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for the Preparation
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Working with Hazardous Chemicals

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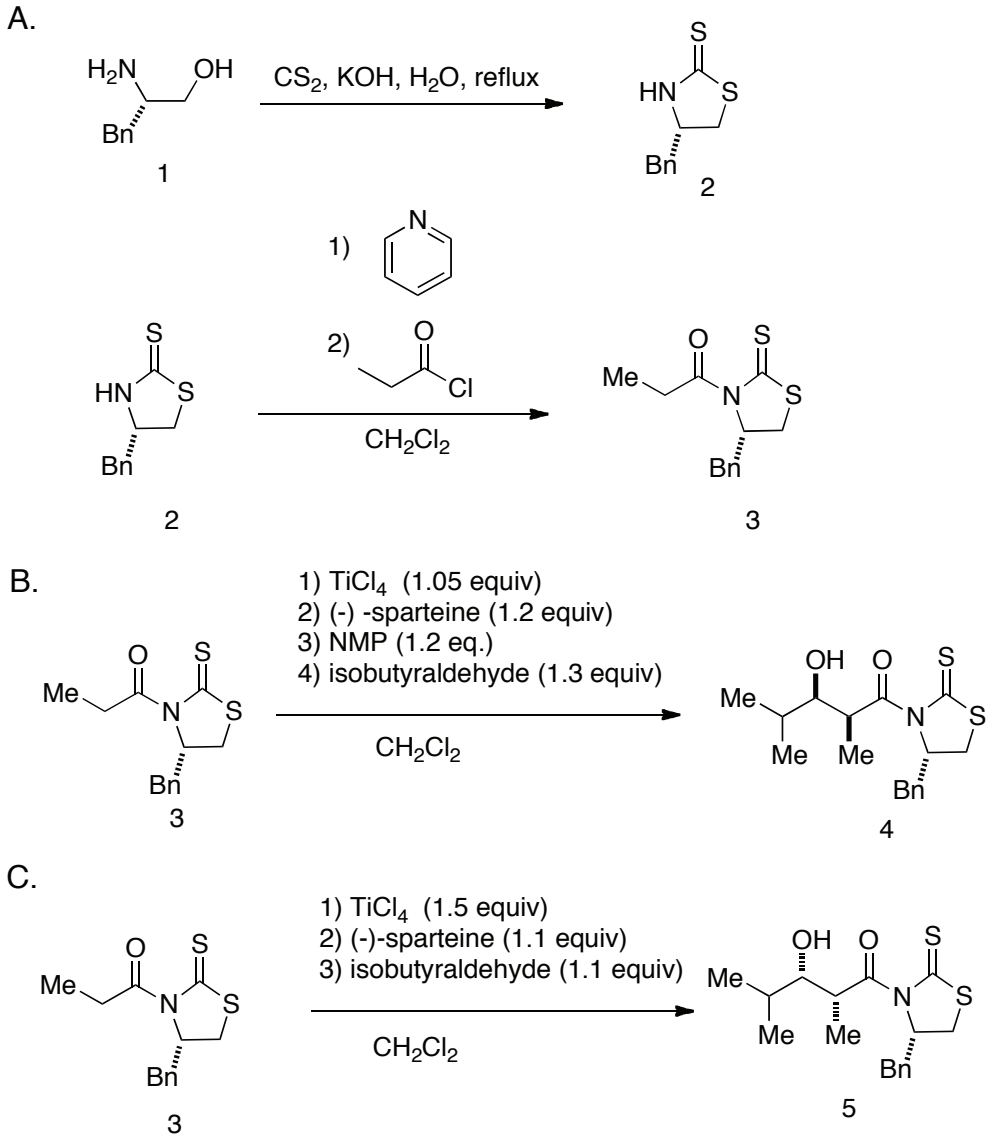
September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

SYNTHESIS AND DIASTEREOSELECTIVE ALDOL REACTIONS OF A THIAZOLIDINETHIONE CHIRAL AUXILIARY



Submitted by Michael T. Crimmins, Hamish S. Christie, and Colin O. Hughes.[1]
Checked by Eric M. Phillips and Jonathan A. Ellman.

1. Procedure

Caution! Carbon disulfide has an auto-ignition temperature of 100 °C, so extreme care should be taken to vent excess CS_2 away from heat sources.

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A. *(S)-1-(4-Benzyl-2-thioxothiazolidin-3-yl)propan-1-one* (**3**) To a 1-L, two-necked, round-bottomed flask equipped with a thermometer and magnetic stirring bar (egg shaped, 3 x 1.5 cm) is added water (250 mL) followed by portion wise addition of potassium hydroxide (KOH) (42 g, 750 mmol) (Note 1) over 5 min with stirring (Note 2). The stirring solution is cooled to ambient temperature, (*S*)-phenylalaninol (18.9 g, 125 mmol) (Note 3) and carbon disulfide (CS_2) (37.6 mL, 625 mmol) (Note 4) are added to the solution. The mixture rapidly becomes a red/orange color. A Friedrichs condenser is attached to the central neck of the flask and a Claisen adapter is attached to the condenser outlet joint. A hose adapter is attached to one joint of the Claisen adapter, with Tygon® plastic tubing leading to the back of the fume hood (Note 5). A septum with an inert gas inlet needle is placed in the remaining joint. A stream of argon is passed through the needle and the stirring reaction mixture is heated gradually using a heating mantle. After all the excess carbon disulfide has been purged (solution at 102–103 °C, Note 6) the red mixture is heated at reflux (110 °C, internal). After 7-8 h (Note 7), heating is discontinued and the heterogeneous mixture is allowed to cool to room temperature. The mixture is poured into a 1-L separatory funnel and extracted with CH_2Cl_2 (1 x 125 mL, 2 x 75 mL). The combined organic solution is dried over sodium sulfate (Na_2SO_4) (20 g), filtered, and evaporated in a 500-mL round-bottomed flask, using a rotary evaporator. The crude solid weighs 24.1 g (Note 8). The flask is equipped with a magnetic stirring bar (egg-shaped, 3 x 1.5 cm) and a rubber septum and flushed with argon. After CH_2Cl_2 (125 mL) (Note 9) is added, the solution is cooled using an ice/water bath. The solution is stirred vigorously and pyridine (12.3 mL, 153 mmol) (Note 10) is added rapidly via syringe, followed by propionyl chloride (12 mL, 137.5 mmol) (Note 11) via syringe over 5 min (Note 12). After 5 min, the ice/water bath is removed and the solution is allowed to warm to room temperature. After stirring for 1 h at room temperature, methanol (750 μL) is added rapidly. After 20 min the solution is poured into a 1-L separatory funnel and washed with water (100 mL) (aqueous solution back-extracted with CH_2Cl_2 (25 mL)), then 1 N $NaHSO_4$ (100 mL) (aqueous solution back-extracted with CH_2Cl_2 (25 mL). The combined organic solution is dried over Na_2SO_4, and evaporated using a rotary evaporator. The bright-yellow solid is dissolved in hot isopropyl alcohol (175 mL) (Note 13), and the solution is allowed to cool, gradually, to room temperature. After standing overnight, the yellow crystals are collected on a sintered 150-mL coarse glass funnel and washed twice with

isopropanol/hexanes (9:1) solution (2 x 63 mL), then dried under vacuum (Note 14), affording 25.2–25.8 g (76–78%) of acylated derivative **3** (Note 15).

