Organic Syntheses

Preparation of Asymmetric Phase-transfer Catalyst, 1,4-Bis((4S,5S)-1,3-bis(3,5-di-tert-butylbenzyl)-4,5-diphenylimidazolidin-2-ylidene)piperazine-1,4-diium chloride

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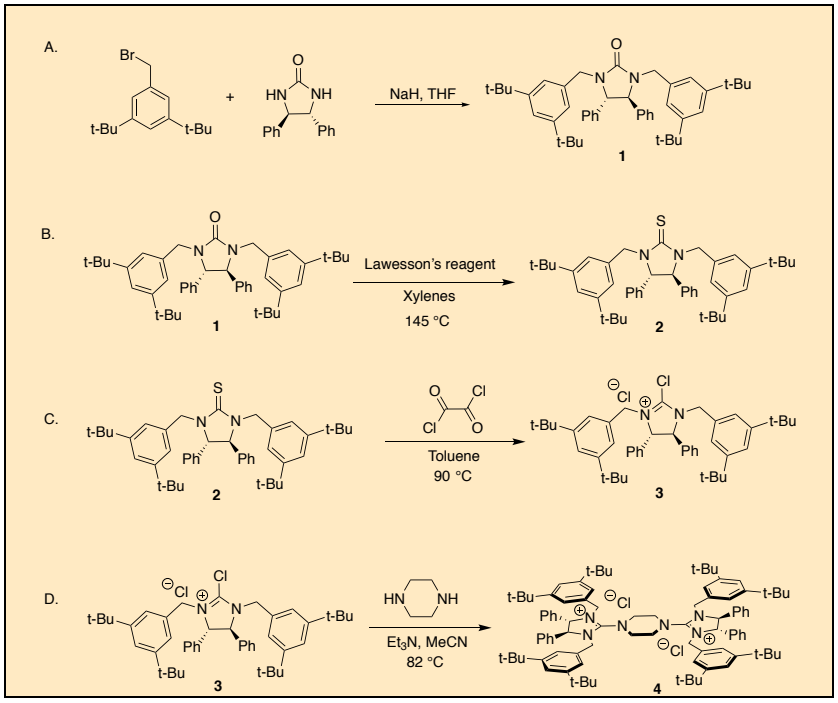
Checked by Prasanth R. Nyalapatla, Hari P. R. Mangunuru, Gopal Sirasani, Joseph Armstrong, and Chris Senanayake



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Procedure (Note 1)

A. *(4S,5S)-1,3-Bis(3,5-di-tert-butylbenzyl)-4,5-diphenylimidazolidin-2-one (**1**).* A 250 mL round-bottomed flask equipped with 3.5 cm Teflon-coated magnetic stir bar is charged with (4*S*,5*S*)-4,5-diphenylimidazolidin-2-one (4.584 g, 19.24 mmol, 1 equiv) (Note 2) and tetrahydrofuran (30.0 mL) (Note 3) at room temperature (21 °C) under a N_2 atmosphere. Sodium hydride (1.385 g, 57.71 mmol, 3.0 equiv) (Note 4) is added slowly in three portions and stirred for 1 h at room temperature (21 °C). 1-(Bromomethyl)-3,5-di-*tert*-butylbenzene (10.90 g, 38.47 mmol, 2.0 equiv) (Note 5) in THF (10 mL) is added dropwise over 10 min to the stirring mixture. The mixture is then allowed to stir at room temperature (21 °C) for 48 h. The reaction mixture is monitored *via* TLC (Notes 6 and 7). The reaction mixture is quenched with a saturated solution of ammonium chloride (25 mL) (Note 8) and the aqueous layer is extracted with diethyl ether (5 x 10 mL) (Note 9). The combined organic layers are washed with brine (20 mL), dried over magnesium sulfate (3 g) (Note 8) and filtered *via* gravitational filtration through a glass funnel equipped with filter paper. The filtrate is concentrated *in vacuo* (2 mmHg, 35 °C) to afford a thick oil. The oil is loaded onto a silica gel column (90 g) (Note 10) and 20 mL fractions are collected. The column is eluted (Note 3) initially with 100% *n*-hexane (fractions 1–36) and subsequently with 9:1 *n*-hexane: EtOAc (fractions 37–60). Fractions 47 to 57 are combined, and solvent is removed *in vacuo* (2 mmHg, 35 °C) to obtain the product as white solid of waxy texture (7.19 g, 58%) (Notes 11, 12, and 13).

B. *(4S,5S)-1,3-Bis(3,5-di-tert-butylbenzyl)-4,5-diphenylimidazolidine-2-thione (**2**).* A 250 mL round-bottomed flask equipped with a 3.5 cm Teflon-coated magnetic stir bar and 30 cm water condenser is charged with *(**1**)* (6.01 g, 9.35 mmol, 1 equiv), Lawesson's reagent (7.56 g, 18.7 mmol, 2 equiv) (Note 14) and *o*-xylene (50 mL) (Note 15). The reaction mixture is refluxed for 24 h under positive nitrogen atmosphere. Before reflux, the solution is a pale-yellow suspension (Figure 1), and the solution turns clear yellow (Figure 2) after the temperature reached 145 °C. The reaction is monitored *via* TLC with 9:1, *n*-hexane:EA as eluent, and the product has an R_f of 0.68 and is observed under UV lamp (254 nm). The reaction mixture is cooled to 25 °C and the phosphine oxide precipitates. The slurry is loaded directly onto a silica gel (120 mL) column and 20 mL fractions are collected. The column is eluted (Note 3) with 100% *n*-hexane (fractions 1 to 40) and subsequently with 20:1 *n*-hexane:EtOAc (fractions 41 to 80). Fractions 65–78 are combined, the solvent

is removed *in vacuo* 2 mmHg, 35 °C) to provide 5.71 g (93 %) of off-white solid with waxy and sticky texture (Notes 16, 17 and 18).

Figure 1. Before reflux

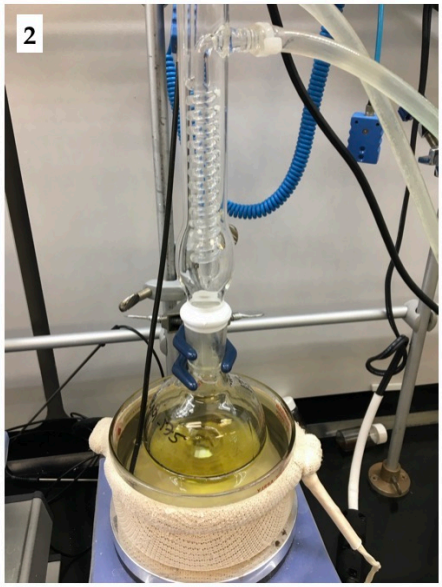


Figure 2. At temperature 145 °C

C. *(4S,5S)-2-Chloro-1,3-bis(3,5-di-tert-butylbenzyl)-4,5-diphenyl-4,5-dihydro-1H-imidazol-3-ium (**3**).* A 250 mL round-bottomed flask, equipped with 3.5 cm Teflon-coated magnetic stir bar is charged with (4S,5S)-1,3-bis(3,5-di-*tert*-butylbenzyl)-4,5-diphenylimidazolidin-2-thione (5.18 g, 7.86 mmol, 1 equiv) and kept under vacuum on the Schlenk line for 4 h, then it is backfilled with nitrogen. A reflux condenser (30 cm) is fitted on the flask, the Schlenk line is connected, and system put under vacuum (4 mmHg) for another 30 min and then back-filled with nitrogen. Toluene (20 mL) (Note 3) and oxalyl chloride (5.3 mL, 62.8 mmol, 8.0 equiv) (Note 19) are added in succession. Once oxalyl chloride is added, reaction mixture turns bright yellow and as the temperature increases, evolution of gases (mixture of hydrogen chloride and carbon monoxide) is observed (Figure 3). The reaction mixture is stirred at 90 °C for 24 h and refluxed for 1 h under nitrogen gas that is passed through a drying agent (Note 20). The reaction mixture is allowed to cool to room temperature (25 °C) under dried nitrogen gas and the flask is swiftly

transferred to the rotary evaporator and the solvent is removed *in vacuo* (2 mmHg, 35 °C) (Figure 4) (Note 21) to yield a golden brown solid (Note 22).

Figure 3. Evolution of CO and HCl gases (photo provided by submitters)

Figure 4 Removal of toluene (photo provided by submitters)

D. *1,4-Bis((4S,5S)-1,3-bis(3,5-di-tert-butylbenzyl)-4,5-diphenylimidazolidin-2-ylidene)piperazine-1,4-diium chloride* (**4**). A 250 mL round-bottomed flask equipped with 3.5 cm Teflon-coated magnetic stir bar is charged with (**3**), kept under vacuum on the Schlenk line for 3 h. A 30 cm reflux condenser is then put on the flask, connected to a Schlenk line, and placed under vacuum (4 mmHg) for an additional 1 h. Acetonitrile (20 mL) (MeCN) (Note 3), piperazine (0.198 g, 2.35 mmol, 0.3 equiv) (Note 23) and triethylamine (3.28 mL, 23.58 mmol, 3.0 equiv) (Note 24) are added in succession and the reaction mixture is refluxed for 12 h. Reaction is monitored *via* TLC (Note 25) (Figure 5). The reaction mixture is evaporated to dryness under reduced pressure 2 mmHg, 35 °C). The mixture is reconstituted in DCM (20 mL) and loaded onto a silica gel (90 g) column from which 20 mL fractions are collected. The column is eluted (Note 3) with 100% EtOAc (fractions 1–17)

and then 20:1, EtOAc:MeOH (fractions from 18–100). Fractions 32–99 are combined, and solvent is removed *in vacuo* 2 mmHg, 35 °C) to yield an off-white powder (2.52 g, 76 %) (Notes 26, 27 and 28).

