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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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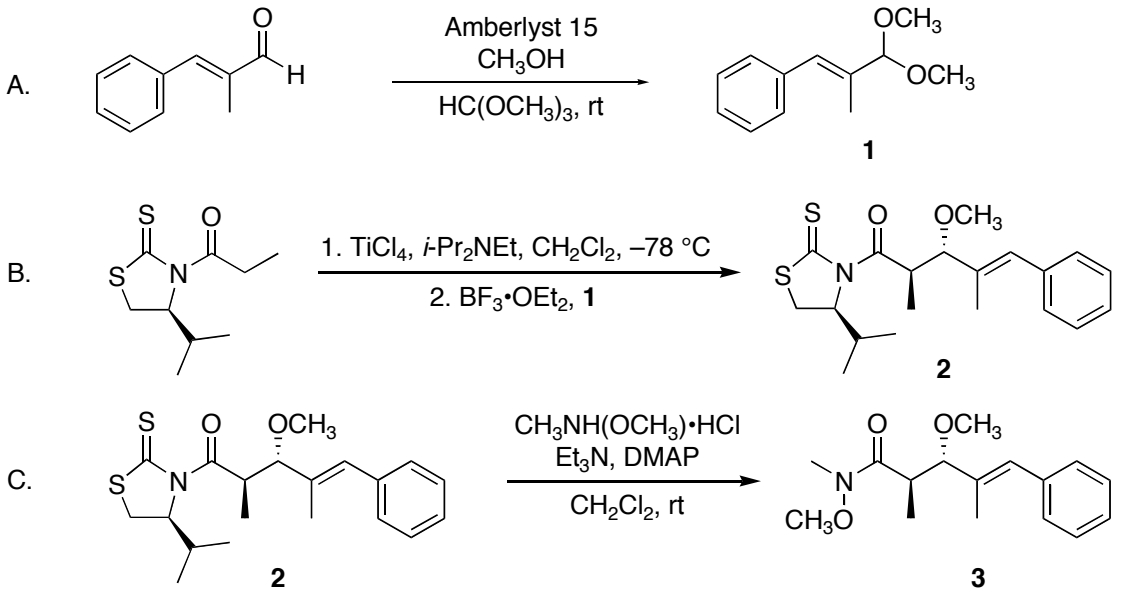
STEREOSELECTIVE SYNTHESIS OF *anti* α-METHYL-β-METHOXY CARBOXYLIC COMPOUNDS



Submitted by Erik Gálvez, Pedro Romea, and Fèlix Urpí.[1]
Checked by Vijaya Bhasker Gondi and Viresh H. Rawal.
Discussion Addendum *Org. Synth.* **2013**, *90*, 182

1. Procedure

A. *[(E)-3,3-dimethoxy-2-methyl-1-propenyl]benzene* (**1**). An oven-dried 25-mL round-bottomed flask equipped with a magnetic stir bar is charged with (*E*)-2-methyl-3-phenylpropenal (6.0 mL, 43 mmol, 1.0 equiv) (Note 1) and Amberlyst 15 (50 mg) (Note 2). The flask is fitted with a rubber septum, flushed with nitrogen, cooled in an ice-water bath, and charged with trimethyl orthoformate (5.8 mL, 53 mmol, 1.2 equiv) (Note 3) and dry methanol (1.0 mL, 25 mmol, 0.56 equiv) (Note 4). The reaction mixture is stirred at room temperature for 36 h. The resin is removed by filtration through a cotton plug, and the volatiles are removed using a rotary evaporator (Note 5). The resultant oil is purified by short path vacuum distillation. The main fraction is collected at 120–130 °C (2.7 mmHg) and provides 6.48 g (78% yield) of the desired *[*(*E*)-3,3-dimethoxy-2-methyl-1-propenyl]benzene (**1**) (Notes 6, 7, 8).

B. *(4S)-N-[(2R,3S,4E)-2,4-Dimethyl-3-methoxy-5-phenyl-4-pentenoyl]-4-isopropyl-1,3-thiazolidine-2-thione* (**2**). An oven-dried 250-mL round-bottomed flask equipped with a magnetic stir bar is charged with

(*S*)-4-isopropyl-*N*-propanoyl-1,3-thiazolidine-2-thione (2.20 g, 10.1 mmol, 1.0 equiv) (Note 9). The flask is fitted with a rubber septum, flushed with nitrogen, and charged with anhydrous CH_2Cl_2 (80 mL) (Note 10). The stirred solution is cooled in an ice-water bath, and neat $TiCl_4$ (1.2 mL, 11 mmol, 1.1 equiv) (Note 11) is added dropwise by syringe over 1 min, which causes the formation of a yellow solid. The resulting suspension is stirred for 5 min, cooled with a liquid nitrogen-ethyl acetate bath (–83 °C), and a solution of dry diisopropylethylamine (1.83 mL, 11.0 mmol, 1.08 equiv) (Note 12) in CH_2Cl_2 (5 mL) is added dropwise *via* canula over 5 min, which produces a deep red homogeneous solution. An additional 5 mL of CH_2Cl_2 are used to transfer the last traces of diisopropylethylamine to the reaction flask. The reaction mixture is stirred in the liquid nitrogen-ethyl acetate bath for 30 min, then transferred to a cryocool (or acetone-dry ice bath) (bath temperature –50 °C to –55 °C) for 2 h. The reaction mixture is cooled again in a liquid nitrogen-ethyl acetate bath, and $BF_3{\cdot}OEt_2$ (1.4 mL, 11 mmol, 1.1 equiv) (Note 13) is added dropwise by syringe over 1 min. After 5 min, a cooled (liquid nitrogen-ethyl acetate bath) solution of *[*(*E*)-3,3-dimethoxy-2-methyl-1-propenyl]benzene (**1**) (2.11 g, 10.9 mmol, 1.08 equiv) in CH_2Cl_2 (5 mL) is added dropwise *via* cannula over 5 min. An additional 5 mL of CH_2Cl_2 are used to transfer the last traces of **1** to the reaction flask. After stirring for 2 h in the liquid nitrogen-ethyl acetate bath, the reaction mixture is quenched with a saturated solution of NH_4Cl (80 mL). The mixture is allowed to warm to room temperature, then transferred to a 250-mL separatory funnel. The aqueous layer is separated and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers are dried ($MgSO_4$), filtered through a cotton plug under water aspirator pressure and concentrated using a rotary evaporator to afford a bright yellow oil (Note 5), a 95:5 ratio of diastereomers (Note 14). The crude product is dissolved in 5 mL of CH_2Cl_2 and loaded on a flash chromatography column of deactivated silica gel (6.5-cm diameter glass column and *ca* 450 g of silica) (Note 15). The column is eluted using a gradient solvent system of hexanes-CH_2Cl_2, 4:1 to 3:1 to 2:1. The fractions containing the desired product are combined and concentrated by rotary evaporator to afford 3.42 g (9.06 mmol, 89% yield) of **2** as a bright yellow oil (Notes 16, 17, 18).

C. *(2R,3S,4E)-N,3-Dimethoxy-N,2,4-trimethyl-5-phenyl-4-pentenamide* (**3**). An oven-dried 25-mL round-bottomed flask equipped with a magnetic stir bar is charged with (4*S*)-*N*-[(2*R*,3*S*,4*E*)-2,4-dimethyl-3-methoxy-5-phenyl-4-pentenoyl]-4-isopropyl-1,3-thiazolidine-2-thione (**2**)

