An Efficient Approach for the Synthesis of Threo-α-Amino Epoxides

Thesis submitted in partial fulfillment of the requirements
for the award of the degree of

Masters of Science
In

Chemistry

Submitted by

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Under the guidance of

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July 2013

Candidate's Declaration

I hereby declare that the work being presented in the dissertation entitled **"An Efficient Approach for the Synthesis of Threo-α-Amino Epoxides"**in partial fulfillment of the requirements for the award of the degree of Masters in Chemistry, School of Chemistry and Biochemistry, Thapar University, Patiala, is my own work during the period of January to July 2013, under the supervision of **Dr. Satyendra Kumar Pandey**. My thesis has not previously formed the basis for award of any degree, diploma, or other similar title or recognition.

Bandhana Sharma

Patiala **Bandhana Sharma**

Date: 15th July 2013

This is to certify that the above statement made by the candidate is correct and true to the best of our knowledge.

15.07.2013

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Certificate

This is to certify that the project entitled **"An Efficient Approach for the Synthesis of Threo-α-Amino Epoxides."** being submitted by **Ms. Bandhana Sharma** in the partial fulfillment of the requirement for the award of the degree of Masters of Science in the School of Chemistry and Biochemistry, Thapar University, Patiala, is a bonified work carried under the supervision of **Dr. Satyendra Kumar Pandey** and no part of this project has been submitted for award of any other degree by me.

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LIST OF CONTENT

1.Introduction

Non-racemic α-amino epoxides are versatile synthetic modules since they undergo regio- and stereoselective attack by various nucleophiles. Nucleophilic ring opening of such epoxides provides a powerful synthetic core unit for the chiral 1,2-amino alcohols and has found widespread application in the synthesis of natural products[1], non-peptidic protease inhibitors[2,3,4], synthesis of hydroxyethylamine, hydroxyethylene dipeptide isosters, anti cancer and antibiotic products[5-8], novel amino acids[9-10], NMDA antagonists[11], potent inhibitors of aspartic acid proteases such as rennin[12] or HIV-protease[13] and are also selective cysteine protease inactivators, while exhibiting no inhibitory activity towards serine proteases[14-16]. In view of such varied utilities, considerable effort has been directed in recent years towards stereoselective synthesis of non-racemic *threo*- and *erythro*-α-aminoepoxides.[17]

The first synthesis of an α-aminoepoxide (derived from an α-amino acid) was non-stereoselective, yielding a racemic mixture of the product. There are several methods currently available by which *erythro*-α-aminoepoxides can be prepared with high diastereoselectivities (90% de)[18]. They include reduction of N-protected-α-aminohalomethyl ketones[19,20] or peptidyl bromomethanes,[21] condensation of dihalomethane with N,N-dibenzyl-α-amino aldehydes,[22] cyclization of 3-amino-1,2-diols,[23] epoxidation of N,N-doubly protected α-amino aldehydes, by sulfonium ylides,[24] and reductive amination of α-ketoepoxides[25] yield preferentially the corresponding erythro-α-amino- or peptidylepoxides. These synthetic routes were applied almost exclusively to hydrophobic α-aminoepoxides, bearing only simple alkyl or aryl side chains, either because they satisfied some specific requirements or in order to avoid synthetic complications. However, in contrast, the stereoselective synthesis of *threo*-α-aminoepoxides is poorly documented and confined to less than a handful of methods that are either lengthy and/or plagued with methodological problems, thus representing a major synthetic hurdle in contemporary asymmetric synthesis. At present, *threo*-α-amino epoxides are best prepared via (i) diastereoselective epoxidation of enantiopure secondary allyl amines (prepared by Wittig reaction of enantiopure α-aminoaldehydes, either the phosphorus ylides of acetone, ethyl acetate, acetonitrile, etc., or phosphonates),[26,27] (ii) reactions of enantiopure *N*-Boc α-amino aldehydes with sulfonium/arsonium ylides,[28,29] and (iii) LAH reduction of chiral pool derived *N,N*-dibenzyl α-amino chloromethylketones followed by MeLi induced epoxide formation.[30] While the former two suffer from methodological problems arising from handling the sensitive

chemicals and racemization-prone α-aminoaldehydes, the latter method which, although avoids the use of α-aminoaldehydes, nevertheless requires a non-conventional procedure for the preparation of the starting chloromethylketones.

In view of these problems, and given the enormous potential of *threo*-α-aminoepoxides in the synthesis of *syn*-1,2- amino alcohols which are common structural units present in a number of anti-HIV dipeptide isosteres and new generation pharmaceutics, it is highly desirable that new and improved procedures be developed for their stereoselective synthesis. To this end, we now describe a facile new synthetic protocol which, while using conventional and chemically stable intermediates, delivers *threo*-α-amino,β-hydroxyepoxides **1a** in a short synthetic pathway and with high diastereoselectivity than erythro-α-amino,β-hydroxyepoxide **1b** (Figure 1).

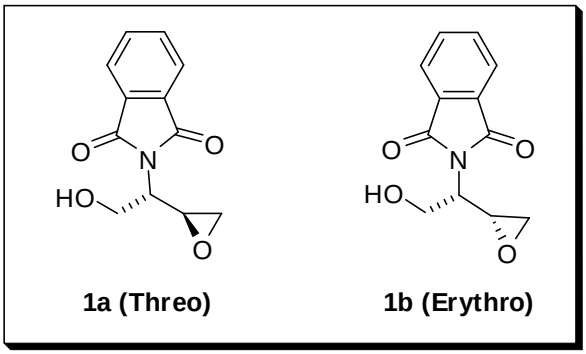
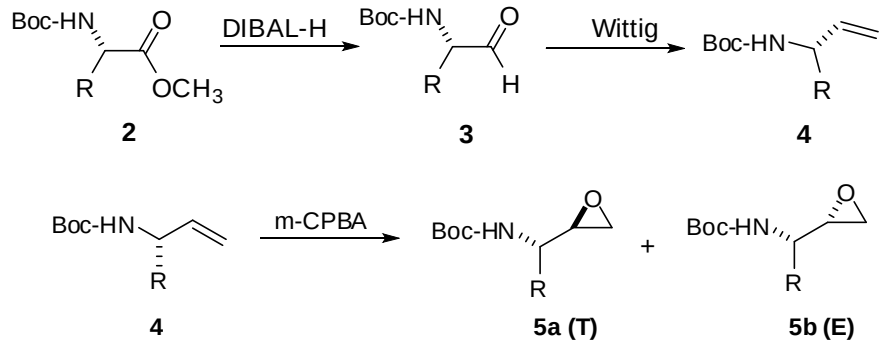


Figure 1.

1. Review of literature

Luly *et al.* (1987) [26]

Luly and co-worker reported an efficient approach for the synthesis, key steps include the synthesis of amino aldehyde **3** by reduction (DIBAL-H) of ester **2** or by oxidation of N-protected amino alcohol.

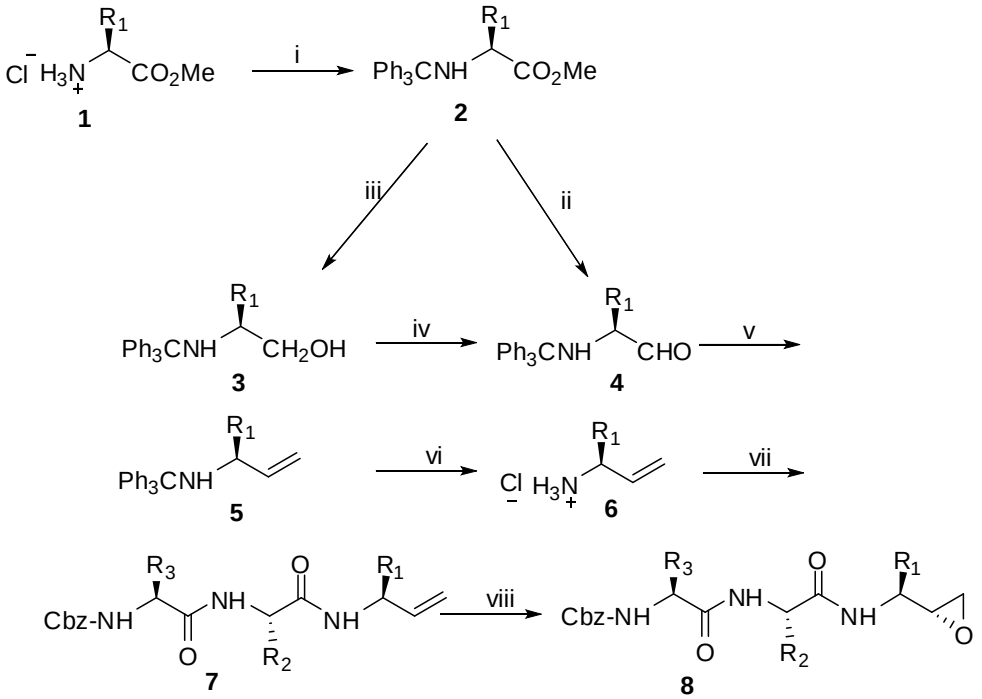


Scheme 1.