B. *(2S,3R)-3-Hydroxy-1-[(4S)-4-benzyl-2-thioxo-thiazolidin-3-yl]-2,4-dimethyl-pentan-1-one (Evans syn aldol adduct)*. An oven-dried 250-mL single-necked, round-bottomed flask equipped with a magnetic stirring bar (egg-shaped, 3 x 1.5 cm) is charged with thiazolidinethione **3** (5.00 g, 18.8 mmol) and fitted with a rubber septum. After purging the flask with argon, anhydrous CH_2Cl_2 (60 mL) (Note 9) is added via syringe, and the flask is cooled to 0 °C using an ice/water bath. While vigorously stirring the solution, titanium tetrachloride (2.16 mL, 19.8 mmol) (Note 16) is added via syringe over three min (Note 17). After 20 min, (–)-sparteine (5.18 mL, 22.6 mmol) (Note 18) is added via syringe over 3 min (Notes 19 and 20). After another 20 min, *N*-methyl-2-pyrrolidone (2.16 mL, 22.6 mmol) (Note 21) is added, via syringe over three min, and the black-red mixture is stirred for 10 min before being cooled in a dry ice/acetone bath to –78 °C. To the cooled reaction mixture is added freshly distilled isobutyraldehyde (2.47 mL, 27.1 mmol) (Note 22) as a solution in 5 mL of dry CH_2Cl_2, dropwise using a syringe. After 30 min, the reaction mixture is warmed to 0 °C by immersion in an ice/water bath. After 30 min at 0 °C, saturated NH_4Cl solution (5 mL) is added to quench the reaction. The reaction mixture is quickly poured (Note 23) into a 250-mL separatory funnel, diluted with brine (80 mL) (Note 24), and extracted with CH_2Cl_2 (2 x 50 mL). The combined organic solution is dried over Na_2SO_4, filtered, and concentrated using a rotary evaporator. The resulting yellow oil (6.05 g) is purified using flash chromatography to provide 5.21 g (82%) of pure product **4** (Notes 25-27).

C. *(2R, 3S)-3-Hydroxy-1-[(4S)-4-benzyl-2-thioxo-thiazolidin-3-yl]-2,4-dimethyl-pentan-1-one* (*non-Evans syn aldol adduct*). An oven-dried 500-mL single-necked, round-bottomed flask equipped with a magnetic stirring bar (egg-shaped, 3 x 1.5 cm) is charged with thiazolidinethione **3** (8.00 g, 30.1 mmol) and fitted with a rubber septum. After purging the flask with argon, anhydrous CH_2Cl_2 (120 mL) (Note 9) is added via syringe, and the flask is cooled to 0 °C, using an ice/water bath. While vigorously stirring the solution, titanium tetrachloride (4.97 mL, 45.3 mmol) (Note 16) is added over three min via syringe (Note 17). After 20 min (–)-sparteine (7.63 mL, 33.2 mmol) (Note 18) is added via syringe over three min (Note 19). After 20 min, the flask is cooled to –78 °C in a dry ice/acetone bath. A solution of freshly distilled isobutyraldehyde (3.03 mL, 33.4 mmol) (Note 22) in 10 mL

of anhydrous CH_2Cl_2 is added dropwise via syringe over 3 min. The resulting solution is stirred for 30 min at –78 °C before being warmed to 0 °C by immersion in an ice/water bath. After stirring for 30 min at 0 °C, saturated NH_4Cl solution (10 mL) is added to quench the reaction. The reaction mixture is quickly poured into a 500-mL separatory funnel, diluted with brine (160 mL) (Note 24), and extracted with CH_2Cl_2 (2 x 100 mL). The combined organic solution is dried over Na_2SO_4 (15 g), filtered, and concentrated using a rotary evaporator. The resulting yellow oil (12.5 g) is purified by flash chromatography to afford 8.1 g (80%) of pure product **5**, eluting with 15:85 EtOAc:hexanes (Notes 28 and 29).

2. Notes

1. Potassium hydroxide was purchased from Fisher Scientific and used as received. A significant loss of color of the solution results during the required reaction time when only 5 equiv of potassium hydroxide is used, as described by le Corre,[2] leading to incomplete conversion.

2. Dissolution of potassium hydroxide in water evolves heat.

3. (*S*)-(–)-2-Amino-3-phenyl-1-propanol [(*S*)-phenylalaninol) was purchased from Aldrich Chemical Company and used as received. The submitters note that this reagent can also be prepared and found that Masamune's[3] procedure is the most convenient of the known procedures[4,5] for preparing (*S*)-phenylalaninol from (*S*)-phenylalanine.

4. Carbon disulfide (99.9%, ACS reagent grade) was purchased from Aldrich Chemical Company and used as received. Carbon disulfide has an auto-ignition temperature of 100 °C,[6] ***so extreme care should be taken to vent excess CS_2 away from heat sources***.

5. To ensure that escaping carbon disulfide does not pass over hot surfaces.

6. The internal temperature reaches 102–103 °C within 1–2 h, at which point any free carbon disulfide, bp = 46 °C, is presumed to be purged from the reaction.

7. The solution has faded somewhat to an orange color. An aliquot is removed (0.5 mL) and that solution is extracted with CH_2Cl_2 (2 x 0.5 mL). The combined organic solution is dried (Na_2SO_4) and evaporated. This sample is examined by ^1H NMR ($CDCl_3$) to confirm complete conversion (disappearance of dd at 2.8 and 2.5 ppm and the appearance of dddd at 4.45 ppm).