(1.85 g, 4.89 mmol, 1.0 equiv). The flask is fitted with a rubber septum, flushed with nitrogen, and charged with anhydrous CH_2Cl_2 (10 mL, Note 10). The septum is temporarily removed and *N,O*-dimethylhydroxylamine hydrochloride (733 mg, 7.50 mmol, 1.53 equiv) (Note 19) and 4-dimethylaminopyridine (610 mg, 5.0 mmol, 1.02 equiv) (Note 20) are quickly added. The septum is replaced, the flask is flushed again with nitrogen, and dry triethylamine (0.75 mL, 5.0 mmol, 1.0 equiv) (Note 21) is added by syringe. The resulting mixture is stirred at room temperature for 15 h, over which period the initial deep yellow solution gradually fades to become almost colorless. The mixture is diluted with CH_2Cl_2 (35 mL), transferred to a 100-mL separatory funnel, and washed successively with 10% citric acid (3 × 30 mL), 1 M NaOH (4 × 30 mL) (Note 22) and brine (30 mL). The organic layer is dried ($MgSO_4$), filtered through a cotton plug under water aspirator pressure, and concentrated with a rotary evaporator to afford a yellowish oil (Note 5). The oily residue is dissolved in 2.5 mL of CH_2Cl_2 and charged on a column (4.1-cm diameter) of silica gel (*ca* 50 g) and eluted with 3:2 hexanes/EtOAc. The desired product is obtained in fractions 10–25 (*ca* 20 mL/fraction), which are concentrated by rotary evaporator (Note 5) to deliver 1.15 g (4.14 mmol, 83% yield) of (2*R*,3*S*,4*E*)-*N*,3-dimethoxy-*N*,2,4-trimethyl-5-phenyl-4-pentenamide (**3**) as a viscous colorless oil that solidifies upon standing in the refrigerator (Note 23). To recover the chiral auxiliary, the basic aqueous layer is treated with 2 M aqueous HCl (60 mL), and the resultant mixture is transferred to a 250-mL separatory funnel and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers are dried ($MgSO_4$), filtered through a cotton plug under water aspirator pressure, and concentrated with a rotary evaporator (Note 5) to afford the thiazolidine auxiliary (638 mg, 81%) as a yellowish solid (mp 67–68 °C) that can be reused.

2. Notes

1. (*E*)-2-Methyl-3-phenylpropenal was purchased from Aldrich Chemical Company, Inc., and used as supplied.

2. Amberlyst 15 was purchased from Aldrich Chemical Company, Inc., and used as supplied.

3. Trimethyl orthoformate was purchased from Aldrich Chemical Company, Inc., and used as supplied.

4. Methanol was purchased from Aldrich Chemical Company, Inc., and distilled over magnesium.

5. Rotary evaporation was performed at 10 mmHg (vacuum pump) with the water bath temperature at 25 °C.

6. By HNMR analysis, the crude product is an 18:1 mixture of *E:Z* diastereomers. After distillation, a 10:1 ratio of *E:Z* diastereomers is present. Fractional distillation using a Vigreux column gives the product in higher *E*/*Z* ratio (>20:1) but in lower yield (38-43%). However, similar yield and dr were obtained when the second step was performed with acetals of 10:1 or 20:1 dr.

7. The submitters reported a lower bp: 75–80 °C (2.5 mmHg).

8. The physical properties and spectral data for the major diastereomer (**1**) are as follows: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.89 (d, J = 1.2 Hz, 3 H), 3.38 (s, 6 H), 4.65 (d, J = 1.2 Hz, 1 H), 6.63 (br s, 1 H), 7.24–7.36 (m, 5 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 13.0, 53.6, 107.7, 126.8, 128.1, 128.5, 129.1, 134.4, 137.0; IR (film) cm^{-1}: 2987, 2932, 2827, 1601, 1445, 1347, 1196, 1073; HRMS calcd for $C_{12}H_{16}O_2Na$ (M^++Na): 215.1043, found 215.1041. Anal. calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39; O, 16.64. Found: C, 75.22; H, 8.42; O, 16.58.

9. The thiazolidine thione was prepared by the method described in the accompanying procedure.

10. Dichloromethane was freshly distilled over calcium hydride. Checkers used the dichloromethane from a solvent purification system (activated alumina column).

11. $TiCl_4$ (reagent plus, 99.9%) was purchased from Aldrich Chemical Company, Inc., and used as supplied.

12. Diisopropylethylamine was purchased from Aldrich Chemical Company, Inc., and freshly distilled over calcium hydride or KOH (checkers).

13. $BF_3{\cdot}OEt_2$ (purified, redistilled grade) was purchased from Aldrich Chemical Company, Inc., and used as supplied.

14. The checkers analyzed the crude product by ^{1}H NMR to determine the ratio of diastereomers. The submitters observed a 96:4 ratio of diastereomers by HPLC. The following HPLC conditions were used by the submitters. Detector: 254 nm; column: Tracer (250 × 4 mm) Spherisorb W Silica 5 μm; eluent: 97:3 hexanes/EtOAc; flow rate: 0.9 mL min^{-1}; retention times: t_R (major diastereomer) = 14.3 min; t_R (minor diastereomer) = 19.1 min.

15. The column is wet-loaded with flash grade silica gel (40-63 μm) using 4:1 hexanes-CH_2Cl_2 solvent mixture containing 3% Et_3N by volume. Further solvent mixtures used for running the column are also treated with 3% Et_3N. The submitters followed a different method for loading and running the column: Deactivated silica is prepared by addition of CH_2Cl_2 (300 mL) to SiO_2 (200 g) kept in a 1-L round-bottomed flask. After shaking carefully, dry triethylamine (5 mL) was added followed by additional CH_2Cl_2 (200 mL). The mixture is carefully shaken and the solvent is removed with a rotary evaporator (*Attention*: a cotton plug is placed at the neck of the flask to keep silica gel from blowing into the evaporator).

16. The product should be kept in the refrigerator under a nitrogen atmosphere to minimize decomposition.

17. The physical properties and spectral data for **2**: $[\alpha]_D^{25}$ +189.7 (*c* 1.05, $CHCl_3$), $[\alpha]_D$ +178.7 (*c* 1.2, $CHCl_3$, submitters); TLC R_f 0.83 (CH_2Cl_2); HPLC (97:3 hexanes/EtOAc) t_R = 14.3 min (submitters); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.01 (d, *J* = 6.8 Hz, 3 H), 1.03 (d, *J* = 6.6 Hz, 3 H), 1.08 (d, *J* = 6.6 Hz, 3 H), 1.85 (br s, 3 H), 2.32–2.40 (m, 1 H), 2.99 (dd, *J* = 11.4, 2.1 Hz, 1 H), 3.16 (s, 3 H), 3.45 (dd, *J* = 11.4, 8.7 Hz, 1 H), 3.92 (d, *J* = 9.9 Hz, 1 H), 5.21 (dq, *J* = 9.9, 7.0 Hz, 1 H), 5.34 (ddd, *J* = 8.7, 5.4, 2.1 Hz, 1 H), 6.52 (br s, 1 H), 7.35–7.24 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 12.1, 14.3, 16.8, 19.0, 28.7, 30.3, 41.3, 55.9, 71.9, 91.8, 126.7, 128.1, 129.0, 131.1, 135.0, 137.0, 177.8, 202.6; IR (film) cm^{-1}: 2940, 1690, 1440, 1365, 1240, 1150; HRMS calcd for $C_{20}H_{27}NO_2S_2Na$ (M^++Na): 400.1375, found: 400.1366. Anal. calcd for $C_{20}H_{27}NO_2S_2$: C, 63.62; H, 7.21; N, 3.71; S, 16.99. Found: C, 63.42; H, 6.97; N, 3.69; S, 17.00.

18. Checkers found that later fractions contain the starting aldehyde, (*E*)-2-methyl-3-phenylpropenal, and a minor diastereomer of **2**. The R_f for the aldehyde is 0.77 (CH_2Cl_2). Properties of the minor diastereomer: R_f = 0.71 (CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.84 (d, *J* = 6.9 Hz, 3 H, $CH_3CC\underline{H}_3$), 0.89 (d, *J* = 6.8 Hz, 3 H, $COCHC\underline{H}_3$), 1.28 (d, *J* = 6.8 Hz, 3 H, $C\underline{H}_3CCH_3$), 1.87 (br s, 3 H, $(C\underline{H}_3)C{=}CHPh$), 2.12–2.16 (m, 1 H, $C\underline{H}(CH_3)_2$), 2.90 (d, *J* = 11.5 Hz, 1 H, $SCH_aC\underline{H}_b$), 3.28 (s, 3 H, $OC\underline{H}_3$), 3.42 (m, 1 H, $SC\underline{H}_aH_b$), 4.07 (d, *J* = 8.1 Hz, 1 H, $C\underline{H}OCH_3$), 5.28 (m, 2 H, $NC\underline{H}$ and $COC\underline{H}CH_3$), 6.51 (br s, 1 H, $PhC\underline{H}{=}C$), 7.20–7.33 (m, 5H, $Ar\underline{H}$). In one run, the checkers also isolated a very small amount (<1%) of another diastereomer, tentatively assigned to be the product of aldol reaction with the *Z* isomeric acetal.

