Organic Syntheses

Homologation of Boronic Esters with Lithiated Epoxides

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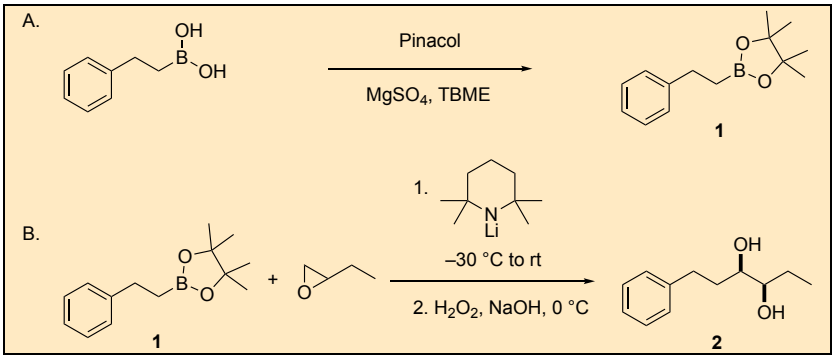
Checked by Philipp Sondermann and Erick M. Carreira



Procedure (Note 1)

A. *4,4,5,5-Tetramethyl-2-phenethyl-1,3,2-dioxaborolane (**1**).* An oven-dried 250 mL two-necked round-bottomed flask equipped with a 2.5 cm magnetic stir bar, a rubber septum and a nitrogen inlet is charged with 2-phenyl-1-ethylboronic acid (10.0 g, 66.7 mmol, 1.00 equiv) (Note 2), pinacol (7.88 g, 66.7 mmol, 1.00 equiv) (Note 2) and oven-dried magnesium sulfate (12.0 g, 99.7 mmol, 1.50 equiv) (Note 2). The flask is evacuated and backfilled with nitrogen three times and then charged by syringe with *tert*-butyl methyl ether (70 mL) (Note 2). The resulting white suspension is stirred under nitrogen at room temperature for 16 h (Figure 1).

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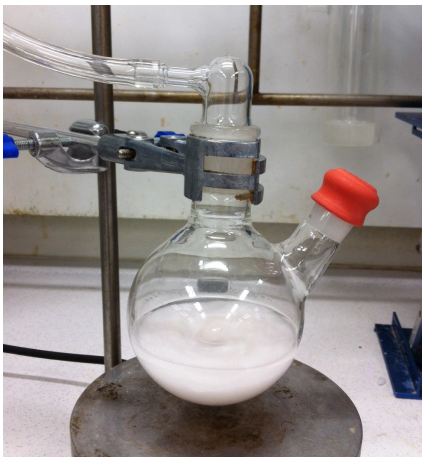


Figure 1. Reaction setup for Step A

The suspension is filtered through a medium porosity glass sinter and the filter cake is washed with *tert*-butyl methyl ether (3 x 20 mL). The filtrate is concentrated under reduced pressure (7.5 mmHg, 30 °C). The colorless residue is diluted with 3:97 ethyl acetate:pentane (30 mL) and charged onto a column (5 x 16 cm) of 150 g of silica gel (Note 3) and eluted with 3:97 ethyl acetate:pentane collecting 45 mL fractions. The desired product is obtained in fractions 7-32, which are concentrated by rotary evaporation (7.5 mmHg, 30 °C) and then dried under reduced pressure (0.2 mmHg) for 2 h to afford a colorless oil which solidifies to form a white solid (Note 4). The resulting solid is dried overnight at 0.2 mmHg to give the analytically pure boronic ester (13.6 g, 88 %) as a white solid (Figure 2) (Note 5).

Figure 2. Boronic ester 1 after purification

B. *(±)-(3R,4R)-1-Phenylhexane-3,4-diol* (**2**). An oven-dried 200 mL (4 cm diameter) Schlenk tube equipped with a 2.5 cm magnetic stir bar and a

rubber septum is evacuated and backfilled three times with nitrogen *via* the side arm. The flask is then charged by syringe with 2,2,6,6-tetramethylpiperidine (8.10 mL, 48.0 mmol, 1.20 equiv) (Note 6) and tetrahydrofuran (50 mL) (Note 6). The resulting solution is cooled to –30 °C (Note 7) and a solution of *n*-butyllithium (2.5 M in hexanes, 19.2 mL, 48.0 mmol, 1.20 equiv) (Note 6) is added to the reaction mixture over ~5 min (Figure 3) (Note 8). The cold bath is removed and the yellow solution is allowed to stir at room temperature for 45 min. The resulting yellow solution of lithium 2,2,6,6-tetramethylpiperidide (LTMP) is then cooled to –33 to –35 °C (Note 9).

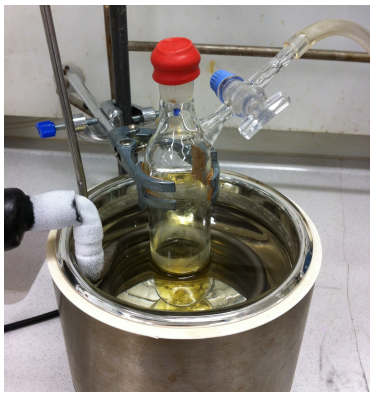


Figure 3. Reaction setup for formation of LTMP

An oven-dried 250 mL two-necked round-bottomed flask equipped with a 2.5 cm magnetic stir bar, a rubber septum and a nitrogen inlet is charged with boronic ester **1** (9.28 g, 40.0 mmol, 1.00 equiv). The flask is evacuated and backfilled with nitrogen three times. The flask is then charged by syringe with tetrahydrofuran (40 mL) (Note 6) and (±)-1,2-epoxybutane (4.18 mL, 48.0 mmol, 1.20 equiv) (Note 6). The resulting solution is cooled to –30 °C (Note 10) and the pre-cooled LTMP solution described above is added *via* insulated cannula over ~6 min (Figure 4) (Note 11). The Schlenk tube is rinsed with an additional portion of tetrahydrofuran (2 mL) which is cooled to –35 °C and added to the reaction mixture *via* insulated cannula.