8. This product is used without further purification, however, the submitters note that recrystallization from ethanol (3 mL per gram of solid) provides colorless blocks, mp 91–92 °C (uncorrected) lit. 84–85 °C.[2] The submitters provided the following characterization data: ^{1}H NMR (400 MHz, $CDCl_3$) the appearance and shift of several resonances varies depending on concentration. δ: 2.92 (dd, J = 13.6, 6.8 Hz, 1 H), 3.01 (dd, J = 13.6, 7.2 Hz, 1 H), 3.5 (dd, J = 11.2, 7.6 Hz, 1 H), 4.43 (dddd, J = 7.2, 7.2, 7.2, 7.2 Hz, 1 H), 7.14–7.18 (band, 2 H), 7.21–7.34 (band, 3 H), 8.17 (variable) (br, s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 37.9, 39.7, 65.0, 127.2, 128.90, 128.92, 135.6, 200.6; $[\alpha]^{24}_D$= –89 (c 4.1, CH_2Cl_2); MS (ESI) calculated for $C_{10}H_{11}NNaS_2$ $[M+Na]^+$: *m/z* 232.0, found *m/z* 232.0.

9. Dichloromethane (99%) purchased from Fisher Scientific was passed through an activated alumina column (50 mm x 400 mm) under argon.

10. Pyridine (anhydrous, 99.8%) was purchased from Aldrich Chemical Company and used as received.

11. Propionyl chloride (98%) was purchased from Aldrich Chemical Company and used as received.

12. A yellow color forms immediately, and a precipitate begins to form by the end of the addition.

13. Isopropanol (99%) was purchased from Fisher Scientific and used as received.

14. Dried overnight at 0.1 mmHg.

15. Short, bright yellow needles, mp 103.4–104.8 °C (uncorrected) (mp does not change upon a second recrystallization from *i*-PrOH) ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.15 (t, J = 7.2 Hz, 3 H), 2.84 (d, J = 11.5 Hz, 1 H), 2.96–3.14 (m, 2 H), 3.18 (dd, J = 13.1, 3.7 Hz, 1 H), 3.33–3.43 (m, 2 H), 5.34 (ddd, J = 10.8, 7.2, 3.8 Hz, 1 H), 7.21–7.32 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 8.8, 31.9, 32.3, 36.8, 68.7, 127.2, 128.9, 129.4, 136.6, 174.9, 201.1: $[\alpha]^{20}_D$ = +45 (*c* 0.01, CH_2Cl_2); MS (EI) calculated for $C_{13}H_{15}NOS_2$ $[M]^+$: *m/z* 265, found: *m/z* 265. Anal. calcd. for $C_{13}H_{15}NOS_2$: C, 58.83; H, 5.70; N, 5.28. Found: C, 58.93; H, 5.67; N, 5.12.

16. Titanium (IV) chloride (99.9%) was purchased from Aldrich Chemical Company and used as received.

17. This mixture becomes a yellow-orange slurry. Since the viscosity of the solution increases notably, an increased stirring power is often necessary.

18. (-)-Sparteine (99%) was purchased from Aldrich Chemical Company and used as received.

19. Triethylamine, diisopropylethylamine, and diisopropylamine were also used as amine bases, however the diastereomeric ratios were much less than 98:2.

20. The viscosity of the solution decreases and the color becomes dark red/brown.

21. 1-Methyl-2-pyrrolidinone ((99.5%, anhydrous) was purchased from Aldrich Chemical Company and used as received.

22. Isobutyraldehyde (98%) was purchased from Aldrich Chemical Company and distilled over CaH_2 immediately prior to use.

23. If left stirring in saturated NH_4Cl solution for too long, the product will decompose.

24. Although not observed by the checkers, the submitters note that an emulsion may form in the separatory funnel, necessitating the addition of approximately 100 mL of a mixture of hexanes and ethyl acetate (1:1).

25. A 5 cm glass column was packed with 250 g of silica gel (60 Å, 40–60 μm, Sorbent Technologies). The crude product was loaded onto the column and eluted with 2.5 L of 1:5 (v:v) EtOAc:hexanes. The product was collected in 25 mL fractions between fraction numbers 44 and 79. $R_f = 0.15$ (15:85 ethyl acetate: hexanes). The product stains blue with *p*-anisaldehyde stain and heating. The product should be placed in a freezer for prolonged storage.

26. The subproduct is essentially pure at this stage, but the submitters state that it can be crystallized from 50 mL of toluene/hexanes solution (1:19, seeding required). Seeds can be obtained by allowing the material obtained after chromatography to stand for several days (the checkers were unable to obtain seed crystals).

27. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.88 (d, J = 6.8 Hz, 3 H), 1.02 (d, J = 6.6 Hz, 3 H), 1.24 (d, J = 6.8 Hz, 3 H), 1.68 (m, 1 H), 2.65 (d, J = 3.9 Hz, 1 H), 2.90 (d, J = 11.5 Hz, 1 H), 3.05 (dd, J = 13.1, 10.6 Hz, 1 H), 3.23 (dd, J = 13.1, 3.8 Hz, 1 H), 3.40 (dd, J = 11.5, 7.1 Hz, 1 H), 3.54 (ddd, J = 7.4, 3.5, 3.5 Hz, 1 H), 4.70 (dddd, J = 6.9, 6.9, 6.9, 3.2 Hz, 1 H), 5.34 (ddd, J = 10.7, 6.9, 3.8 Hz, 1 H), 7.37–7.27 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 10.2, 18.9, 19.0, 31.1, 32.0, 36.7, 41.0, 68.8, 77.4, 127.2, 128.9, 129.4, 136.3, 178.5, 201.1; IR (cm^{-1}) 3494 (br), 2960, 1687 (w); $[\alpha]^{20}_D$= +152 (c 0.017, CH_2Cl_2); MS (ESI) calculated for $C_{17}H_{23}NNaO_2S_2$ $[M+Na]^+$: *m/z*

360, found *m/z* 360. Anal. calcd. for $C_{17}H_{23}NO_2S_2$: C, 60.50; H, 6.87; N, 4.15. Found: C, 60.82; H, 6.81; N, 4.10.

28. The submitters used a 7.5 cm glass column packed with 340 g of silica gel (60 Å, 40 – 60 μm, Sorbent Technologies). The crude product was loaded onto the column and eluted with 4 L of 15:85 (v:v) EtOAc:hexanes. The product was collected in 25 mL fractions between fraction numbers 41 and 80. R_f = 0.33 (15:85 ethyl acetate: hexanes).

29. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (d, *J* = 6.8, 3 H), 1.06 (d, *J* = 6.5 Hz, 3 H), 1.18 (d, *J* = 6.8 Hz, 3 H), 1.66–1.75 (m, 1 H), 2.89 (d, *J* = 11.6 Hz, 1 H), 2.95 (d, *J* = 2.8 Hz, 1 H) (may appear as a broad singlet), 3.05 (dd, *J* = 10.5, 13.2 Hz, 1 H), 3.25 (dd, *J* = 3.9, 13.2 Hz, 1 H), 3.37 (dd, *J* = 7.1, 11.5 Hz, 1 H), 3.64 (ddd, *J* = 2.3, 2.3, 8.9 Hz, 1 H), 4.93 (qd, *J* = 2.1, 7.1 Hz, 1 H), 5.35 (ddd, *J* = 4.1, 6.9, 10.7 Hz, 1 H) 7.27–7.37 (m, 5 H); ^{13}C (100 MHz, $CDCl_3$) δ: 10.3, 18.8, 19.7, 30.7, 31.7, 36.9, 40.3, 68.9, 76.0, 127.3, 128.9, 129.4, 136.4, 179.2, 201.4; IR ν 3550 (br), 2960 (s), 1675 (s) $[\alpha]^{20}_D$= +146 (c 0.026, CH_2Cl_2); MS (ESI) calculated for $C_{17}H_{23}NNaO_2S_2$ $[M+Na]^+$: *m/z* 360, found *m/z* 360. . Anal. calcd. for $C_{17}H_{23}NO_2S_2$: C, 60.50; H, 6.87; N, 4.15. Found: C, 60.78; H, 6.78; N, 4.03.

Safety and 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.

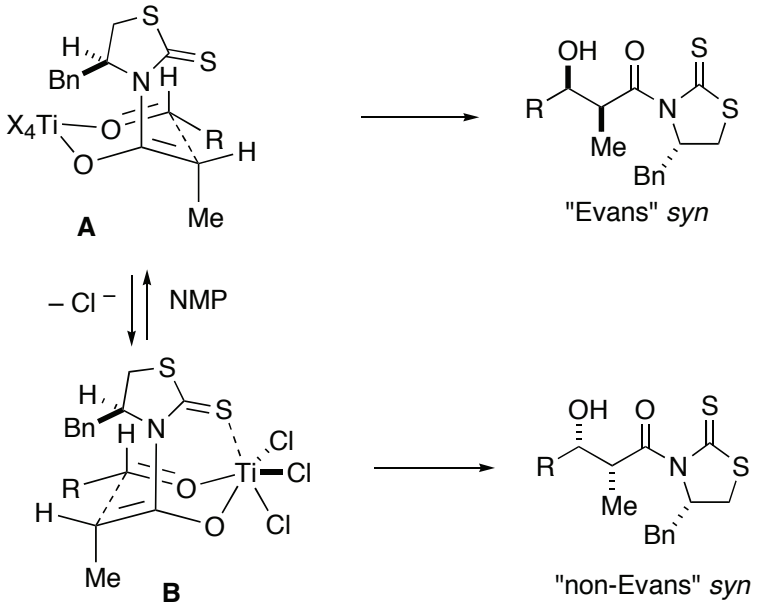
3. Discussion

The preparation and use of thiazolidinethione reagent **3** for the synthesis of aldol products, described in this procedure, is simple and offers many advantages over other available methods. The aldol reaction has found many applications in the total synthesis of natural products.[7] Chiral auxiliary based methods continue to be the most versatile and reliable of the stereoselective aldol reactions. The high selectivities observed with a range of aldehyde reactants, coupled with relatively easy separations, due to the diastereomeric nature of any mixed products, makes these user friendly processes. The Evans syn-aldol procedure employing amino acid-derived oxazolidinone chiral auxiliaries.[4,8] is particularly useful and is widely applied. A useful modification to the Evans procedure has been to replace

the oxazolidinone chiral auxiliaries with the thiazolidinethione counter parts.[9] The aldol reaction using these compounds is more user friendly for several reasons: 1) Inexpensive, easily handled, and readily available $TiCl_4$ can be used as the Lewis acid source, rather than Bu_2BOTf, required for the Evans procedure. 2) The use of a chlorotitanium enolate also permits a standard acidic work-up to be used, as opposed to the oxidative process needed when alkyl boranes are employed as the Lewis acid. Importantly, as demonstrated in this procedure, the choice of base, and base stoichiometry, allows the preparation of either the typical Evans syn- or the non-Evans syn-aldol product.[9] A variety of functional and protecting groups are tolerated in the reactions (see Tables 1 and 2).

The change in facial selectivity in the aldol additions is postulated to be the result of a switch between chelated and nonchelated transition states as illustrated in Scheme 1. In each case, the aldehyde approaches the enolate from the face opposite the benzyl substituent on the auxiliary and the

Scheme 1



aldehyde carbonyl oxygen is coordinated to the metal center allowing for a six-membered transition state. When the enolate formation and aldol addition are carried out in the absence of excess diamine or another additional ligand for the metal, it is proposed that the nucleophilic thiocarbonyl displaces chloride from the metal center and the reaction proceeds through a chelated transition state **B** giving rise to "non-Evans" *syn* aldol adducts. When NMP or additional diamine are added as an extra

Table 1: Evans syn aldol reactions of aldehydes and *N*-propionylthiazolidinethione **3**