Figure 5. Dark purple spot is product 4 (photo provided by submitters)

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 4*S*,5*S*)-4,5-diphenylimidazolidin-2-one, tetrahydrofuran, sodium hydride, 1- (bromomethyl)-3,5-di-*tert*-butylbenzene, *n*-hexane, ethyl acetate,

ammonium chloride, diethyl ether, brine, magnesium sulfate, Lawesson's reagent, *o*-xylene, silica gel, toluene, Drierite™, oxalyl chloride, hydrogen chloride, carbon monoxide, acetonitrile, piperazine, triethylamine, potassium permanganate, dichloromethane, deuterated chloroform, and (methylsulfonyl)methane.

2. (4*S*,5*S*)-4,5-Diphenylimidazolidin-2-one used as received from authors.
3. Solvents (*n*-hexane (45%, ACS grade) and ethyl acetate (99.9%) was obtained from Oakwood Chemicals and used as received. Dichloromethane (>99.8%), toluene (99.8%), acetonitrile (99.8%), and tetrahydrofuran(>99.9%) were obtained from Sigma-Aldrich (sure seal bottles,) and used as received.
4. Sodium hydride (60% dispersion in mineral oil) was bought from Sigma-Aldrich and used as received.
5. 1-(Bromomethyl)-3,5-di-*tert*-butylbenzene was provided to the checkers by the authors. The material (97% purity) is commercially available from Sigma-Aldrich and suitable for the described chemistry.
6. TLC plates were bought from SiliCycle, Glass-Backed, Silica, 250 μm, 10 x 20 cm, F254 (TLG-R10011B-723). Product has an R_f of 0.50 when the plate is developed with 9:1 *n*-hexane:ethyl acetate (EA) as an eluent, observed under UV lamp (254 nm).
7. The reaction will not be 100% complete; however, 1-(bromomethyl)-3,5-di-*tert*-butylbenzene and (4*S*,5*S*)-4,5-diphenylimidazolidin-2-one can be recovered through column chromatography. 1-(Bromomethyl)-3,5-di-*tert*-butylbenzene elutes at 100% *n*-hexane, (**1**) elutes at 9:1 *n*-hexane: EA and (4*S*,5*S*)-4,5-diphenylimidazolidin-2-one elutes at 9:1 DCM:MeOH. 1-(Bromomethyl)-3,5-di-*tert*-butylbenzene has R_f of 0.9, (**1**) has R_f of 0.5 and (4*S*,5*S*)-4,5-diphenylimidazolidin-2-one has R_f of 0.03 at solvent system of 9:1 *n*-hexane: EA. All spots can be observed under UV lamp (254nm).
8. Magnesium sulfate (anhydrous) and ammonium chloride were purchased from Oakwood Chemical and used as received.
9. Diethyl ether (HPLC-grade) was bought from Sigma-Aldrich and used as received.
10. Silica gel (Chromatographic silica) (40 to 63 μm) was bought from SiliCycle and used as received.
11. (4*S*,5*S*)-1,3-Bis(3,5-di-*tert*-butylbenzyl)-4,5-diphenylimidazolidin-2-one (**1**) has the following characterization data: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.28 (s, 36H), 3.61 (d, J = 14.5 Hz, 2H), 3.99 (s, 2H), 5.11 (d, J = 14.6 Hz, 2H), 6.94–6.99 (m, 8H), 7.22–7.29 (m, 8H). ^{13}C NMR (151 MHz, $CDCl_3$)

δ: 31.6, 34.9, 46.5, 65.5, 121.2, 123.1, 127.4, 128.3, 128.8, 135.9, 139.6, 151.0, 160.0.

12. The purity was determined to be 98.3% wt. by qNMR spectroscopy in $CDCl_3$ using 31.1 mg of the compound (**1**) and 28.3 mg of (methylsulfonyl) methane (100%) as an internal standard.
13. A second run on 4.83 g (20.3 mmol) provided 7.2 g (55%) of the product.
14. Lawesson's reagent was bought from Acros Organics (99% purity) and used as received.
15. *o*-Xylene (97% pure) was bought from Sigma-Aldrich and used as received.
16. (4*S*,5*S*)-1,3-Bis(3,5-di-*tert*-butylbenzyl)-4,5-diphenylimidazolidine-2-thione (**2**) has the following characterization data: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.29 (s, 36H), 3.76 (d, J = 14.6 Hz, 2H), 4.26 (s, 2H), 5.90 (d, J = 14.6 Hz, 2H), 6.97 – 6.99 (m, 4H), 7.03 (d, J = 1.6 Hz, 4H), 7.27–7.33 (m, 8H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 31.6., 34.9, 49.9, 68.9, 121.5, 123.0, 127.2, 128.7, 129.1, 135.3, 139.3, 151.1, 182.2.
17. The purity was determined to be 99.3% wt. by qNMR spectroscopy in $CDCl_3$ using 29.6 mg of compound (**2**) and 25.5 mg of (methylsulfonyl) methane (100%) as an internal standard.
18. A second run on 5.45 g (8.48 mmol) scale provided 5.34 g (96%) of the product.
19. Oxalyl chloride (>99%) was bought from Sigma-Aldrich and used as received.
20. Drierite™ is the laboratory gas drying unit that was used to dry the nitrogen gas supply, it was bought from W.A. Hammond Drierite Co. Ltd.
21. As compound **3** is extremely moisture sensitive, a water bath cannot be used when evaporating toluene. A dryer was employed to provide the thermal energy required for solvent evaporation.
22. A yield of 100% was assumed and the unpurified product taken to the next step.
23. Piperazine (99%) was bought from Sigma Aldrich and used as received.
24. Triethylamine (≥ 99%) was bought from Sigma Aldrich and used as received.
25. The product has an R_f of 0.51 when eluted with 9:1, DCM:MeOH. When stained with $KMnO_4$, the product spot stains dark purple and turns dark brown over time.
26. 1,4-Bis((4S,5S)-1,3-bis(3,5-di-*tert*-butylbenzyl)-4,5-diphenylimidazolidin-2-ylidene)piperazine-1,4-diium chloride (**4**) ^{1}H NMR (600 MHz, CD_2Cl_2)

δ: 1.14 (s, 72H), 3.99 (s, 4H), 4.49 (d, J = 9 Hz, 4H), 4.76 (d, J = 9 Hz, 4H), 4.84 (d, J = 14.9 Hz, 4H), 5.19 (d, J = 14.9 Hz, 4H), 6.94–6.96 (m, 8H), 7.03–7.07 (m, 8H), 7.20–7.21 (m, 4H), 7.28–7.32 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 31.2, 34.9, 49.3, 54.9, 70.7, 122.6, 123.7, 126.8, 129.4, 129.9, 132.2, 138.0, 151.6, 163.0.

27. The purity was determined to be 98.3% wt. by ^{1}H NMR spectroscopy in $CDCl_3$ using 19.8 mg of the compound (**4**) and 1.8 mg of (methylsulfonyl) methane (100%) as an internal standard.
28. A second run performed in 3.78 mmol scale of compound **3** provided 1.19 g (75%) of compound **4**.

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.

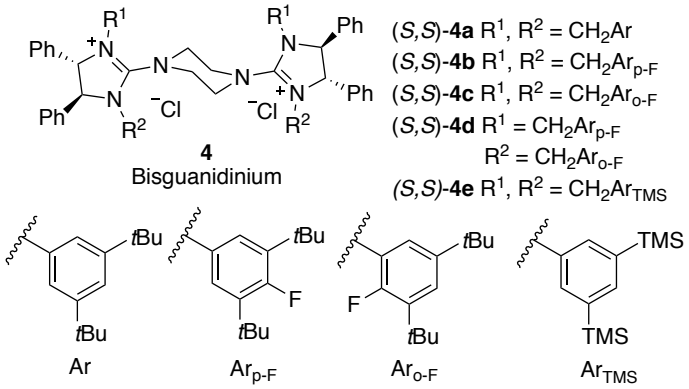
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or

damages claimed to have resulted from or related in any way to the procedures herein.

