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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.

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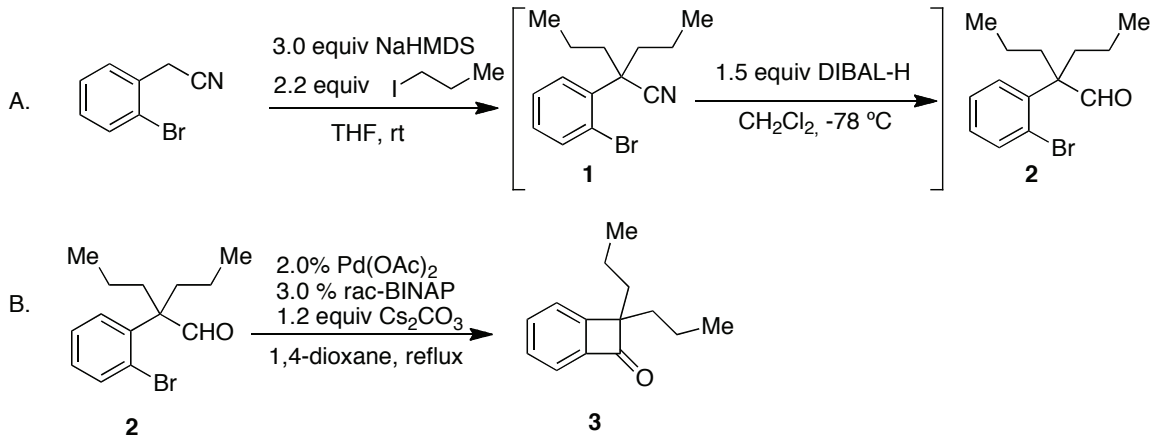
Synthesis of 8,8-Dipropylbicyclo[4.2.0]octa-1,3,5-trien-7-one via Pd-catalyzed Intramolecular C-H Bond-Acylation



Submitted by Ruben Martin and Areli Flores-Gaspar.[1]
Checked by Hongqiang Liu and Mark Lautens.

1. Procedure

A. *2-(2-Bromophenyl)-2-propylpentanenitrile* (**1**). An oven-dried, 500-mL, round-bottomed flask containing 2-bromophenylacetonitrile (8.0 g, 40.8 mmol, 1.0 equiv) (Note 1) is equipped with an oval magnetic stirring bar (32 mm x 15 mm), argon inlet, and a rubber septum. An argon atmosphere is maintained throughout the reaction using an argon manifold system. The flask is charged through the septum via syringe with anhydrous THF (150 mL) (Note 2) and NaHMDS (122.4 mL, 122.4 mmol, 3.0 equiv) (Note 3) is added dropwise over a 4 min period, which results in the solution becoming brown. After stirring for 20 min, the flask is immersed in a room temperature water bath and 1-iodopropane (8.8 mL, 89.8 mmol, 2.2 equiv) (Note 4) is added dropwise over a 3 min period, resulting in a pale brown slurry. The reaction is followed by TLC analysis (Note 5). After stirring for 2.5 h, the septum is removed and saturated NH_4Cl solution (100 mL) is added (Note 6). The organic layer is separated using a 500-mL separatory funnel and the aqueous solution is extracted with diethyl ether (3 x 20 mL) (Note 7). The combined organic layers are dried over $MgSO_4$ (10 g) (Note 8), filtered and concentrated by rotary evaporation (from 760 mmHg to 26 mmHg, 40 °C). The residue is transferred to a 500-mL round-bottomed flask and dried for 4 h under vacuum (10 mmHg). The crude compound **1**

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thus obtained is used directly in the next step without further purification (Note 9).

2-(2-Bromophenyl)-2-propylpentanal (**2**). The previous 500-mL round-bottomed flask with the crude 2-(2-bromophenyl)-2-propylpentanenitrile (**1**) is equipped with an oval stirring bar (32 mm x 15 mm), argon inlet and a rubber septum. An argon atmosphere is maintained throughout the reaction using an argon manifold system. The flask is charged through the septum (*via* syringe) with anhydrous CH_2Cl_2 (150 mL) (Note 10) and immersed in a previously cooled dry ice/acetone bath at –78 ºC (internal temperature) (Note 11). Then, DIBAL-H (45 mL, 45.0 mmol, 1.1 equiv) is added dropwise via syringe over a 15 min period (Note 12), resulting in a pale orange solution. The reaction progress is followed by TLC analysis (Note 13) or GC analysis (Note 14). After 2 h reaction time, additional DIBAL-H (20.4 mL, 20.4 mmol, 0.5 equiv) is added dropwise via syringe; after stirring for an additional 1 h, no more starting material is observed by TLC analysis (Note 15). The flask is removed from the cooled bath, and the reaction is then quenched by slow addition of ethyl acetate (150 mL) (Note 16) and 2M HCl (100 mL) (Note 17) over a 10 min period. The organic phase is separated using a 1-L separatory funnel and the aqueous solution is extracted with ethyl acetate (2 x 50 mL). The combined organic layers are dried over magnesium sulfate (8 g) and concentrated by rotary evaporation (from 760 mmHg to 26 mmHg, 40 °C). The residue is purified by column chromatography on silica gel (Note 18). The title compound is thus obtained as a yellow oil (8.00–8.09 g, 69–70% yield) (Note 19).

B. *8,8-Dipropylbicyclo[4.2.0]octa-1,3,5-trien-7-one* (**3**). An oven-dried 500-mL Schlenk flask equipped with a reflux condenser and a stirring bar (32 mm x 15 mm) is charged with $Pd(OAc)_2$ (134.7 mg, 2.0 mol%) (Note 20), *rac*-BINAP (560.4 mg, 3.0 mol%) (Note 21), Cs_2CO_3 (11.73 g, 36.01 mmol, 1.2 equiv) (Note 22). The Schlenk flask is evacuated and back-filled with argon (this sequence was repeated three times over a period of 3 min). Under an argon atmosphere, the 1,4-dioxane (150 mL) solution of *2-(2-bromophenyl)-2-propylpentanal* (**2**) (8.50 g, 30.01 mmol), (Note 23) is then added by syringe. The mixture is then placed in a pre-heated oil bath (Note 24) at 110 °C for 22 h under argon atmosphere, resulting in a black slurry. The mixture is then allowed to cool to room temperature, diluted with EtOAc (3 x 50 mL) and filtered through a Celite® plug (19.4 g, 50 mL) (Note 25) eluting with additional EtOAc (2 x 30 mL). The filtrate is

concentrated and purified by column chromatography on silica gel (Note 26), obtaining 4.24 g (20.96 mmol, 70% yield) of the title compound as a yellow oil (Notes 27 and 28).

2. Notes

1. 2-Bromophenylacetonitrile (97%) was purchased from Alfa Aesar and used as received.

2. THF was distilled from Na/benzophenone ketyl. Submitters used THF anhydrous (content in H_2O <10 ppm) that was dried from an Instrument Solvent Purification System (MBraun-SPS).

3. NaHMDS (1.0 M in THF) was purchased from Aldrich and used as received.

4. 1-Iodopropane (99%) was purchased from Aldrich and used as received.

5. TLC analysis (performed using EMD TLC silica gel 60 F254 plates thin-layer chromatography) using hexanes:EtOAc (95:5) as the eluent; visualization with $KMnO_4$ stain; 2-bromophenylacetonitrile: R_f= 0.49, mono-alkylated product: R_f=0.79 and compound **1**: R_f=0.89

6. NH_4Cl was purchased from ACP; the solution was prepared using 110 g of NH_4Cl and 100 mL of distilled water.

7. Diethyl ether (stabilized with ~1 ppm of 2,6 di-*tert* butyl-*p*-cresol) was purchased from Caledon and used as received.