Figure 4. Addition of LTMP to 1 and epoxide *via* cannula

The pale yellow reaction mixture is stirred at –30 °C for 5 h and then the cooling bath is removed and the solution is stirred at room temperature for a further 1 h (Figure 5).

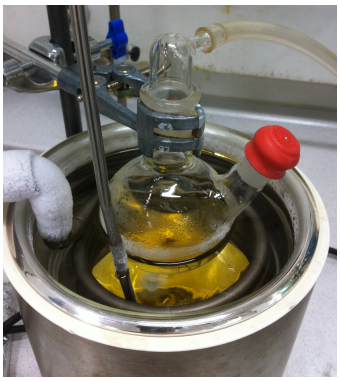


Figure 5. Reaction mixture stirring at –30 °C after addition of LTMP

The resulting solution is then poured into a rapidly stirred ice-cold mixture of aqueous 2M sodium hydroxide (40 mL) (Note 6) and tetrahydrofuran (20 mL) in a 500 mL Erlenmeyer flask equipped with a 4 cm magnetic stir bar. The reaction flask is rinsed with an additional portion of tetrahydrofuran (10 mL), which is also added to the stirring solution in the Erlenmeyer flask (Note 12). The resulting cloudy white solution is stirred in the ice bath for 4-5 min (Note 13) (Figure 6a). A chilled solution of hydrogen peroxide (30 % w/w, 20 mL) (Note 6) is added carefully by Pasteur pipette

over ~7 min (Note 14) and the resulting mixture is stirred in the ice bath for 1 h (Figure 6b).

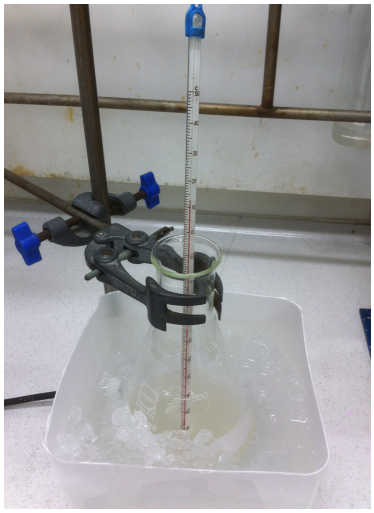
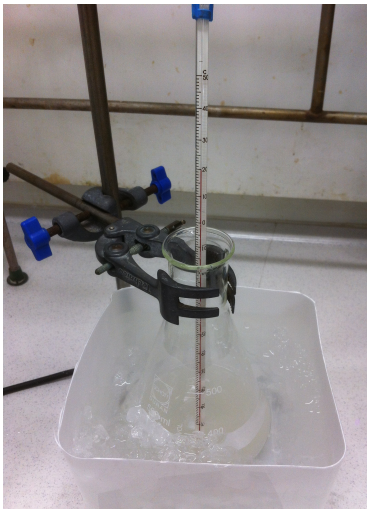
(a)  (b) 

Figure 6. (a) After pouring the reaction mixture into THF and NaOH (b) After addition of aqueous H_2O_2

The resulting milky solution is poured into a 1 L separatory funnel containing 300 mL of 2M NaOH. The reaction flask is rinsed with ethyl acetate (2 x 100 mL), which is added to the separatory funnel. After thorough mixing, the aqueous layer is separated and extracted with ethyl acetate (2 x 200 mL). The combined organic phases are washed with saturated aqueous sodium thiosulfate (2 x 100 mL), brine (100 mL), 3 M HCl (100 mL) and water (100 mL). The organic phase is poured into a 1 L round bottomed flask and concentrated under reduced pressure (7.5 mmHg, 30 °C) to afford a light brown oil (Note 15).

The crude residue is azeotroped twice with 1:1 methanol/water (200 mL), concentrating by rotary evaporation (7.5 mmHg, 50 °C) (Note 16). The resulting pale brown oil is diluted with 1:4 ethyl acetate:dichloromethane (30 mL) and charged onto a column (5 x 16 cm) of 150 g of silica gel (Note 2) and eluted with 1:4 ethyl acetate:dichloromethane collecting 45 mL fractions. The desired product is obtained in fractions 14-40 (Note 17), which are concentrated by rotary evaporation (7.5 mmHg, 30 °C) and then dried under reduced pressure (0.2 mmHg) to afford a colorless oil, which solidifies to form an off-white solid (Note 18). The resulting solid is

dried overnight at 0.2 mmHg to give the analytically pure diol (5.43–5.48 g, 70–71%, >95:5 d.r.) as an off-white solid (Notes 19 and 20) (Figure 7).

Figure 7. Diol 2 after purification

Notes

1. Prior to performing each reaction, a thorough hazard analysis and risk assessment should be carried out with regard to each chemical substance and experimental operation on the scale planned and in the context of the laboratory where the procedures will be carried out. Guidelines for carrying out risk assessments and for analyzing the hazards associated with chemicals can be found in references such as Chapter 4 of "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at https://www.nap.edu/catalog/12654/prudent-practices-in-the-laboratory-handling-and-management-of-chemical). See also "Identifying and Evaluating Hazards in Research Laboratories" (American Chemical Society, 2015) which is available via the associated website "Hazard Assessment in Research Laboratories" at https://www.acs.org/content/acs/en/about/governance/committees/chemicalsafety/hazard-assessment.html. In the case of this procedure, the risk assessment should include (but not necessarily be limited to) an evaluation of the potential hazards associated with 2-phenyl-1-ethylboronic acid, pinacol, magnesium sulfate, *tert*-butyl methyl ether, silica gel, 2,2,6,6-tetramethylpiperidine, *n*-butyllithium, hydrogen peroxide, (±)-1,2-epoxybutane, and tetrahydrofuran.