Discussion

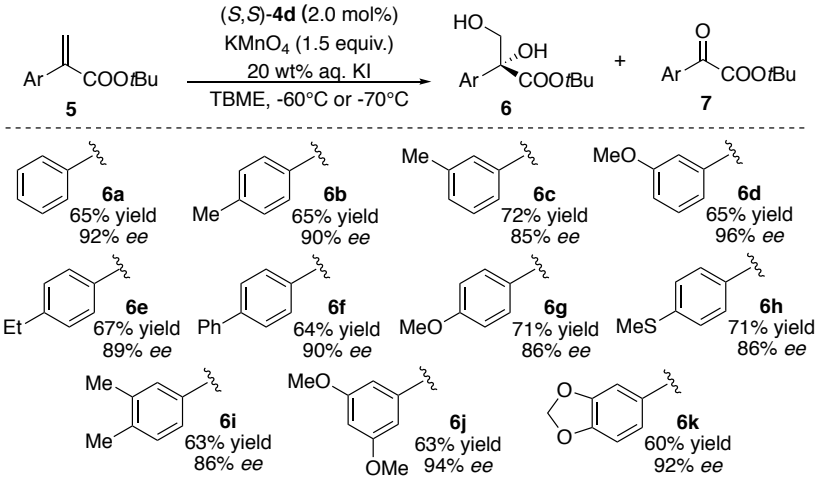
The control of enantioselectivity in reaction outcomes has been extremely useful in natural product synthesis, pharmaceutical development, or preparation of materials with optical properties, to name a few.[3] Asymmetric catalysis is immensely useful as one molecule of the chiral catalyst is able to impart chiral information to produce enantioenriched products.[4] Chemical reactions occur due to some extent of charge polarization and in many organic reactions, the intermediate is a charged species. Being able to control the charged intermediate allows control over the stereochemical outcome of the reaction.[5] Our group has been utilizing bisguanidinium-type cationic salts and pairing them with various metal anionic species, such as permanganate[6] in the dihydroxylation of alpha-aryl acrylates and oxohydroxylation of trisubstituted enolates, as well as tungstate[7] and molybdate[8] in the asymmetric oxidation of organo-sulfur compounds to form chiral sulfoxides. In addition, catalytic asymmetric alkylation of indanones[9] and asymmetric [1,2]-Brook rearrangement of acyl silanes[10] can also be performed. Bisguanidinium-type catalysts have found potential industrial application in the synthesis of for example, armodafinil and (*S*)-lansprazole, where the sulfoxide group can be installed in gram-scale reactions with high yields and enantiopurities.

Compound **4**, which features two guanidinium moieties linked by a piperazine spacer, has been found to act as effective and efficient chiral cationic catalyst that is able to pair with anions such as metal oxides and catalyse oxidation reactions under phase transfer conditions to furnish products with high enantioselectivity. Compound **4** can be amended into various forms with variations to the described procedure, thereby producing different catalytic activities (Scheme 1).

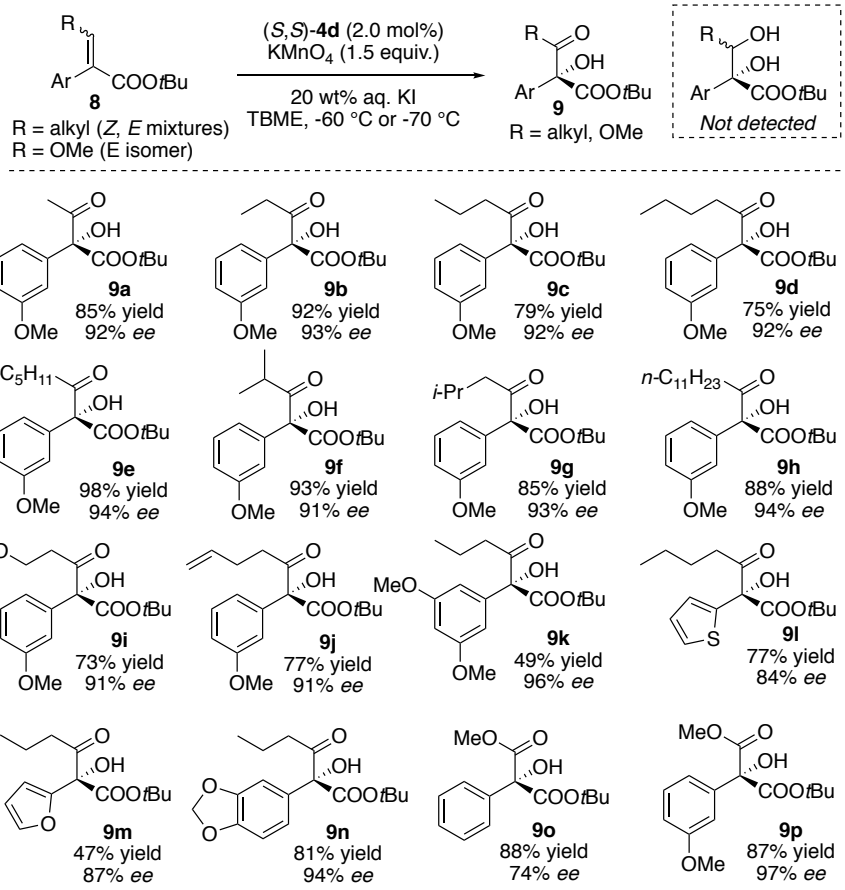


Scheme 1. Various types of bisguanidinium salts that can be synthesized

Permanganate was found to be an effective catalyst in the dihydroxylation and oxohydroxylation of alpha-aryl acrylates (Schemes 2 and 3). The catalyst used in this case was **4d**.[6] Based on experimental results, rate acceleration was mainly attributed to transition state stabilization through strong electrostatic interaction between dicationic **4d** and enolate anion.

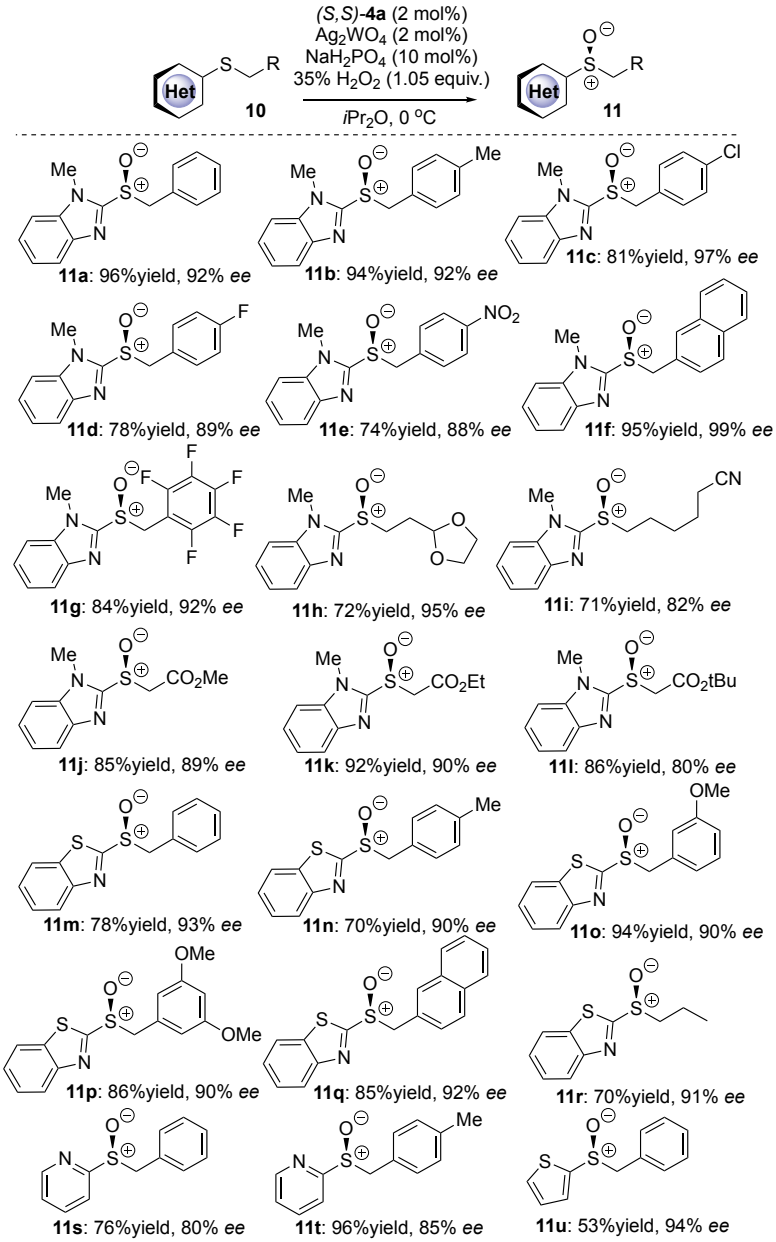


Scheme 2. Application of 4d in catalytic dihydroxylation of α-aryl acrylates

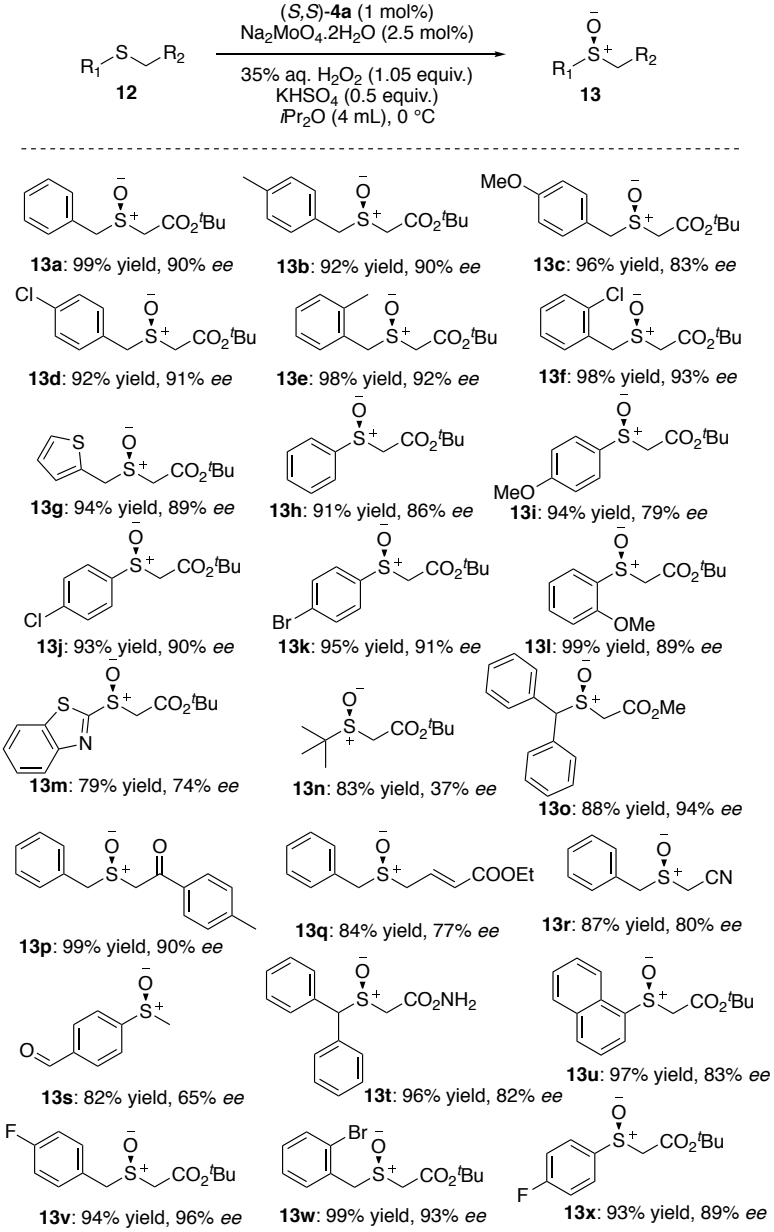


Scheme 3. Application of 4d in catalytic oxohydroxylation of trisubstituted enolates