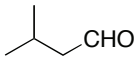
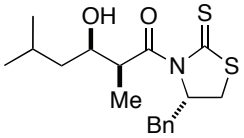
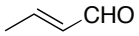
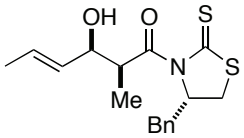
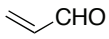
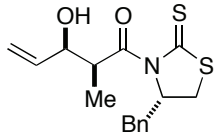
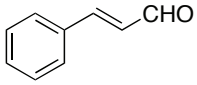
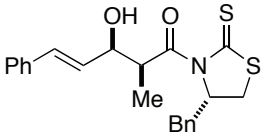
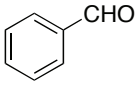
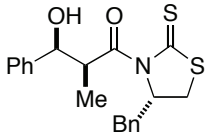
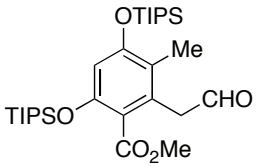
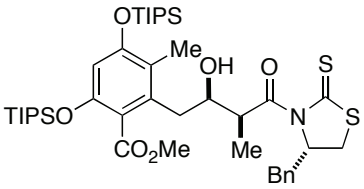
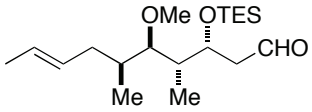
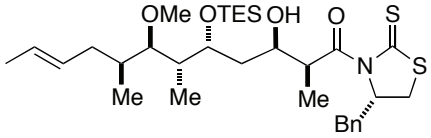
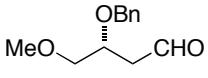
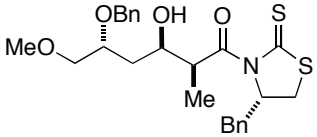
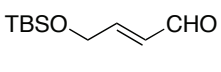
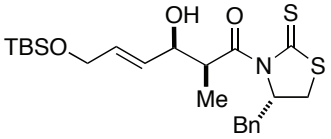
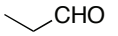
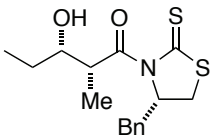
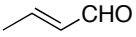
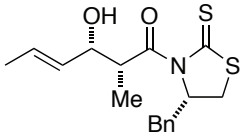
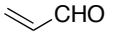
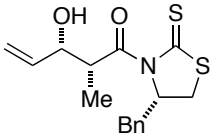
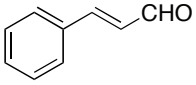
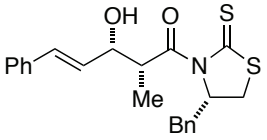
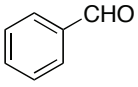
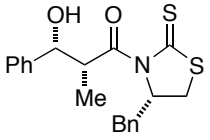
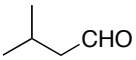
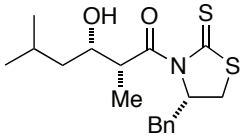
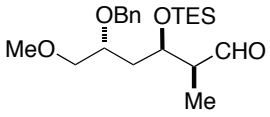
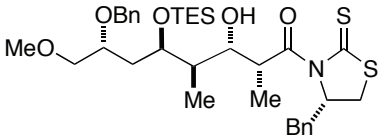
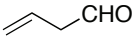
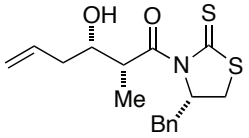
Aldehyde	Evans Syn aldol adduct	yield(%)	ratio
		74	96:4
		84	98:2
		97	98:2
		98	96:4
		99	96:4
		94	>95:5
		65	>95:5
		90	>95:5
		78	>95:5

Table 2: non-Evans syn aldol reactions of aldehydes and *N*-propionylthiazolidinethione **3**

Aldehyde	non-Evans Syn aldol adduct	yield(%)	ratio
		91	>95:5
		45	99:1
		49	99:1
		58	97:3
		52	99:1
		57	98:2
		62	>95:5
		73	>95:5

ligand for the metal center, the chelation between the sulfur of the thiocarbonyl of the auxiliary and titanium is disrupted, leading to a dipole-minimized, non-chelated transition state **A** giving rise to the "Evans" *syn* aldol adduct.

The change in diastereoselectivity through changing reaction conditions enables the use of the same enantiomer of chiral auxiliary to form

either enantiomer of a syn-aldol product (after removal of the auxiliary). Once the thiazolidinethione aldol products are formed they are more versatile (than the oxazolidinone products) in the range of transformations that they can undergo. One step reductive removal of the auxiliary to form an aldehyde,[10] and addition of carbon nucleophiles, such as phosphonates[11] and ester enolates[12] are examples of reactions that cannot be directly performed with the equivalent oxazolidinone aldol products.

1. Department of Chemistry, CB 3290, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599-3290; Crimmins@email.unc.edu.

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Appendix
Chemical Abstracts Nomenclature; (Registry Number)

(*S*)-1-(4-Benzyl-2-thioxothiazolidin-3-yl)propan-1-one: 1-Propanone, 1-[(4*S*)-4-(phenylmethyl)-2-thioxo-3-thiazolidinyl]-; (263764-23-4)

(2*S*, 3*R*)-3-Hydroxy-1-[(4*S*)-4-benzyl-2-thioxo-thiazolidin-3-yl]-2,4-dimethyl-pentan-1-one: 1-Pentanone, 3-hydroxy-2,4-dimethyl-1-[(4*S*)-4-(phenylmethyl)-2-thioxo-3-thiazolidinyl]-, (2*S*,3*R*)-; (263764-33-6)

(2*R*, 3*S*)-3-Hydroxy-1-[(4*S*)-4-benzyl-2-thioxo-thiazolidin-3-yl]-2,4-dimethyl-pentan-1-one: 1-Pentanone, 3-hydroxy-2,4-dimethyl-1-[(4*S*)-4-(phenylmethyl)-2-thioxo-3-thiazolidinyl]-, (2*R*,3*S*)-; (331283-30-8)

(*S*)-Phenylalaninol: Benzenepropanol, β-amino-, (βS)-: (3182-95-4)

Carbon disulfide; (75-15-0)

Propionyl chloride: Propanoyl chloride: (79-03-8)

Pyridine; (110-86-1)

2-Thiazolidinethione, 4-(phenylmethyl)-, (4*S*)-; (171877-39-7)

N-Methyl-2-pyrrolidone: 2-Pyrrolidinone, 1-methyl-**:** **(**872-50-4)

(–)-Sparteine: 7,14-Methano-2*H*,6*H*-dipyrido[1,2-a:1',2'-e][1,5]diazocine, dodecahydro-, (7*S*,7a*R*,14*S*,14a*S*)-; (90-39-1)

Isobutyraldehyde: Propanal, 2-methyl-; (78-84-2)

