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of Organic Compounds

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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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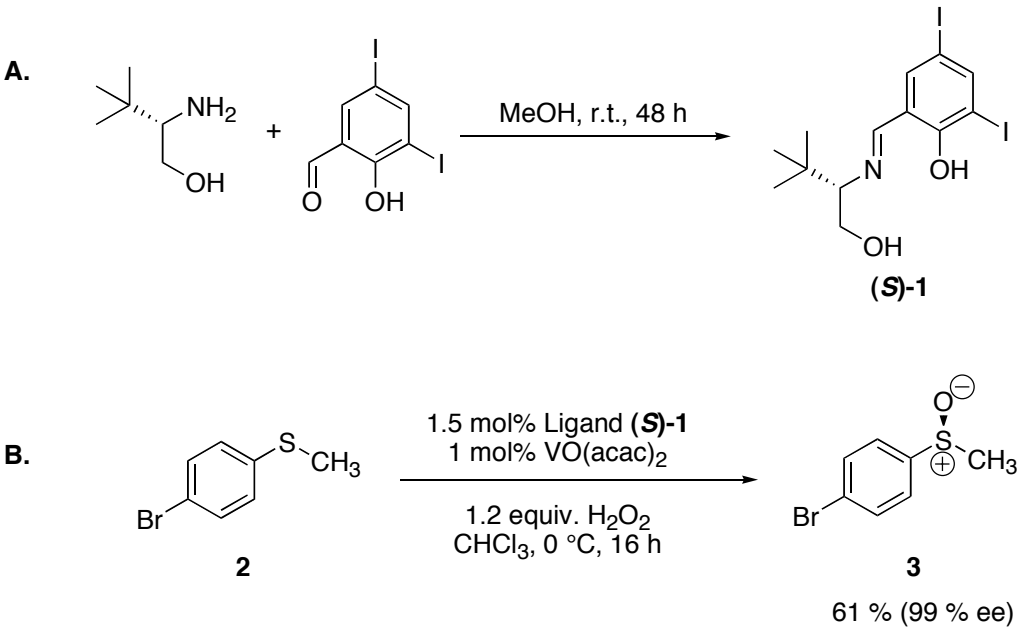
# ENANTIOSELECTIVE OXIDATION OF AN ALKYL ARYL SULFIDE: SYNTHESIS OF (*S*)-(–)-METHYL *P*-BROMOPHENYL SULFOXIDE




Submitted by Carmelo Drago, Emma-Jane Walker, Lorenzo Caggiano and Richard F. W. Jackson.[1]
Checked by Katherine Rawls and Jonathan A. Ellman.

## 1. Procedure

*A. (S)-(–)-2-(N-3,5-Diiodosalicyliden)amino-3,3-dimethyl-1-butanol [(S)-1]:* To a solution of (L)-(+)-*tert*-leucinol (350 mg, 3.0 mmol, 1.13 equiv) (Note 1) dissolved in 15 mL of MeOH (Note 2) in a flame-dried 50-mL round-bottomed flask kept under positive nitrogen pressure during the reaction is added 3,5-diiodosalicylaldehyde (1.00 g, 2.66 mmol, 1.0 equiv) (Note 3). The reaction mixture is stirred at room temperature (25 °C) for 48 h (Note 4). The solvent is evaporated under reduced pressure (30 °C, 40 mmHg) and the crude product is transferred to a 25-mL Erlenmeyer flask and purified by dissolving in 5 mL of hot EtOH (Note 5). The resulting yellow solution is allowed to reach room temperature slowly over a two-hour period (25 °C), allowing partial solvent evaporation (~1 mL), and needle crystal formation is observed. At this point, the Erlenmeyer flask is plugged and left overnight (17 h) in a refrigerator at 3 °C. The crystals are filtered in a Büchner funnel and washed with ice-cold EtOH (3 x 2 mL), and

then dried under vacuum (0.02 mmHg) to afford the ligand **(*S*)-1** as a yellow solid (1.04 g, 82% yield) (Note 6).

*B.* (*S*)-(–)-*p*-*Bromophenyl methyl sulfoxide (3)*. A flame-dried, three-necked, 250-mL round-bottomed flask is equipped with a rubber septum, a 25-mL pressure-equalizing addition funnel, a thermometer adaptor fitted with a suitable thermometer, and a magnetic stir bar (30 mm length, oval) and is placed under positive nitrogen pressure. The apparatus is charged with (*S*)-(-)-2-(*N*-3,5-diiodosalicyliden)amino-3,3-dimethyl-1-butanol **(*S*)-1** (425.8 mg, 0.90 mmol, 1.5 mol%) and 15 mL of $CHCl_3$ (Note 7). A green solution of vanadyl acetylacetonate ($VO(acac)_2$, 159.0 mg, 0.60 mmol, 1.0 mol%) (Note 8) in 15 mL of chloroform is added dropwise via the addition funnel to the stirred bright yellow solution at room temperature over 3 minutes. The stirred translucent solution immediately turns from yellow to green and then finally dark brown as it is left stirring for 30 min at room temperature open to the atmosphere. *p*-Bromophenyl methyl sulfide (2) (12.19 g, 0.060 mol, 1.0 equiv) (Note 9) is added in one portion to the reaction mixture, followed by $CHCl_3$ (30 mL) and the solution is cooled to 0 ºC by means of a cryocool with an isopropanol bath. Once the internal temperature reaches 0 °C (20–30 minutes), an aqueous solution of hydrogen peroxide (7.75 g of a 31.6% solution in $H_2O$, 0.072 mol, 1.2 equiv) (Note 10) is added dropwise over a period of 25 min via the dropping funnel, keeping the internal temperature between 0-5 °C. The reaction mixture is then kept at 0 °C (± 1 °C) and vigorously stirred for 16 h (Note 11).