Peroxotungstate[9] (Scheme 4) and peroxomolybdate[10] (Scheme 5) species are known to catalyze oxidation reactions such as epoxidation and sulfoxidation. Since these metal oxolates species are anions, peroxotungstate and peroxomolybdate were paired with **4a** to catalyze the sulfoxidation reactions in Schemes 4 and 5, respectively. Excellent yields and enantioselectivity were achieved in the two catalytic systems.

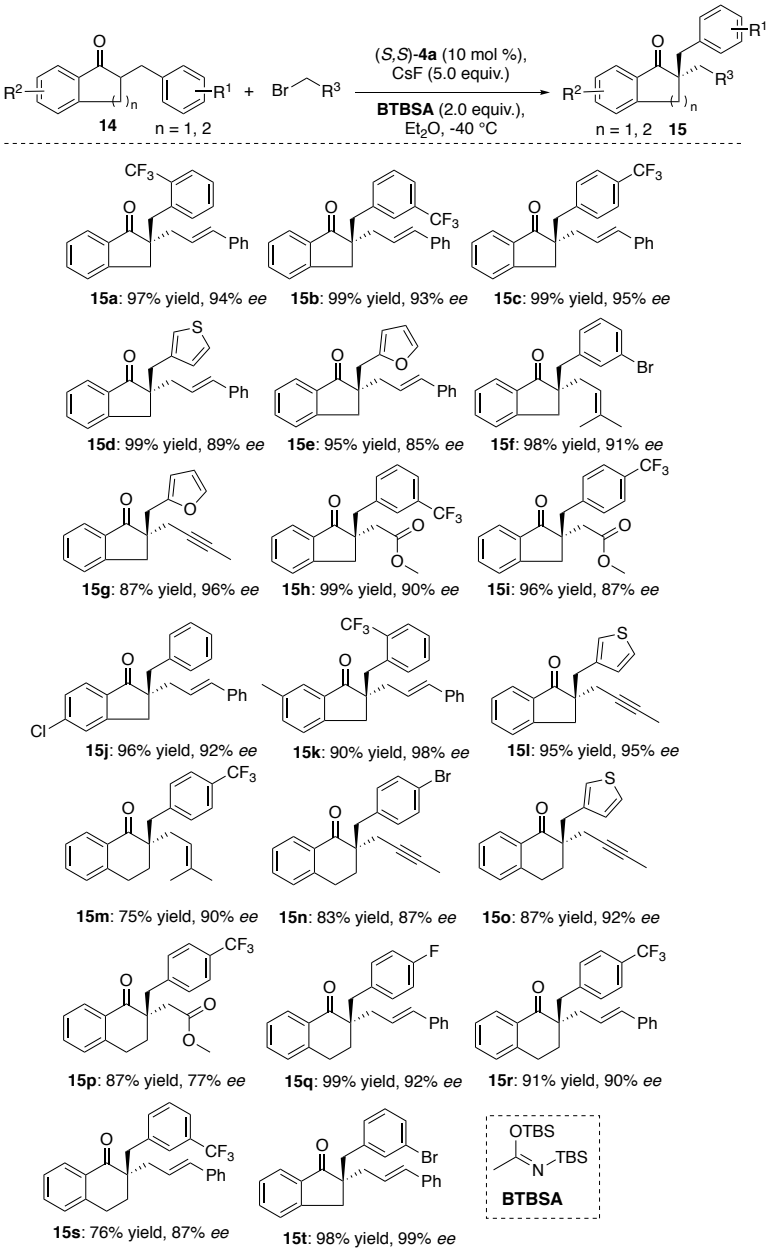


Scheme 4. Application of 4a in diphosphatobisperoxotungstate-catalyzed sulfoxidation



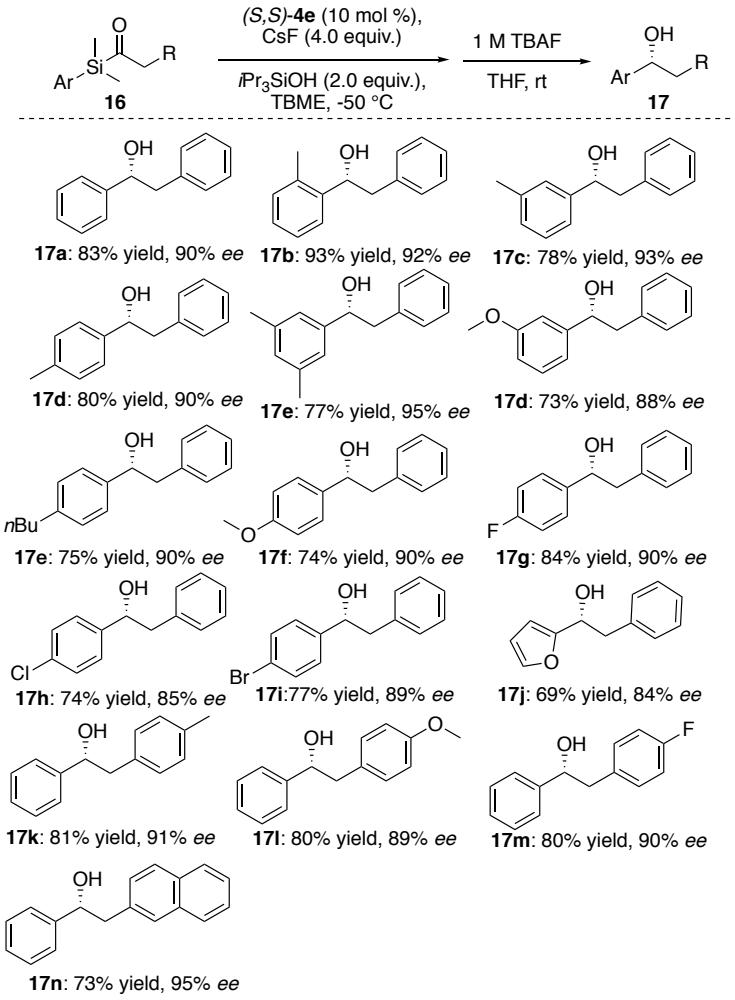
Scheme 5. Use of 4a in dinuclear oxodiperoxomolybdosulfate-catalyzed sulfoxidation

Fragile substrates, such as lactones, can be activated without hydrolysis by use of a Brønsted base generated *in situ* from a silylamide (*N*,*O*-bis(*tert*-butyldimethylsilyl)acetamide (BTBSA) is used as the probase) and cesium fluoride. In this approach a strong base, which is transient and not generated in excess is formed *in situ*, thereby reducing background and side reactions (Scheme 6). Hypervalent silicates form an ion-pair with the bisguanidinium phase transfer catalyst as an intermediate in the reaction, which determines the enantiofacial approach of the electrophile.[9]



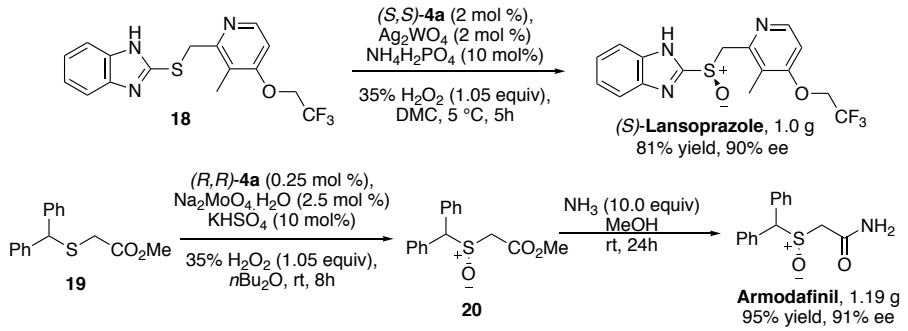
Scheme 6. Application of 4a in catalytic alkylation of indanones

Asymmetric tandem 1,2-anionotropic/Brook arrangements of acylsilane to produce highly enantio-enriched secondary alcohols (up to 95% ee) (Scheme 7) can be achieved using **4e**.



Scheme 7. Application of 6e in catalytic asymmetric [1,2]-Brook rearrangement of acylsilanes

4a was shown to catalyze gram-scale reactions (Scheme 8) with low catalyst loading and to provide products in high enantioselectivity and high yield, demonstrating its applicability in industrial settings.