8. Magnesium sulfate anhydrous was purchased from ACP and used as received.

9. Crude compound **1** has the following properties: Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.92 (t, *J* = 7.2 Hz, 6 H), 1.06–1.19 (m, 2 H), 1.39–1.52 (m, 2 H), 1.97 (ddd, *J* = 14.0, 12.4, 4.4 Hz, 2 H), 2.61 (ddd, *J* = 14.0, 12.0, 4.4 Hz, 2 H), 7.16 (ddd, *J* = 8.0, 7.2, 1.2 Hz, 1 H), 7.32 (ddd, *J* = 8.0, 7.2, 1.2 Hz, 1 H), 7.61 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.72 (dd, *J* = 8.0, 1.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.9, 18.9, 39.3, 50.9, 120.3, 123.0, 127.6, 129.2, 131.5, 135.3, 135.9.

The pure compound **1** was prepared following the procedure *A* using 2-bromophenylacetonitrile (1.46 g, 7.44 mmol, 1.0 equiv), 20 mL of anhydrous THF, NaHMDS (22 mL, 22 mmol, 3.0 equiv), 1-iodopropane (1.60 mL, 16.4 mmol, 2.2 equiv). Column chromatography was performed on 75 mL of Silica gel 230-400 mesh SiliaFlash®P60, purchased from Silicycle. It was wet packed in a 3 cm diameter column using hexanes/ethyl

Acetate: 90/10 and the crude material was directly loaded to the column (the remaining residue was loaded in the minimal amount of hexanes/ethyl acetate 90/10). 10 mL fractions were collected at 0.15 mL/s rate, eluting with hexanes/ethyl Acetate: 90/10. All the fractions (9 to 18) containing the desired product were combined and concentrated by rotary evaporation (from 760 mmHg to 26 mmHg, 40 °C), and dried under high vacuum (10 mmHg), to yield 1.77 g (9.23 mmol, 85% yield) of the title compound as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.92 (t, *J* = 7.2 Hz, 6 H), 1.04–1.21 (m, 2 H), 1.37–1.54 (m, 2 H), 1.97 (ddd, *J* = 16.8, 12.0, 4.5 Hz, 2 H), 2.61 (ddd, *J* = 16.8, 12.3, 4.5 Hz, 2 H), 7.16 (ddd, *J* = 8.7, 7.5, 1.5 Hz, 1 H), 7.32 (ddd, *J* = 8.7, 7.5, 1.2 Hz, 1 H), 7.60 (dd, *J* = 7.8, 1.2 Hz, 1 H), 7.71 (dd, *J* = 7.8, 1.5 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13.9, 18.9, 39.2, 50.8, 120.2, 123.0, 127.5, 129.2, 131.5, 135.2, 135.9. IR (neat, cm^{-1}): 2961, 2932, 2874, 2359, 2233, 1629, 1470, 1391, 1021, 758. HRMS calcd. for ($C_{14}H_{18}BrN+NH_4$): 297.0966, Found 297.0953. Anal. calcd. for $C_{14}H_{18}BrN$: C, 60.01; H, 6.47; N, 5.00 Found: C, 59.80; H, 6.46; N, 4.89.

10. Dichloromethane anhydrous (content in H_2O <10 ppm) was dried from an Instrument Solvent Purification System (MBraun-SPS).

11. Submitter used an immersion cooler HAAKE EK90 with methanol bath for –78 ºC.

12. Diisobutyl aluminiumhydride (DIBAL-H), 1M solution in hexane, Sureseal ™ was purchased from Aldrich and used as received. Submitters used DIBAL-H, 1M solution in hexane, Acroseal™ that was purchased from Acros Organics and titrated before use with the following procedure: Hoye, T. R.; Aspaas, A. W.; Eklov, B. M.; Ryba, T. D. *Org. Lett.* **2005**, *7*, 2205.

13. TLC is run twice using a mixture of Hexanes:EtOAc (40:1) as eluent (compound **1**: R_f= 0.50, compound **2** R_f=0.46), using a $KMnO_4$ stain.

14. Submitters also used GC to monitor the reaction progress. Compounds **1** and **2** are easily distinguished by GC: $t_{r\mathbf{1}}$=5.04 min; $t_{r\mathbf{2}}$=5.24 min.

GC-method (Agilent 19091J-413): Initial Temp: 70ºC; Maximum Temp: 300ºC; Initial Time: 1.0 min, Equilibration Time: 3.0 min; Ramp: Rate = 50.0 °/min; Final Temp = 250 °C, Final Hold Time= 1.50 min; Run Time: 6.10 min; Pressure: 10.10 psi; Split flow: 97.1 mL/min; Gas type: Helium; Capillary column: HP-5, 5% phenyl methyl siloxane

15. Addition of DIBAL-H at the start of experiment rather than semi-batch addition led to incomplete reduction in a 3 h period.

16. Ethyl acetate was purchased from Fisher Scientific and used as received.

17. HCl (37-38%) was purchased from Fisher Scientific; a 2M HCl solution is preparing by adding 16.7 mL of HCl (37-38%) to a 250-mL volumetric flask containing 83.3 mL of distilled water.

18. Column chromatography was performed on 260 mL of silica gel (230-400 mesh SiliaFlash®P60), purchased from Silicycle. It was wet packed in a 5-cm diameter column using hexanes/ethyl acetate (96/4) and the crude material was directly loaded to the column (The remaining residue was loaded in the minimal amount of hexanes/ethyl acetate (96/4)). Fractions of 30 mL were collected at 0.5 mL/s rate, eluting with hexanes/ethyl acetate (96/4). All fractions (10-18) containing the desired product were combined, concentrated by rotary evaporation (from 760 mmHg to 26 mmHg, 40 ºC), and dried overnight at 10 mmHg. In order to avoid any decomposition, compound **2** was kept under argon atmosphere.

19. Compound **2** has the following physical properties: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, J = 7.2 Hz, 6 H), 0.97–1.11 (m, 2 H), 1.16–1.30 (m, 2 H), 2.00 (ddd, J = 26.0, 12.0, 4.8 Hz, 4 H), 7.13–7.19 (m, 1 H), 7.33–7.38 (m, 2 H), 7.60 (d, J = 8.0 Hz, 1 H), 9.86 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.9, 17.0, 35.1, 58.6, 123.9, 127.5, 129.1, 130.4, 135.0, 140.2, 204.4. IR (neat, cm^{-1}): 2957, 2872, 1716, 1564, 1466, 1432, 1380, 1264, 1167, 1113, 1067, 1029, 971. HRMS calcd. for ($C_{14}H_{19}BrO+NH_4$): 300.0963, Found 300.0959. Anal. calcd. for $C_{14}H_{19}BrO$: C, 59.37; H, 6.76. Found: C, 59.42; H, 6.91**.** Submitters also determined the purity of **2** using GC analysis. The range of yield for different runs is from 63% to 70%.

20. $Pd(OAc)_2$ (min. 98%; 99.9% Pd) was purchased from Strem Chemicals and used as received. Submitters noted that $Pd(OAc)_2$ (99.98% (metal basis); Pd 47% min) purchased from Alfa-Aesar gave similar efficiency.

21. Racemic 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl 98% was purchased from Strem Chemicals and used as received. Submitters noted that racemic 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl 98% from Atomax chemicals gave similar efficiency.

22. Cs_2CO_3 99.9% [metal basis] was purchased from Aldrich and was stored in the glove box. The exact amount of cesium carbonate was weighed out inside the glove box and then added to the reaction mixture under an

argon stream outside the glove box. Submitters used Cs_2CO_3 99% [metal basis] purchased from Alfa Aesar.

23. 1,4-Dioxane was distilled over sodium, and used directly without degassing. Submitters used dioxane anhydrous, 99.8% that was purchased from Sigma Aldrich. Instead of the addition of a dioxane solution of 2-(2-bromophenyl)-2-propylpentanal (**2**), submitters added **2** to the flask at the start of experiment followed by air exclusion and addition of dioxane.

24. Oil Bath: silicone oil δ=0.97, was purchased from Fisher Scientific and used as received (working temperature from –40 ºC to +200 ºC).