The olefination of aldehyde **3** with unstabilized ylides gave the protected allylic amine **4** in good to excellent optical purity. As desired, epoxidation of olefin **4** with 3-chloroperoxybenzoic acid afforded mainly the threo stereochemistry **5a**.

Albeck *et al.* (1994) [28]

Amnon Albeck' and co-worker reported a synthetic route for the preparation of *threo* peptidyl epoxides (Scheme 2). Tritylation of α-amino esters **1** was followed by DIBAL-H reduction. *N*-trityl-α-amino aldehydes **4** were obtained either directly or, in the case of full reduction, after a subsequent Swern oxidation of the corresponding alcohols **3**. Both steps proceeded in

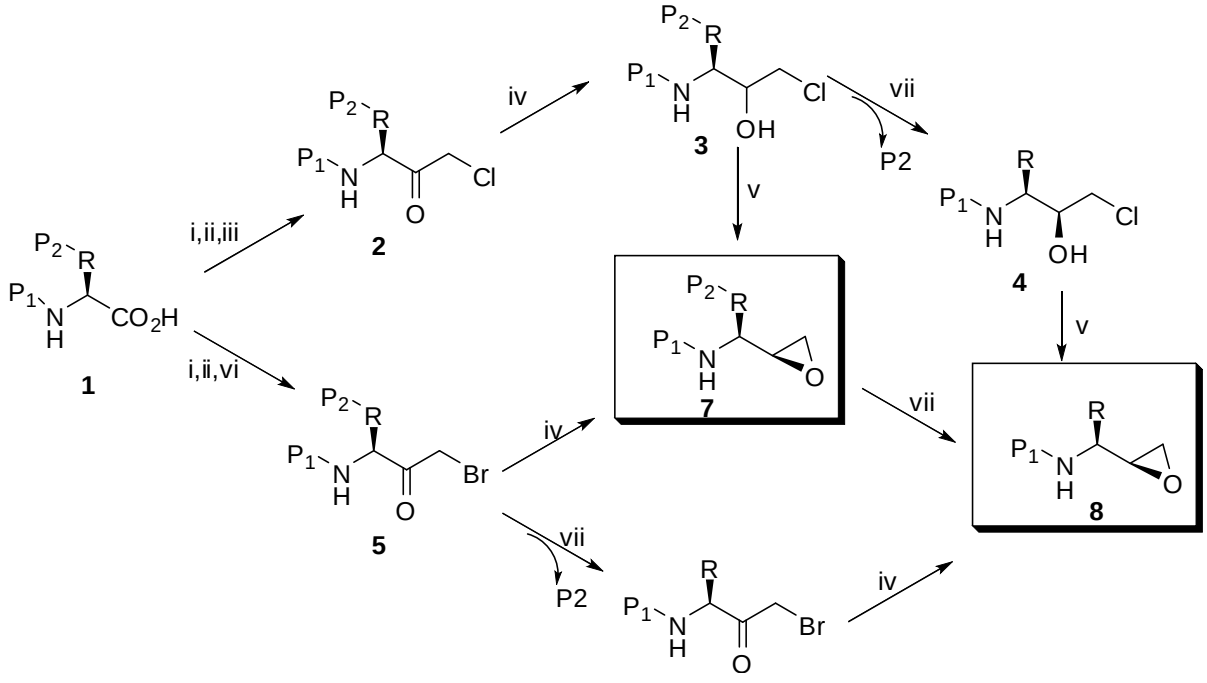


Scheme 2. Reagents and conditions: (i) Ph_3CCl, Et_3N, CH_2Cl_2; (ii) DIBAL-H, toluene; (iii) LAH, Et_2O; (iv) DMSO, $(COC1)_2$; (v) $Ph_3P{=}CH_2$, THF (vi) HC1, acetone; (vii) Cbz-aa_3aa_2, DCC, NHS; (viii) *m*-CPBA, CH_2Cl_2.

very high yield**.** Wittig reaction of the *N*-trityl-a-amino aldehydes **4** with methylidene triphenylphosphorane afforded the corresponding olefins **5** in high yield**.** Deprotection under acidic conditions yielded allylamines **6.** Reprotection (form *N*-Boc or *N*-Cbz allylamines) and epoxidation furnished the known *threo N*-protected α-amino epoxides.

Albeck *et al.* (1997) [18]

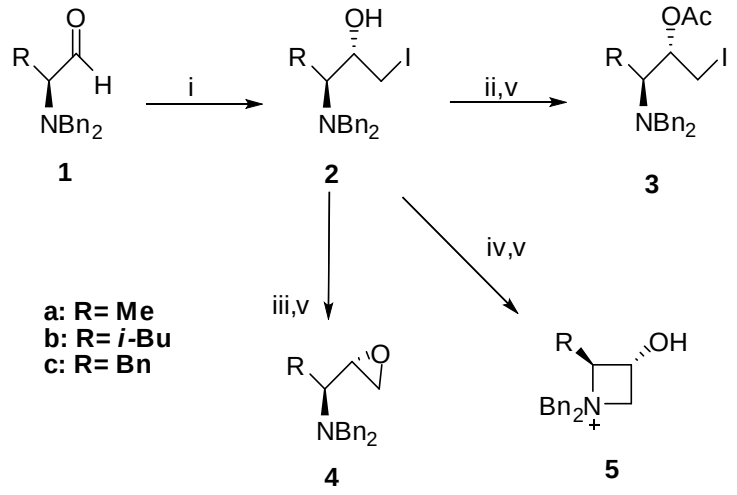
Amnon Albeck and and co-worker reported an efficient approach for the synthesis of erythro *N*-protected α-amino epoxides, which is based on a key stereoselective reduction of α-amino haloketones. It utilizes the chirality of α-amino acids to induce a preferred configuration at the new adjacent chiral center. The fate of the reduction depends very much on the halide, chloroketones being reduced to the corresponding chlorohydrins and bromoketones being reduced and spontaneously cyclized to the corresponding epoxides under the reaction conditions. In this study, they used the α-amino acids bearing a protected functional group at their side chains were subjected to the same procedure, yielding the corresponding doubly protected α-amino epoxides. In addition, removal of the side chain protecting group either prior or subsequent to the epoxide formation was also carried out. This general approach is summarized in Scheme 3.



Scheme 3. Reagents and conditions: (i) $ClCO_2CH_2CHMe_2$; NMM. THF; (ii) CH_2N_2, Et_2O; (iii) HCl (g); (iv) $NaBH_4$, EtOH; (v) NaOMe, MeOH; (vi) HBr (aq); (vii) selective deprotection: 1,4-cyclohexadiene, Pd/C, EtOH; or TFA, CH_2CI_2.

Jose M. Concellon *et al.* (1997) [30]

Jose M. Concellon and co-worker reported the synthesis of erythro-α-aminoepoxide in which they treated a mixture of diiodomethane and different *N*,*N*-dibenzylated R-amino aldehydes **1** with samarium metal at 0°C gave, after hydrolysis, the corresponding iodohydrins **2** (Scheme 4). When iodohydrins were taken to dryness they became unstable and decomposed to a mixture of several products. In order to characterize compounds **2** they were transformed into their *O*-acetyl derivatives **3** by treatment with acetic anhydride at room temperature, and these could be isolated and purified by flash column chromatography. Reaction of iodohydrins **2** with NaH at room temperature led to *erythro* amino epoxides **4**. The stereochemistry of amino epoxides **4** was established unambiguously by comparison of their NMR spectra with those previously reported. The iodomethylation of amino aldehydes **1** with Sm/CH_2I_2 took place with good diastereoselectivity. The diastereomeric excess (de) of compounds **2a-c** was higher than 80%, as determined by 300-MHz ^1H NMR and quantitative ^{13}C NMR spectroscopy.