Scheme 8. Gram-scale synthesis of commercial drugs using 4a

References

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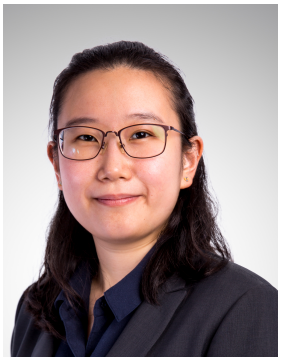
Appendix
Chemical Abstracts Nomenclature (Registry Number)

(4S,5S)-4,5-Diphenylimidazolidin-2-one; (191599-79-8)
1-(Bromomethyl)-3,5-di-*tert*-butylbenzene; (62938-08-3)
Magnesium sulfate; (7487-88-9)
Sodium hydride; (7646-69-7)
Ammonium chloride; (12125-02-9)
Lawesson's Reagent; (19172-47-5)
Oxalyl chloride; (79-37-8)
Piperazine; (110-85-0)
Triethylamine; (121-44-8)

Choon-Hong Tan received his BSc (Hons), First Class from NUS in 1995 and completed his PhD from the University of Cambridge in 1999. He carried out two years postdoctoral training at the Department of Chemistry and Chemical Biology, Harvard University. Subsequently, he worked as Research Associate at Harvard Medical School for another year. He joined the Department of Chemistry, NUS as Assistant Professor in 2003. He was promoted to Associate Professor in 2010. He moved to NTU in 2012 and was promoted to Full Professor in 2016. Currently he is the school Chair, CN Yang Scholars Program Director, as well as President of the Singapore National Institute of Chemistry. His research interests include synthetic chemistry and asymmetric catalysis.

Xinyi Ye received Bachelor of Engineering, from Zhejiang University of Technology, China, in 2013. Following which, she obtained Doctor of Philosophy from Nanyang Technological University, Singapore in 2019 under the supervision of Prof. Tan Choon-Hong. Later the same year, she received an offer from Collaborative Innovation Center of Yangtze River Delta Region Green Pharmaceuticals, Zhejiang University of Technology as a young scholar. Her research interests include synthetic chemistry and asymmetric chemistry.



Esther C. X. Ang received Bachelor of Science from Nanyang Technological University in 2019 where she carried out research in the laboratory of Professor Tan Choon-Hong. She is currently pursuing PhD under the supervision of Prof. Tan C-H.

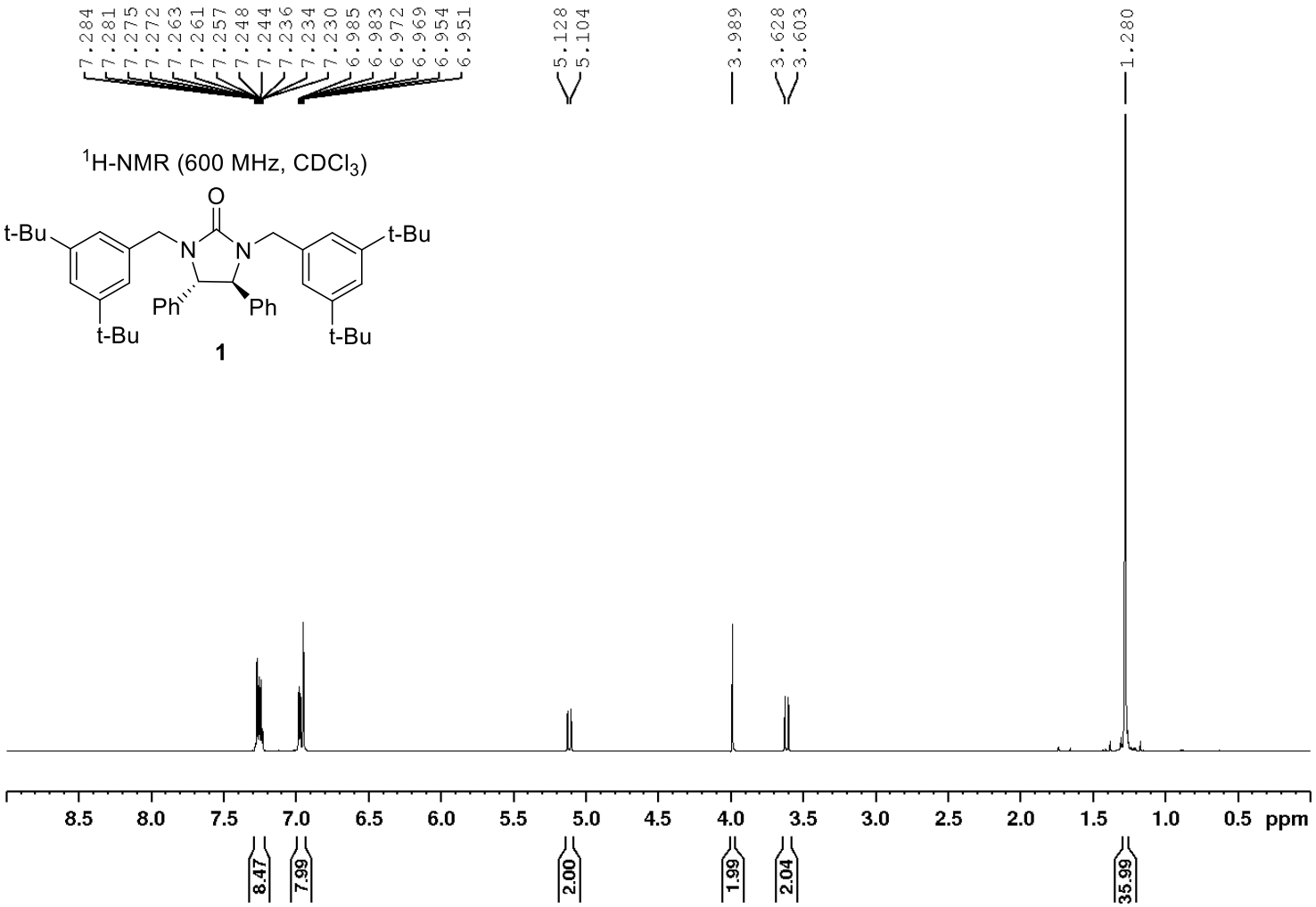
Prasanth R. Nyalapatla was born in Hyderabad, India. He received his M.S. chemistry from Texas A&M University-Kingsville, TX with Apurba Bhattacharya. He earned his Ph.D. in organic chemistry in 2017 at Purdue University, IN under the guidance of Prof. Arun K. Ghosh. In 2017, he joined Prof. Peter Wipf's group as a postdoctoral research associate where he made contributions to two distinct areas of research: a new synthesis of gefitinib and synthesis of small molecule antagonists for the treatment of Castration-Resistant Prostate Cancer. In 2019, Prasanth began his industrial career at TCG GreenChem, Inc. in Richmond, VA where currently he is a Senior Scientist.

Hari P. R. Mangunuru earned his Ph.D. in organic chemistry from the Old Dominion University, 2012 under the guidance of Prof. Guijun Wang, where his research focused on developing carbohydrate based hydrogelators as drug delivery carriers. After completing his graduate studies, he joined the Department of Process Research & Development at Boehringer Ingelheim, Ridgefield, CT, USA, as a postdoctoral fellow until May 2016. After that he moved to Virginia Commonwealth University as a postdoctoral fellow to work with Prof. B. Frank Gupton. Currently he is working as a Senior scientist in Process Chemistry at TCG GreenChem, Inc.