25. Celite® 545 coarse was purchased from Sigma-Aldrich and used as received.

26. Column chromatography was performed on 500 mL of silica gel 230-400 mesh SiliaFlash®P60, purchased from Silicycle. The column was wet packed in a 8-cm diameter column with hexanes and the crude material was directly loaded to the column (The remaining residue was loaded in the minimal amount of hexanes/ethyl acetate (10/1)). Fractions of 30 mL were collected at 0.8 mL/s rate eluting with the following gradient: 500 mL hexane, 850 mL hexanes/ethyl acetate: 30/1, 300 mL hexanes/ethyl acetate: 20:1, 400 mL hexanes/ethyl acetate: 10/1, 300 mL hexanes/ethyl acetate: 5/1. The fractions (10-17) containing compound **3** (R_f=0.65; hexanes:EtOAc (90:10)) are collected, combined and concentrated by rotary evaporation (from 760 mmHg to 26 mmHg, 40 ºC). In order to avoid any decomposition, compound **3** was kept under argon atmosphere.

27. Compound **3** has the following physical properties: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.83 (t, *J* = 7.2 Hz, 6 H), 1.13–1.30 (m, 4 H), 1.74 (ddd, *J* = 8.8, 6.4, 2.4 Hz, 4 H), 7.32 (dt, *J* = 6.8, 0.8 Hz, 1 H), 7.37 (td, *J* = 6.8, 0.8 Hz, 1 H), 7.42 (dt, *J* = 6.8, 0.8 Hz, 1 H), 7.48 (td, *J* = 6.8, 0.8 Hz, 1 H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ: 14.7, 19.1, 37.4, 74.2, 120.9, 123.2, 129.2, 135.1, 146.1, 160.6, 197.1. IR (neat, cm^{-1}): 3064, 2958, 2873, 2845, 1754, 1582, 1461, 1441, 1379, 1274, 1142, 1092, 926. HRMS calcd. for ($C_{14}H_{19}O+NH_4$): 203.1436, Found 203.1433. Anal. calcd. for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.97; H, 8.79**.** The range of yields for different runs is from 67% to 71%.

28. The only by-product generated in the reaction is [(1*E*)-1-propylbut-1-enyl]benzene (**4**) as a mixture of diastereoisomers (16:1, favoring *E* isomer, as judged by NOESY) in 9.0% yield. This by-product elutes prior to the main fraction in the column chromatography and is readily removed (R_f=0.90; hexanes:EtOAc (90:10)). Compound **4** has the following physical

properties: Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.06 (t, *J* = 7.6 Hz, 3 H), 1.23 (t, *J* = 7.6 Hz, 3 H), 1.51–1.60 (m, 2 H), 2.38 (q, *J* = 7.2 Hz, 2 H), 2.65 (t, *J* = 7.2 Hz, 2 H), 5.83 (t, *J* = 7.2 Hz, 1 H), 7.33–7.37 (m, 1 H), 7.42–7.46 (m, 2 H), 7.49–7.52 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.9, 14.4, 21.8, 21.9, 31.6, 126.32, 126.34, 128.1, 130.9, 139.4, 143.4. IR (neat, cm^{-1}): 3058, 2930, 2871, 1599, 1491, 1457, 1443, 1377, 1074, 1030, 754, 697. HRMS Calcd for ($C_{13}H_{19}$): 175.14868, Found 175.14834. Anal. Calcd for $C_{13}H_{18}$: C, 89.59; H, 10.41. Found: C, 89.39; H, 10.33.

Waste Disposal Information

All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995

3. Discussion

Benzocyclobutenones are an intriguing class of four-membered ring ketones that have been used extensively as powerful synthetic intermediates in organic synthesis[2]. The reactivity of benzocyclobutenones is primarily associated to their unique high electrophilicity of the carbonyl unit, allowing

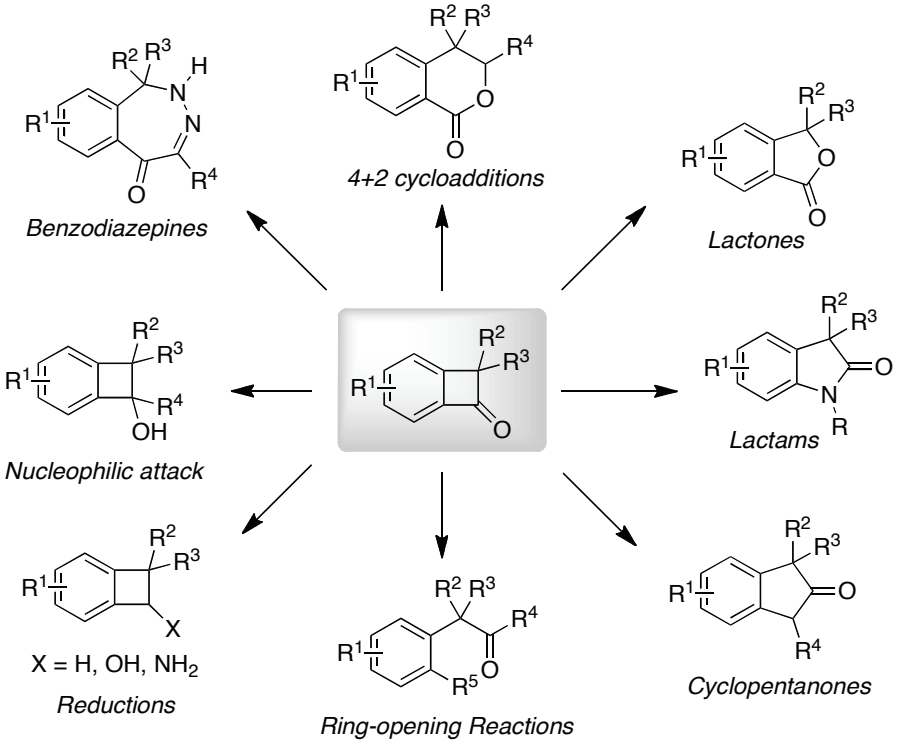

Figure 1. Benzocyclobutenones in Organic Synthesis

a myriad of different transformations, ranging from classical 1,2-additions, ring-expansion, ring-opening reactions, cycloadditions, heterocycle synthesis or preparation of complex benzocyclobutanes via reduction of the carbonyl backbone, among many others (Figure 1).

Despite their potential as synthetic intermediates, benzocyclobutenones are elusive compounds to prepare in a straightforward and general fashion. To the best of our knowledge, the synthesis of benzocyclobutenones is usually accomplished via two different routes: (1) intramolecular addition of organolithium or Grignard reagents to Weinreb amides (route 1, Figure 2)[3] or (2) [2+2]-cycloaddition of silyl enol ethers and benzyne (route 2, Figure 2),[4] as elegantly described by Suzuki and coworkers. The application profile of these methods, unfortunately, is quite limited, as only a limited set of substitution patterns can be accessed; additionally, these procedures do not tolerate the presence of functional groups, as stochiometric amounts of organolithium derivatives are required.

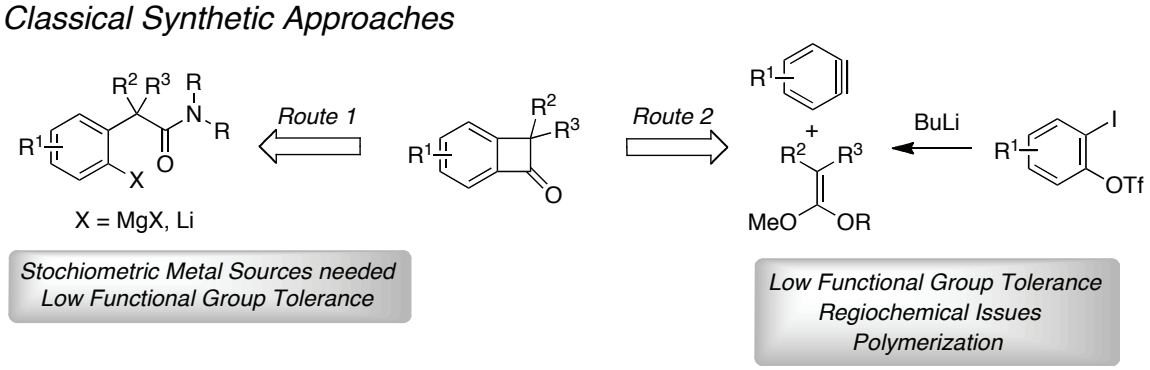

Figure 2. Alternative Pathways to Benzocyclobutenones

In recent years, metal-catalyzed C-H bond-functionalization strategies have become one of the most popular areas of research in organic (organometallic) chemistry.[5] The attractiveness of such methodologies is based on the ability to build up molecular complexity from rather inert and abundant C-H bonds, thus allowing unconventional and elegant bond disconnection strategies for assembling valuable organic structures. Our group has recently reported that benzocyclobutenones can be prepared by intramolecular Pd-catalyzed acylation via C-H bond-functionalization.[6] Such an approach has the advantage of using readily available precursors and controlling the substitution pattern over the aryl backbone; additionally, the method tolerates a wide range of functional groups, allowing for the first

time, the preparation of highly complex benzocyclobutenones in a straightforward manner. The scope of this procedure is illustrated in Table 1.