The reaction is quenched at 0 °C by the addition of 10 % w/v aqueous solution of sodium thiosulfate (100 mL) added dropwise via the addition funnel and then transferred to a 500-mL separatory funnel, rinsing with $CH_2Cl_2$ (2 x 50 mL) (Note 12). The layers are separated and the aqueous fraction is washed with $CH_2Cl_2$ (2 x 50 mL). The combined organic fractions are washed with saturated aqueous sodium chloride (50 mL) and dried over magnesium sulfate (10 g). The solution is filtered, and the magnesium sulfate is washed with 100 mL $CH_2Cl_2$. The organic solvent is evaporated under reduced pressure (30°C, 40 mmHg) to give the crude product as a dark brown solid (13.83 g, Sample 1, Note 13). The solid is dissolved in $CH_2Cl_2$ (17 mL) and layered on a silica pad (50 g $SiO_2$, Note 14) in a 7-cm diameter glass-sintered filter funnel (Note 15) and a mixture of sulfoxide and sulfone is eluted using EtOAc and petroleum ether (50:50, 200 mL) (Notes 16 and 17). The mixture is collected and evaporated under reduced pressure (3.37 g brown solid, Sample 2.1, Note 18). Elution with EtOAc (300 mL) and

evaporation under reduced pressure gives pure sulfoxide as a pale yellow solid (9.3 g, Sample 2.2, 71% yield) (Note 19).

Column chromatography is performed on the mixed fraction Sample 2.1 (Note 20) and elution with a mixture of EtOAc and petroleum ether (50:50, 550 mL, until complete elution of ligand **(*S*)-1** and sulfone) followed by EtOAc (1.4 L) and evaporation of the EtOAc fraction under reduced pressure gives pure sulfoxide as a yellow-brown solid (0.93 g, 7% yield, Sample 3) (Note 21).

The pure sulfoxide fractions, Samples 2.2 and 3, are combined in a 250-mL Erlenmeyer flask and dissolved in a mixture of hot EtOAc and heptane (20:80, 75 mL, Notes 22 and 23). Recrystallization occurs as the solution sits at room temperature (12 h, 25 °C), allowing for partial solvent evaporation (5 mL). Filtration on a Büchner funnel gives the sulfoxide, which is dried under vacuum (0.02 mmHg) to afford off-white needles (8.07 g, 61%, Sample 4) (Note 24). Further purification is performed by sublimation of the solid at a pressure of 0.02 mmHg over a period of 4 h in a standard sublimation apparatus, with a water-cooled cold finger and with the external oil bath at 90 °C, which gives (*S*)-(-)-*p*-bromophenyl methyl sulfoxide as a white powder (8.07 g, 99 % ee, 61% yield) (Note 25).

## 2. Notes

1. The submitters received (L)-*tert* leucinol from Degussa AG Industrie, who prepared the reagent by $I_2/NaBH_4$ reduction of (L)-*tert* leucine.[3] $\{[\alpha]_D^{20}$ +40.3, (EtOH, c 1.0), lit. +35.3 (EtOH, c 3.05)$\}$[2] The checkers purchased (S)-*tert*-leucinol from Aldrich Chemical Company, and it was used as received.

2. HPLC Grade methanol from Fisher Scientific (submitters) or Spectro Grade from Fisher Scientific (checkers) was used as received.

3. 3,5-Diiodosalicylaldehyde (97%), from Aldrich Chemical Company, was used as received.

4. Reaction progress was monitored by silica gel TLC, using 2:1 hexanes:EtOAc as eluent, and UV and ninhydrin stain to visualize (checkers). The aldehyde starting material has an $R_f$ value of 0.65 (UV only), the desired imine product has an $R_f$ value of 0.38 (yellow), and (*S*)-*tert*-leucinol (pink) remains at the baseline.

5. HPLC Grade ethanol from Fisher Scientific was used as received. The checkers heated the product in ethanol in a 25 mL Erlenmeyer flask in an oil bath at 90 °C (bath temperature) until all product dissolved.

6. The submitters reported a yield of 1.08 g, 86%. Characterization of (*S*)-(–)-2-(*N*-3,5-diiodosalicyliden)amino-3,3-dimethyl-1-butanol [**(*S*)-1**] is as follows: mp 162–163 °C, lit. mp 163–164 °C;[3] $[\alpha]_D^{20}$ –16.0 (acetone, c 1.0), lit.[4] $[\alpha]_D^{20}$ –16.6 (acetone, c 1.0); $\nu_{max}$ ($cm^{-1}$) 3303 (O-H), 2965 (CH=N, C-H), 1637 (CH=N, C-N); $^1$H NMR (400 MHz, $CDCl_3$) δ: 0.99 (s, 9 H), 2.73 (br s, 1 H), 3.09 (dd, 1 H, *J* = 9.2, 2.5 Hz), 3.69 (dd, 1 H, *J* = 11.2, 10.4 Hz), 4.00 (dd, 1 H, *J* = 11.5, 2.5 Hz), 7.50 (d, 1 H, *J* = 2.1 Hz), 7.99 (d, 1 H, *J* = 2.0 Hz), 8.09 (s, 1 H), 14.88 (br s, 1 H,); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 26.8, 32.9, 61.8, 75.7, 78.0, 93.0, 116.8, 141.1, 150.0, 164.7, 167.0; *m/z* (EI) 474 ($MH^+$, 22%), 473 ($M^+$, 100), 442 (22), 416 (73) and 359 (30); Anal. Calcd. for $C_{13}H_{17}I_2NO_2$: C, 33.00; H, 3.62; N, 2.96. Found: C, 33.02; H, 3.73; N, 2.83.