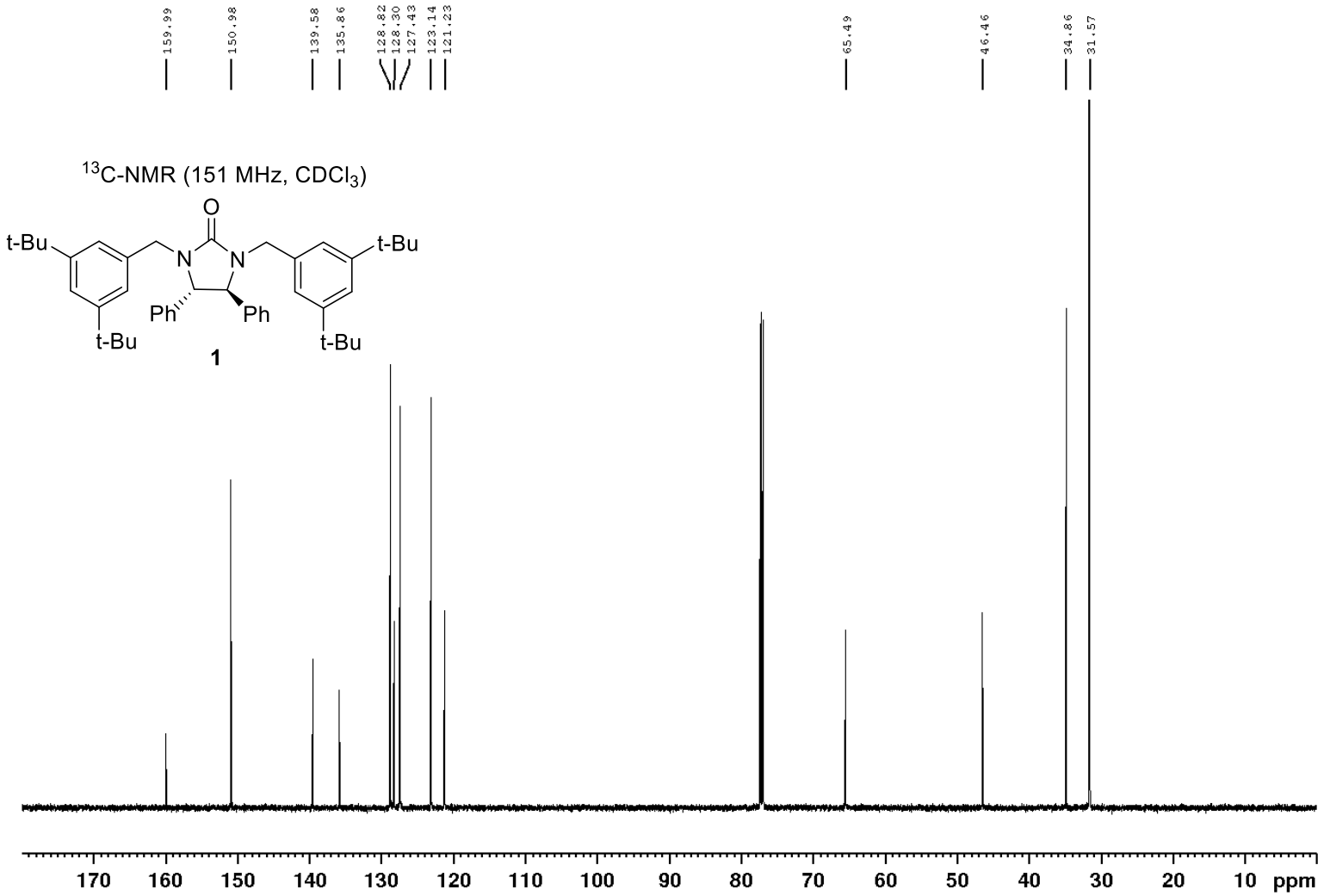
Dr. Gopal Sirasani received his Bachelor's and Master's degrees in Hyderabad, India. He obtained his Ph.D. in in 2011 from Temple University under the guidance of Prof. Rodrigo B. Andrade. His doctoral research was focused on developing novel methodologies, total syntheses of natural products and their analogs thereof. He received post-doctoral training in the laboratory of Prof. Emily Balskus at Harvard University, where he developed biocompatible organic reactions utilizing microbially-generated reagents to realize transition metal catalysis in the presence of microbes. In 2013, Gopal began his industrial career at Melinta Therapeutics, New Haven, CT. He is currently working at TCG GreenChem, Inc. as an Associate Director in the department of process research and development.

Dr. Joseph Armstrong received his Ph.D. in organic chemistry in 1988 with Prof. David Walba at University of Colorado, Boulder followed by postdoctoral training in the laboratory of Prof. Robert Ireland at University of Virginia. He has over 28 years of process R&D experience. Some of the positions he held at Merck & Co include Executive Director for process R&D, Director of Formulation, Executive Director of Project Management. In 2006 he won the Presidential Green Chemistry Challenge Award. He is currently working at TCG GreenChem, Inc. as Executive Vice President, Global Head of R&D and Business Development. He is the co-author of more than 50 publications and patents.

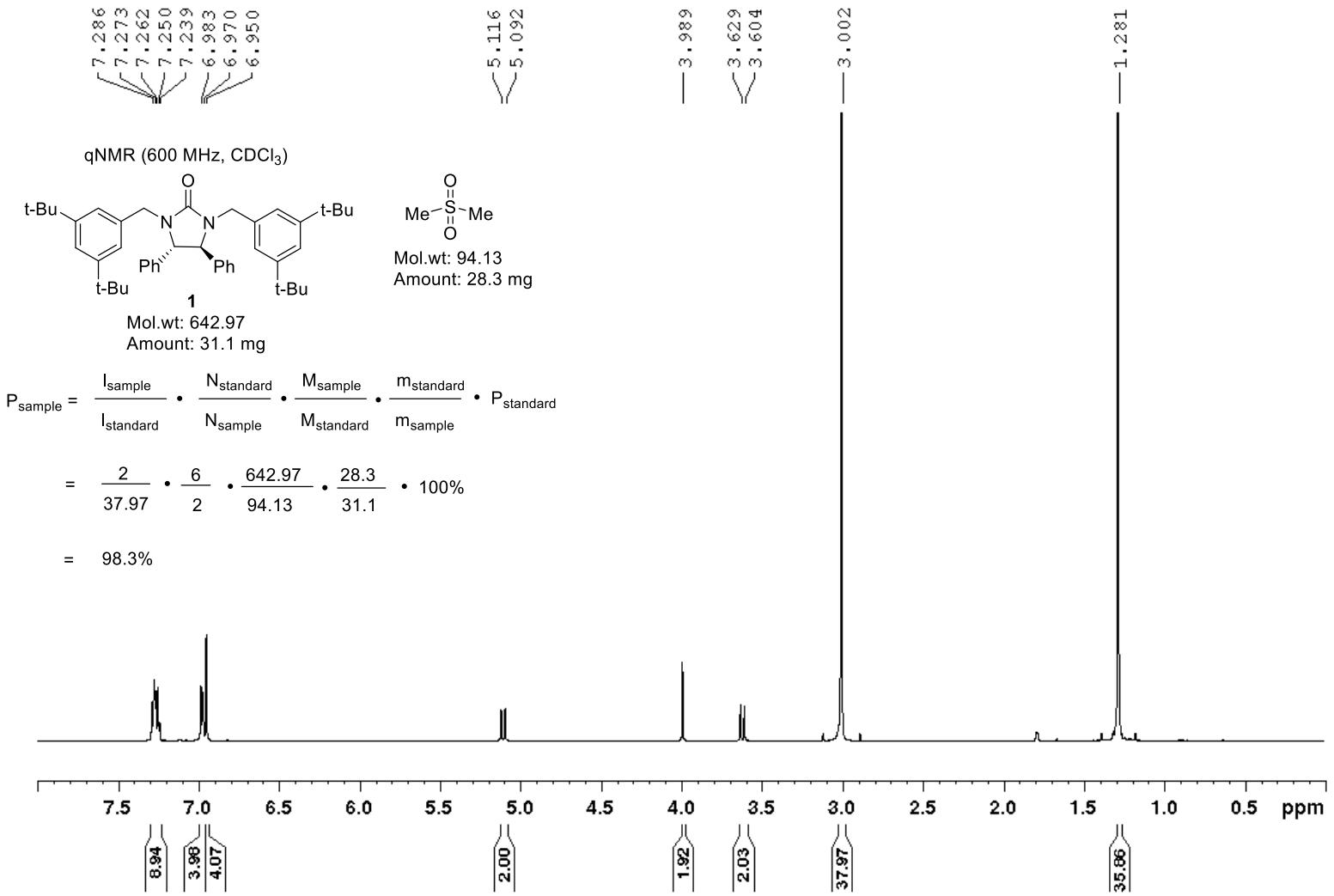
[1]H-NMR of (4*S*,5*S*)-1,3-*bis*(3,5-*di*-*tert*-butylbenzyl)-4,5-diphenylimidazolidin-2-one (**1**)



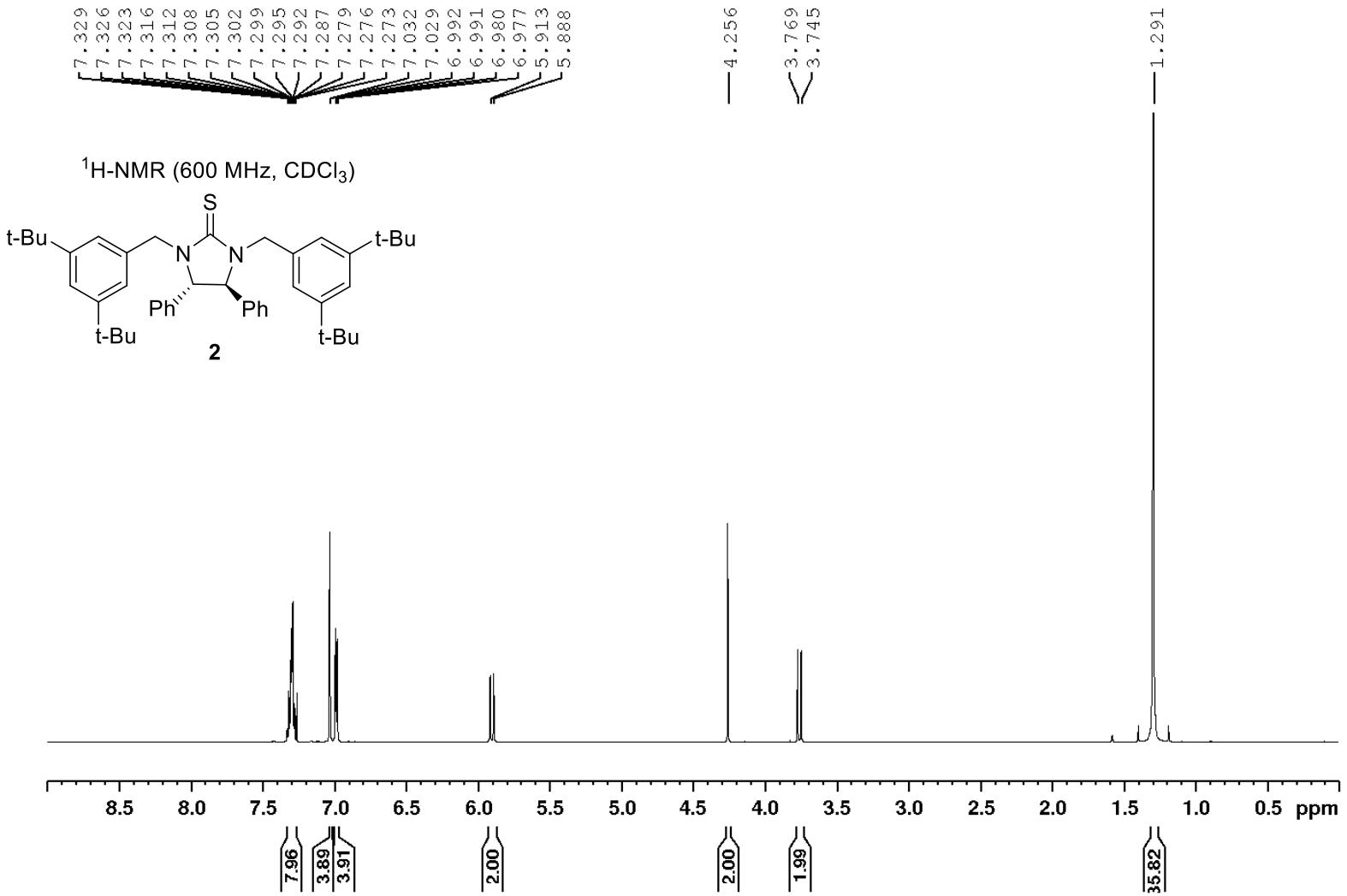
^{13}C-NMR of (4*S*,5*S*)-1,3-*bis*(3,5-*di*-*tert*-butylbenzyl)-4,5-diphenylimidazolidin-2-one (**1**)