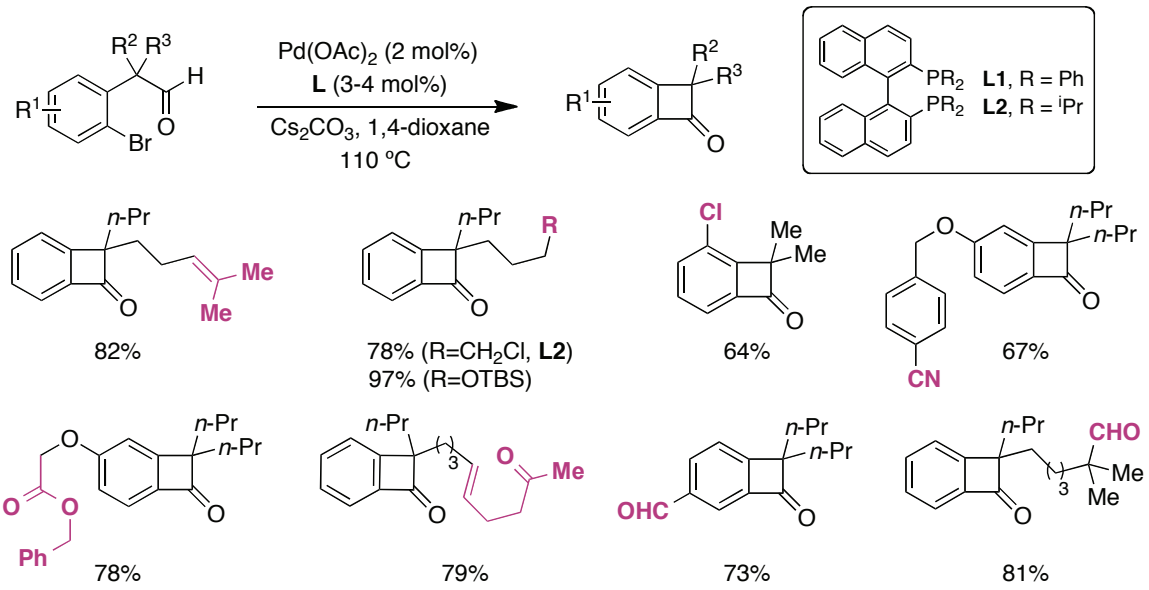

Table 1. Pd-catalyzed Synthesis of Benzocyclobutenones via C-H Bond-Functionalization

Herein, we describe the preparation of the model compound [8,8-dipropylbicyclo[4.2.0]octa-1,3,5-trien-7-one], thus illustrating the simplicity of our new protocol for the direct conversion of commonly employed and readily available α-aryl aldehydes into benzocyclobutenones. This user-friendly methodology nicely complements the existing routes to benzocyclobutenones in the literature.[3,4] Given the practicality and flexibility, it is expected that this method will find immediate application in advanced organic synthesis.

1. Institute of Chemical Research of Catalonia (ICIQ), AV. Països Catalans 16, 43007 Tarragona, Spain, E-mail: rmartinromo@iciq.es; We thank ICIQ Foundation, Consolider Ingenio 2010 (CSD2006-0003) and MICINN (CTQ2009-13840) for financial support. Johnson Matthey, Umicore, and Nippon Chemical Industrial are acknowledged for gifts of metal and ligand sources. R. M and A. F-G thank MICINN for RyC and FPU fellowships.

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Appendix
Chemical Abstracts Nomenclature; (Registry Number)

2-Bromophenylacetonitrile: Benzeneacetonitrile, 2-bromo-; (19472-74-3)

NaHMDS: Silanamine, 1,1,1-trimethyl-N-(trimethylsilyl)-, sodium salt (1:1); (1070-89-9)

1-Iodopropane: Propane, 1-iodo-; (107-08-4)

DIBAL-H: Aluminum, hydrobis(2-methylpropyl)-; (1191-15-7)

$Pd(OAc)_2$: Acetic acid, palladium (2+) salt (2:1); (3375-31-3)

Rac-BINAP: Phosphine, 1, 1'-[1,1'binaphthalene]-2,2'-diylbis[1,1-diphenyl-; (98327-87-8)

Cs_2CO_3: Carbonic acid, cesium salt (1:2); (534-17-8)

2-(2-Brommophenyl)-2-propylpentanal: Benzeneacetaldehyde, 2-bromo-α,α-dipropyl-; (1206450-98-7)

[8,8-Dipropylbicyclo[4.2.0]octa-1,3,5-trien-7-one]: Bicyclo[4.2.0]octa-1,3,5-trien-7-one, 8,8-dipropyl-; (1206451-50-4)

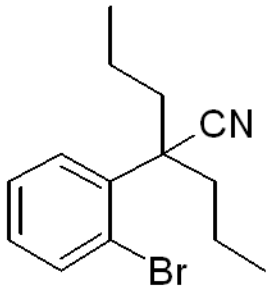
[(1*E*)-1-Propylbutyl-1-enyl]benzene: Benzene, [(1*E*)-1-propyl-1-buten-1-yl]-; (1151654-13-5)

Ruben Martin was born in 1976. He received his Ph.D in 2003 at the Universitat de Barcelona with Prof. Antoni Riera. After two postdoctoral stages at the Max-Planck-Institut für Kohlenforschung with Prof. Alois Fürstner and at the Massachusetts Institute of Technology with Prof. Stephen L. Buchwald, he initiated his independent career in 2008 at the Institute of Chemical Research of Catalonia (ICIQ). His interests are primarily focused on the metal-catalyzed activation of inert bonds.

Areli Flores-Gaspar was born in Mexico, City. She did her Bachelor studies and a M.Sc. at the Universidad Nacional Automoma de México. She is currently a Ph.D. student in Dr. Ruben Martin's group at Institut Català d'Investigació Química in Tarragona, Spain. Her work is focused on the development of novel synthetic transformations based upon C-H bond-activation protocols.

Hongqiang Liu was born in China. He did his B. Sc. and M. Sc, at Peking University and Peking Union Medical College respectively. He finished his Ph.D. degree in 2010 under supervision of Dr. John Vederas at the University of Alberta. He is currently a postdoctoral fellow at Dr. Mark Lautens group at the University of Toronto. His work is focused on molecular motor synthesis using palladium-catalyzed and norbornene-mediated domino reactions.