2. 2-Phenyl-1-ethylboronic acid (96%) and pinacol (98%) were purchased from Fluorochem and were used as received. Magnesium sulfate (Laboratory Reagent Grade) was purchased from Fischer Scientific and was stored in an open 500 mL beaker in a 200 °C oven for several days prior to use. *tert*-Butyl methyl ether (99.8%, HPLC Grade) was purchased from Sigma Aldrich and stored over activated 3 Å molecular sieves for several days prior to use.
3. Silica gel (technical grade, 40-63 μm) was purchased from Sigma Aldrich and was used as supplied.
4. The fractions containing product were determined by TLC. After 2 h at 0.2 mmHg, crystallization was initiated by holding a pellet of dry ice against the outside of the round-bottomed flask containing the product. Once crystallization was complete, the solid cake was broken up into a coarse powder with a spatula before drying overnight.
5. A second reaction on equivalent scale provided 13.6 g (88%) of the product. 4,4,5,5-Tetramethyl-2-phenethyl-1,3,2-dioxaborolane (**1**) has the following physical and spectroscopic properties: R_f = 0.47 (3:97, ethyl acetate:pentane), the checkers report the following values for **1**: R_f = 0.09 (3:97 ethyl acetate:pentane); R_f = 0.52 (10% EtOAc in hexanes); Merck silica gel 60 F254 plate; mp 38–39 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ : 1.18 (t, *J* = 8.4 Hz, 2H), 1.26 (s, 12H), 2.79 (t, *J* = 8.0 Hz, 2H), 7.16–7.22 (m, 1H), 7.23–7.32 (m, 4H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ : 25.0, 30.1, 83.2, 125.6, 128.1, 128.3, 144.6 [*N.B.* the carbon attached to boron was not observed due to quadrupolar relaxation]; HRMS (ESI^+) calculated for $C_{14}H_{22}BO_2^+$ = 233.1707, mass found = 233.1710; IR (film): 3026, 2978, 2929, 1372, 1318, 1139, 848, 755, 703 cm^{-1}; Anal. calcd for $C_{14}H_{21}BO_2$: C, 72.44; H, 9.12. Found: C, 72.18; H, 9.28.
6. Tetrahydrofuran was purified by passage through a column of activated alumina using equipment from Anhydrous Engineering based on the Grubbs design.[2] 2,2,6,6-Tetramethylpiperidine (99%) was purchased from Fluorochem and distilled from CaH_2 under an atmosphere of N_2 (bp 154–156 °C). *n*-Butyllithium (2.5 M in hexanes) and (±)-1,2-epoxybutane (99%) were purchased from Sigma Aldrich and were used as received. Sodium hydroxide pellets (>97%) were purchased from Fisher Scientific and were dissolved in deionized water to form a 2 M solution. Hydrogen peroxide (>30% w/v in water) was purchased from Fisher Scientific and was used as received.

7. Cooling was achieved using an acetone bath with the bath temperature maintained at –30 °C using a LabPlant cryostat. The checkers used an acetone bath kept at –30 °C by addition of small portions of dry ice.
8. Upon addition of *n*-butyllithium a yellow color developed which persisted upon warming to room temperature.
9. The solution of LTMP was cooled in an acetone bath, maintaining a bath temperature between –33 °C to –35 °C by careful addition of dry ice. It is important to avoid cooling the solution below this temperature in order to avoid precipitation of LTMP.
10. The solution of boronic ester and epoxide was cooled in an acetone bath with the bath temperature maintained at –30 °C using a LabPlant cryostat. The checkers used an acetone bath kept at –30 °C during the addition of LiTMP and switched to a Cryostat for cooling after the addition was finished.
11. A 24", 16 G cannula wrapped with cotton wool was used to connect the acceptor and donor flasks. A double skinned N_2 balloon was used to pressurize the head space of the donor flask.
12. The internal temperature of the conical flask (monitored with a thermometer) rose from 5 °C to ~15 °C upon addition of the reaction mixture and washings.
13. The solution was stirred in the ice bath until the internal temperature fell from ~15 °C to below 10 °C (typically 4-5 min). At this point, addition of H_2O_2 was commenced. The checkers observed a persisting faint yellow color of the suspension, which did not change the reaction outcome.
14. Upon addition of hydrogen peroxide, the internal temperature of the reaction mixture rose from 10 °C to ~25 °C. After addition is complete, the internal temperature fell to ~5 °C.
15. Prior to concentration, an aliquot from the organic phase was spotted onto KI-starch paper (obtained from Sigma Aldrich) to verify that all active oxygen compounds had been removed. The checkers observed a positive peroxide test (ca. 10mg/L) after one wash with sat. aq. sodium thiosulfate solution. A second wash with sat. aq. sodium thiosulfate solution alleviated this problem.
16. The crude reaction mixture contained a mixture of **2**, $PhCH_2CH_2OH$ and pinacol. The ratios of these compounds was determined by ^1H NMR (400 MHz, $CDCl_3$) by integration of the following diagnostic peaks: **2** (δ = 3.36–3.43, m, 1H), $PhCH_2CH_2OH$ (δ = 3.90 ppm, t, J = 7.0 Hz, 2H) and pinacol (δ = 1.27 ppm, s, 12H) (chemical shifts are relative to the

submitter's ^{1}H NMR data (Note 19)). A typical crude reaction mixture contained a 100:23:49 mixture of **2**:$PhCH_2CH_2OH$:pinacol. Azeotroping the reaction mixture facilitates chromatographic purification by removing some of the pinacol and $PhCH_2CH_2OH$. After two water/MeOH azeotropes, a typical mixture contained a 100:13:15 mixture of **2**:$PhCH_2CH_2OH$:pinacol. The checkers observed that the endpoint of azeotropic removal can be determined by the fact that the milky suspension becomes a clear oil when the water/methanol mixture has been completely evaporated.

17. 2-Phenylethanol ($PhCH_2CH_2OH$) (R_f = 0.63 in 1:4 ethyl acetate:dichloromethane) elutes first from the column, followed by the desired product **2** (R_f = 0.27 in 1:4 ethyl acetate:dichloromethane) followed by pinacol (R_f = 0.12 in 1:4 ethyl acetate:dichloromethane). Visualization was achieved by staining with potassium permanganate or *p*-anisaldehyde (Figure 8) [*N.B.* staining with *p*-anisaldehyde is particularly effective for visualization of pinacol].