The submitters synthesized (*R*)-(-)-2-(*N*-3,5-diiodosalicyliden)amino-3,3-dimethyl-1-butanol [**(*R*)-1**] from (D)-(–)-*tert*-Leucinol (kindly provided as a gift from Degussa AG Industrie) according to the procedures outlined above, in similar yields. Use of the (*R*)-**1** ligand in the sulfoxidation reaction afforded the corresponding (*R*)-sulfoxide product in similar yields and enantioselectivity.

7. HPLC Grade Chloroform from Fisher Scientific, was used as received.

8. Vanadyl acetylacetonate [$VO(acac)_2$], from Alfa Aesar, was used as received.

9. *p*-Bromophenyl methyl sulfide (4-bromothioanisole, 98 %), from Alfa Aesar, was used as received.

10. Hydrogen peroxide solution (~30% w/w in water) from Aldrich Chemical Company was used. The concentration of $H_2O_2$ was determined to be 31.6 % by titration with $KMnO_4/H_2SO_4$ using a procedure based on the Degussa analytical method WM 09 / WM 11.[5]

11. Reaction progress was monitored by silica gel TLC, using diethyl ether as eluent, and UV or *p*-anisaldehyde to visualize (checkers). The desired sulfoxide product has an $R_f$ value of 0.29 (white-yellow), the overoxidation product sulfone has an $R_f$ of 0.67 (UV only), and the starting sulfide has an $R_f$ of 0.90 (UV only).

12. HPLC Grade dichloromethane from Fisher Scientific, was used as received.

13. The checkers obtained a crude ee of 93.4% using a Chiralpak AS chiral column from Chiral Technologies (250 x 4.6 mm) on an Agilent 1100 Series LC equipped with a multiwavelength detector (85:15

heptane:isopropanol, 1 mL/min, λ = 222, 254, and 280 nm, $t_R$ (minor) = 35.96 min, $t_R$ (major) = 43.20 min). The checkers obtained a ratio of sulfoxide:sulfone of 86:14 by $^1$H NMR.

14. The submitters purchased silica gel from BDH. The checkers purchased silica gel from Sorbent Technologies (60 Å, 230–400 mesh).

15. The submitters used a fritted funnel with pore size 2. The checkers used a 150-mL fritted funnel, ASTM, 40–60 C.

16. HPLC Grade Ethyl Acetate from Fisher Scientific was used as received.

17. Analytical Reagent Grade petroleum ether (40–60 °C) from Fisher Scientific (submitters) or Certified ACS Grade petroleum ether (30–60 °C) from Fisher Scientific (checkers) was used as received.

18. The submitters report a ratio of sulfoxide:sulfone of 67:33 by $^1$H NMR for 6.09 g of mixed fractions. The checkers obtained a ratio of sulfoxide:sulfone of 37:63 for 3.37 g of mixed fractions.

19. The submitters report collection of 7.21 g (55%) of pure product.

20. The checkers used a column with diameter = 4.5 cm, length = 38.1 cm, loaded with 100 g of silica gel (see Note 13). The compound was loaded onto the column with 13 mL of $CH_2Cl_2$.

21. The submitters report collection of 3.3 g of pure product, 25% yield.

22. HPLC Grade heptane from Fisher Scientific was used as received.

23. The submitters used 100 mL of 80:20 heptane:EtOAc for recrystallization. The checkers found that the enantiomeric purity and yield of the product was highly dependent on the amount of solvent used for recrystallization. The checkers heated the product in 80:20 heptane:EtOAc in a 250-mL Erlenmeyer flask in an oil bath at 90 °C (bath temperature) until all solid dissolved.

24. The submitters reported the isolation of 9.3 g (70.7 %).

25. The submitters reported the isolation of 9.2 g (70%) at >99% ee. The checkers collected the sublimation product in two batches due to the small size of the sublimation apparatus. **(*S*)-(–)-4-Bromophenyl methyl sulfoxide (3)**: mp 77–78 °C; $[\alpha]_D^{20}$ –106.9 (acetone, c 1.8), 99 % ee; lit. $[\alpha]_D^{20}$ –97.5 (acetone, c 1.8) for 94 % ee;[4] $^1$H NMR (500 MHz, $CDCl_3$) δ: 2.69 (s, 3 H), 7.49 (d, 2 H, $J$ = 8.4 Hz), 7.64 (d, 2 H, $J$ = 8.3 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 43.9, 125.0, 125.3, 132.5, 144.8; Anal. Calcd. for $C_7H_7BrOS$: C, 38.37; H, 3.22; S, 14.63. Found C, 38.36; H, 3.17; S 14.85. Chiral HPLC using a Chiralpak AS chiral column from Chiral Technologies

(250 x 4.6 mm) on an Agilent 1100 Series LC equipped with a multiwavelength detector (85:15 heptane:isopropanol, 1 mL/min, λ = 222, 254, and 280 nm) retention times are as follows: *p*-bromophenyl methyl sulfide $t_R$ 5 min.; *p*-bromophenyl methyl sulfone $t_R$ 30 min.; (*R*)-*p*-bromophenyl methyl sulfoxide $t_R$ 37 min. and (*S*)-*p*-bromophenyl methyl sulfoxide $t_R$ 45 min.

## Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academic Press: Washington, DC, 1995.

## 3. Discussion

Asymmetric oxidation of alkyl aryl sulfides has received a substantial amount of attention, due to the synthetic utility of the product sulfoxides. An existing *Organic Syntheses* procedure describes the preparation of (*S*)-(−)-methyl *p*-tolyl sulfoxide by oxidation of methyl *p*-tolyl sulfide using a stoichiometric reagent derived from (*S*,*S*)-(–)-diethyl tartrate and titanium(IV) isopropoxide, employing cumene hydroperoxide as the oxidant.[6] Purification of the product is achieved by flash chromatography. Herein is presented an alternative catalytic procedure for the asymmetric oxidation of *p*-bromophenyl methyl sulfide, based on our optimization[7,8] of the asymmetric sulfur oxidation procedure discovered by Bolm,[9] which employs a catalyst derived from $VO(acac)_2$ and an amino alcohol Schiff base ligand. A significant feature of this procedure is that the enantiomeric excess of the initially formed product is enhanced by a subsequent kinetic resolution process,[10] in which the minor enantiomer of the product is selectively oxidized to the corresponding sulfone. The key parameter is the use of chloroform as solvent, which promotes initial asymmetric oxidation and subsequent efficient kinetic resolution at the same temperature (namely 0 °C). In addition to the catalytic nature of the procedure, the main advantage is the use of hydrogen peroxide as oxidant.

From a practical point of view, the challenge is not achieving high levels of enantiomeric excess, but rather finding a convenient purification procedure that allows the separation of the by-product sulfone that is always produced (typically 10%). While flash column chromatography is an

effective method, we have made a substantial effort to purify the product sulfoxide without recourse to chromatography. However, in the case of both methyl p-tolyl sulfoxide and *p*-bromophenyl methyl sulfoxide, it has proved impossible to remove the corresponding sulfone by-product using distillation, trituration, crystallization or sublimation. The compromise purification method presented in this procedure, namely the use of a pad of silica gel in a sintered filter funnel, allows separation of pure sulfoxide product in reasonable yield, due to the large $R_f$ difference between the sulfone and sulfoxide. The yield can be enhanced by conventional flash chromatographic purification of the mixed fraction that is eluted first.

Another application of Bolm's system to the asymmetric synthesis of (*R*)-(+)-2-methyl-2-propanesulfinamide has been recently reported by Ellman in *Organic Syntheses*.[11]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**2.** Romo, D.; Romine, J. L.; Midura, W.; Meyers, A. I. *Tetrahedron* **1990**, *46*, 4951-4994.

**3.** McKennon, M. J.; Meyers, A. I.; Drauz, K.; Schwarm, M. *J. Org. Chem.* **1993**, *58*, 3568-3571.

**4.** Legros, J.; Bolm, C. *Chem. Eur. J.* **2005**, *11*, 1086-1092.

**5.** http://www.degussa.com.au/australia/MCMSbase/Pages/ProvideResource.aspx?; respath=/NR/rdonlyres/EC5E6FED-34E5-4AD1-9D59E2ADB8840764/0/; Application_Determination_of_Hydrogen_Peroxide_Concentration.pdf

**6.** Zhao, S. H.; Samuel, O.; Kagan, H. B. *Org. Synth.* **1990**, *68*, 49-55.

**7.** Pelotier, B.; Anson, M. S.; Campbell, I. B.; Macdonald, S. J. F.; Priem, G.; Jackson, R. F. W. *Synlett* **2002**, 1055-1060.

**8.** Drago, C.; Caggiano, L.; Jackson, R. F. W. *Angew. Chem., Int. Ed. Engl.* **2005**, *44*, 7221-7223.

**9.** Bolm, C.; Bienewald, F. *Angew. Chem., Int. Ed. Engl.* **1996**, *34*, 2640-2642.

**10.** Mohammadpoor-Baltork, I.; Hill, M.; Caggiano, L.; Jackson, R. F. W. *Synlett* **2006**, 3540-3544.

**11.** Weix, D. J.; Ellman, J. A.; Wang, X.; Curran, D. P. *Org. Synth.* **2005**, *82*, 157-165.

## Appendix
## Chemical Abstracts Nomenclature; (Registry Number)

(*S*)-(–)-2-(*N*-3,5-Diiodosalicyliden)amino-3,3-dimethyl-1-butanol; (477339-39-2)

(L)-(+)-tert-leucinol: 1-Butanol, 2-amino-3,3-dimethyl-, (2*S*)-; (112245-13-3)

3,5-Diiodosalicylaldehyde: Benzaldehyde, 2-hydroxy-3,5-diiodo-; (2631-77-8)

(*S*)-(–)-*p*-Bromophenyl methyl sulfoxide: Benzene, 1-bromo-4-[(*S*)-methylsulfinyl]-; (145266-25-0)

Vanadyl acetylacetonate; (3153-26-2)

*p*-Bromophenyl methyl sulfide: Benzene, 1-bromo-4-(methylthio)-; (104-95-0)