19. *N,O*-Dimethylhydroxylamine hydrochloride (98%) was purchased from Aldrich Chemical Company, Inc., and kept overnight under vacuum before use.

20. 4-Dimethylaminopyridine (99%) was purchased from Aldrich Chemical Company, Inc., and used as supplied.

21. Triethylamine was purchased from Aldrich Chemical Company, Inc., and freshly distilled over calcium hydride.

22. The basic aqueous solution contains the deprotonated chiral auxiliary.

23. The physical properties and spectral data for **3** are as follows: $[\alpha]_D^{25}$ +58.0 (*c* 1.18, $CHCl_3$); TLC R_f 0.40 (hexanes/EtOAc, 3:2); HPLC (85:15 hexanes/EtOAc) t_R = 23.4 min; chiral HPLC (97:3 hexanes/*i*-PrOH) t_R = 8.2 min; mp 40–42 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.99 (d, *J* = 7.0 Hz, 3 H), 1.83 (br s, 3 H), 3.20 (s, 3 H), 3.25 (s, 3 H), 3.23–3.25 (m, 1 H), 3.76 (s, 3 H), 3.86 (d, *J* = 10.2 Hz, 1 H), 6.54 (br s, 1 H), 7.23–7.37 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 11.9, 14.3, 32.1, 37.5, 56.2, 61.4, 89.9, 126.7, 128.1, 129.0, 131.0, 135.0, 137.1, 175.0; IR (film) cm^{-1}: 2976, 2935, 2819, 1660, 1448, 1418, 1386, 1178; HRMS calcd. for $C_{16}H_{23}NNaO_3$ $[M+Na]^+$ 300.1576, found 300.1563. Anal. calcd for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.36; N, 5.05; Found: C, 68.87; H, 8.13; N, 5.11.

Safety and Waste Disposal Information

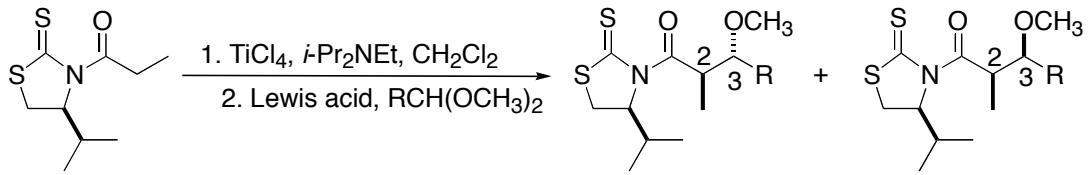
All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

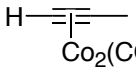
The reported experimental procedure can be also applied to other dimethyl acetals from aromatic and α,β-unsaturated aldehydes (see entries 1–6 in Table 1), whereas less reactive substrates, such as acetals from deactivated aromatic or aliphatic aldehydes, require a stronger Lewis acid ($SnCl_4$) and higher temperatures to obtain similar yields and diastereomeric ratios (see entries 7–10 in Table 1). Thus, the addition of the titanium enolate from (*S*)-4-isopropyl-*N*-propanoyl-1,3-thiazolidine-2-thione to a wide range of dimethyl acetals in the presence of a Lewis acid ($BF_3{\cdot}OEt_2$ or

$SnCl_4$) constitutes an efficient one-step entry to the stereoselective synthesis of *anti* β-methoxy-α-methyl carboxylic adducts.[2]

Table 1. Stereoselective synthesis of *anti* β-methoxy-α-methyl carboxylic adducts



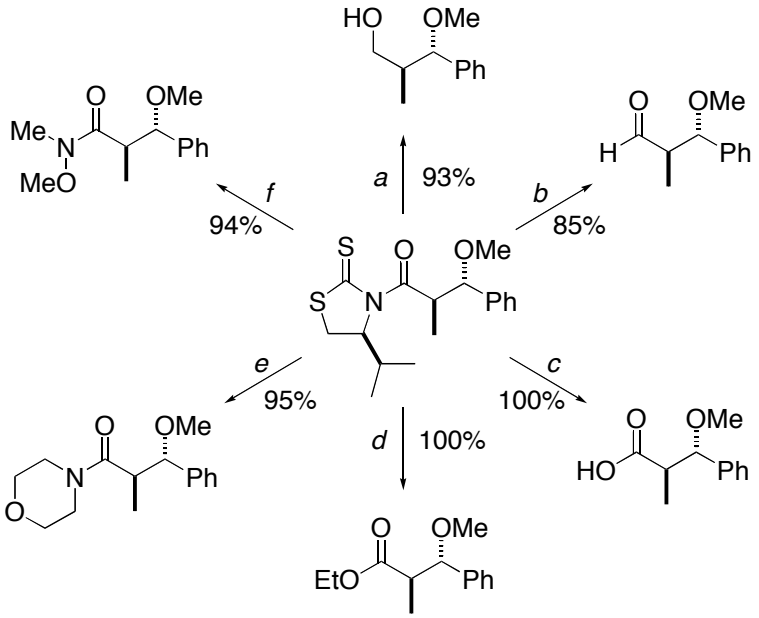
2,3-*anti* 2,3-*syn*

Entry	R	Lewis acid	Reactions conditions (T, t)	dr[a] 2,3-*anti*/2,3-*syn*	Yield (%)[b]
1	(*E*)-PhCH=C(CH_3)	BF_3•OEt_2	–78 °C, 2.5 h	96:4	94
2[c]		BF_3•OEt_2	–78 °C, 2.5 h	99:1	84
3	Ph	BF_3•OEt_2	–78 °C, 2.5 h	86:14	75
4	4-CH_3OPh	BF_3•OEt_2	–78 °C, 2.5 h	81:19	77
5	3-CH_3OPh	BF_3•OEt_2	–78 °C, 2.5 h	92:8	79
6	4-ClPh	BF_3•OEt_2	–78 °C, 2.5 h	91:9	81
7	4-NO_2Ph	$SnCl_4$	–78 °C, 2 h	86:14	70
8	$CH_3CH_2CH_2$	$SnCl_4$	–50 °C, 2 h	93:7	64[d]
9	$(CH_3)_2CHCH_2$	$SnCl_4$	–20 °C, 2 h	92:8	76
10	$(CH_3)_2CH$	$SnCl_4$	–20 °C, 2 h	88:12	50

a Established by HPLC. *b* Isolated yield at 1 mmol scale. *c* Diethyl acetal was used. *d* Isolated yield of the corresponding ethyl ester.

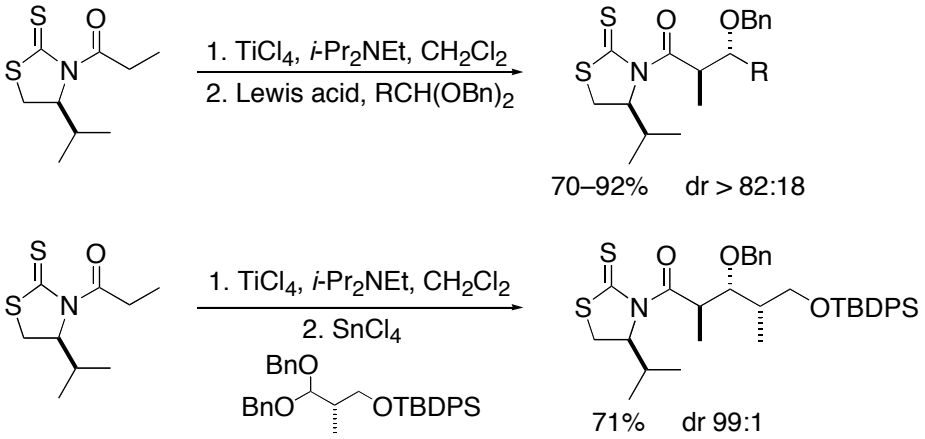
As shown by the preparation of the Weinreb amide **3**, one of the most appealing advantages of the 1,3-thiazolidine-2-thione auxiliaries is that they are removed under very mild conditions.[3,4] Indeed, the above mentioned

adducts are easily transformed into a large number of enantiopure 1,3-dioxygenated compounds with high interest in organic synthesis (Scheme 1).