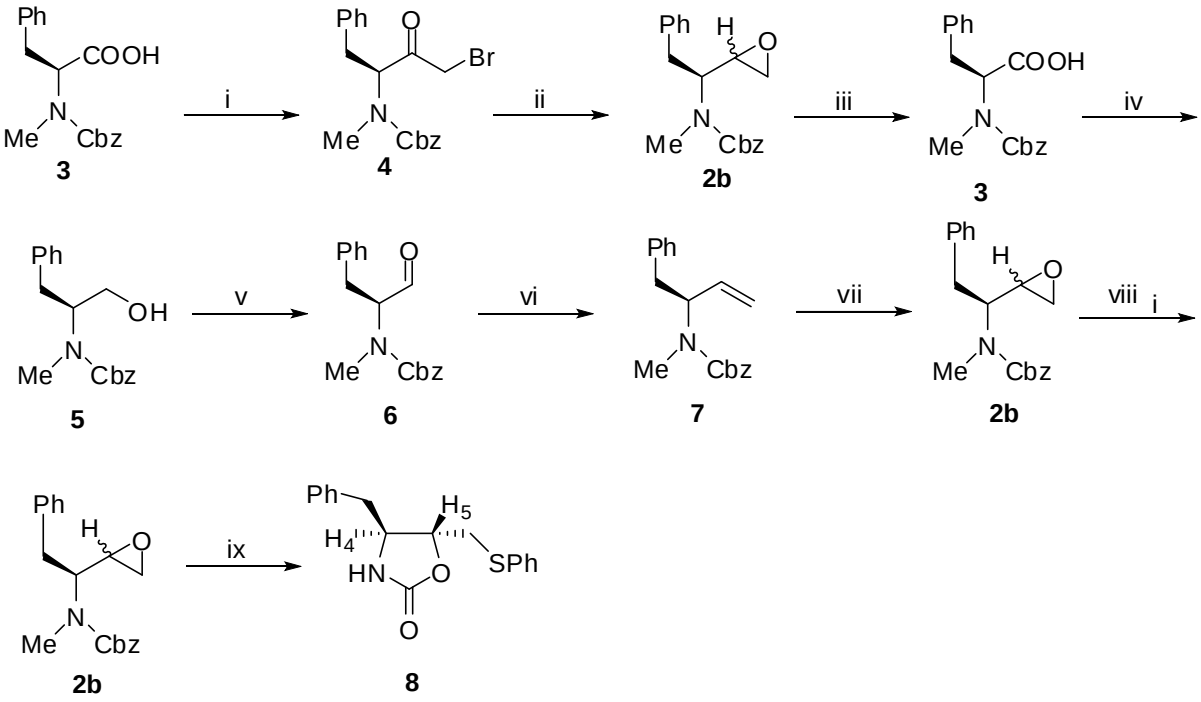


Scheme 4. Reagents and conditions: (i) Sm^0/CH_2I_2, THF, 0 °C, 40 min, then H_3O^+; (ii) Ac_2O, pyridine, rt; (iii) NaH, CH_2Cl_2, rt; (iv) $AgBF_4$, Et_2O, rt; (v) H_2O.

Ernst Schaumann *et al.* (1998) [1]

Ernst Schaumann and co-worker reported the synthesis of *threo N*-methyl oxirane **3** from (*S*)-*N*-methyl phenylalanine by bromoketone reduction or by epoxidation routes. The most extensively used pathways for the synthesis of amino epoxides are the epoxidation of the corresponding allyl amine for the *threo* isomer **3.** Epoxidation of olefin **6** gave the diastereomer **3** in only 39% yield along with considerable decomposition. Similar side

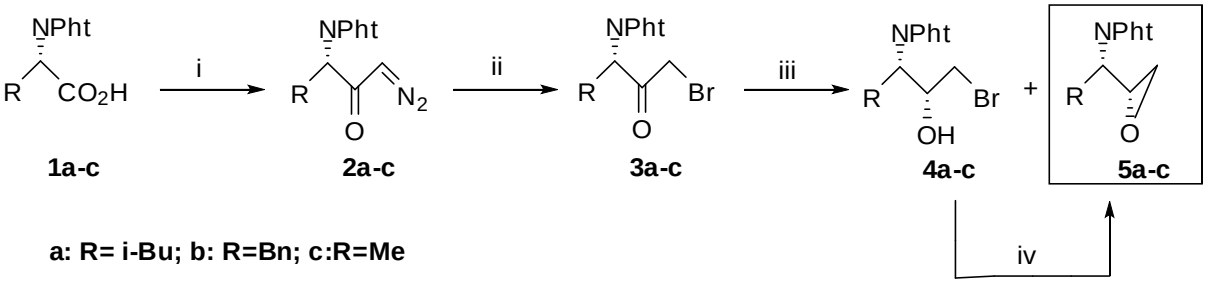
reactions leading to oxazolidinones and particularly decomposition had been observed by Rich on oxidation of an *N*-Boc- *N*-methyl derivate. To establish the relative configuration of the isolated oxirane, epoxide **3** was treated with sodium thiophenoxide leading to substituted *N*-methyl-oxazolidinone **7**.



Scheme 4. i) NMM/*i*-BuCO_2Cl/THF, CH_2N_2, 48% HBr, 72%, ii) $NaBH_4$/EtOH, -78^{0}C→RT, 78%, iii) BH_3/THF, 0^{o}C, 2h, 62%, iv) Py-SO_3/NEt_3/CH_2Cl_2/DMSO, 0^{o}C→RT, 0.5h, 95%) $Ph_3PCH_3^+$ Br^- /KHMDS, THF/DMSO, -78^{o}C→ 40^{o}C, 12h, 85%, vi) *m*-CPBA/CH_2Cl_2, 0^{o}C →RT , 39% vii) PhSH/NaH/DMF, 2h , 88%.

Sengupta, S. *et al.* (1999)[31]

Saumitra Sengupta and co-worker reported the synthesis of *threo*-α-aminoepoxides started with the readily available *N*-phthaloyl (*N*-Pht) α-amino acids **1a**–**c**. The corresponding enantiopure α-amino diazoketones **2a**–**c** were prepared in good yields (60–70%) by



Scheme 5. Reagents and conditions: (i) $SOCl_2$, benzene, reflux, then CH_2N_2, ether, 0°C; (ii) 47% HBr, ether, 0°C; (iii) LiAlH(OBu-*t*)$_3$ (2 equiv.), THF, −20°C; (iv) NaH, THF, rt.

conventional procedures and were easily converted *via* HBr treatment (47% HBr, ether, 0°C) to the corresponding bromoketones **3a**–**c** in near quantitative yields (Scheme 5). The latter were subsequently reduced with LiAlH(OBu-*t*)$_3$ (2 equiv., THF, −20°C) to produce the respective bromohydrins **4a**–**c** (60–62%) with virtually complete *syn*-selectivity (*syn*:*anti*=95:5). LiAlH(OBu-*t*)$_3$, a bulky and highly chemoselective reducing agent, was found to be absolutely essential for this reduction since other reducing agents viz. $NaBH_3$(CN) or $NaBH_4$ caused extensive attack on the phthaloyl moiety. Small amounts of the *threo*-epoxides **5a**–**c** were also produced in this reduction step *via* in situ cyclization of the bromohydrins. Although the bromohydrins could be easily separated from the epoxides and cyclized to the latter, separately with NaH, they found it more convenient to treat this product mixture with NaH in THF at room temperature which smoothly produced the *threo*-α-amino epoxides **5a**–**c** in good overall yields (62–70%), starting from the respective bromoketones.
The opposite result of the reduction of **3** leading to the *threo* and not to the expected *erythro* isomer may be explained by the Felkin-Anh (Figure 4) and the chelated Cram models (Figure 3) for addition reactions to a-chiral carbonyl compounds (Scheme 5). In the case of the unmethylated α- bromoketone the *erythro* selectivity is controlled by the formation of a chelate intermediate from the α-heterosubstituted carbonyl compound and the organometallic reagent.

Chelated Cram model[32]

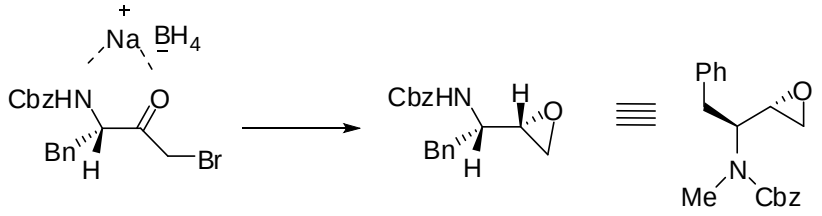


Figure 2.

Felkin Anh model[33,34]

The high *syn*-selectivity observed in the bromoketone reductions can be rationalized by a Felkin non-chelation model such as **3**, in which the *N*-Pht moiety acts as a large electronegative group and the bulky reducing agent attacks this TS from the less hindered side. An alternative TS that would have led to the *anti*-bromohydrins is disfavored since it

would lead to severe non-bonding and dipolar repulsions between the *N*-Pht and the carbonyl groups. It is worthy of mention that such a high degree of *syn*-selectivity in the reduction of α-amino ketones has otherwise been observed only with the *N*,*N*-dibenzyl systems. The present observation that *N*-Pht α-amino ketones, having a more conventional amino protecting group than the *N*,*N*-Bn_2 system, can also be reduced with high *syn*selectivity, thereby promises a more attractive synthetic protocol for homochiral *syn*-1,2-amino alcohols, in general.