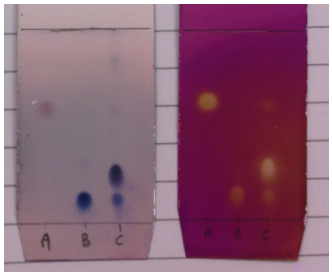


Figure 8. TLC for Step B (1:4 ethyl acetate-dichloromethane). Left plate stained with *p*-anisaldehyde; right plate stained with potassium permanganate. A = $PhCH_2CH_2OH$, B = pinacol, C = crude reaction mixture after two MeOH/H_2O azeotropes.

18. After 2 h at 0.2 mmHg, a solid cake had formed, which was broken up into a coarse powder with a spatula before drying overnight.
19. (±)-(3*R*,4*R*)-1-Phenylhexane-3,4-diol (**2**) has the following physical and spectroscopic properties: R_f = 0.27 (1:4 ethyl acetate:dichloromethane; Merck silica gel 60 F254 plate); mp 50 °C; Checker's ^{1}H NMR data: ^{1}H NMR ($CDCl_3$, 400 MHz) δ : 0.97 (t, *J* = 7.5 Hz, 3H), 1.44 (ddq, *J* = 14.4, 8.3, 7.3 Hz, 1H), 1.58 (dqd, *J* = 13.9, 7.6, 4.1 Hz, 1H), 1.73-1.88 (m, 2H), 2.06 (s, 2H), 2.71 (ddd, *J* = 13.8, 9.1, 7.2 Hz, 1H), 2.85 (ddd, *J* = 13.8, 9.1, 6.1 Hz, 1H), 3.37 (ddd, *J* = 8.3, 5.3, 4.1 Hz, 1H), 3.41-3.52 (m, 1H), 7.16–

7.32 (m, 5H); Submitter's ^{1}H NMR data: ^{1}H NMR ($CDCl_3$, 400 MHz) δ : 0.99 (t, *J* = 7.5 Hz, 3H), 1.41-1.53 (m, 1H), 1.60 (dqd, *J* = 13.8, 7.5, 4.1 Hz, 1H), 2.73 (ddd, *J* = 13.8, 9.2, 7.2 Hz, 1H), 1.74–1.92 (m, 2H), 2.26 (d, *J* = 5.2 Hz, 1H, O*H*), 2.38 (d, *J* = 5.3 Hz, 1H, O*H*), 2.88 (ddd, *J* = 13.9, 9.1, 6.1 Hz, 1H), 3.36-3.43 (m, 1H), 3.44-3.52 (m, 1H), 7.18–7.26 (m, 3H), 7.28–7.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ : 10.1, 26.6, 32.1, 35.5, 73.6, 76.1, 126.0, 128.56, 128.58, 142.1; HRMS (ESI^{+}) calculated for $C_{12}H_{18}NaO_2^{+}$ = 217.1199, mass found 217.1194; IR (film): 3368, 3027, 2960, 2934, 2877, 1496, 1455, 699 cm^{-1}; Anal. calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.94; H, 9.27.

20. The d.r. of the purified material was typically in the range 97:3 to 98:2. The submitters report that the minor diastereoisomer displays the following diagnostic ^{1}H NMR signals: (400 MHz, $CDCl_3$): δ (ppm) = 3.52–3.59 (m, 1H) and 3.61–3.69 (m, 1H) (chemical shifts are relative to the ^{1}H NMR data (Note 19)). The d.r. was determined from the ^{1}H NMR by integration of the peak for the minor diastereoisomer against one of the ^{13}C satellites of the major diastereomer as described by Davies and co-workers.[3]

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards

associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

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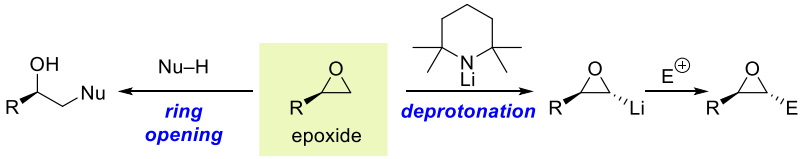
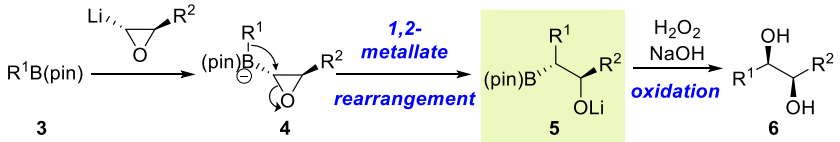
Discussion

Epoxides are versatile building blocks, which, due to their highly strained nature can act as electrophiles in a range of ring opening processes.[4] This high ring strain also confers additional acidity upon the C_α–H bonds (relative to acyclic ethers) which can be deprotonated by a non-nucleophilic base for example lithium 2,2,6,6-tetramethylpiperidide (LTMP). The resulting metallated epoxides are useful intermediates and a wide range of reactions have been developed that rely upon their carbanionic and carbenic behavior (Scheme 1a).[5]