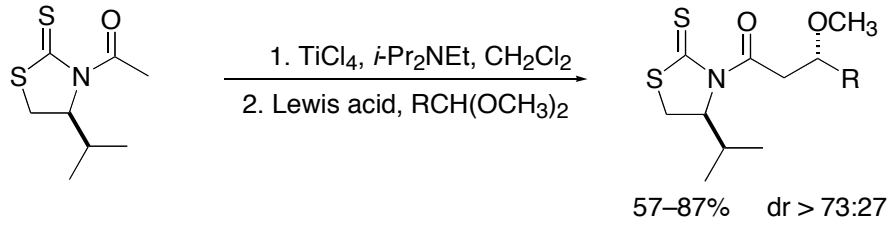
Scheme 1. *Experimental conditions: (a)* $NaBH_4$ (4.5 equiv), THF-H_2O, rt, 4 h. *(b)* DIBAL-H (1.1 equiv), CH_2Cl_2, -78 °C, 3 h. *(c)* $LiOH{\cdot}H_2O$ (6 equiv), CH_3CN-H_2O, rt, 12 h. *(d)* EtOH, DMAP cat., rt, 24 h. *(e)* Morpholine (4 equiv), THF, rt, 12 h. *(f)* MeONHMe·HCl (1.5 equiv), Et_3N (1 equiv), DMAP cat., CH_2Cl_2, rt, 24 h.

Further studies have established that this methodology can be generalized to other substrates. Dibenzyl acetals afford in high yields and diastereomeric ratios the corresponding *anti* adducts, which may be considered as protected *anti* aldol structures (Scheme 2). Importantly, *matched* pairs in double asymmetric reactions with chiral dibenzyl acetals deliver the Felkin adduct as the sole diastereomer.[5]



Scheme 2

Finally, this methodology has been applied to titanium enolates from (*S*)-*N*-acetyl-4-isopropyl-1,3-thiazolidine-2-thione (Scheme 3). Compared to the results summarized in Table 1, the diastereoselectivity of this process is slightly lower, but it achieves sufficiently good results to be used in asymmetric synthesis,[6] and has been successfully applied to the stereoselective synthesis of the C9–C21 fragment of debromoaplysiatoxin.[7]



Scheme 3

1. Departament de Química Orgànica, Universitat de Barcelona, Martí i Franqués 1-11, 08028 Barcelona, Catalonia, Spain. E-mail: pedro.romea@ub.edu; felix.urpi@ub.edu.

2. Cosp, A.; Romea, P.; Talavera, P.; Urpí, F.; Vilarrasa, J.; Font-Bardia, M.; Solans, X. *Org. Lett.* **2001**, *3*, 615–617.

3. Chiral 1,3-thiazolidine-2-thiones were introduced and identified as easy removable chiral auxiliaries in asymmetric synthesis by Nagao and Fujita. For instance, see: (a) Reference 2. (b) Nagao, Y.; Dai, W.-M.; Ochiai, M.; Tsukagoshi, S.; Fujita, E. *J. Org. Chem.* **1990**, *55*, 1148–1156.

4. For a review on the application of thiazolidinethiones in asymmetric synthesis, see: Velázquez, F.; Olivo, H. F. *Curr. Org. Chem.* **2002**, *6*, 303-340.

5. Cosp, A.; Larrosa, I.; Vilasís, I.; Romea, P.; Urpí, F.; Vilarrasa, J. *Synlett* **2003**, 1109–1112.

6. Cosp, A.; Romea, P.; Urpí, F.; Vilarrasa, J. *Tetrahedron Lett.* **2001**, *42*, 4629–4631.

7. Cosp, A.; Llàcer, E.; Romea, P.; Urpí, F. *Tetrahedron Lett.* **2006**, *47*, 5819–5823.

Appendix
Chemical Abstracts Nomenclature; (Registry Number)

(*E*)-2-Methyl-3-phenylpropenal; (15174-47-7)
Trimethyl orthoformate; (149-73-5)
(*E*)-3,3-Dimethoxy-2-methyl-1-propenyl]benzene: Benzene, [(1*E*)-3,3-dimethoxy-2-methyl-1-propen-1-yl]-: (137032-32-7)
(*S*)-4-(1-Methylethyl)-3-(1-oxopropyl)-2-thiazolidinethione; (102831-92-5)
Diisopropylethylamine: 2-Propanamine, *N*-ethyl-*N*-(1-methylethyl)-; (7087-68-5)
Titanium tetrachloride; (7550-45-0)
Boron trifluoride etherate: $BF_3 \cdot OEt_2$ (109-63-7)
(4*S*)-3-[(2*R*,3*S*,4*E*)-3-Methoxy-2,4-dimethyl-1-oxo-5-phenyl-4-pentenyl]-4-(1-methylethyl)-2-thiazolidinethione; (332902-42-8)
N,O-Dimethylhydroxylamine hydrochloride: Methanamine, *N*-methoxy-, hydrochloride; (6638-79-5)
4-Dimethylaminopyridine: 4-Pyridinamine, *N*,*N*-dimethyl-; (1122-58-3)
Triethylamine: thanamine, *N*,*N*-diethyl-; (121-44-8)

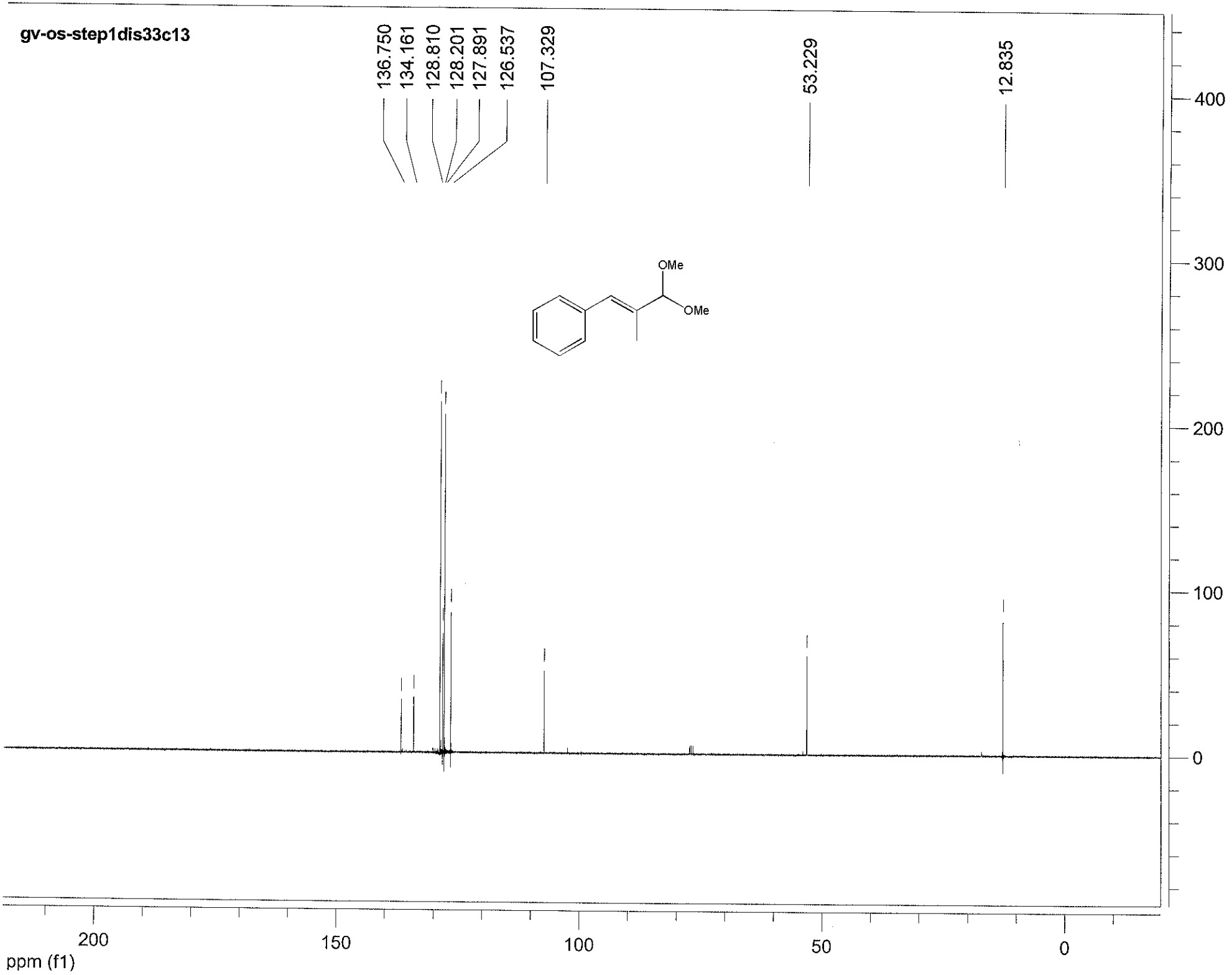
Pedro Romea completed his B.Sc. in Chemistry in 1984 at the University of Barcelona. That year he joined the group of Professor Jaume Vilarrasa, at the University of Barcelona, receiving his Masters Degree in 1985, and he followed Ph.D. studies in the same group from 1987 to 1991. Then, he joined the group of Professor Ian Paterson at the University of Cambridge (UK), where he participated in the total synthesis of oleandolide. Back to the University of Barcelona, he became Associate Professor in 1993. His research interests have focused on the development of new synthetic methodologies and their application to the stereoselective synthesis of naturally occurring molecular structures.