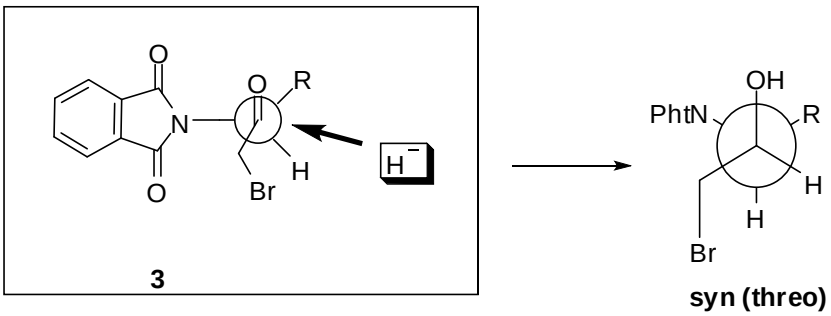


Figure 3.

2. Present Work

Objective:

Non-racemic α-amino epoxides are versatile synthetic modules since they provides a powerful synthetic core unit for homochiral 1,2-amino alcohols and in the synthesis of natural products. Various methods for the synthesis of *threo*-α-amino,β-hydroxyepoxide **1a** and *erythro*-α-amino,β-hydroxyepoxide **1b** have been documented in the literature. Most of these approaches employed chiral pool starting materials. As part of our research program aimed at developing enantioselective synthesis of α-amino epoxides, we became interested to develop a new and highly enantioselective synthesis of α-amino epoxides employing (*S*,*S*)-DACH-Phenyl Trost Ligand **2** (Figure 4) and *m*-CPBA as the source of diasteroselective epoxidation.

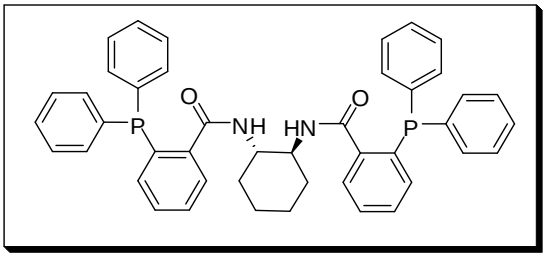
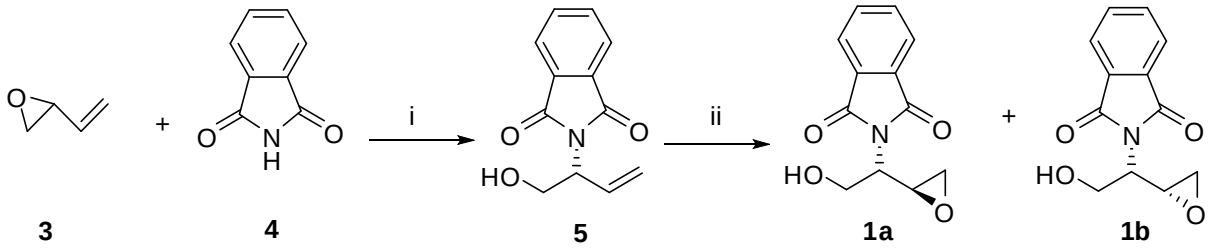


Figure 4. Structure of (*S*,*S*)-DACH-Phenyl Trost Ligand **2**.

3. Results and discussion

The synthesis of *threo*-α-amino epoxides **1a** started from commercially available pthalimide **4** as illustrated in Scheme 8. The compound pthalimide **4** was treated with butadiene monoepoxide **3** using (*S*,*S*)-DACH-Phenyl Trost Ligand **2** to afford 2-(*R*)-*N*-phthalimido-3-bueten-1-ol **5** as a single isomer in 95% yield with 100% ee. With enantiomerically pure 2-(*R*)-*N*-phthalimido-3-bueten-1-ol **5** in hand, we then subjected it to epoxidation with *m*-CPBA to afford the *threo*-α-amino epoxides **1a** and *erythro*-α-amino epoxides **1b** in excellent yield of 85% (80% de). The IR spectrum of 2-(*R*)-*N*-phthalimido-3-bueten-1-ol **5** shows the



Scheme 8. Reagents and conditions: i) (*S*,*S*)-DACH-naphtyl, 0.4 mol % $[n^3\text{-}(C_3H_5)PdCl]_2$, Na_2CO_3 in DCM, rt, 14h; ii) *m*-CPBA, rt, 12h.

hydroxyl peak at 3460 cm^{-1}, carbonyl absorption at 1774 cm^{-1} and olefinic C=C strecting at 1708 cm^{-1}. The proton NMR spectrum of 2-(*R*)-*N*-phthalimido-3-bueten-1-ol **5** indicates the aromatic peak at 7.74 (dd, two protons), 7.85 (dd, two protons) hydrogen at chiral carbon at 4.15 (ddd, one proton) and olefinic hydrogen at 6.12-6.19 (multiplet, one proton). The ^{13}C NMR spectrum of 2-(*R*)-*N*-phthalimido-3-bueten-1-ol **5** shows carbonyl carbon at 168.7, olefinic carbon at 131.8 and chiral carbon appeared at delta 56. The DEPT-135 NMR of 2-(*R*)-*N*-phthalimido-3-bueten-1-ol **5** gave two peaks showing two $–CH_2$ at delta 63.0 and 119.0. The IR spectrum of **1a** gave hydroxyl peak at 3467 cm^{-1}, carbonyl absorption at 1775 cm^{-1} and aromatic C=C strecting at 1713 cm^{-1}. The proton NMR spectrum of **1a** gave methoxy peak at 4.04-4.08 (multiplet, one proton), hydrogen at chiral carbon at 4.11-4.15 (multiplet, two proton) and 2.93 (triplet, one proton). The ^{13}C NMR of **1a** gave carbonyl carbon at 168.6 and chiral carbon appeared at δ 49.7 and δ 55.8. The IR spectrum of **1b** gave hydroxyl peak at 3465 cm^{-1}, carbonyl absorption at 1774 cm^{-1} and aromatic C=C strecting at 1712 cm^{-1}. The proton NMR spectrum of **1b** gave methoxy peak at 4.09 (dd, two proton), hydrogen at chiral carbon at 4.30 (quartet, two protons) and 2.80 (triplet, one proton). The ^{13}C

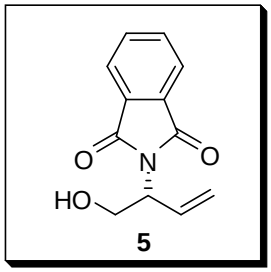
NMR of **1b** gave carbonyl carbon at 168.7 and chiral carbon appeared at δ 49.6 and δ 55.6. The DEPT-135 NMR of **1a** and **1b** gave two peaks showing two $-CH_2$ at delta 46.0 and 61.0.

4. Conclusion

In conclusion, a practical and distereoselective synthesis of *threo*-α-amino epoxides **1a** has been achieved employing (*S*,*S*)-DACH-Phenyl Trost Ligand and *m*-CPBA epoxidation. The synthesis strategy describe as significant potential for further extension to other isomers and related analogues including natural products, non-peptidic protease inhibitors, synthesis of hydroxyethylamine, hydroxyethylene dipeptide isosters, anti cancer and antibiotic products, novel amino acids, NMDA antagonists, potent inhibitors of aspartic acid proteases such as rennin or HIV-protease.

5. Experimental section

6.1 Synthesis of 2-(*R*)-*N*-phthalimido-3-bueten-1-ol 5:



5

In a 250 mL flamed-dried flask, Na_2CO_3 (53 mg, 0.05 mmol), phthalimide (**4**) (1.47 g, 10 mmol), $[(\eta^3\text{-}C_3H_5)PdCl]_2$ (14.6 mg, 0.04 mmol) and *S*,*S* ligand **2** (94.6 mg, 0.12 mmol) were added under argon being the flask purged three times with argon. Then dry dichloromethane (80 mL) was added to the mixture and the solution was stirred 15 min at rt. Butadiene monoepoxide **3** (810 μl, 10 mmol) was added in one portion and the resulting mixture was stirred at rt for 14h. The resulting mixture was concentrated and purified by flash chromatography, using 1:1 hexanes:ethyl acetate as a solvent, to afford compound **5** (99%) as a white solid.

Yield: 2.08g, 96%

Mp: 276 ºC.

IR: (neat,cm^{-1}): ν_{max}3460, 1774, 1708, 1388.