Scheme 1a. Ring opening and deprotonation of epoxides



Scheme 1b. Homologation of boronic esters with lithiated epoxides

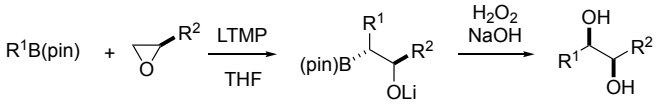


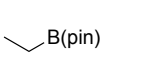
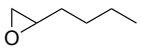
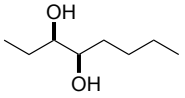
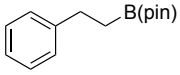
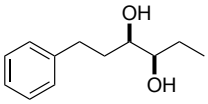
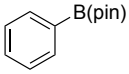
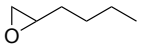
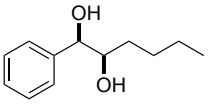
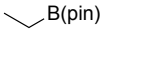
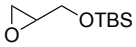
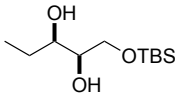
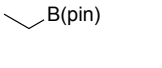
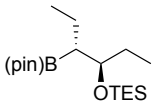
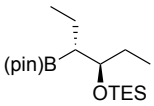
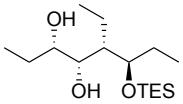
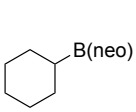
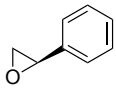
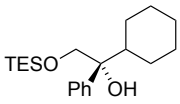
Building upon our previous studies directed towards lithiation-borylation of enantioenriched lithium carbenoids,[6] we recently reported a

method for the homologation of boronic esters with lithiated epoxides (Scheme 1b).[7] In this process, epoxides were deprotonated with LTMP in the presence of a boronic ester. The resulting lithiated epoxide reacted with the boronic ester resulting in the formation of a strained boronate complex. This intermediate underwent stereospecific 1,2-metallate rearrangement affording β -hydroxyboronic esters, which upon treatment with alkaline peroxide were oxidized to the corresponding 1,2-diols.[8]

These conditions were applied to the synthesis of a series of 1,2-diols (Table 1). A range of aliphatic boronic esters and epoxides were well tolerated in this process (Table 1, entries 1-2) and aromatic boronic esters also underwent homologation in good yield and high diastereoselectivity (Table 1, entry 3). Functionalized epoxides were also effective substrates, including a glycidol derivative (Table 1, entry 4). In all cases where enantioenriched epoxides were employed, the products were obtained with complete enantiospecificity. The β -hydroxyboronic esters obtained in this

Table 1. Selected examples of boronic ester homologation with lithiated epoxides



Entry	Boronic ester	Epoxide	Product	Result[a]
1				76% yield >95:5 d.r.
2				**70-71% yield** **(40 mmol scale)** **>95:5 d.r.**
3				57% yield >95:5 d.r.
4				54% yield >95:5 d.r.
5[b]				57% yield 99:1 e.r.; >95:5 d.r.
6				45% yield >95:5 d.r.
7[c]				69% yield 99:1 e.r.

[a] Isolated yields. [b] TESOTf was added to the crude reaction mixture instead of H_2O_2 and NaOH. [c] TESOTf was added to the ate complex followed by oxidation.

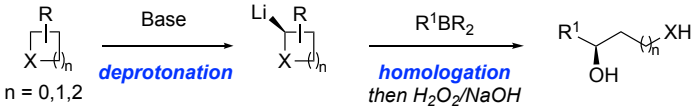
process are somewhat unstable with respect to elimination, but can be isolated after protection of the hydroxyl group. For example, following addition of TESOTf to the crude reaction mixture, a silyl protected derivative was isolated in good yield and essentially complete stereocontrol

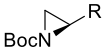
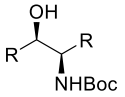
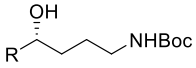
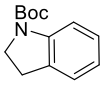
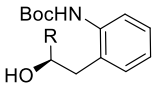
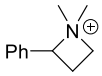
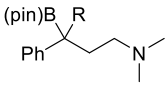
(Table 1, entry 5). These protected β -hydroxyboronic esters could be further homologated with a second lithiated epoxide affording triols with complete stereoselectivity (Table 1, entry 6). Such motifs are commonly found in natural products and their ease of synthesis using this method is particularly noteworthy. Styrene oxide could also be employed in this chemistry (Table 1, entry 7). In this case, stereospecific lithiation of the epoxide at the benzylic position resulted in the formation of tertiary alcohol products.

We have also extended this chemistry to the homologation of boronic esters with several other lithiated heterocycles (Table 2). *N*-Boc-aziridines were lithiated with LTMP and following homologation and oxidation, β -amino alcohols were obtained in good yields and complete stereocontrol.[9] (Table 2, entry 2). The homologation of boranes with Boc protected pyrrolidines and indolines has also been investigated (Table 2, entries 3-4).[10] In this case, enantioselective lithiation of the achiral heterocycle starting materials was carried out using a combination of *s*BuLi and sparteine. Addition of TMSOTf was found to be critical to facilitate 1,2-metallate rearrangements. 2-Phenyl-azetidinium ylides can also be employed as carbenoid reagents, enabling the efficient synthesis of γ -dimethylamino boronic esters (Table 2, entry 5).[11]

In summary, the homologation of boronic esters using lithiated epoxides is a powerful method, enabling the convergent and stereoselective assembly of 1,2-diols. The process is extremely scalable and has been carried out with 40 mmol of boronic ester with no reduction in efficiency. The β -hydroxyboronic ester intermediates can also be protected and subjected to further homologations. This chemistry has also been successfully extended to homologation processes with other lithiated heterocycles such aziridines, pyrrolidines, indolines and azetidines.

Table 2. Summary of methods for homologation of boranes and boronic esters with lithiated heterocycles



Entry	Heterocycle	Base	Product	Result[a]
1		LTMP		38-86% yield >95:5 d.r.; >99% e.s.
2		LTMP		63-93% yield >95:5 d.r.; 99 % e.e.
3[b,c]		^{s}BuLi·(–)-Sp		58-59% yield 95:5 to 92:8 e.r.
4[b,c]		^{s}BuLi·(–)-Sp		64-67% yield 97:3 to 96:4 e.r.
5[d]		LDA		44-69% yield

[a] Isolated yields. [b] Boranes were used since boronic esters did not undergo 1,2-migration. [c] TMSOTf was added to facilitate 1,2-migration. [d] The boronic esters were isolated without oxidation.

References

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11. Casoni, G.; Myers, E.; Aggarwal, V. *Synthesis* **2016**, *48*, 3241–3253.