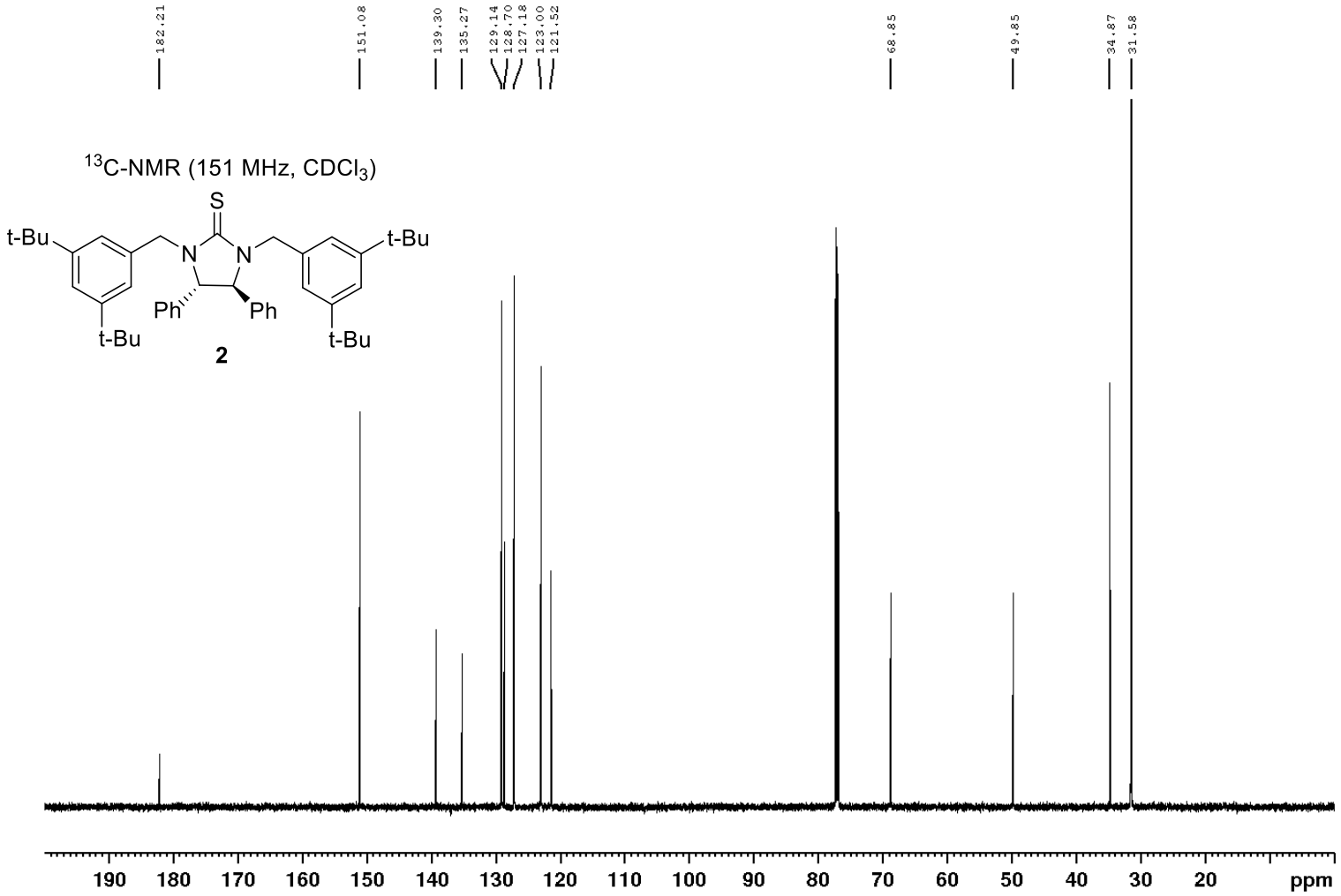
qNMR of (4*S*,5*S*)-1,3-*bis*(3,5-*di*-*tert*-butylbenzyl)-4,5-diphenylimidazolidin-2-one (**1**)



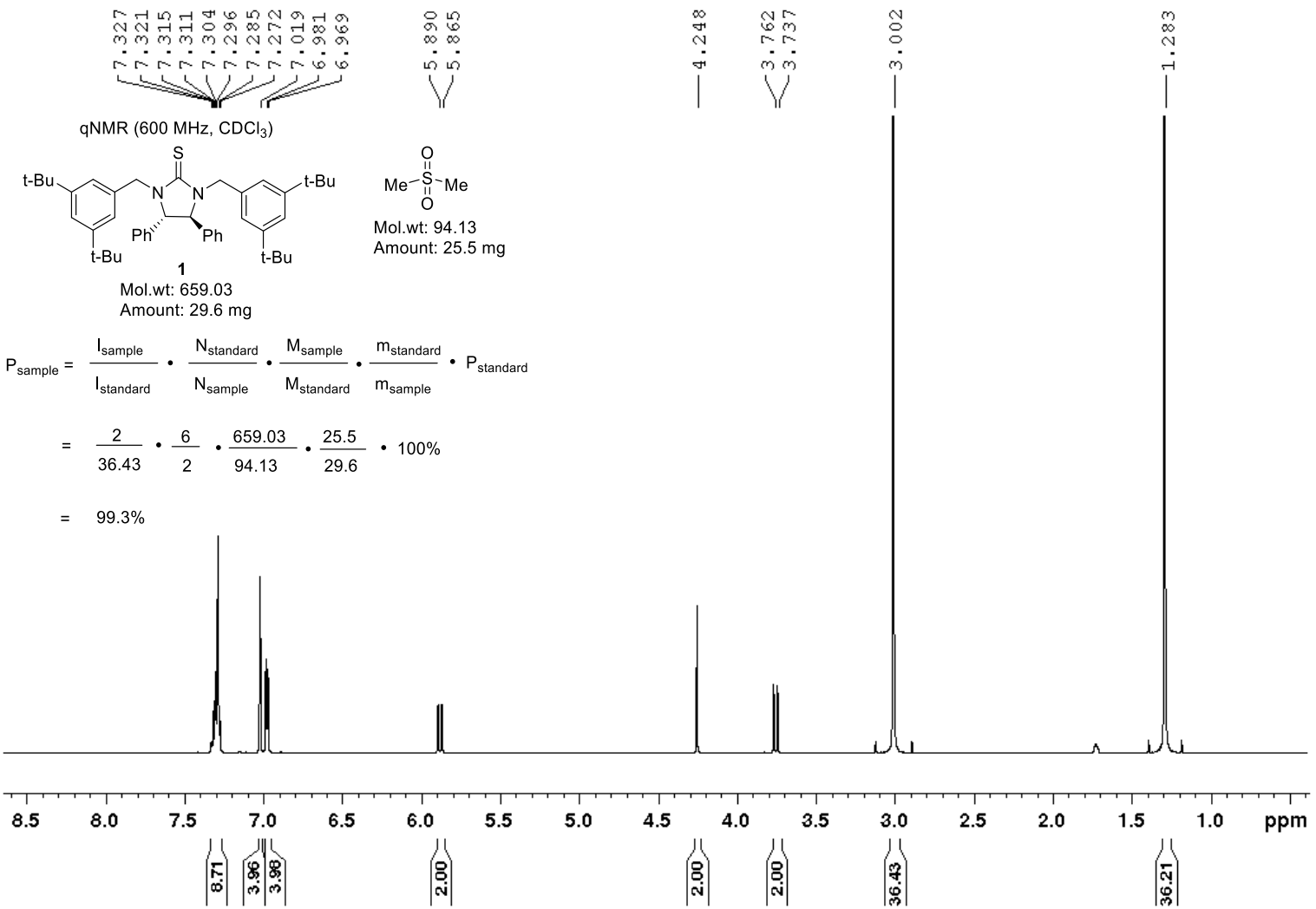
^{1}H-NMR of (4*S*,5*S*)-1,3-*bis*(3,5-*di*-*tert*-butylbenzyl)-4,5-diphenylimidazolidine-2-thione (**2**)