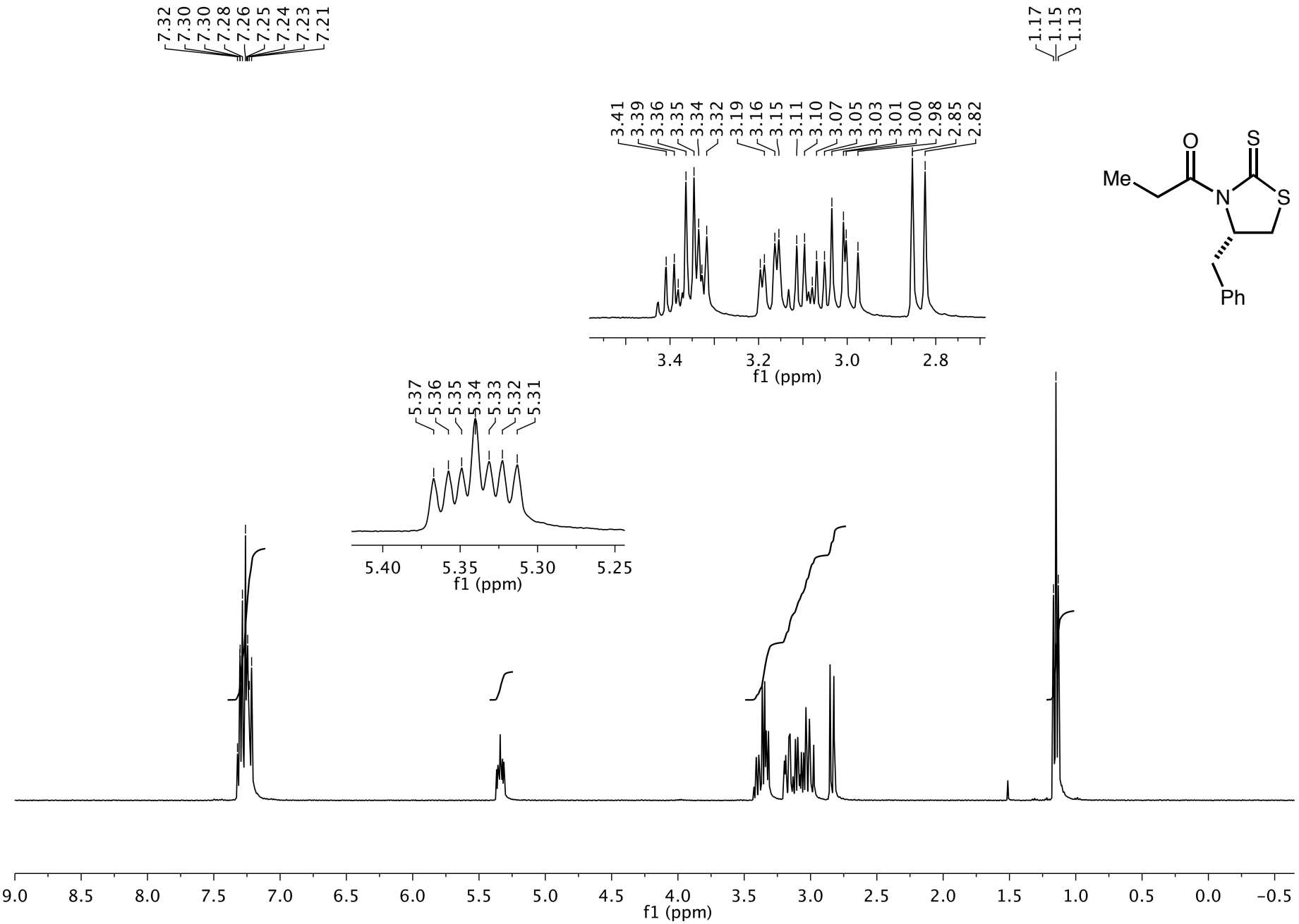
Titanium tetrachloride: (7550-45-0)

Michael T. Crimmins is currently Mary Ann Smith Distinguished Professor of Chemistry and Senior Associate Dean for the Natural Sciences in the College of Arts and Sciences. He received his B.A. degree from Hendrix College, his Ph.D. from Duke and was a postdoctoral associate at the California Institute of Technology. His research interests are in the development of new synthetic methods and their application to the total synthesis of biologically active compounds. Professor Crimmins' research has been recognized by a number of awards including the Charles H. Herty Medal and the Ernest Guenther Award in the Chemistry of Natural Products.

Hamish Christie received his B. Sc. and M. Sc. degrees in Chemistry in 1996 and1998 respectively, from the University of Adelaide, Australia. He then conducted his Ph.D. studies at the University of California, Berkeley working on the total synthesis of marine alkaloids under the supervision of Clayton Heathcock. In 2003 he began post-doctoral research with Michael Crimmins at the University of North Carolina, Chapel Hill, working on polyketide natural product synthesis. In 2006 he joined the faculty of the University of Arizona. His research interests include the development of small molecule catalysts and the total synthesis of complex organic compounds.

Colin Hughes was born in Berkeley California in 1984. He earned his B.S degree in Chemistry from the University of California at Berkeley in 2006. Later that year he joined the lab of Professor Michael Crimmins at the University of North Carolina at Chapel Hill, where his research has focused on the total synthesis of aldingenin B.