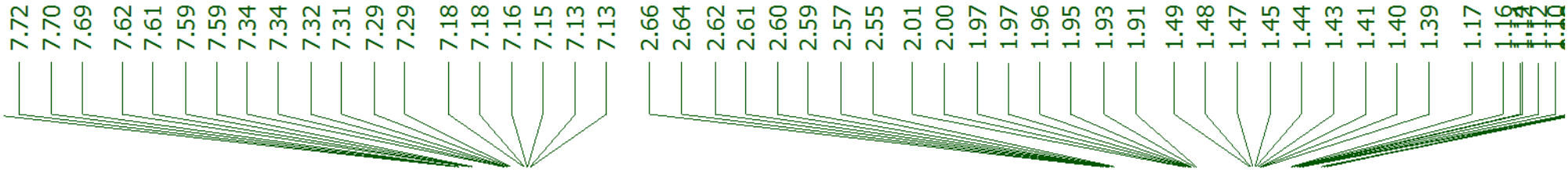
HL-2-31-400Hz-CDCl3, before column

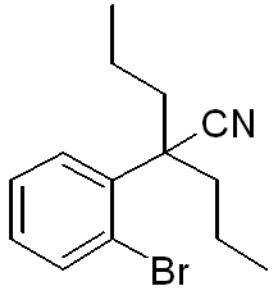


Compound **1**

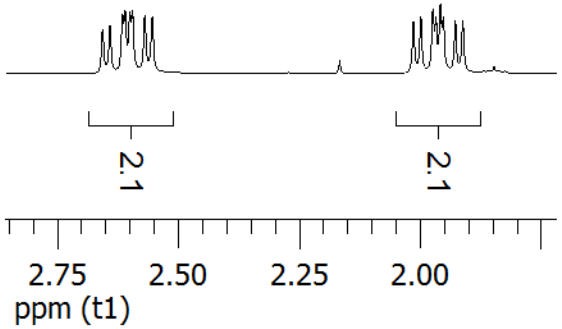
ppm (t1)