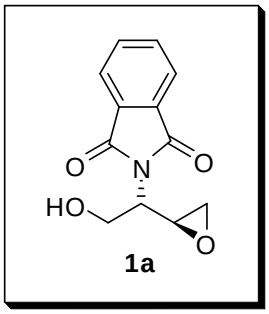
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.76 (dd, *J*=3.68Hz, 8.24Hz, 1H), 3.97 (ddd, *J*=4.16Hz, 12.44 Hz, 8.12Hz, 1H), 4.15 (ddd, *J*=3.96Hz, 7.6Hz, 12.22Hz, 1H), 4.94 (q, *J*= 3.20Hz,

7.76Hz, 1H), 5.29 (dd, *J*=0.88Hz, 9.6Hz, 2H), 6.12-6.19 (m, 1H), 7.74(dd, *J*=3.2Hz, 5.48Hz, 2H), 7.85 (dd, *J*= 2.76Hz, 5.52Hz, 2H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 56.0, 62.9, 118.9, 123.5, 131.8, 132.0, 134.3, 168.7.

DEPT-135 ^{13}C NMR (100 MHz, $CDCl_3$): δ for $-CH_2$ carbon 56, 119.

6.2 Synthesis of 2-((S)-2-hydroxy-1-((S)-oxiran-2-yl)ethyl)isoindoline-1,3-dione.



1a

General Procedure: To 250mg (1.5 mmol) of 2-(*R*)-*N*-phthalimido-3-bueten-1-ol **5** in DCM (70ml) was added 380mg (0.2 mmol) and *m*-CPBA. The reaction mixture was then stirred at 0^{o}C to room temperature over 12 hours. Then the reaction mixture was quenched with saturated $NaHCO_3$ solution and extracted with $CHCl_3$ (3 x 20ml) and concentrated under reduced pressure to get the crude product. Silica gel column chromatography (100-200 mesh) purification of the crude compound by using hexane/EtOAc (7:3) furnished epoxides **1a** and **1b** in diastereomeric ratio of 80% de.

6.2.1 2-((S)-2-hydroxy-1-((S)-oxirane-2-yl)ethyl)isoindoline-1,3-dione 1a:

Yield: 182.56mg, 85%.

Mol. Formula: $C_{12}H_{10}NO_2$

M.P: 324 ºC

IR: (neat,cm^{-1}): ν_{max}3467, 1775, 1713, 1387.

^{1}H NMR (400 MHz, $CDCl_3$): (LS): δ 2.77 (dd, J=2.76Hz,5.6Hz,1H), 2.93 (t, J=4.6Hz, 1H), 3.37 (s,1H), 3.59-3.61 (m,1H), 4.04-4.08 (m, 1H), 4.11-4.15 (m,2H), 7.73 (dd, J=3.2Hz, 5.48, 2H), 7.84 (dd, J= 3.2Hz, 5.48, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) : δ 46.4, 49.7, 55.8, 60.9, 123.4, 131.5, 134.2, 168.6

DEPT-135 ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.0, 61.0.

6.2.2 2-((*S*)-2-hydroxy-1-((*R*)-oxirane-2-yl)ethyl)isoindoline-1,3-dione 1b:

Yield: 45.64mg, 85%.

Mol. Formula: $C_{12}H_{10}NO_2$

M.P: 324 ºC

IR: (neat,cm^{-1}): ν_{max}3465, 1774, 1712, 1387.

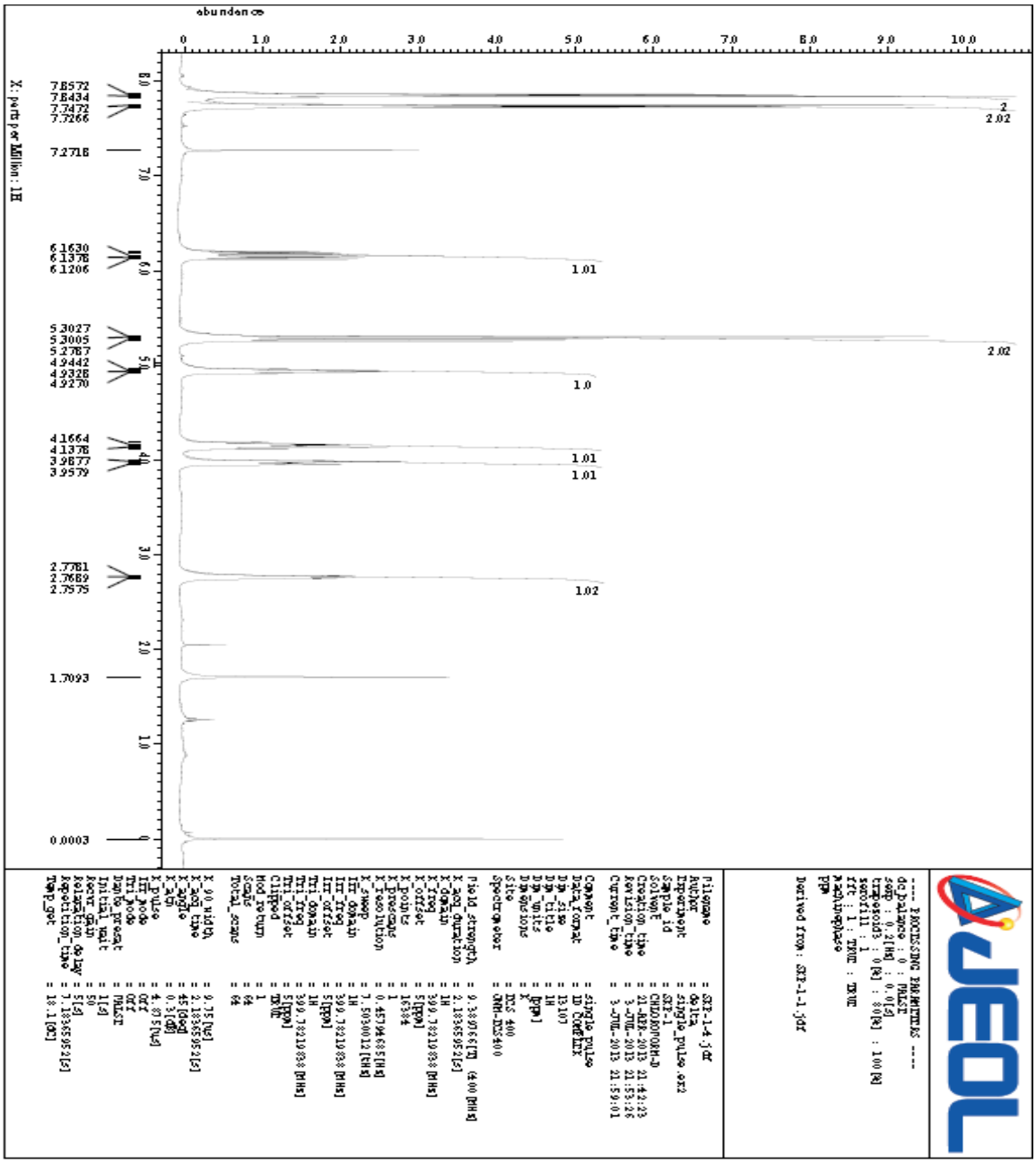
^{1}H NMR (400 MHz, $CDCl_3$): (US): δ 1.29 (s, 1H), 2.65-2.67 (m,1H), 2.80 (t, J=3.68Hz, 1H), 3.55-3.56 (m,1H), 4.07-4.09 (dd, J=5.04Hz, 10.52Hz, 2H), 4.30 (q, J=2.28Hz, 8.24Hz, 1H), 7.76 (dd, J=0.92Hz, 3.64Hz, 2H), 7.86 (dd, J=1.84Hz, 3.0Hz,2H).

^{13}C NMR (100 MHz, $CDCl_3$) : δ 46.1, 49.6, 55.6, 61.4, 123.7, 131.7, 134.5, 168.7.

DEPT-135 ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.0, 61.0.

7. Spectra

1. IR, ^{1}H, ^{13}CNMR and DEPT-135 ^{13}CNMR spectra of **5**.
2. IR, ^{1}H, ^{13}CNMR and DEPT-135 ^{13}CNMR spectra of **1a**.
3. IR, ^{1}H, ^{13}CNMR and DEPT-135 ^{13}CNMR spectra of **1b**.