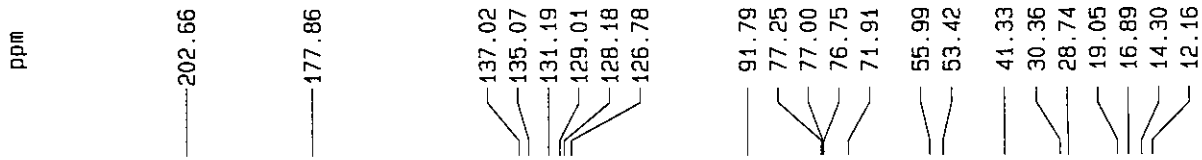
Erik Gálvez was born in Barcelona, Spain, in 1982. He received his B.Sc. in Chemistry in 2005 at the Universitat de Barcelona and joined the group of Pedro Romea and Fèlix Urpí. In 2006 he received his Masters Degree and is now pursuing the Ph.D. in the same group. His research concerns asymmetric methodologies involving cross-coupling reactions using 1,3-thiazolidine-2-thiones as source of chirality.

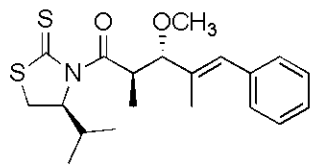
Fèlix Urpí received his B.Sc. in Chemistry in 1980 at the University of Barcelona. In 1981, he joined the group of Professor Jaume Vilarrasa, at the University of Barcelona, receiving his Masters Degree in 1981 and Ph.D. in 1988, where he was an Assistant Professor. He then worked as a NATO postdoctoral research associate in titanium enolate chemistry with Professor David A. Evans, at Harvard University in Cambridge, MA. He moved back to the University of Barcelona and he became Associate Professor in 1991. His research interests have focused on the development of new synthetic methodologies and their application to the stereoselective synthesis of naturally occurring molecular structures.

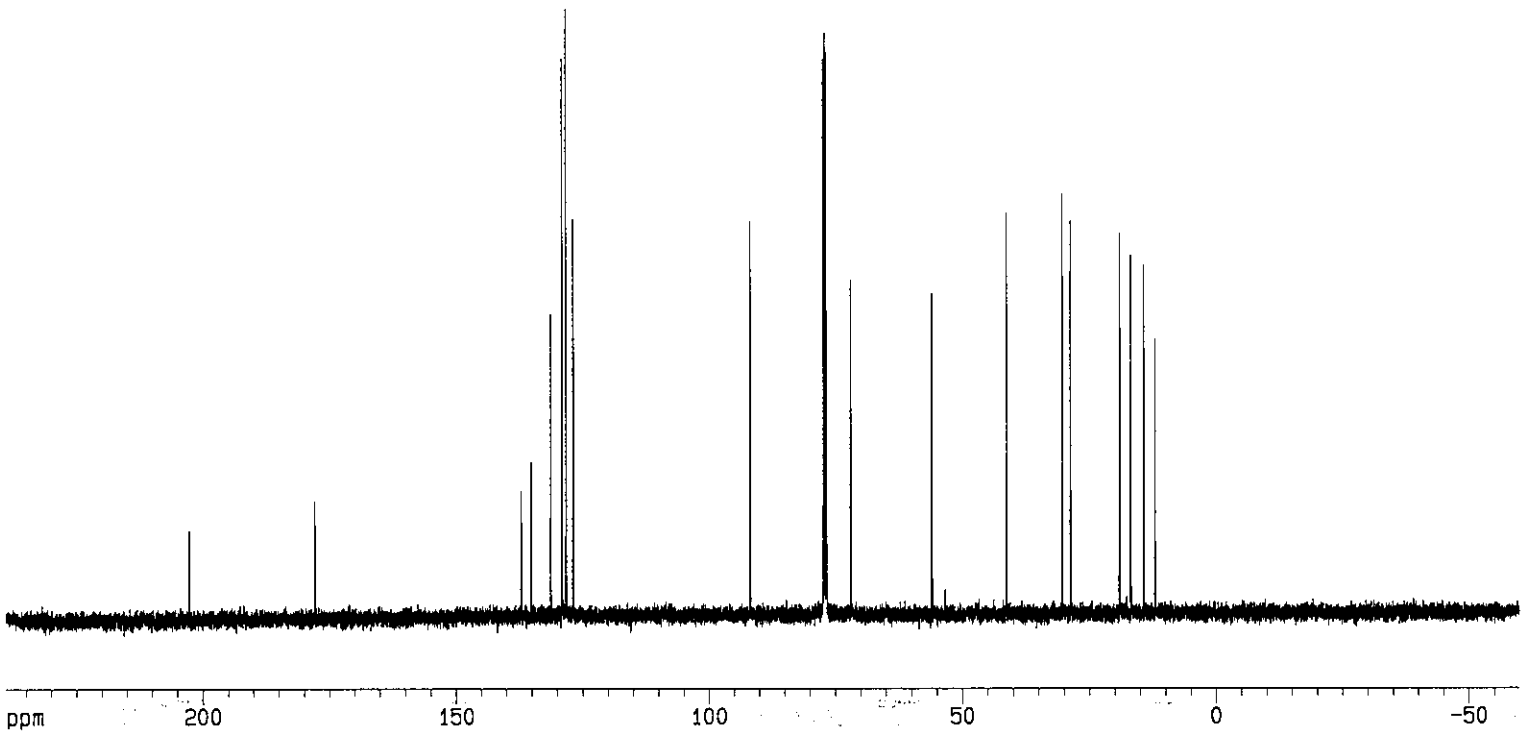
Vijaya Bhasker Gondi was born in Amrabad, India in 1979. He received his B.Sc. and M.Sc. in Industrial Chemistry from Indian Institute of Technology, Kharagpur, in 2002, and in the same year went to the University of Chicago for graduate studies. He completed his Ph.D. in chemistry with Prof. Viresh Rawal in 2008, working on the asymmetric catalysis of carbon-carbon bond forming reactions through hydrogen bonding. Soon thereafter, he began his postdoctoral studies at The Scripps Research Institute, La Jolla, with Prof. K. C. Nicolaou.

gv-os-step1dis33c13









Current Data Parameters

NAME	OS-step2flc13
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20080116
Time	18.00
INSTRUM	spect
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PULPROG	zgdc
TD	75184
SOLVENT	CDCl3
NS	1490
DS	0
SWH	37593.984 Hz
FIDRES	0.500026 Hz
AQ	0.9999972 sec
RG	8192
DW	13.300 usec
DE	7.50 usec
TE	300.0 K
D1	0.10000000 sec
d11	0.03000000 sec