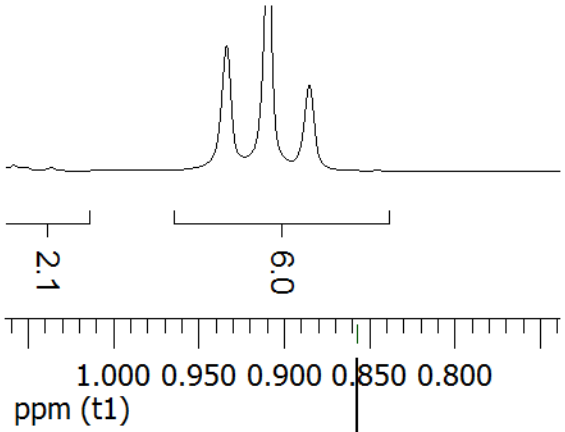
HL-2-32-300MHz-CDCl3

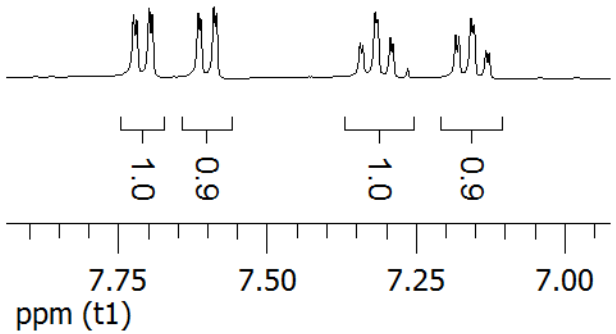


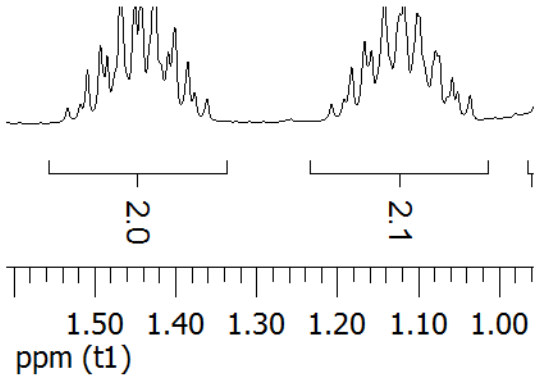


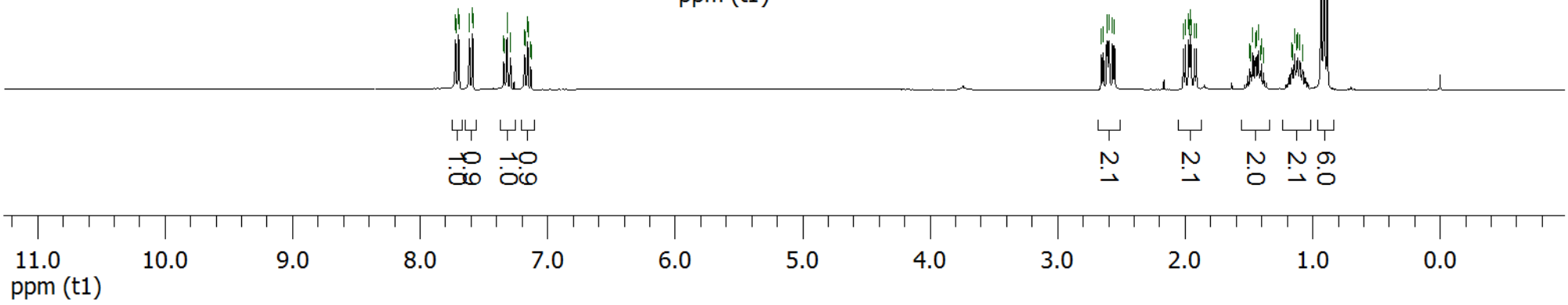
Compound **1**



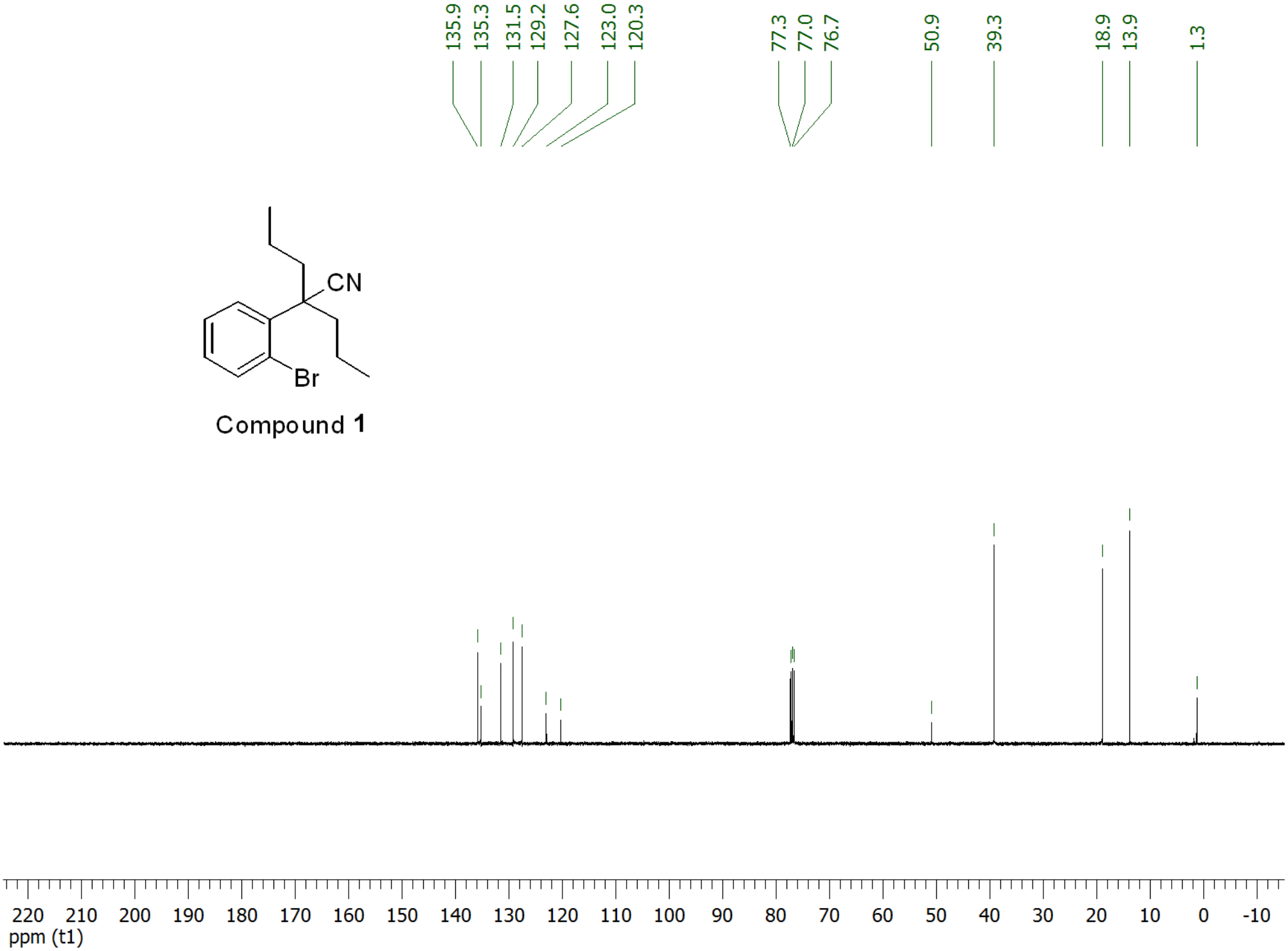






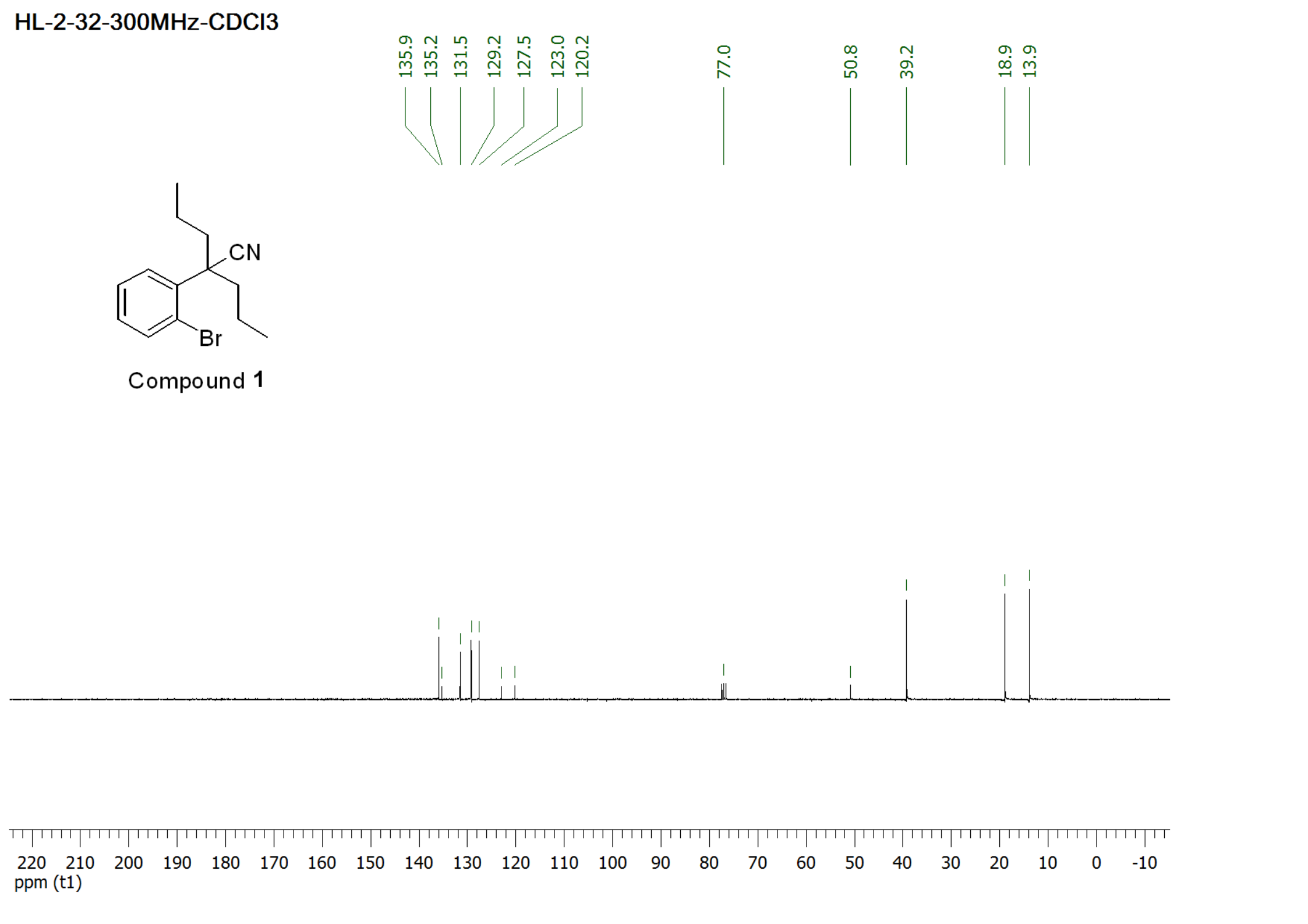


HL-2-31-400Hz-CDCl3- Before column