abundance
X : parts per Million : 1H
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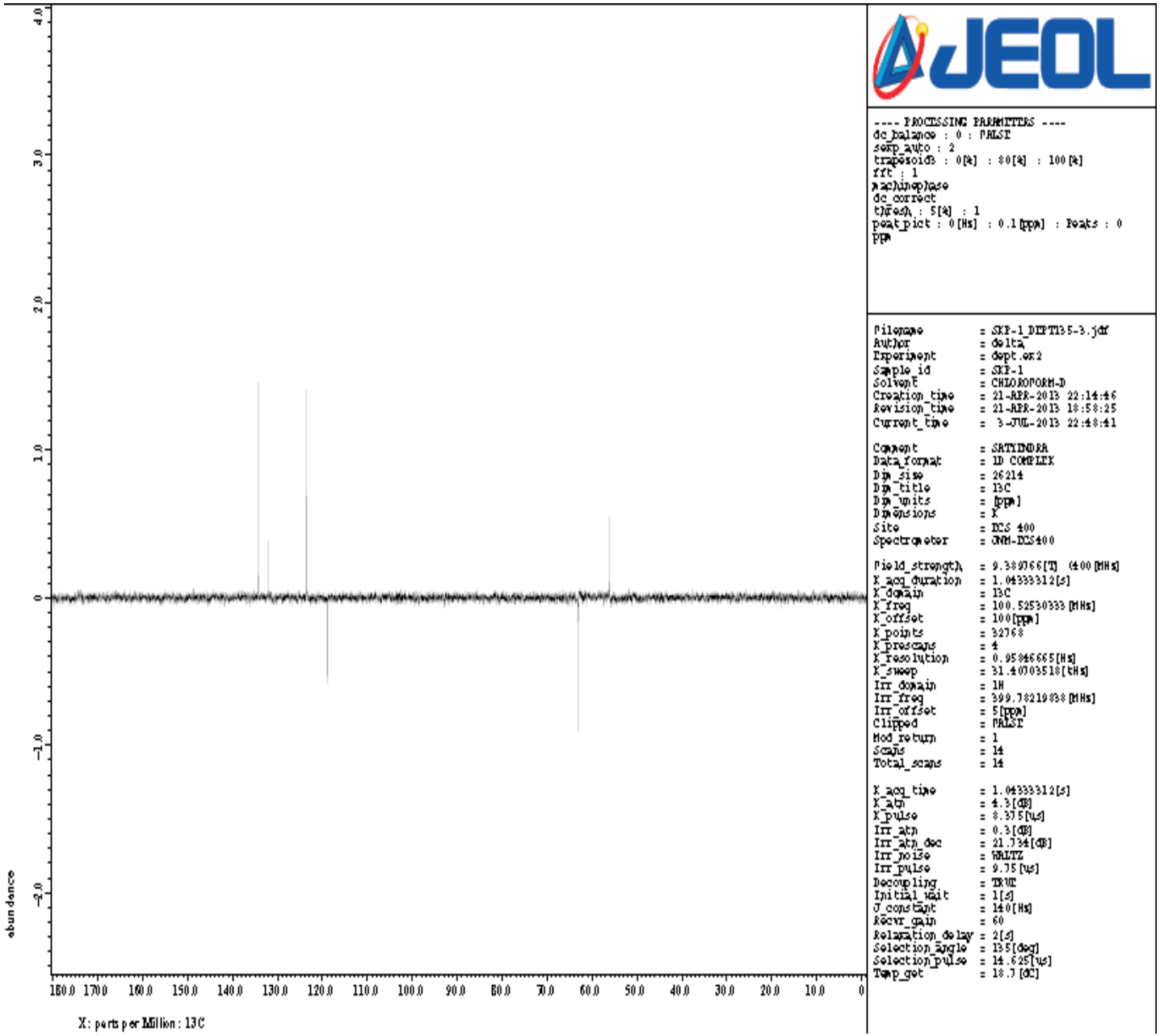
7.7472
7.7266
7.2718
6.1630
6.1378
6.1206
5.3027
5.3005
5.2767
4.9442
4.9328
4.9270
4.1664
4.1378
3.9877
3.9579
2.7781
2.7682
2.7575
1.7093
0.0003
2
2.02
1.01
2.02
1.0
1.01
1.01
1.02
---- PROCESSING PARAMETERS ----
do_balance : 0 : FALSE
sadp : 0.2[Hz] : 0.0[s]
trapezoids : 0[%] : 80[%] : 100[%]
zerofill : 1
fft : 1 : TRUE : TRUE
magnitude
PPM
Derived from: SZP-1-1.jdf
Filename = SZP-1-4.jdf
Author = Optics
Experiment = single_pulse.exp
Sample_id = SZP-1
Solvent = CHLOROFORM-D
Creation_time = 21-AUG-2013 21:42:23
Revision_time = 3-JUL-2013 21:53:26
Current_time = 3-JUL-2013 21:59:01
Comment = single pulse
Data_format = 1D ComplEX
Dim_size = 13107
Dim_title = 1H
Dim_units = [PPM]
Site = JEOL 400
Spectrometer = GSHH-JES400
Field_strength = 9.389716[T] (400[MHz])
X_acq_duration = 2.183655[s]
X_domain = 1H
X_freq = 399.782198[MHz]
X_offset = 5[PPM]
X_points = 16384
X_prescans = 1
X_resolution = 0.457946[Hz]
X_sweep = 7.503012[kHz]
Irr_domain = 1H
Irr_freq = 399.782198[MHz]
Irr_offset = 5[PPM]
Tri_domain = 1H
Tri_freq = 399.782198[MHz]
Tri_offset = 5[PPM]
Clipped = TRUE
Mod_protocol = 1
Scans = 64
Total_scans = 64
X_90_width = 9.75[us]
X_acq_time = 2.183655[s]
X_angle = 45[deg]
X_atn = 0.3[dB]
X_pulse = 4.87[us]
Tri_mode = off
Tri_pulse = off
Dam_mode = FALSE
Initial_wait = 1[s]
Recvr_gain = 50
Relaxation_delay = 5[s]
Repetition_time = 7.183655[s]
Temp_set = 18.1[DC]

JEOL
---- PROCESSING PARAMETERS ----
dc_balance : 0 : FALSE
sort_auto : 2
transients : 0[#] : 80[#] : 100[#]
rfl : 1
rfp : 1
zerohidephase
dc_correct
thresh : 5[%] : 1
peak_pick : 0[Hz] : 0.1[ppm] : Peaks : 0
ppm
filename = SEF-1_CARBON-4.jdf
Author = delta
Experiment = single_pulse_dec
sample_id = SEF-1
solvent = CHLOROFORM-D
Creation_time = 21-APR-2015 22:13:31
Revision_time = 3-JUL-2015 22:16:01
Current_time = 3-JUL-2015 22:22:07
Comment = STANDARD
Data_format = 1D COMPLEX
Dim_size = 65214
Dim_title = 13C
Dim_units = [PPM]
Dim_quantities = X
Site = NMR-EC5400
Spectrometer = NMR-EC5400
Field_strength = 9.389916[T] (400 MHz)
X_acq_duration = 1.043333312[s]
X_domain = 13C
X_freq = 100.525030339 [MHz]
X_offset = 100[ppm]
X_points = 32768
X_prescans = 4
X_resolution = 0.957846665[Hz]
X_sweep = 31.470035218[kHz]
Irr_domain = 1H
Irr_freq = 399.782190838 [MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Method_num = 1
Scans = 14
Total_scans = 14
X_90_width = 8.375[us]
X_acq_time = 1.043333312[s]
X_angle = 30[deg]
X_atn = 4.31[dB]
X_pulse = 2.791666667[us]
Irr_atn_dec = 21.734[dB]
Irr_atn_noe = 21.734[dB]
Irr_noise = 6817[Hz]
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recyc_drain = 60
Relaxation_delay = 2[s]
Repetition_time = 3.043333312[s]
Temp_set = 18.7 [DC]
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
X: parts per Million: 13C
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
168.6776
134.2959
132.0267
131.8264
123.5313
118.9643
62.9391
56.0360