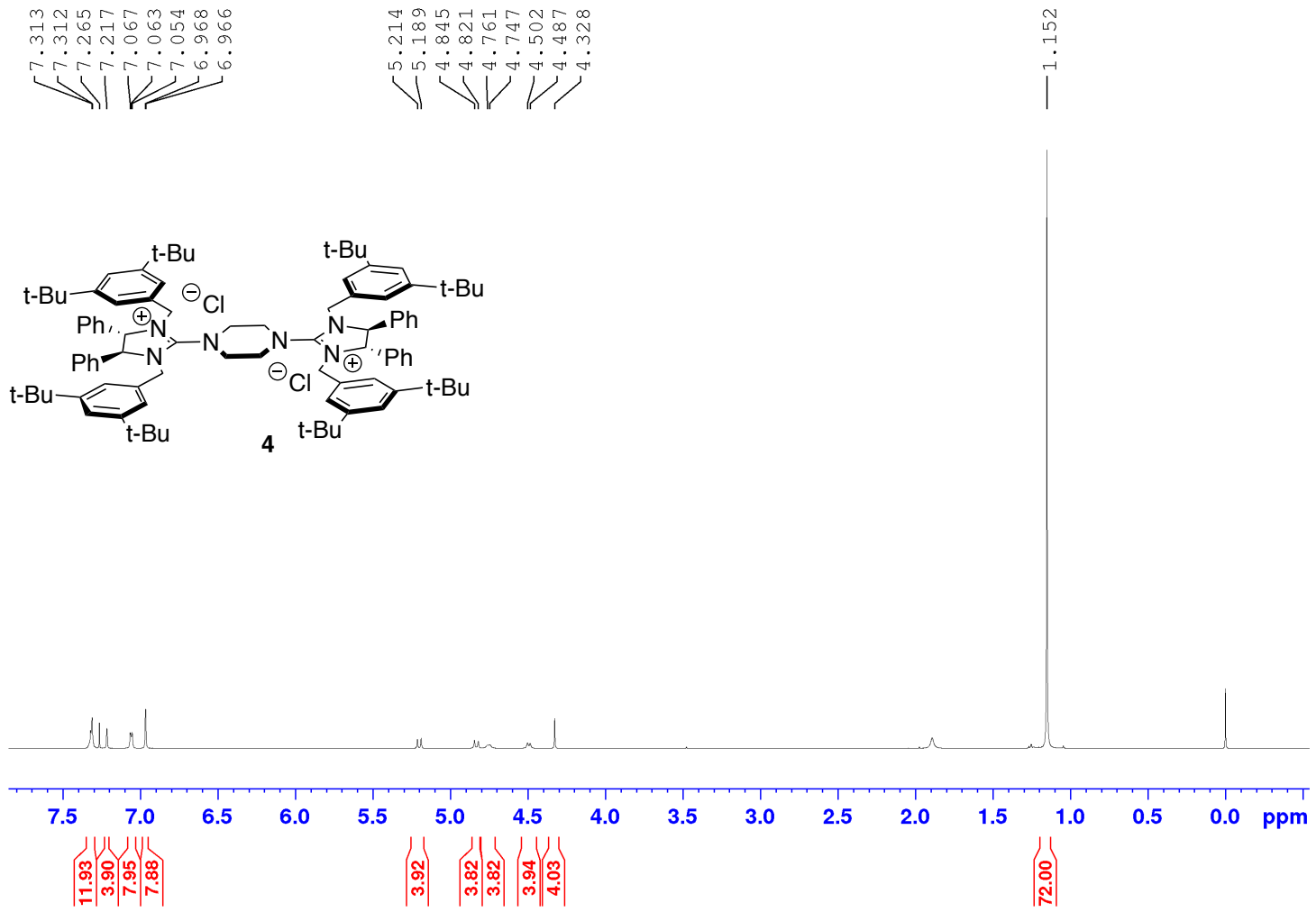


^{13}C-NMR of (4*S*,5*S*)-1,3-*bis*(3,5-*di*-*tert*-butylbenzyl)-4,5-diphenylimidazolidine-2-thione (**2**)



qNMR of (4*S*,5*S*)-1,3-*bis*(3,5-*di*-*tert*-butylbenzyl)-4,5-diphenylimidazolidine-2-thione (**2**)

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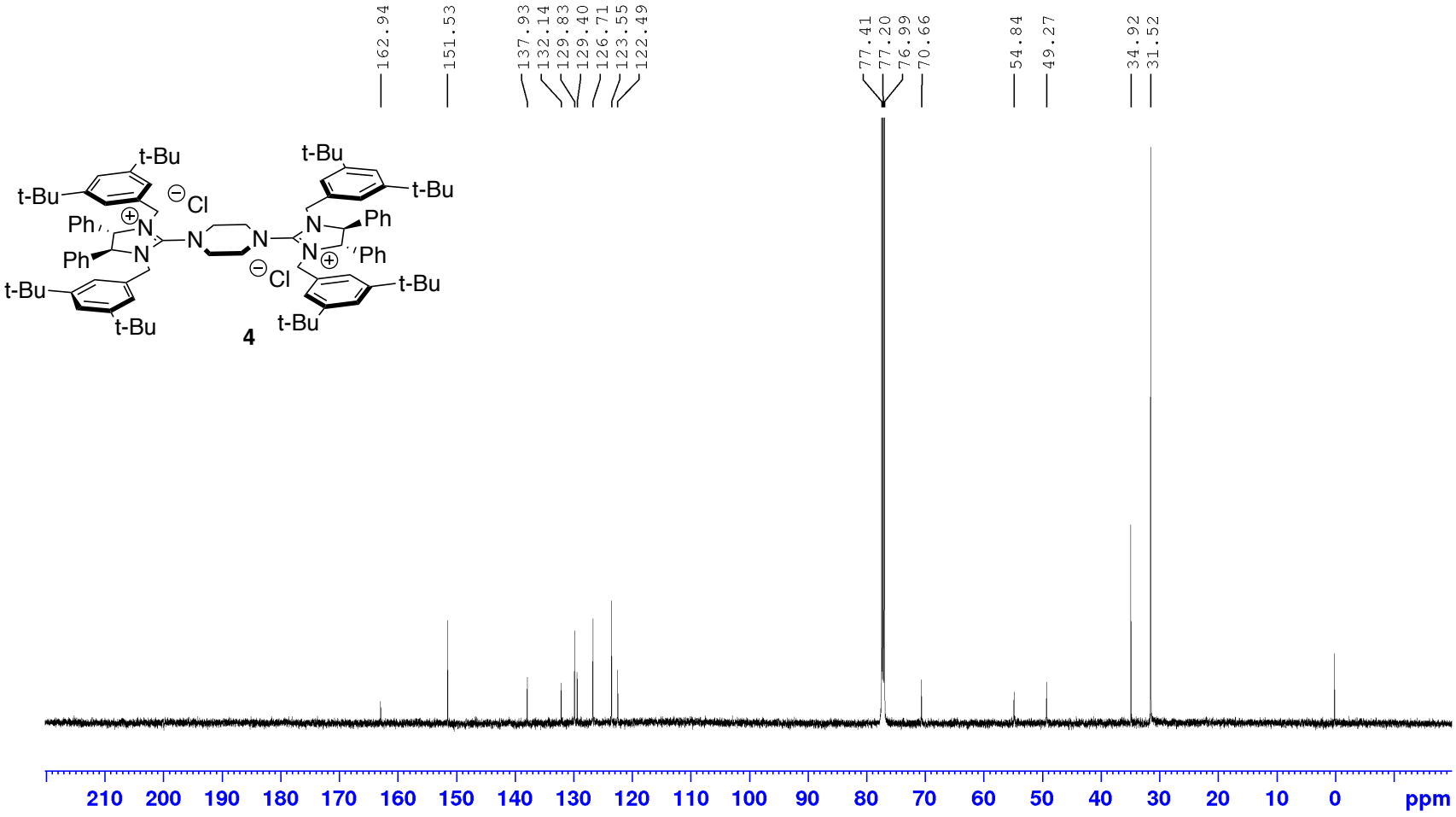
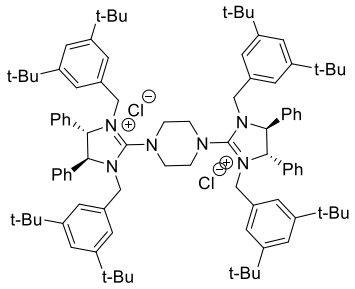
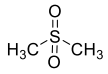
7.312
7.265
7.217
7.067
7.063
7.054
6.968
6.966
5.214
5.189
4.845
4.821
4.761
4.747
4.502
4.487
4.328
1.152
t-Bu
Cl
Ph
N
4
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
11.93
3.90
7.95
7.88
3.92
3.82
3.82
3.94
4.03
72.00


162.94
151.53
137.93
132.14
129.83
129.40
126.71
123.55
122.49
77.41
77.20
76.99
70.66
54.84
49.27
34.92
31.52
t-Bu
Cl
Ph
N
4
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



Weight = 19.5 mg
Mwt= 1406.3



Standard, Weight = 1.5 mg
MWt= 94.3

$$\text{Purity\%} = \frac{2.9 \times 6 \times 1.8 \times 1406.3}{6 \times 4 \times 19.8 \times 94.3} \times 100$$

$$= 98.3\%$$