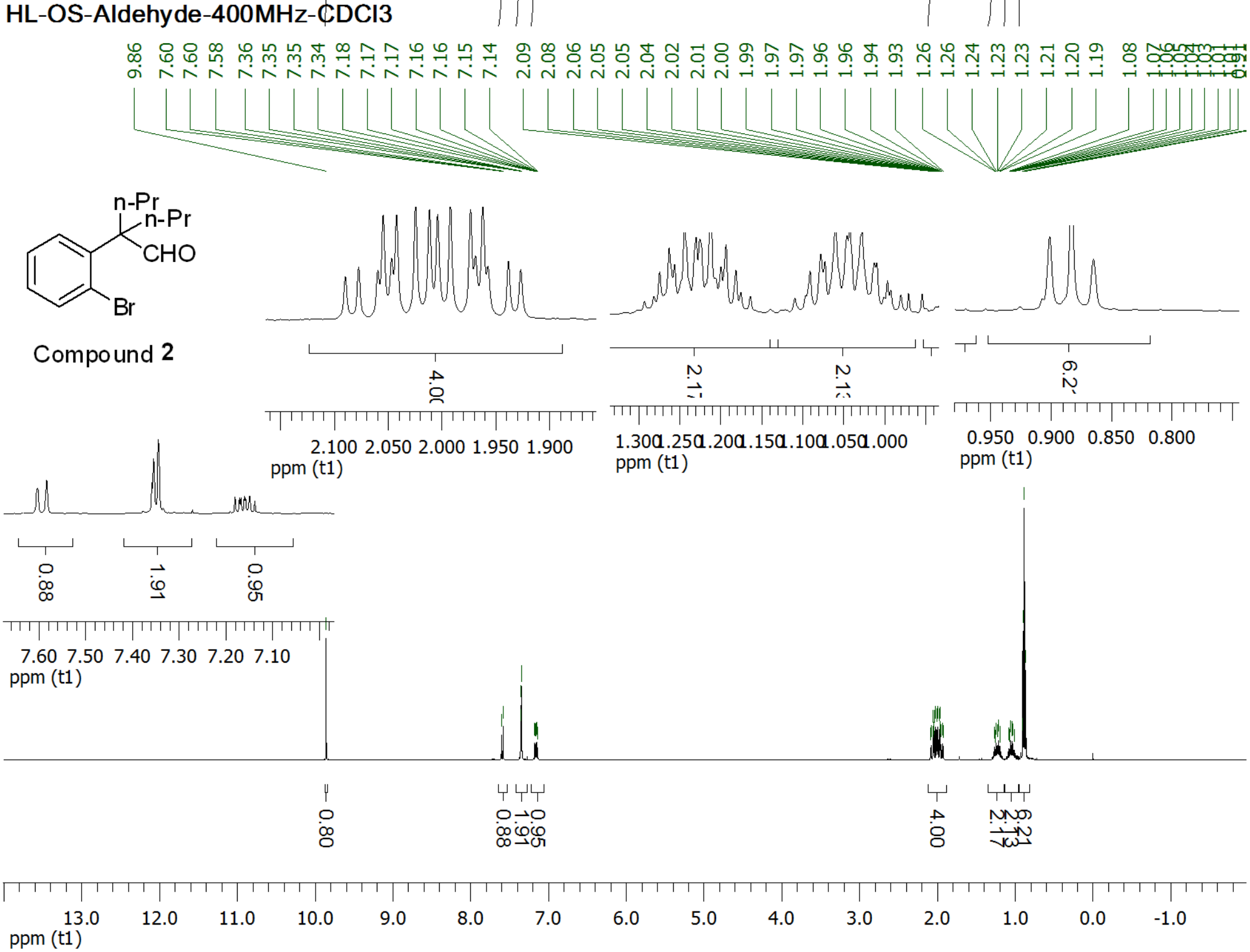
Compound **1**

HL-2-32-300MHz-CDCl3



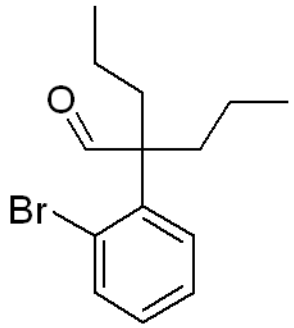
Compound **1**

HL-OS-Aldehyde-400MHz-CDCl3

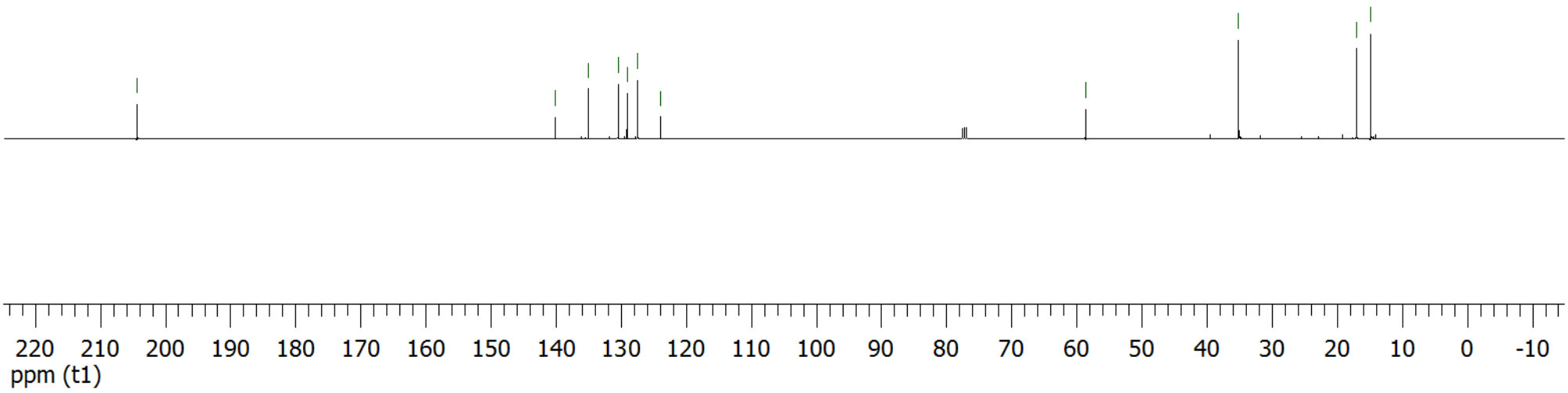


HL-OS-aldehyde-400MHz CDCl3

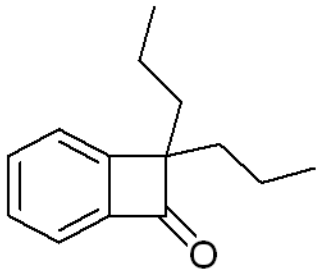
204.4
140.2
135.0
130.4
129.1
127.5
123.9
58.6
35.1
17.0
14.9