abundance
4.0
3.0
2.0
1.0
0
-1.0
-2.0
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
X: parts per Million : 13C
---- PROCESSING PARAMETERS ----
dc_balance : 0 : FALSE
autp_auto : 2
trapezoid3 : 0[%] : 80[%] : 100[%]
fft : 1
magnitude
dc_correct
thres\ : 5[%] : 1
peak_pick : 0[Hz] : 0.1[ppm] : Peaks : 0
ppm
Filename = SKP-1_DEPT135-3.jdf
Author = delta
Experiment = dept.ex2
Sample_id = SKP-1
Solvent = CHLOROFORM-D
Creation_time = 21-APR-2013 22:14:46
Revision_time = 21-APR-2013 18:58:25
Current_time = 3-JUL-2013 22:48:41
Comment = SATYENDRA
Data_format = 1D COMPLEX
Dim_size = 26214
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = DCS 400
Spectrometer = JNM-DCS400
Field_strength = 9.389766[T] (400[MHz])
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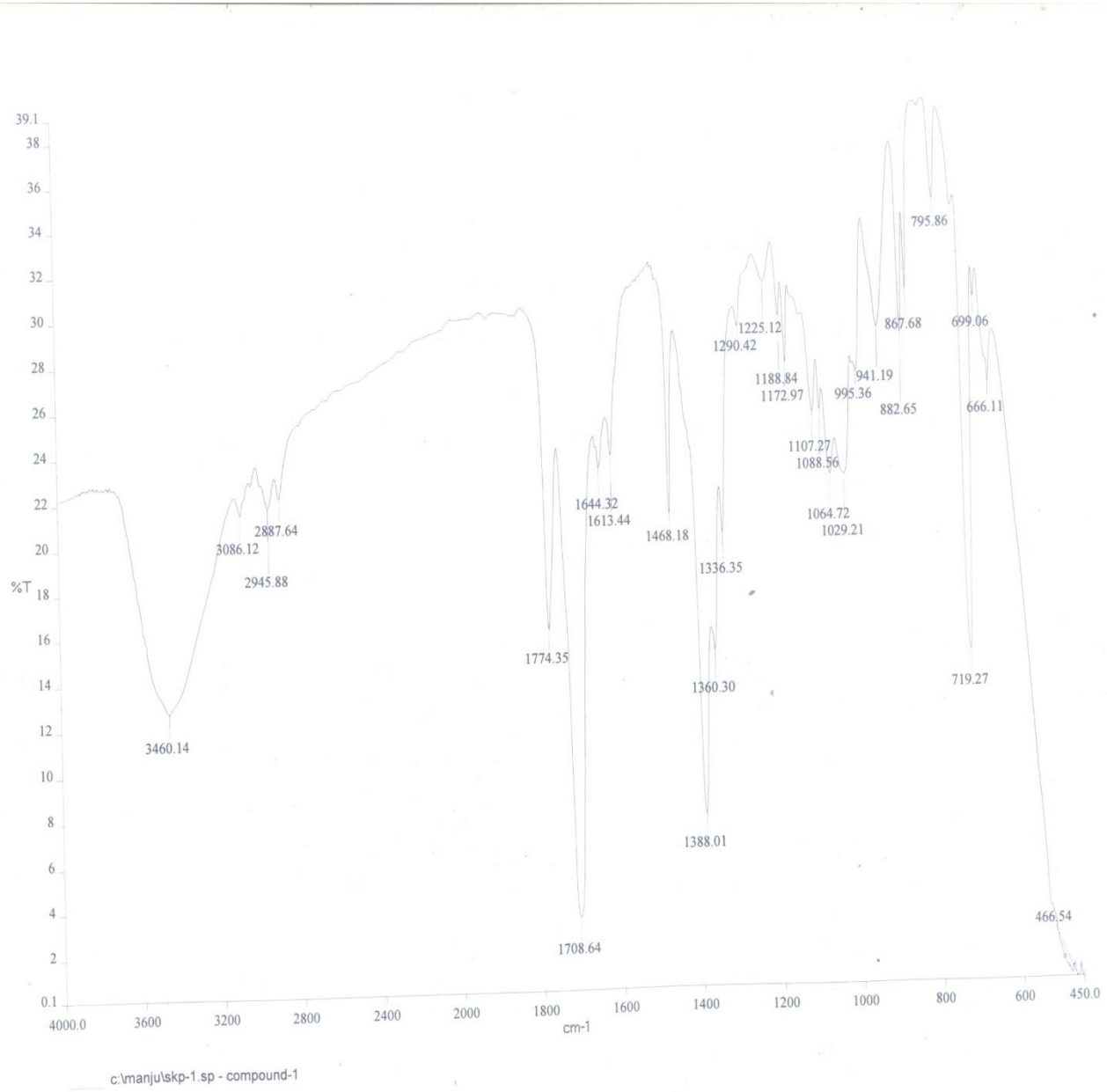
X_domain = 13C
X_freq = 100.52530333[MHz]
X_offset = 100[ppm]
X_points = 32768
X_prescans = 4
X_resolution = 0.95846665[Hz]
X_sweep = 31.40703518[kHz]
Irr_domain = 1H
Irr_freq = 399.78219838[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 14
Total_scans = 14
X_acq_time = 1.04333312[s]
X_atn = 4.3[dB]
X_pulse = 8.375[us]
Irr_atn = 0.3[dB]
Irr_atn_dec = 21.734[dB]
Irr_noise = WALTZ
Irr_pulse = 9.75[us]
Decoupling = TRUE
Initial_wait = 1[s]
J_constant = 140[Hz]
Recvr_gain = 60
Relaxation_delay = 2[s]
Selection_angle = 135[deg]
Selection_pulse = 14.625[us]
Temp_get = 18.7 [deg]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cm-1
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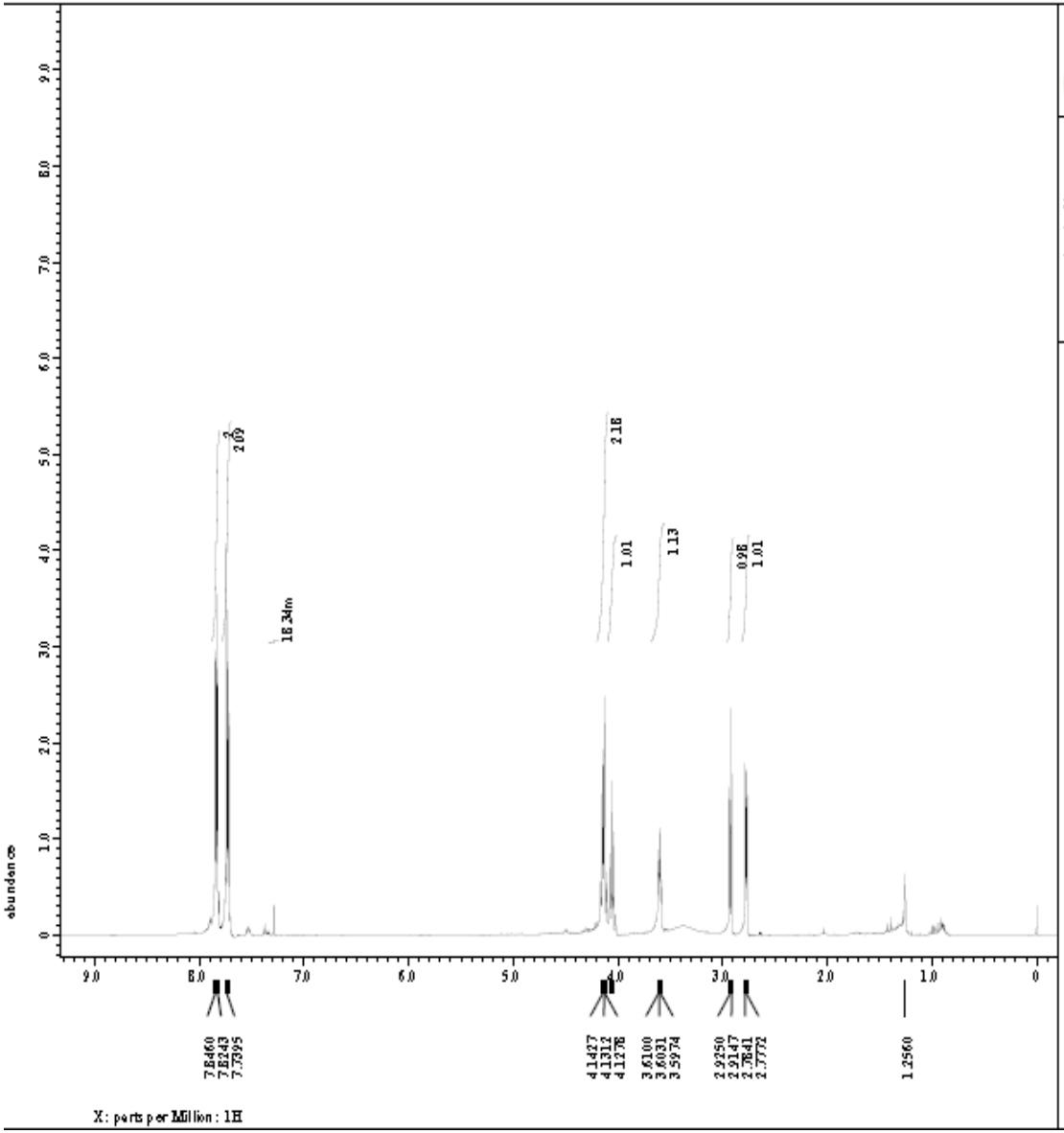
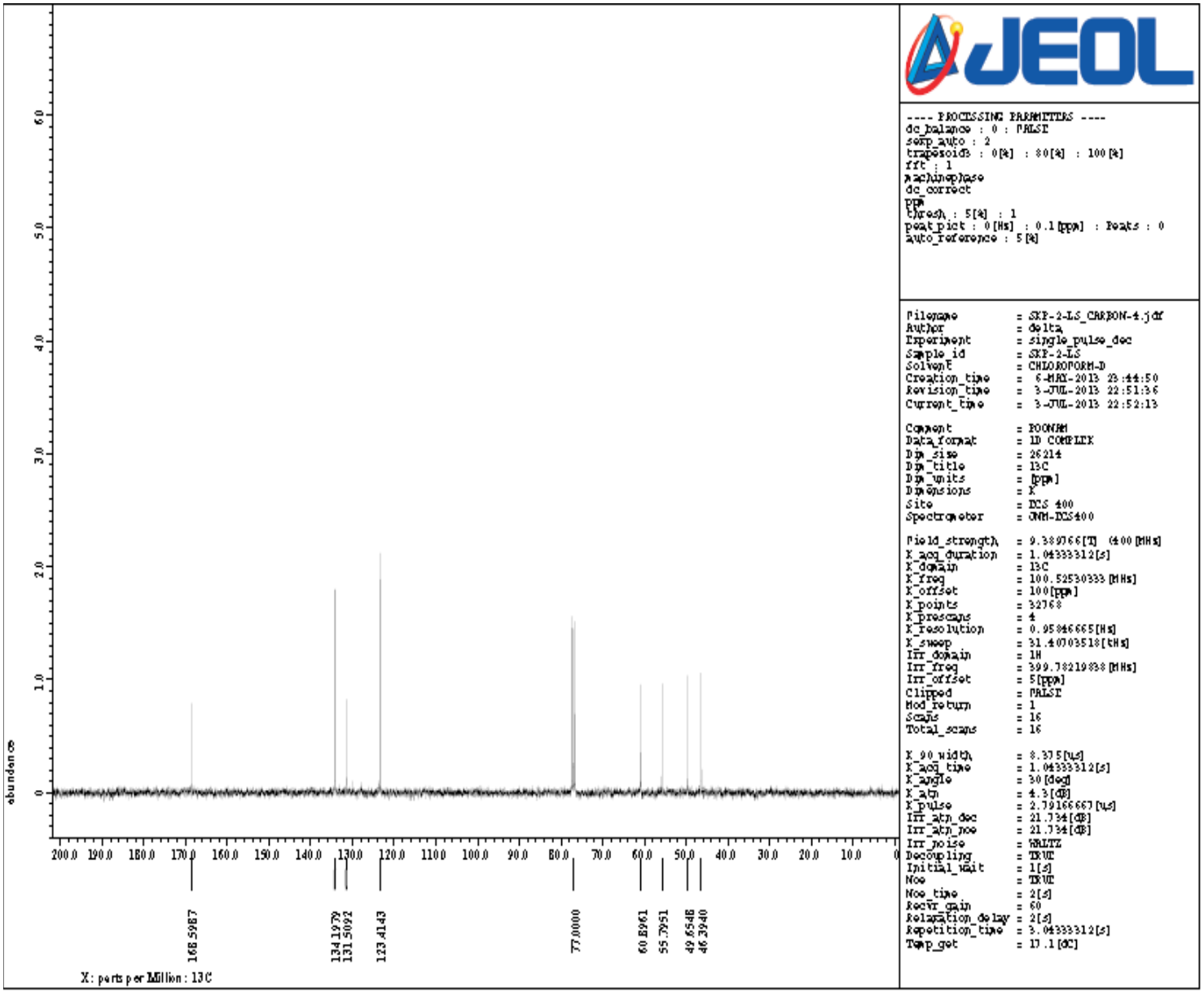
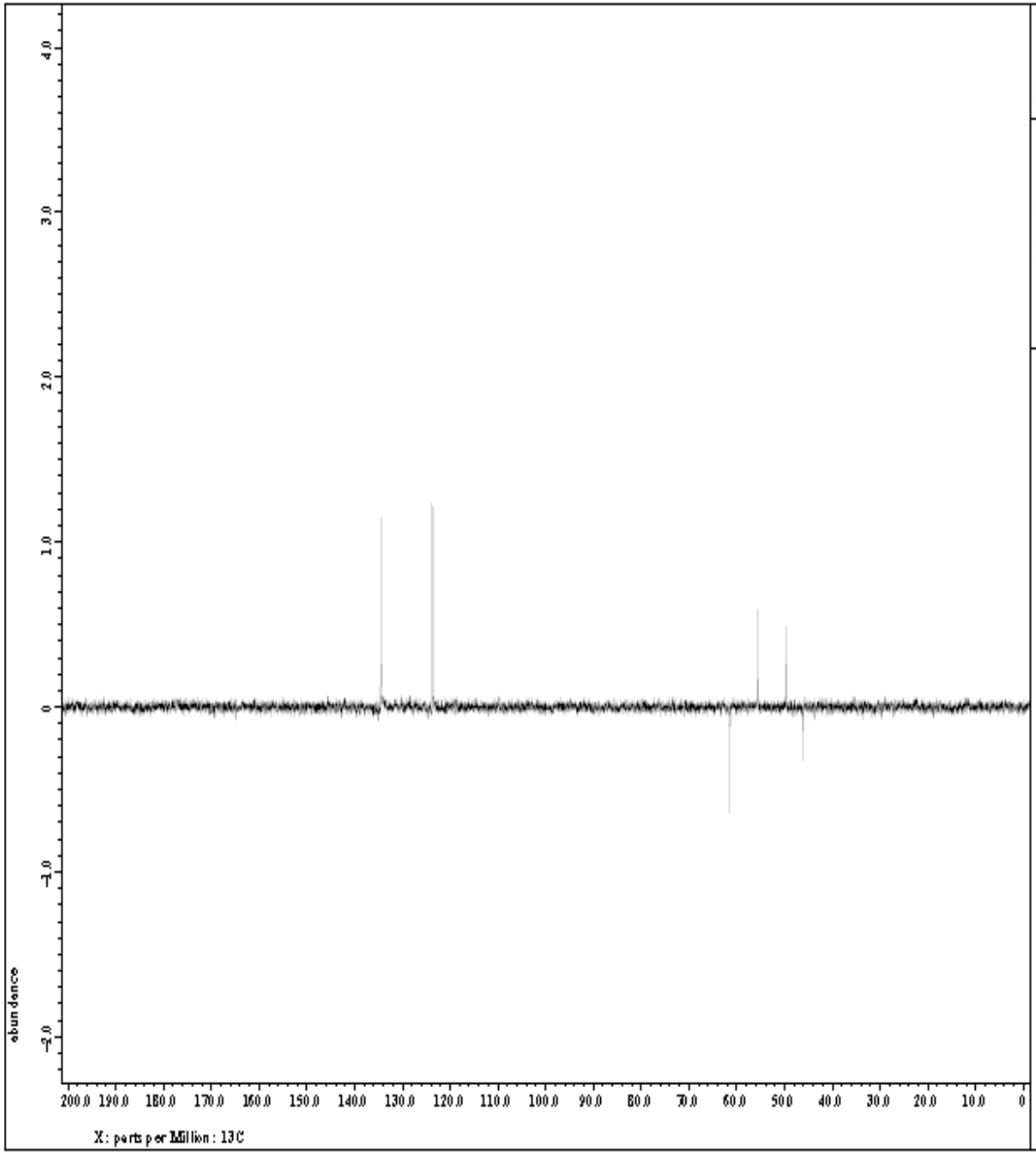
2945.88
2887.64
1774.35
1708.64
1644.32
1613.44
1468.18
1388.01
1360.30
1336.35
1290.42
1225.12
1188.84
1172.97
1107.27
1088.56
1064.72
1029.21
995.36
941.19
882.65
867.68
795.86
719.27
699.06
666.11
466.54
c:\manju\skp-1.sp - compound-1