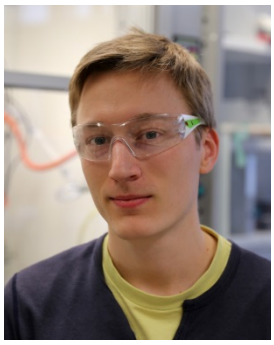
Appendix
Chemical Abstracts Nomenclature (Registry Number)

2-Phenyl-1-ethylboronic acid: Boronic acid, B-(2-phenylethyl)-; (34420-17-2)
Pinacol: 2,3-Dimethylbutane-2,3-diol; (76-09-5)
tert-Butyl methyl ether: Methyl *tert*-butyl ether; (1634-04-4)
2,2,6,6-Tetramethylpiperidine; (768-66-1)
n-Butyllithium; (109-72-8)
Hydrogen peroxide; (7722-84-1)
(±)-1,2-Epoxybutane; (106-88-7)

4,4,5,5-Tetramethyl-2-phenethyl-1,3,2-dioxaborolane: 4,4,5,5-Tétraméthyl-2-(2-phényléthyl)-1,3,2-dioxaborolane; (165904-22-3)
(±)-(3R,4R)-1-Phenylhexane-3,4-diol: 3,4-Hexanediol, 1-phenyl-, (3*R*,4*R*)-: (1095498-29-5)

Roly J. Armstrong graduated with an MSci in Natural Sciences from Pembroke College, Cambridge (2011) spending his final year working in the laboratory of Prof. Steven Ley. He subsequently moved to Merton College, Oxford to carry out a DPhil under the supervision of Prof. Martin Smith (2011-2015) working on asymmetric counter-ion directed catalysis. In October 2015 he joined the group of Prof. Varinder Aggarwal at the University of Bristol as a postdoctoral research associate.

Varinder K. Aggarwal studied chemistry at Cambridge University and received his Ph.D. in 1986 under the guidance of Dr. Stuart Warren. After postdoctoral studies (1986–1988) under Prof. Gilbert Stork, Columbia University, he returned to the UK as a Lecturer at Bath University. In 1991 he moved to Sheffield University, where he was promoted to Professor in in 1997. In 2000 he moved to Bristol University where he holds the Chair in Synthetic Chemistry. He was elected Fellow of the Royal Society in 2012.



Philipp Sondermann obtained his B.Sc. and M.Sc. degree in Chemistry from the University of Heidelberg, conducting research with Professor G. Helmchen at the same institution, Professor F. Gagosz at Ecole Polytechnique, France and Professor D. W. C. MacMillan at Princeton University, USA. He then joined the research group of Professor E. M. Carreira at the ETH Zürich for Ph.D. studies to work on the synthesis of complex natural products.

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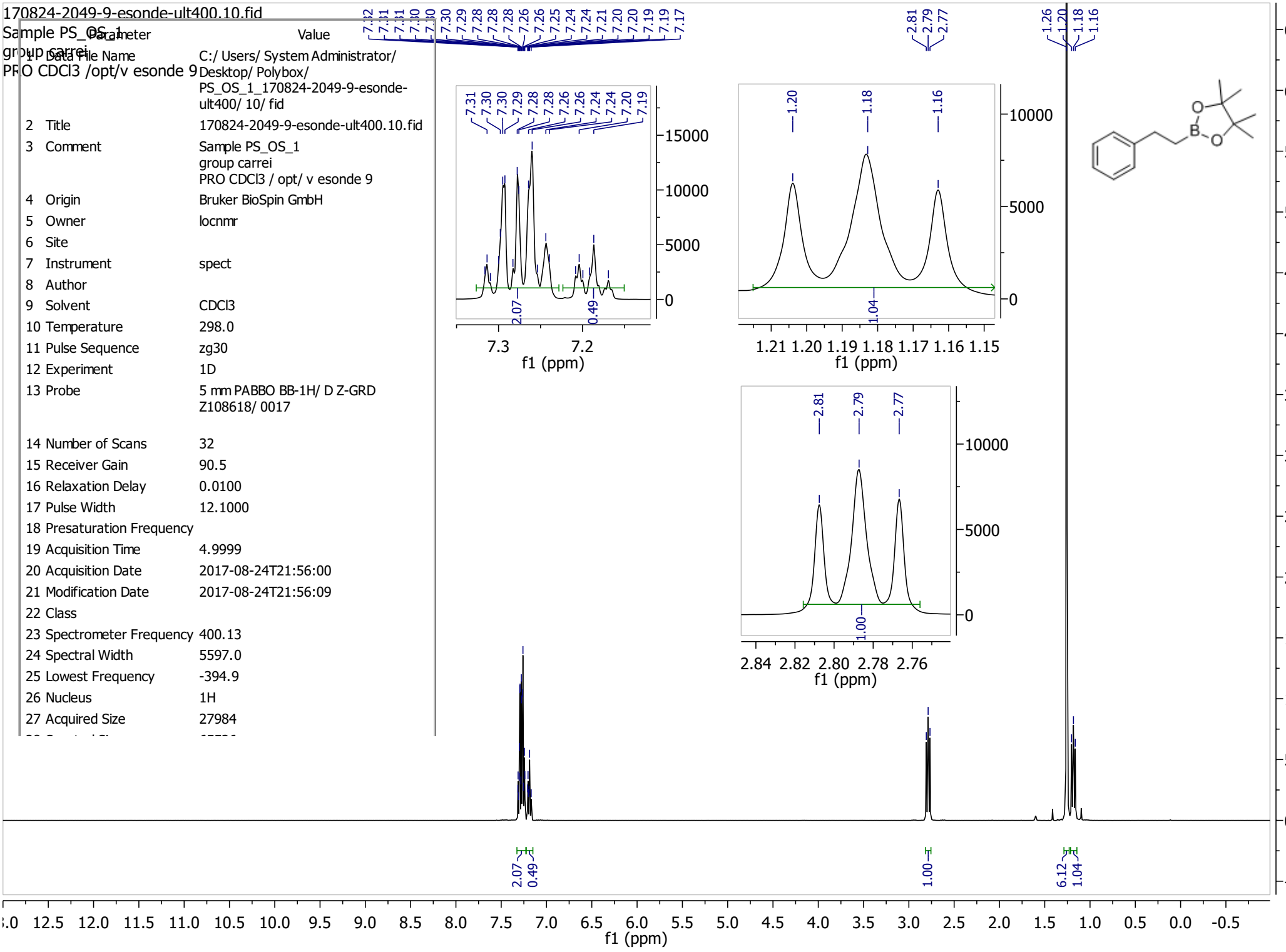