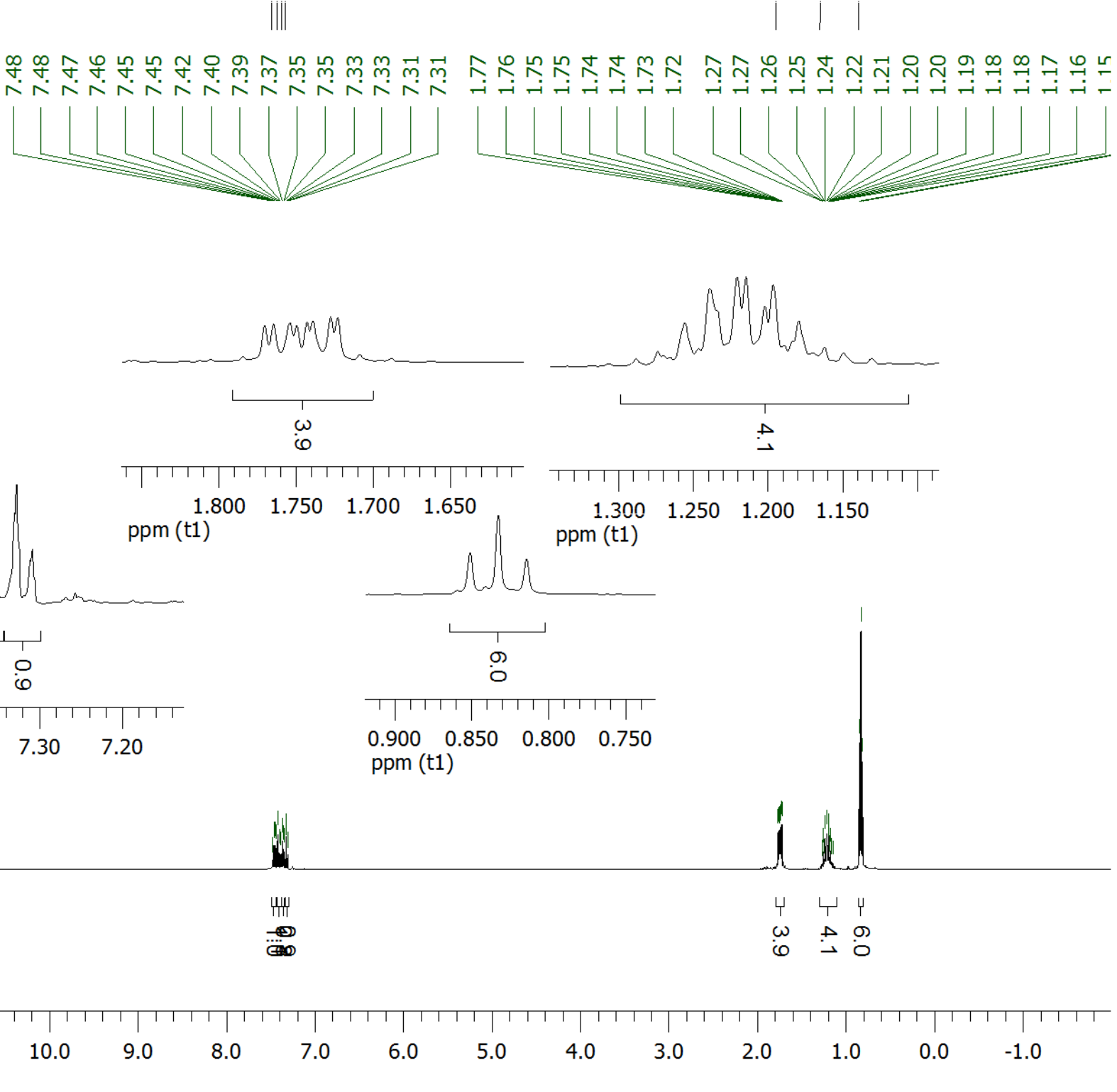
Compound **2**



HL-2-47 CDCl3 400MHz

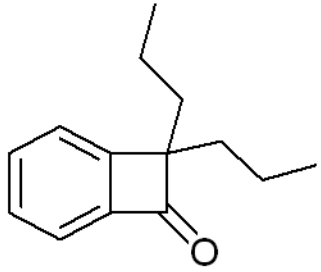


Compound **3**

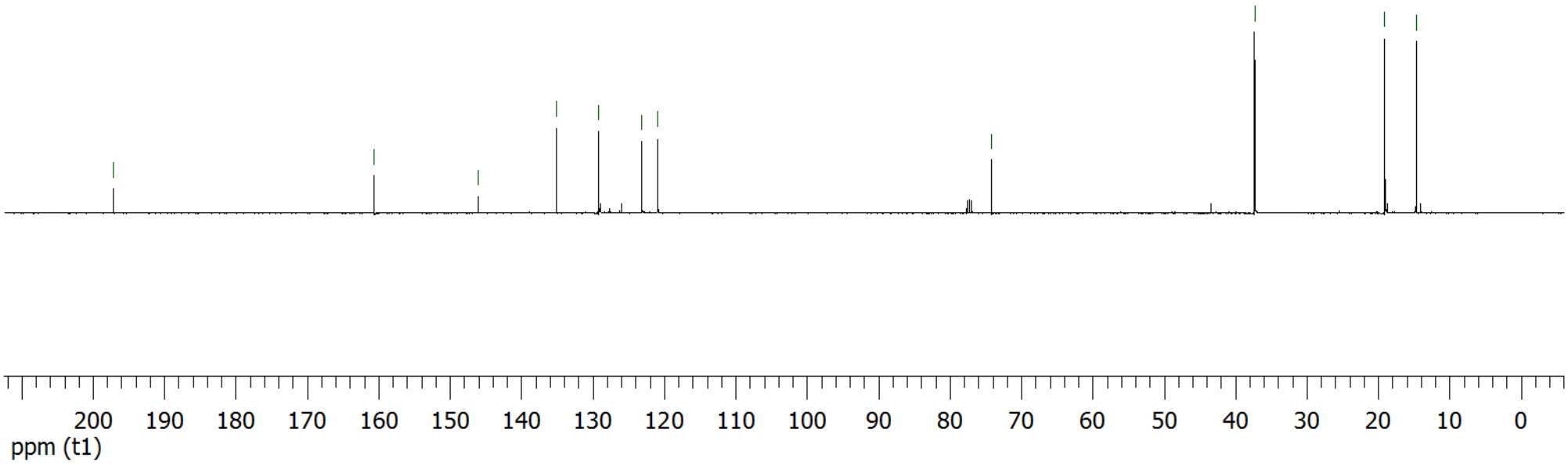


HL-2-47-400 MHz, CDCl3

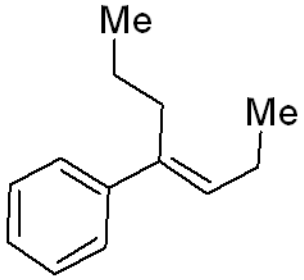
197.1 160.6 146.1 135.1 129.2 123.2 120.9 74.2 37.4 19.1 14.7



Compound **3**



HL-2-47-2-400Hz-CDCl3

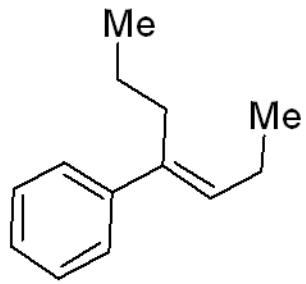


Compound **4**

16:1 (***E*:*Z***)

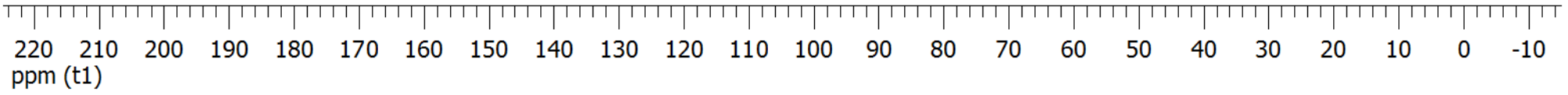
HL-2-47-2-400Hz-CDCl3

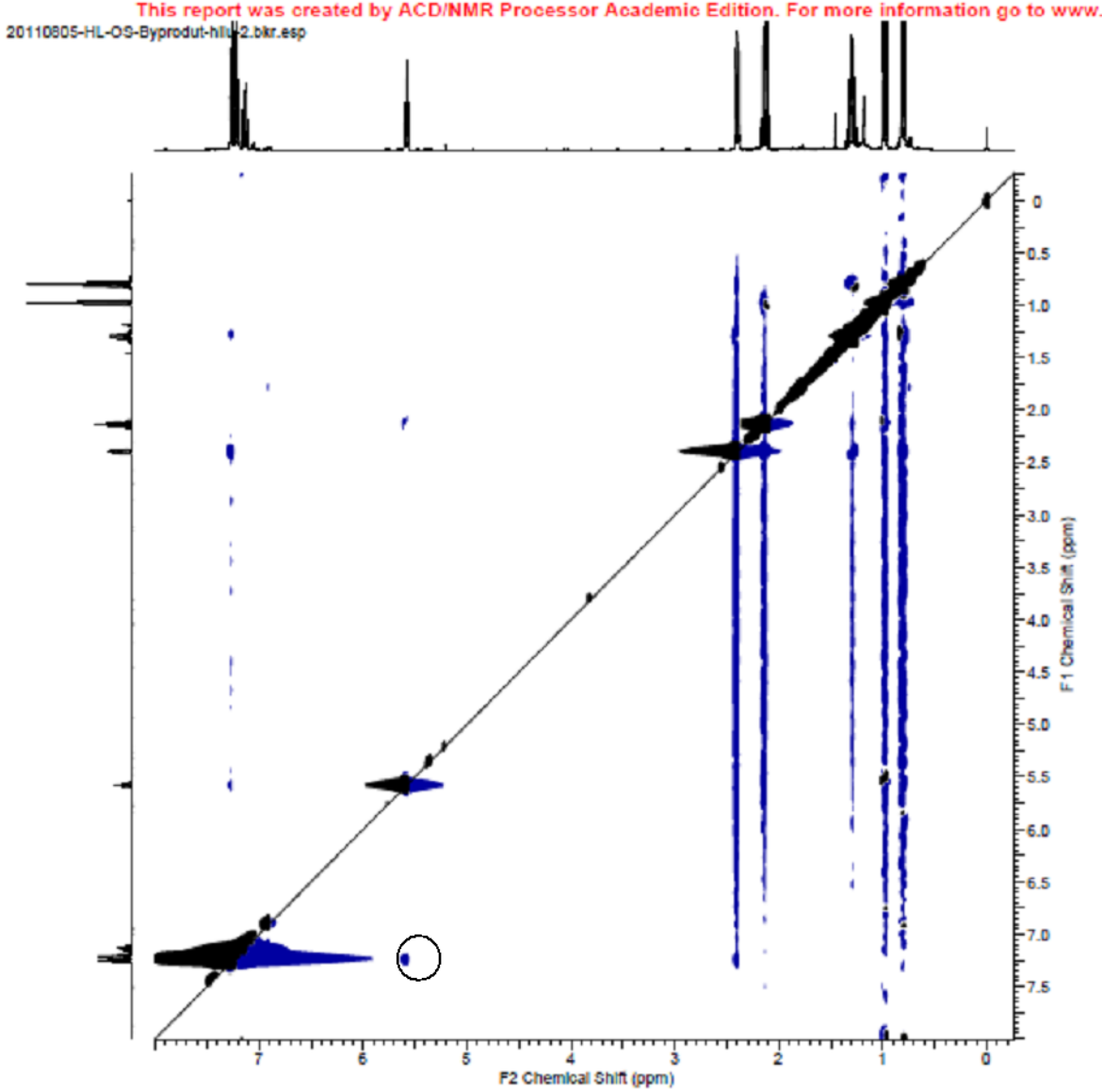
143.43
139.37
130.88
128.08
126.34
126.32
77.32
77.00
76.68
31.63
21.87
21.84
14.43
13.93

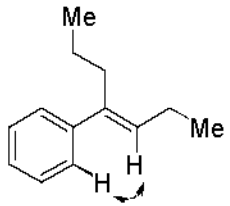


Compound **4**

16:1 (***E:Z***)







NOESY