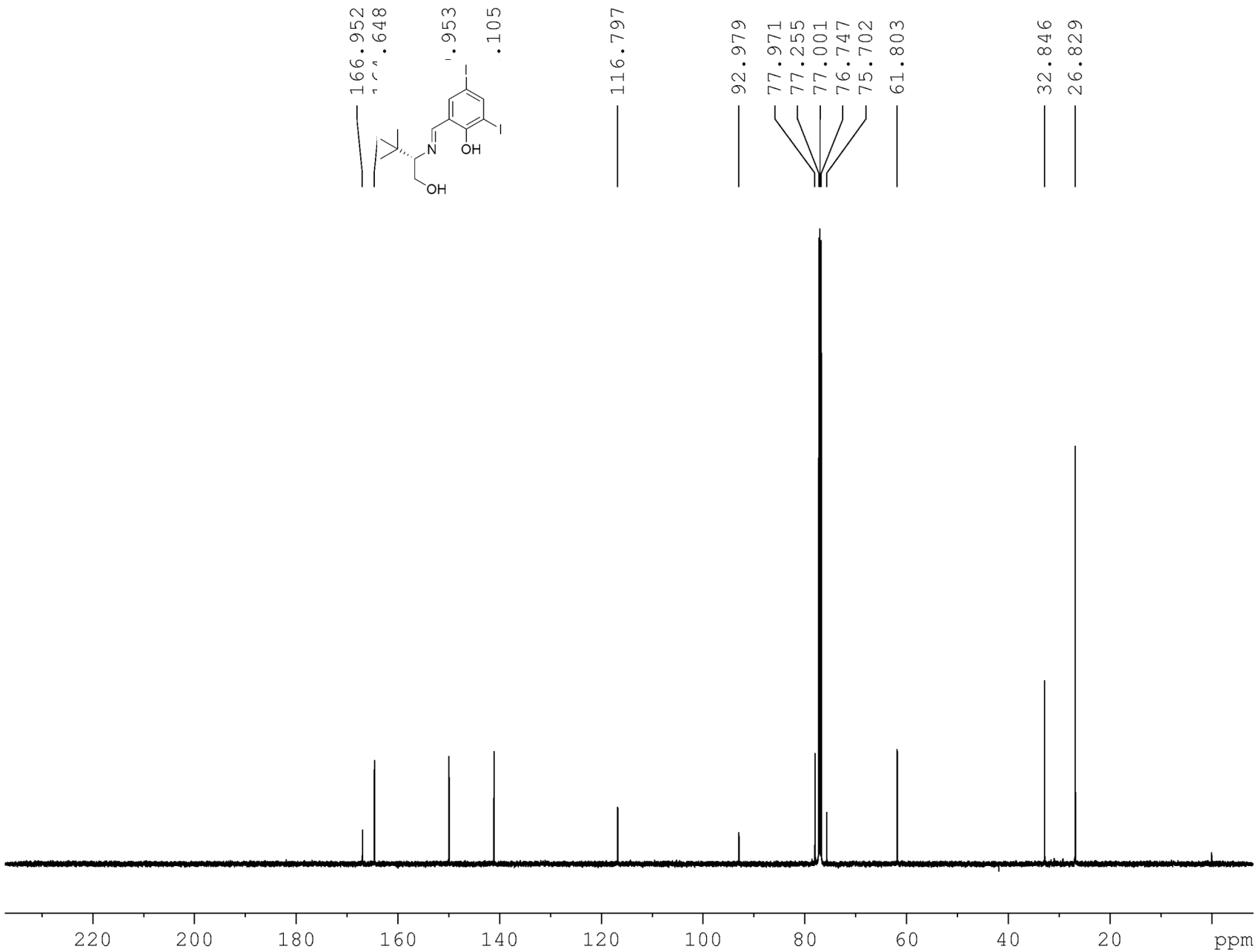
Richard Jackson obtained his Ph.D. in 1984 under the supervision of the late Professor Ralph Raphael, developing a new route to dihydrofuranones, and completing a synthetic approach to the pseudomonic acids. He spent a year at the ETH, Zürich, working with Professor Dieter Seebach on total synthesis, before starting his independent career at the University of Newcastle. His research interests range from applications of organometallic chemistry in non-proteinogenic amino acid synthesis to catalytic asymmetric oxidation reactions. In 2001 he moved to a Chair in Synthesis at the University of Sheffield, serving as Head of Department from 2003 to 2007.

Carmelo Drago obtained his first degree in Chemistry from the University of Catania in 2001, undertaking a final year project on asymmetric oxidation reactions mediated by enzymes under the supervision of Dr. Giovanni Nicolosi at the CNR (National Research Council). He moved to Sheffield for his Ph.D., working on asymmetric sulfur oxidation under the supervision of Professor Richard F. W. Jackson. In 2005, he joined the group of Professor Carlo Scolastico, at the CISI (Centre for Bio-molecular Interdisciplinary Studies and Industrial applications – University of Milan) where he is working on design, synthesis and characterization of proapoptotic agents for cancer therapy.

Emma Walker obtained her M.Chem. with Industrial Experience from the University of Edinburgh in 2003 before moving to the University of Sheffield to undertake her Ph.D. on the development of new methods for screening catalysts for kinetic resolution under the supervision of Professor Richard F.W. Jackson. In 2008 Emma joined the Whisky Technical Specialist Team within Diageo Scotland as a Project Chemist.