========== CHANNEL f1 ==========

NUC1	13C
P1	4.60 usec
PL1	0.00 dB
SFO1	125.7690572 MHz

========== CHANNEL f2 ==========

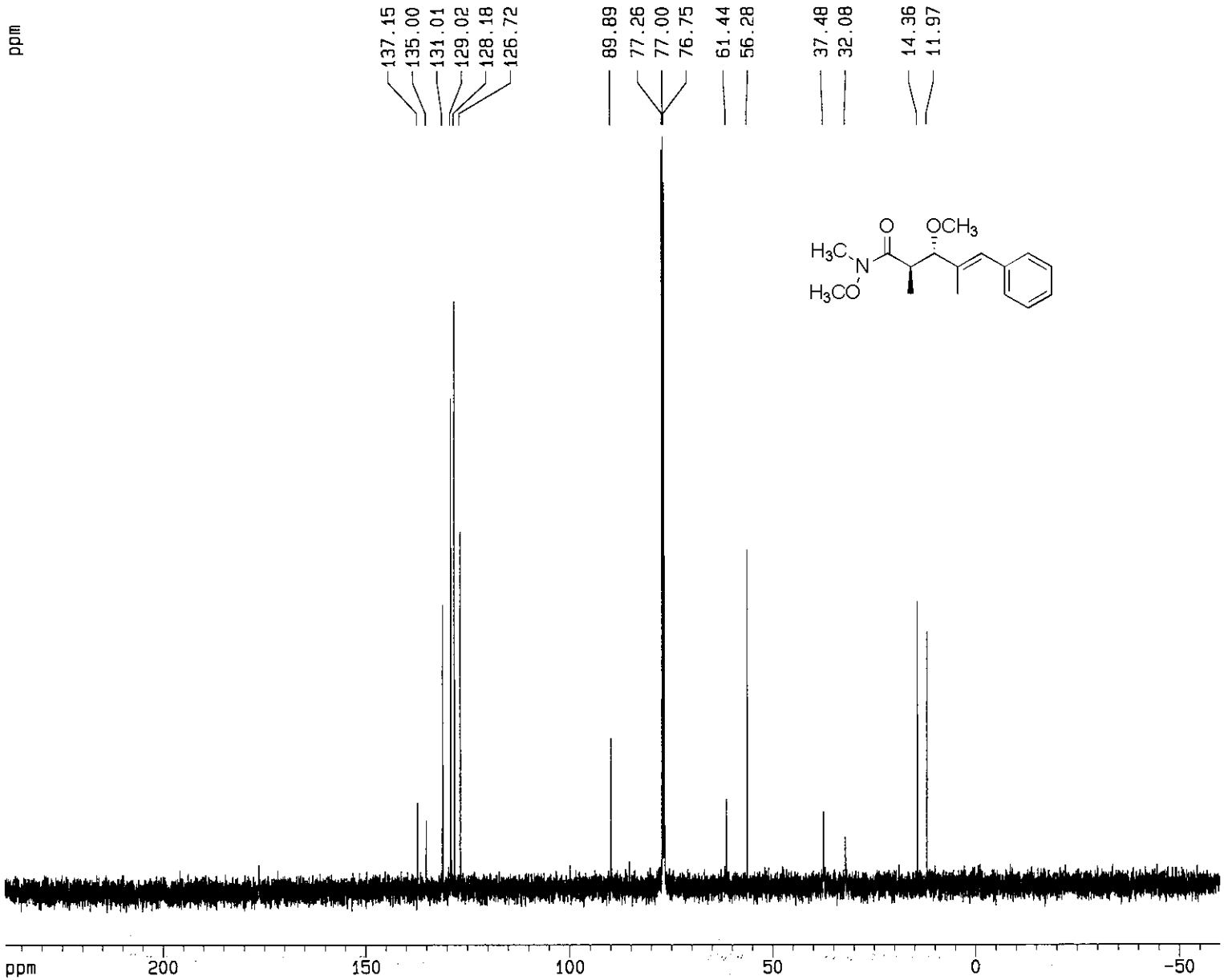
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	120.00 dB
PL12	19.00 dB
SFO2	500.1320005 MHz

F2 - Processing parameters

SI	32768
SF	125.7577941 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
F1P	239.032 ppm
F1	30060.14 Hz
F2P	-59.908 ppm
F2	-7533.85 Hz
PPMCM	14.94698 ppm/cm
HZCM	1879.69934 Hz/cm



Current Data Parameters

NAME	os-step3-crpro
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20080119
Time	13.35
INSTRUM	spect
PROBHD	5 mm QNP 1H
PULPROG	zgdc
TD	75184
SOLVENT	CDCl3
NS	1279
DS	0
SWH	37593.984 Hz
FIDRES	0.500026 Hz
AQ	0.9999972 sec
RG	8192
DW	13.300 usec
DE	7.50 usec
TE	300.0 K
D1	0.10000000 sec
d11	0.03000000 sec

========== CHANNEL f1 ==========

NUC1	13C
P1	4.60 usec
PL1	0.00 dB
SFO1	125.7690572 MHz

========== CHANNEL f2 ==========

CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	120.00 dB
PL12	19.00 dB
SFO2	500.1320005 MHz

F2 - Processing parameters

SI	32768
SF	125.7577929 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

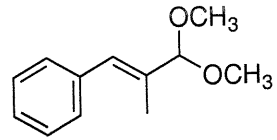
1D NMR plot parameters

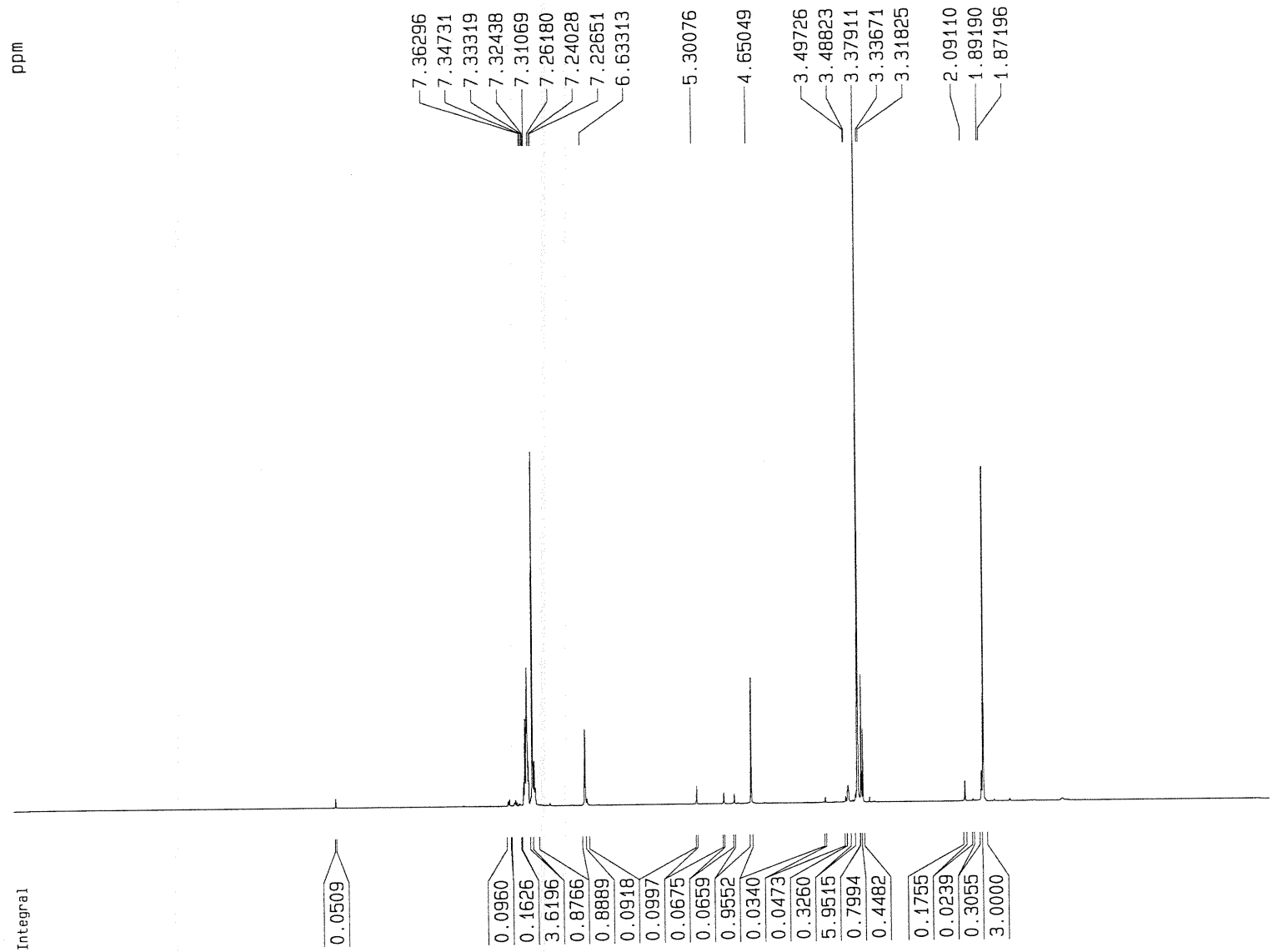
CX	20.00 cm
F1P	239.041 ppm
F1	30061.28 Hz
F2P	-59.898 ppm
F2	-7532.70 Hz
PPMCM	14.94698 ppm/cm
HZCM	1879.69922 Hz/cm