Eric Phillips was born in Grand Rapids, MI in 1983. After receiving his B.S. degree in chemistry from Western Michigan University in 2005, he attended graduate school under the guidance of Prof. Karl Scheidt. Upon graduating in 2010, he became a Ruth Kirschstein NIH post-doctoral fellow in Prof. Jon Ellman's lab at Yale University where his research is focused on transition metal-catalyzed C-H insertion reactions.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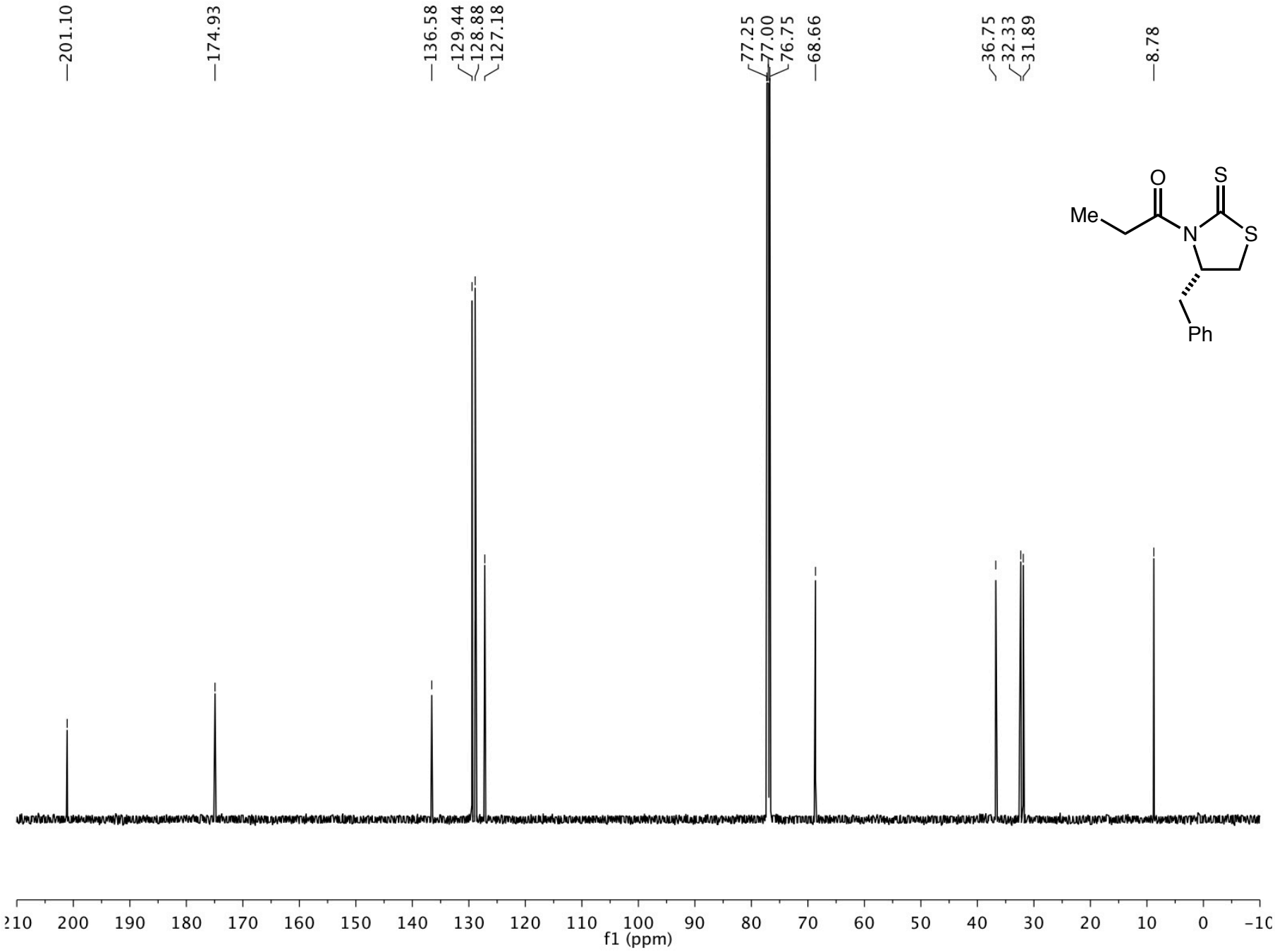
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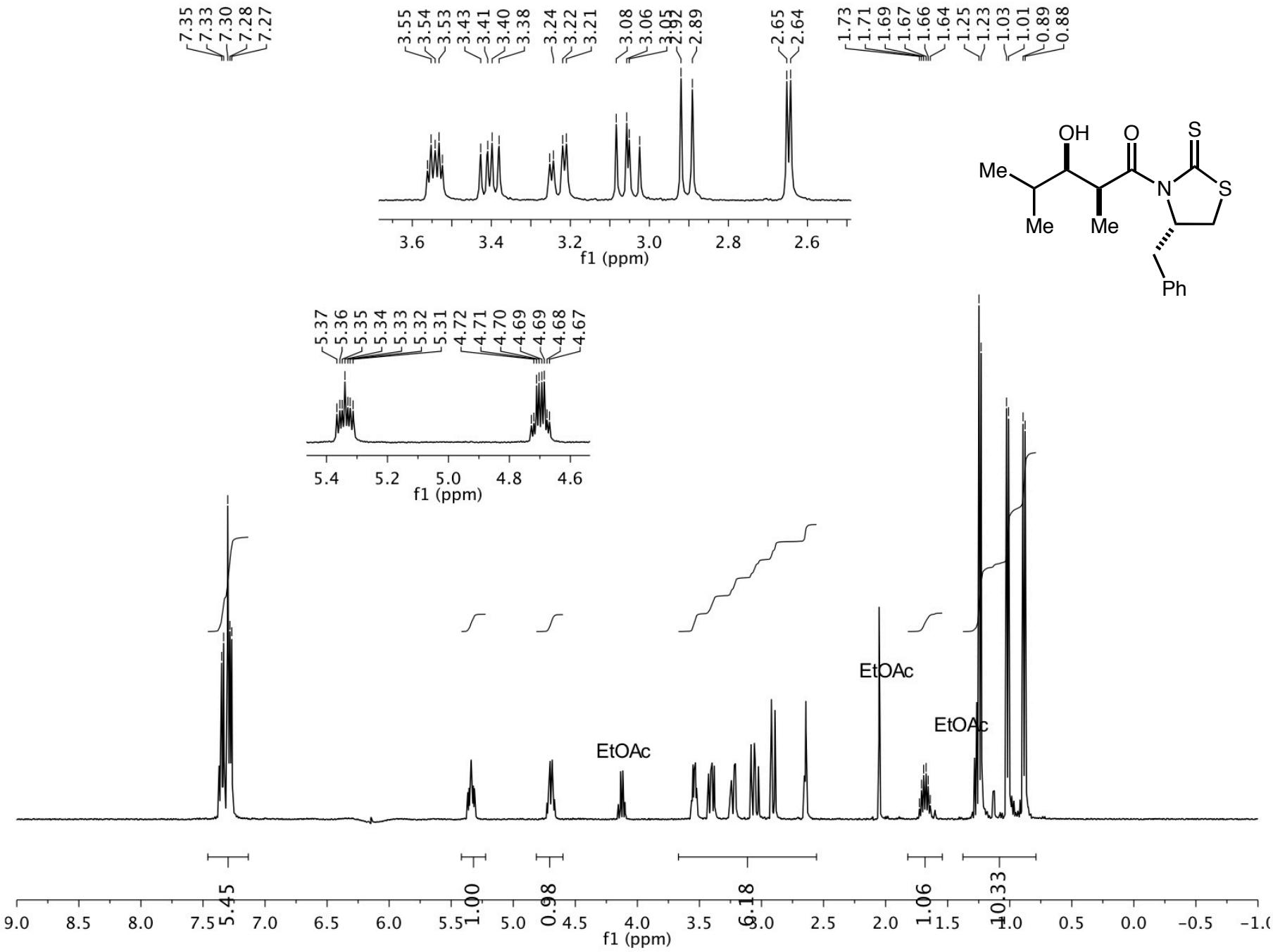
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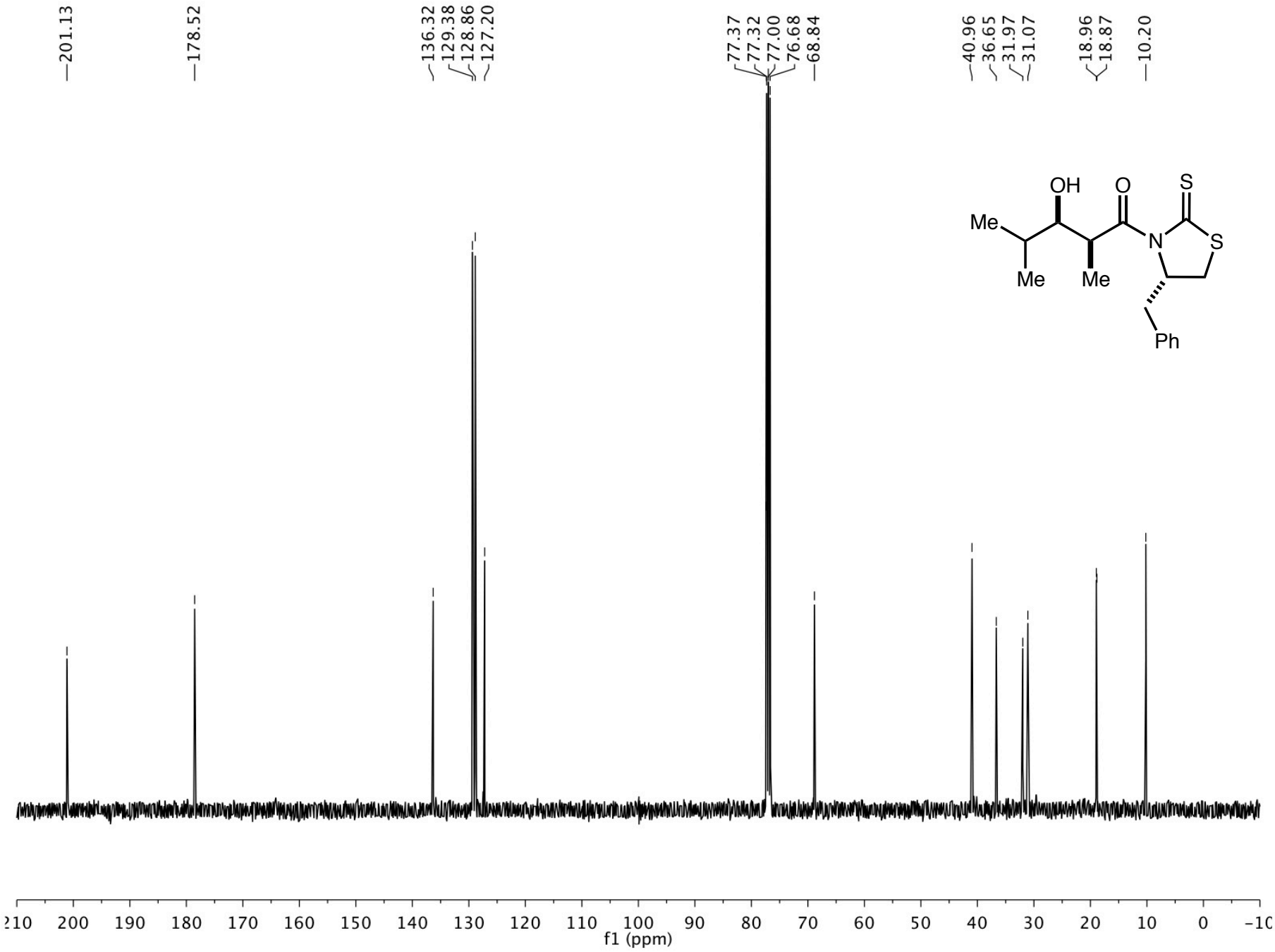
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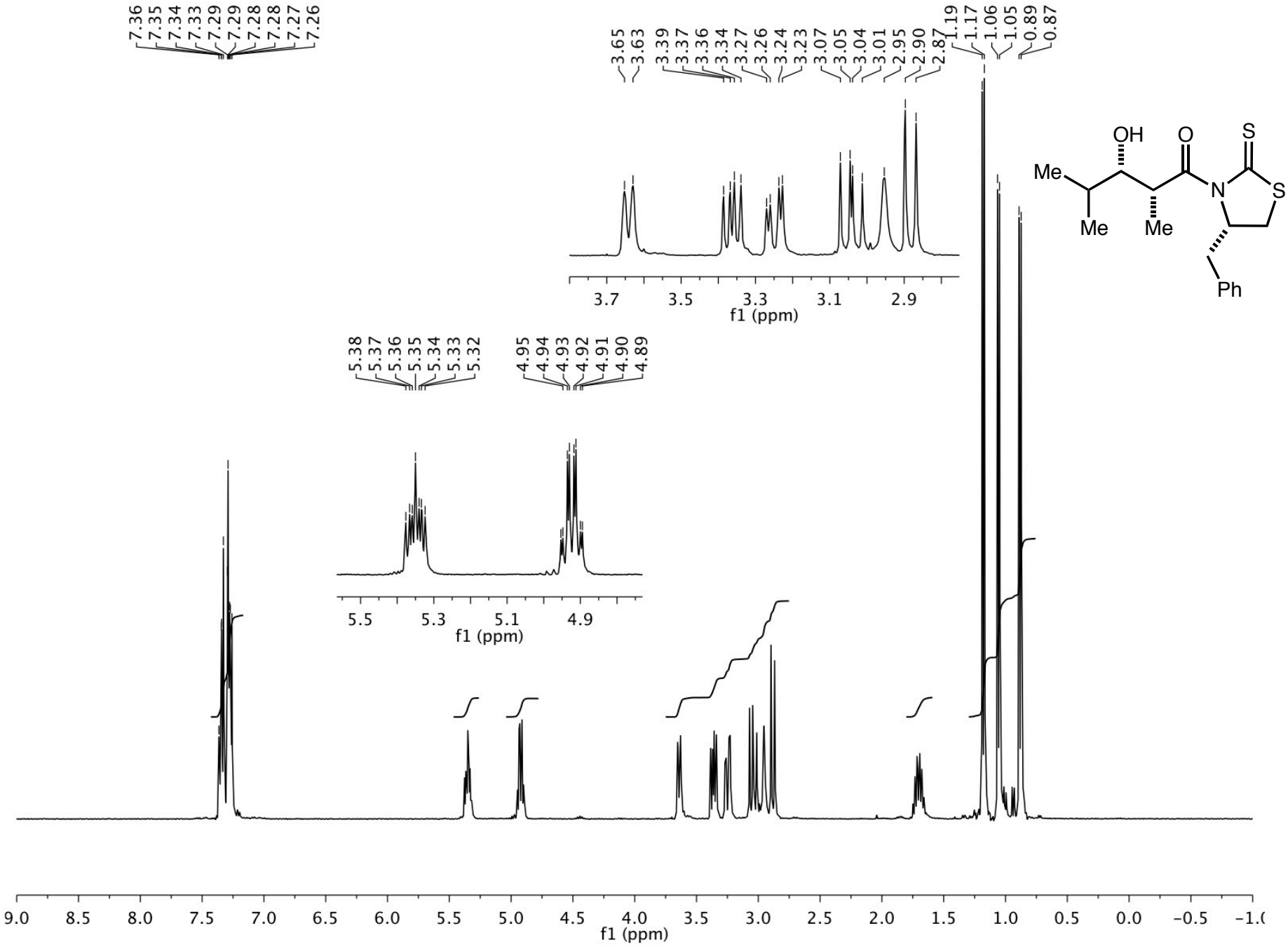
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