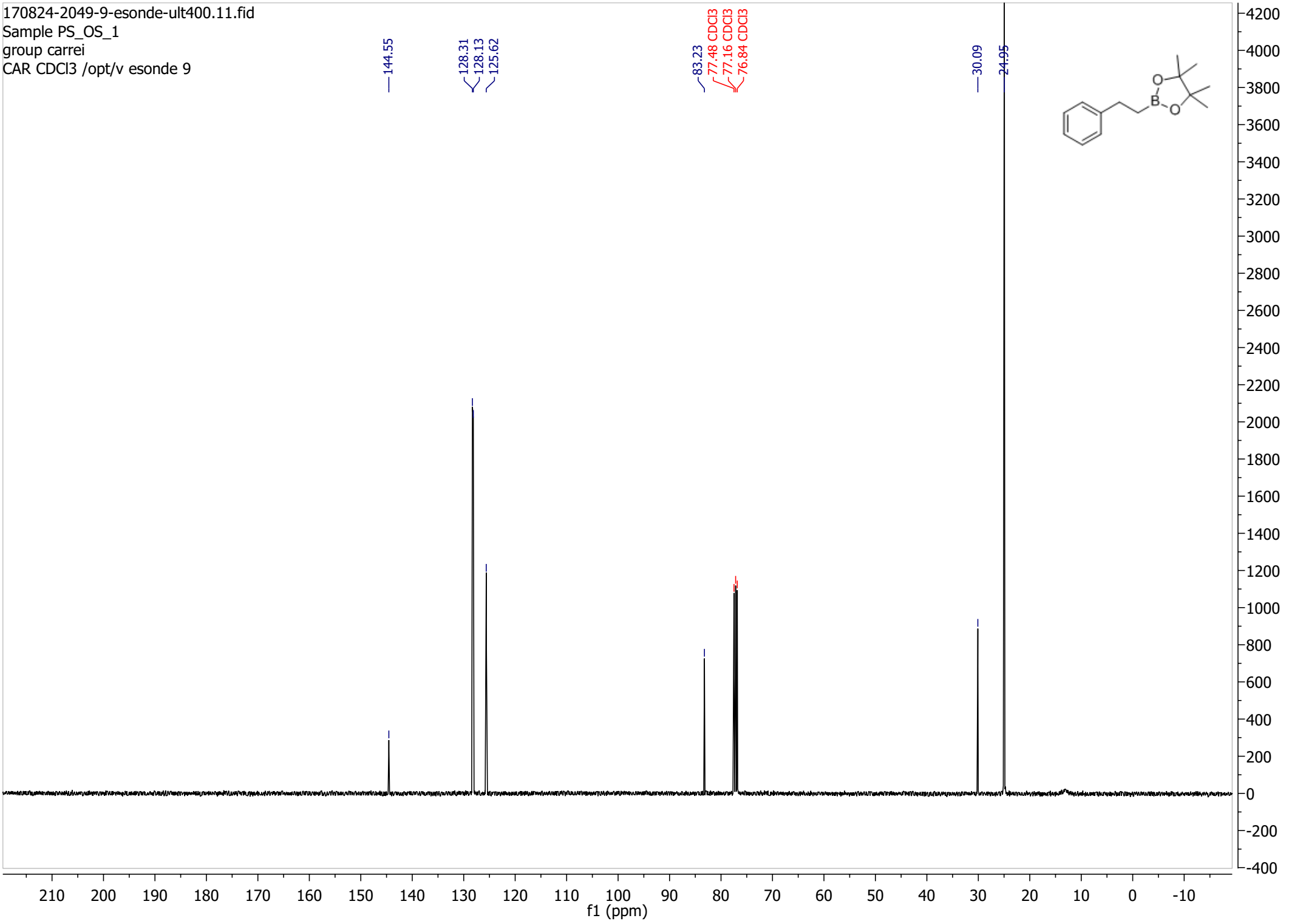
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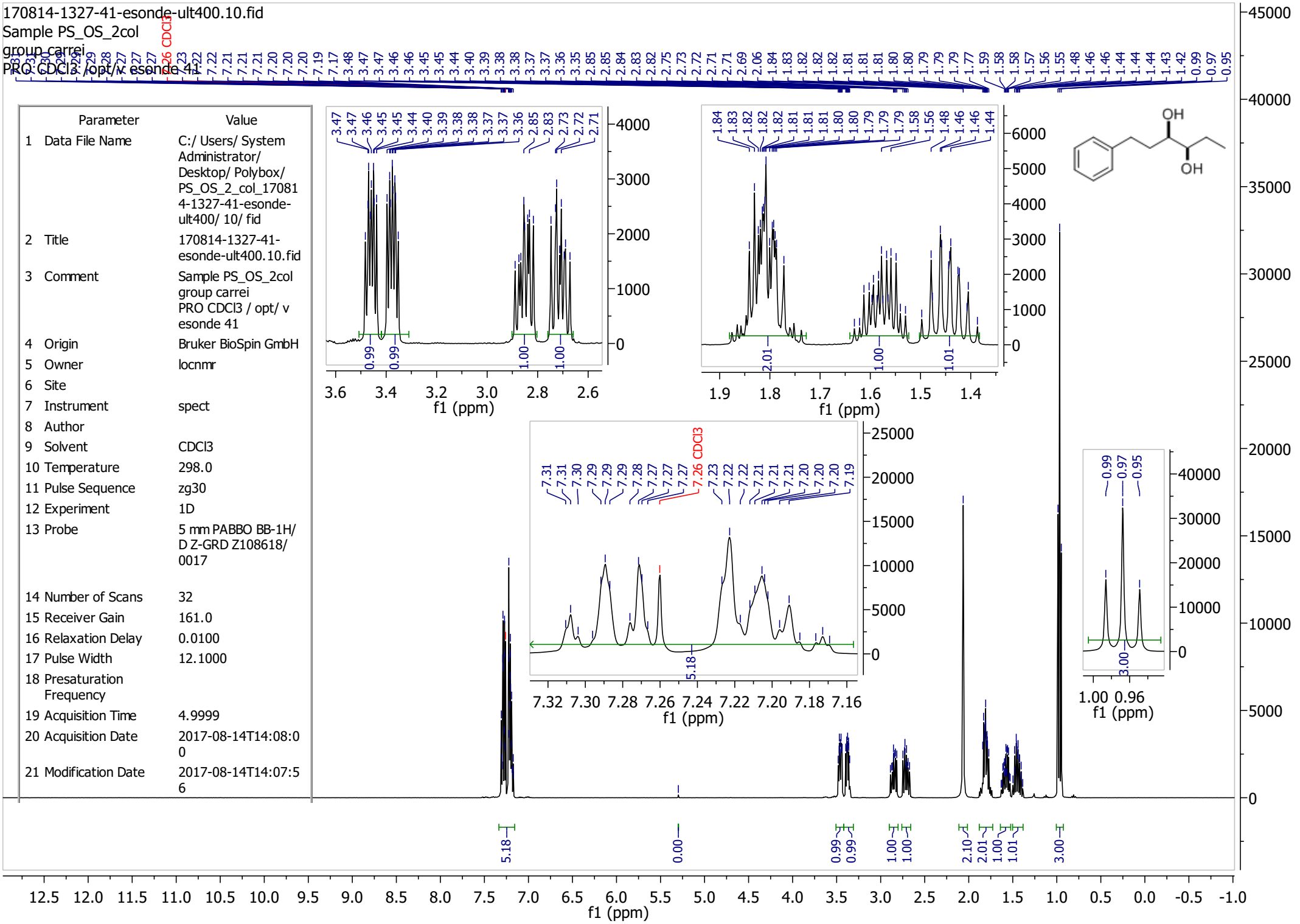