~14:1

Crude

~95% Conversion





Current Data Parameters

NAME	OS-2-step1cr
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20080508
Time	11.40
INSTRUM	spect
PROBHD	5 mm BBI 1H-BB
PULPROG	zg
TD	45044
SOLVENT	CDCl3
NS	32
DS	0
SWH	7507.507 Hz
FIDRES	0.166671 Hz
AQ	2.9999804 sec
RG	57
DW	66.600 usec
DE	4.50 usec
TE	300.0 K
D1	1.00000000 sec

======== CHANNEL f1 ========

NUC1	1H
P1	5.80 usec
PL1	0.00 dB
SFO1	499.8779993 MHz

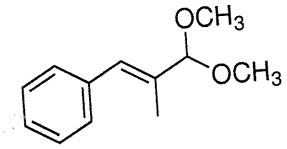
F2 - Processing parameters

SI	32768
SF	499.8750140 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	15.00 cm
F1P	13.481 ppm
F1	6739.04 Hz
F2P	-1.537 ppm
F2	-768.46 Hz
PPMCM	0.75094 ppm/cm
HZCM	375.37537 Hz/cm

Step I
Distilled
major fraction
~ 10:1



Current Data Parameters

NAME	OS2-step1dis2
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20080519
Time	8.04
INSTRUM	spect
PROBHD	5 mm BBI 1H-BB
PULPROG	zg
TD	45044
SOLVENT	CDCl3
NS	4
DS	0
SWH	7507.507 Hz
FIDRES	0.166671 Hz
AQ	2.9999804 sec
RG	45.3
DW	66.600 usec
DE	4.50 usec
TE	300.0 K
D1	1.00000000 sec

======== CHANNEL f1 ========

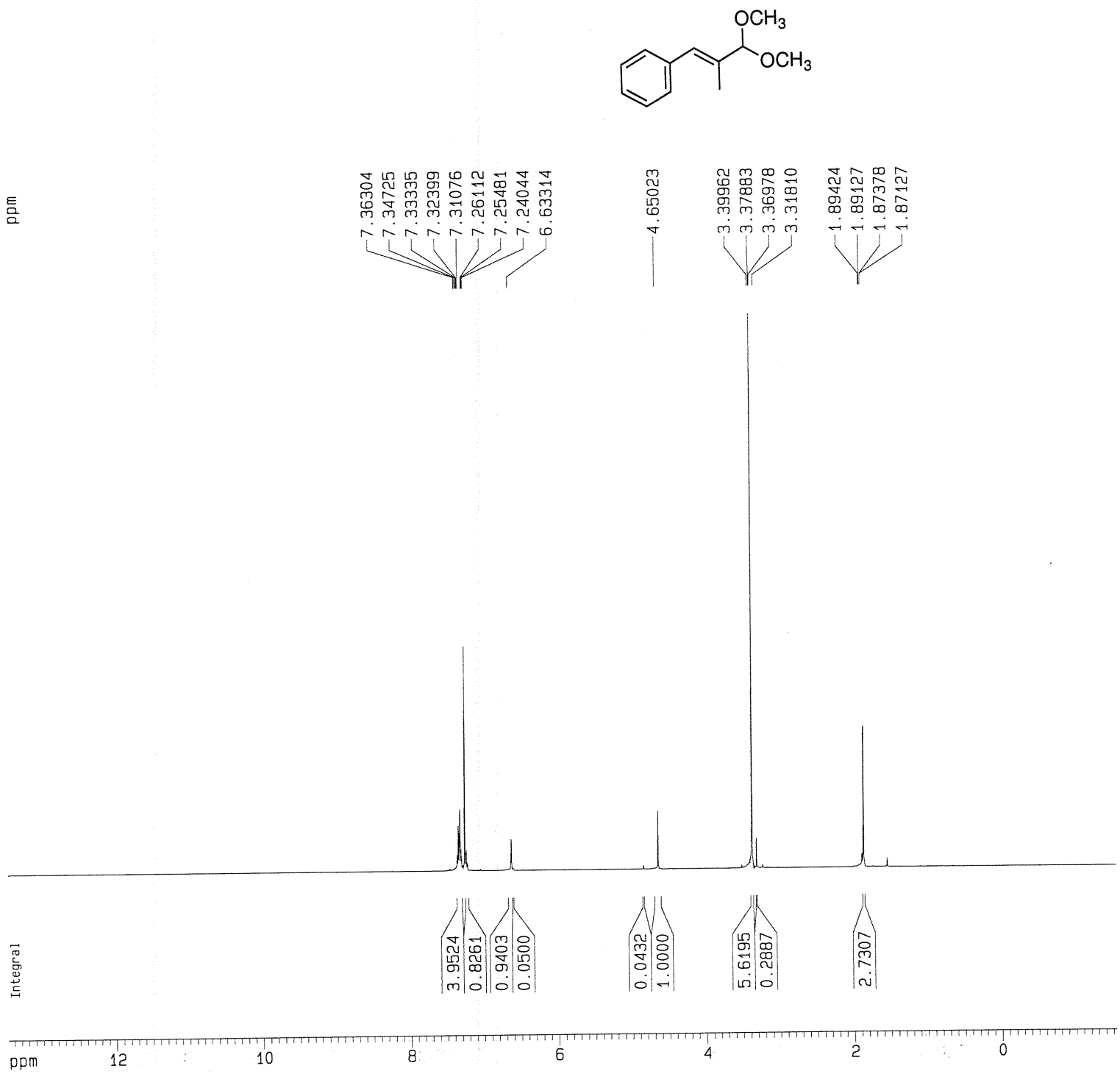
NUC1	1H
P1	5.80 usec
PL1	0.00 dB
SFO1	499.8779993 MHz

F2 - Processing parameters

SI	32768
SF	499.8750140 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	13.481 ppm
F1	6739.04 Hz
F2P	-1.537 ppm
F2	-768.47 Hz
PPMCM	0.75094 ppm/cm
HZCM	375.37537 Hz/cm