After obtaining his degree from the University of Liverpool in 1998, Lorenzo Caggiano performed his Ph.D. with Dr. Stuart Warren at the University of Cambridge. In 2002 as a European Network Fellow in the group of Professor Cesare Gennari at the University of Milan, he was involved in the formal synthesis of eleutherobin. In February 2004 he became a Research Officer in the group of Professor Richard F. W. Jackson at the University of Sheffield. In January 2007, he started his independent career as a RCUK Research Fellow at the Department of Pharmacy and Pharmacology, University of Bath, UK.

Katherine Rawls was born in 1983 in Wheat Ridge, Colorado. She graduated from Santa Clara University in 2005 with a B.S. in Chemistry and Mathematics. There she worked on chemoselective "post-translational" modifications of *N*-alkylaminooxy containing peptides under the mentorship of Professor Michael Carrasco. Currently, she is a fourth year graduate student at the University of California, Berkeley, working under the direction of Prof. Jonathan A. Ellman. Her research includes the development and application of the Substrate Activity Screening (SAS) method for the identification of nonpeptidic tyrosine phosphatase inhibitors.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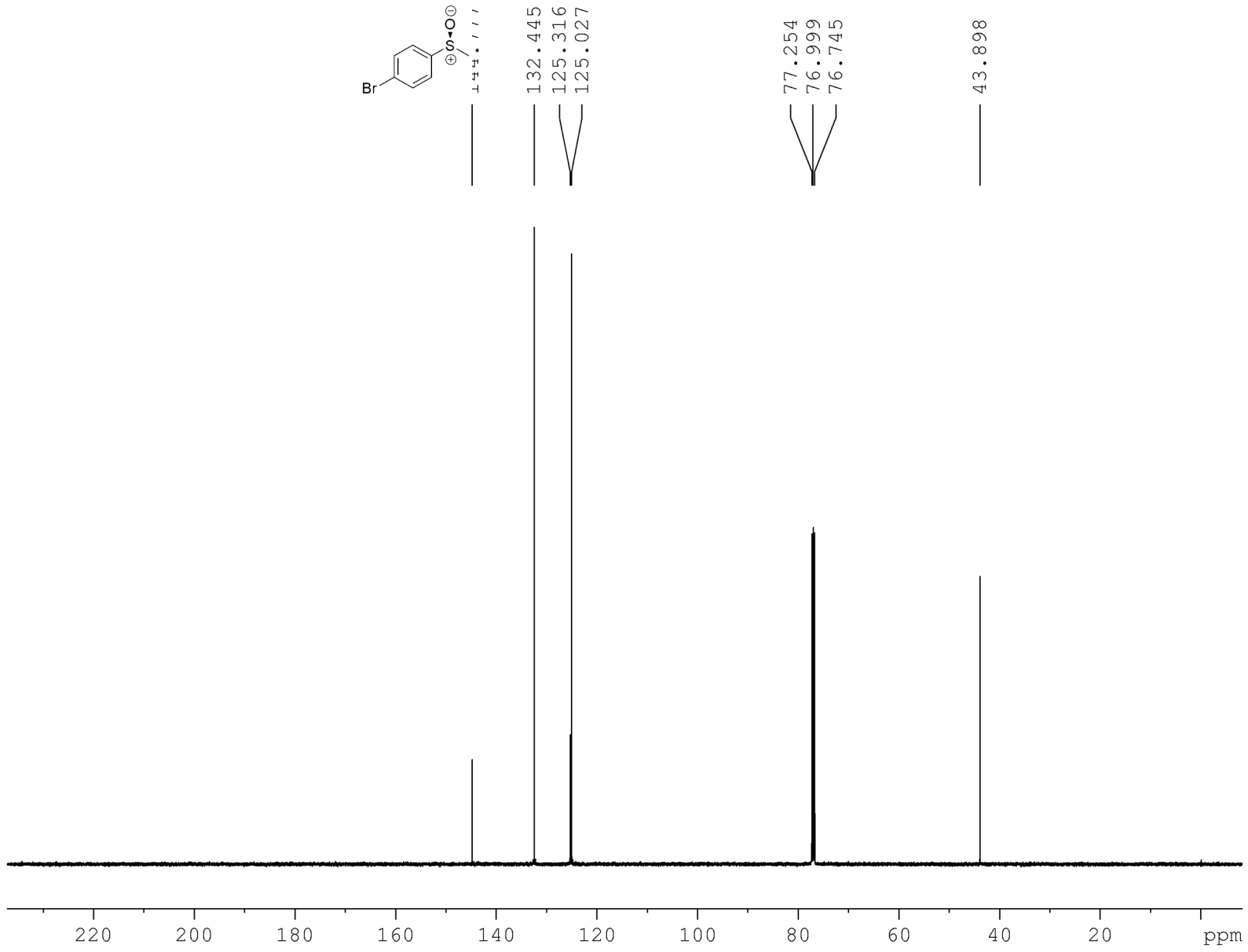
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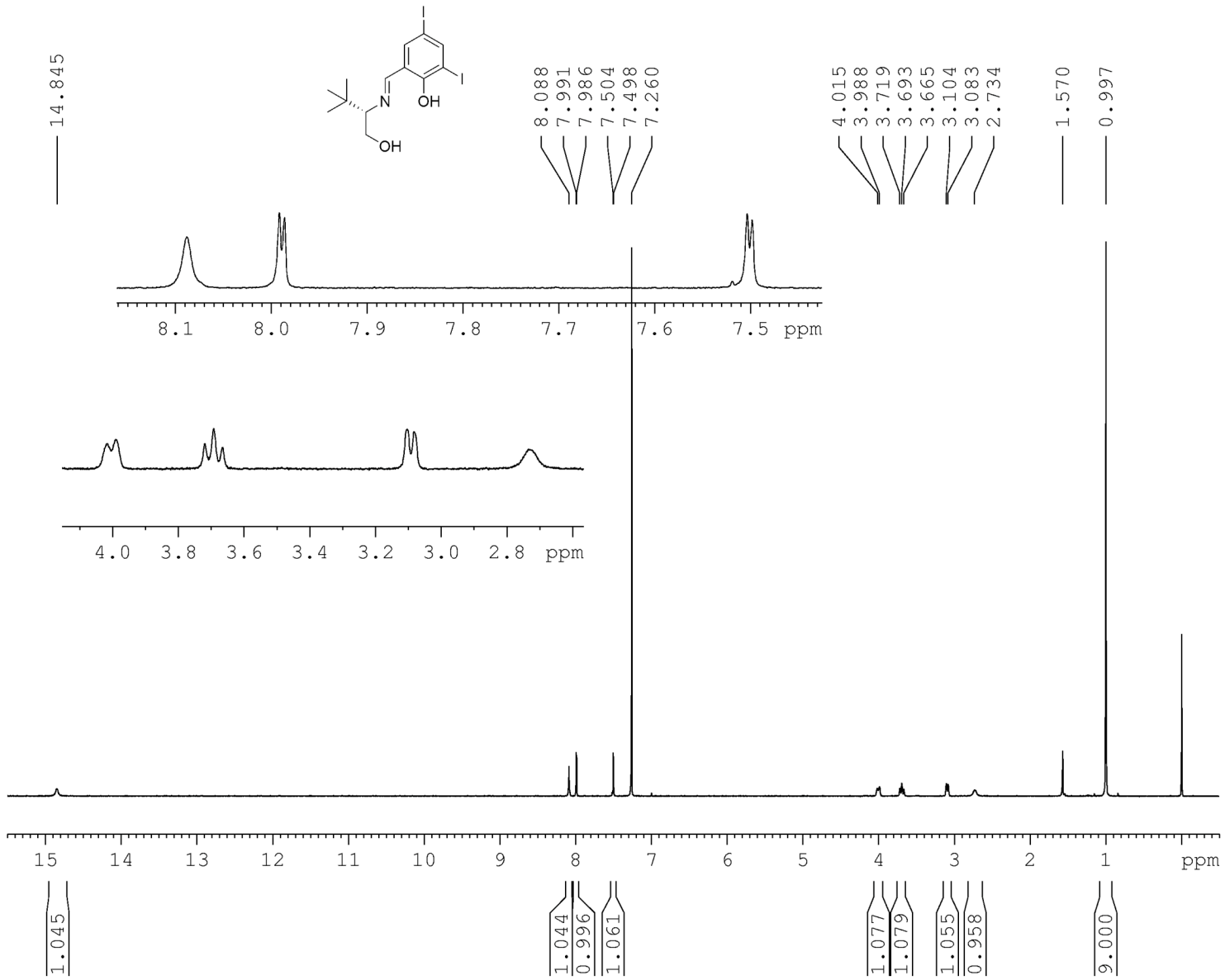
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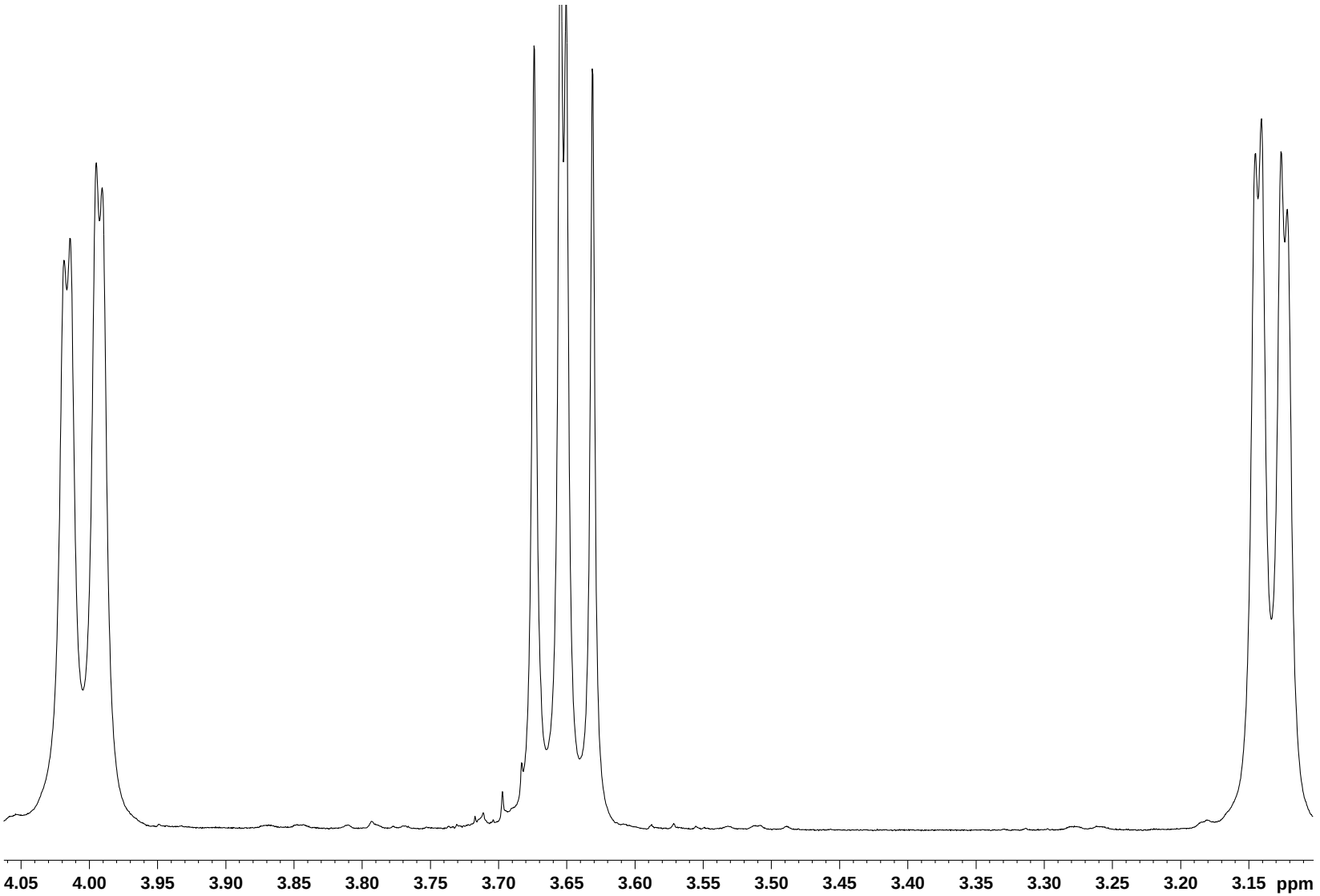
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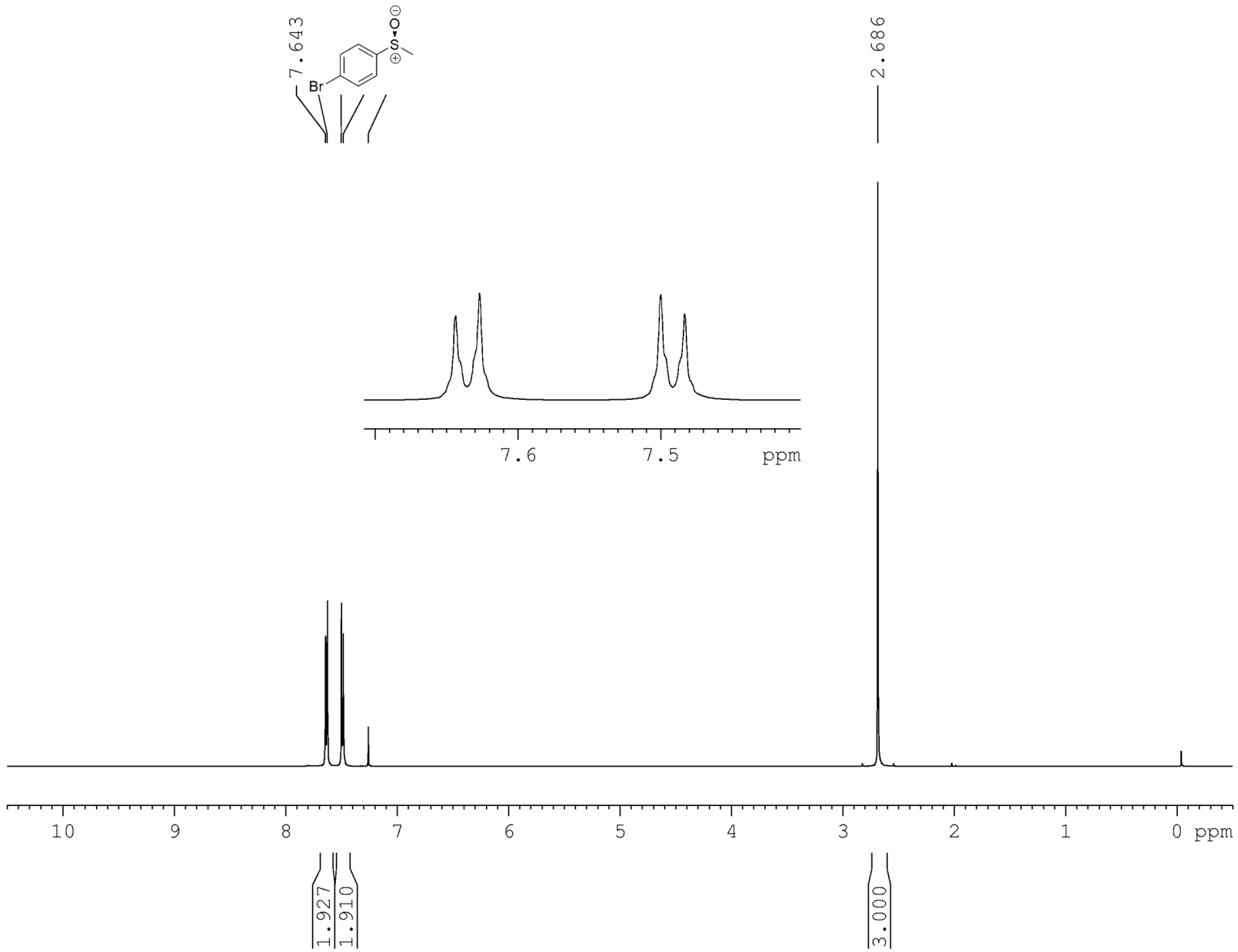
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