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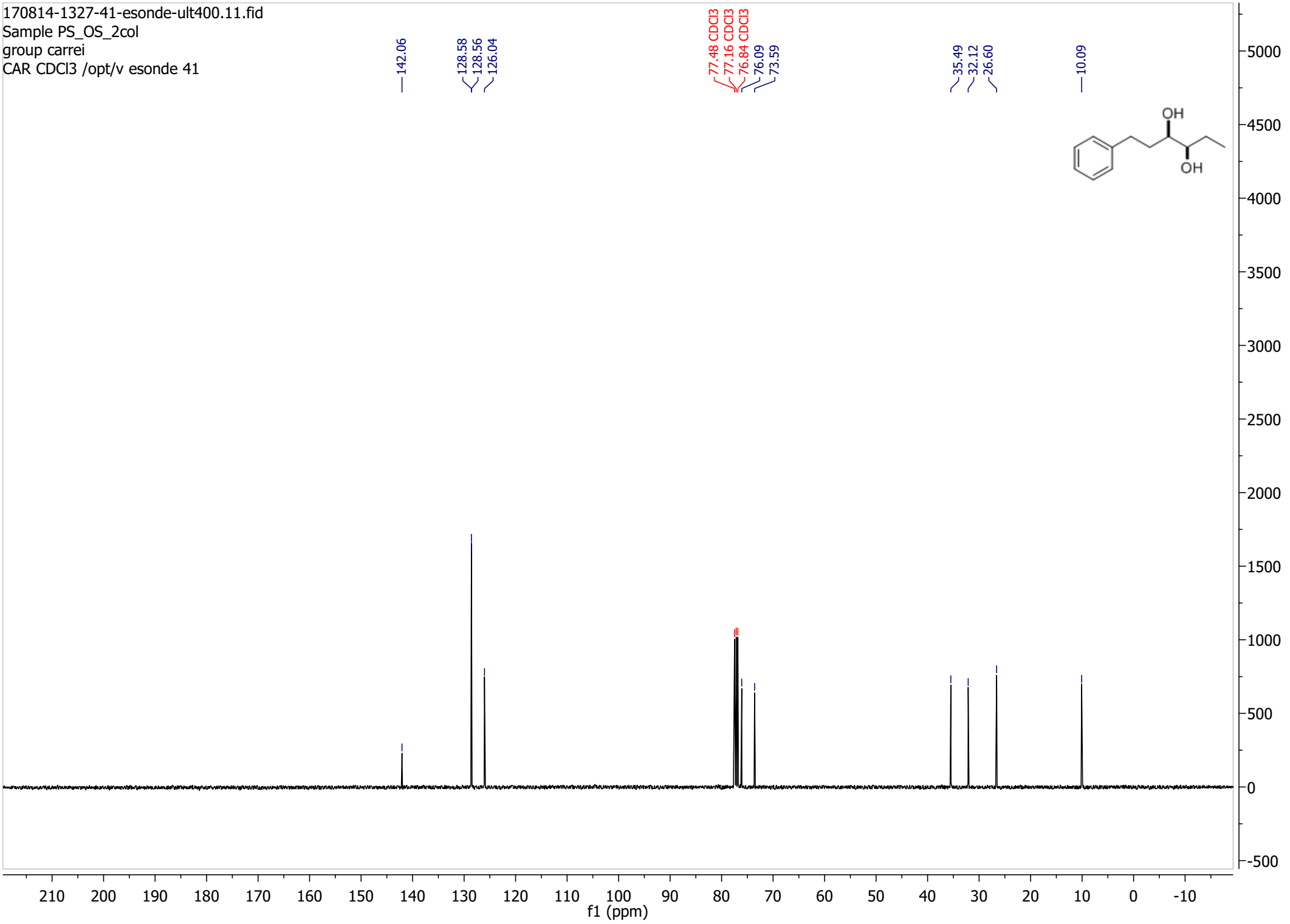
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