~23:1

final fraction

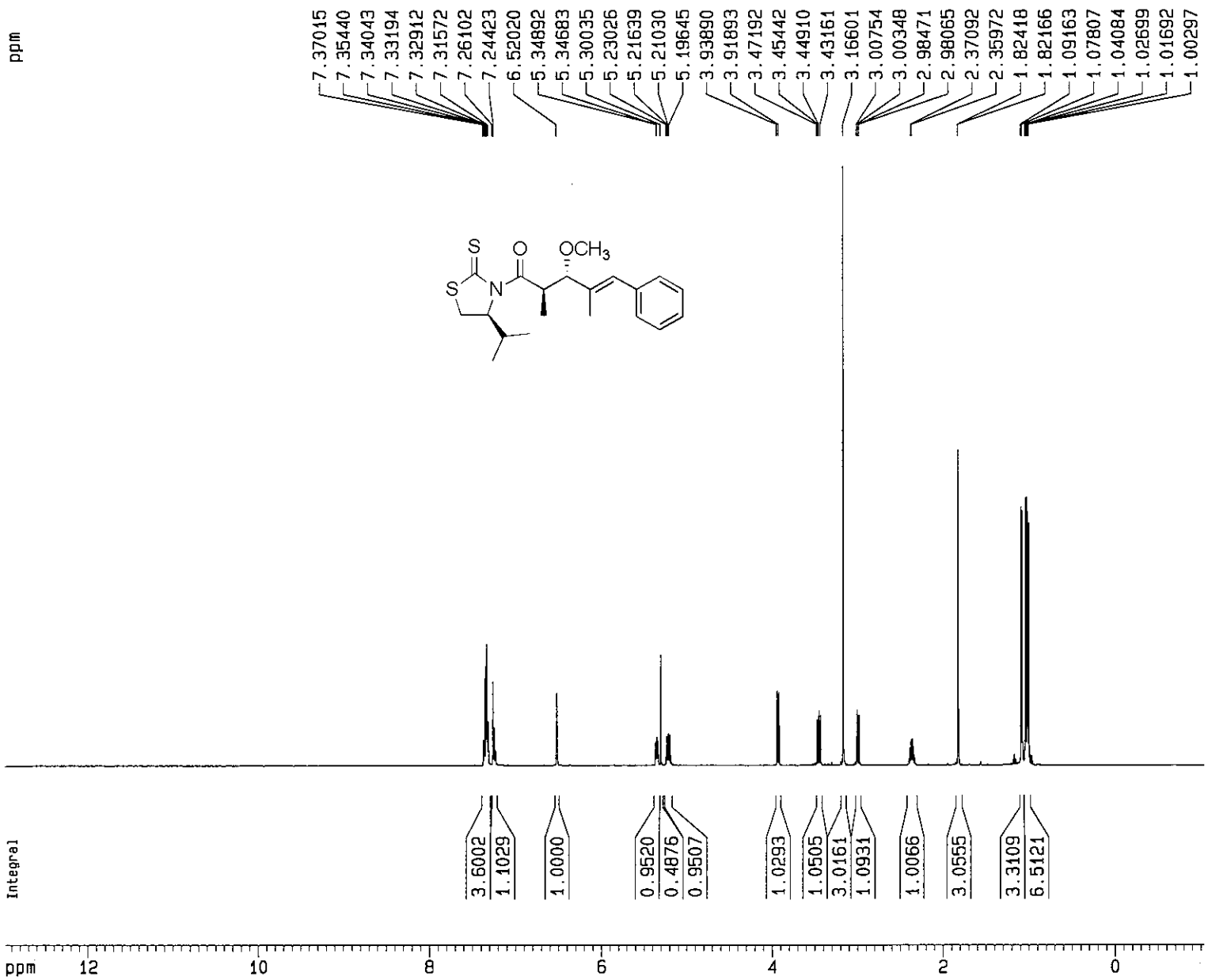
Current Data Parameters
NAME OS2-step1dis3
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20080519
Time 8.09
INSTRUM spect
PROBHD 5 mm BBI 1H-BB
PULPROG zg
TD 45044
SOLVENT CDCl3
NS 4
DS 0
SWH 7507.507 Hz
FIDRES 0.166671 Hz
AQ 2.9999804 sec
RG 80.6
DW 66.600 usec
DE 4.50 usec
TE 300.0 K
D1 1.00000000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 5.80 usec
PL1 0.00 dB
SFO1 499.8779993 MHz

F2 - Processing parameters
SI 32768
SF 499.8750140 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 13.481 ppm
F1 6739.04 Hz
F2P -1.537 ppm
F2 -768.47 Hz
PPMCM 0.75094 ppm/cm
HZCM 375.37537 Hz/cm



Current Data Parameters

NAME	os-step2-fl
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20080116
Time	17.55
INSTRUM	spect
PROBHD	5 mm BBI 1H-BB
PULPROG	zg
TD	28010
SOLVENT	CDCl3
NS	4
DS	0
SWH	7002.801 Hz
FIDRES	0.250011 Hz
AQ	1.9999640 sec
RG	64
DW	71.400 usec
DE	4.50 usec
TE	300.0 K
D1	1.00000000 sec

======== CHANNEL f1 ========

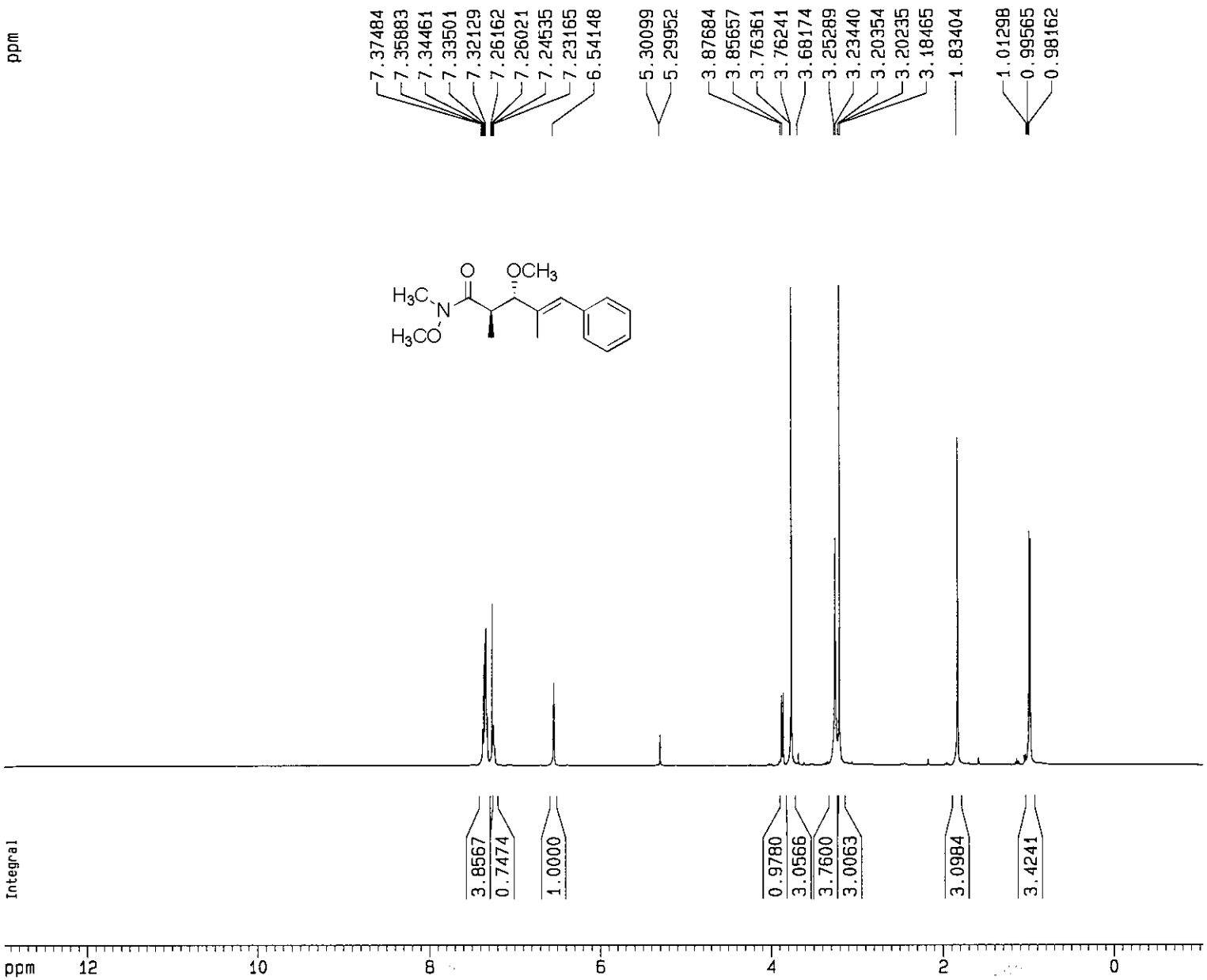
NUC1	1H
P1	5.60 usec
PL1	0.00 dB
SFO1	499.8779993 MHz

F2 - Processing parameters

SI	32768
SF	499.8750141 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	12.976 ppm
F1	6486.59 Hz
F2P	-1.033 ppm
F2	-516.21 Hz
PPMCM	0.70046 ppm/cm
HZCM	350.14005 Hz/cm



Current Data Parameters

NAME	os-step3-crprod
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20080119
Time	13.19
INSTRUM	spect
PROBHD	5 mm BBI 1H-BB
PULPROG	zg
TD	28010
SOLVENT	CDCl3
NS	4
DS	0
SWH	7002.801 Hz
FIDRES	0.250011 Hz
AQ	1.9999640 sec
RG	256
DW	71.400 usec
DE	4.50 usec
TE	300.0 K
D1	1.00000000 sec

======== CHANNEL f1 ========

NUC1	1H
P1	5.80 usec
PL1	0.00 dB
SFO1	499.8779993 MHz

F2 - Processing parameters

SI	32768
SF	499.8750141 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	8.00 cm
F1P	12.976 ppm
F1	6486.59 Hz
F2P	-1.033 ppm
F2	-516.21 Hz
PPMCM	0.70046 ppm/cm
HZCM	350.14005 Hz/cm