---- PROCESSING PARAMETERS ----
dc_balance : 0 : FALSE
sexp_auto : 0.2
trapezoid3 : 0[%] : 80[%] : 100[%]
fft : 1
zerofill
dc_correct
ppm
thresh : 5[%] : 1
peak_pick : 0[Hz] : 0.1[ppm] : both : 0[
auto_reference : 5[%]

Filename	= SKP-2_LS_PROTON-4.jdf
Author	= delta
Experiment	= single_pulse.ex2
Sample_id	= SKP-2_LS
Solvent	= CHLOROFORM-D
Creation_time	= 6-MAY-2013 02:57:14
Revision_time	= 3-JUL-2013 22:43:08
Current_time	= 3-JUL-2013 22:43:57
Comment	= SKP-2 LS
Data_format	= 1D COMPLEX
Dim_size	= 13107
Dim_title	= 1H
Dim_units	= [ppm]
Dimensions	= F
Site	= DLS 400
Spectrometer	= GNM-DLS400
Field_strength	= 9.389766[T] (400[MHz]
F_acq_duration	= 2.18365952[s]
F_domain	= 1H
F_freq	= 399.78219838[MHz]
F_offset	= 5[ppm]
F_points	= 16384
F_prescans	= 1
F_resolution	= 0.45794685[Hz]
F_sweep	= 7.5030012[kHz]
Irr_domain	= 1H
Irr_freq	= 399.78219838[MHz]
Irr_offset	= 5[ppm]
Tri_domain	= 1H
Tri_freq	= 399.78219838[MHz]
Tri_offset	= 5[ppm]
Clipped	= FALSE
Mod_return	= 1
Scans	= 200
Total_scans	= 200
F_90_width	= 9.75[us]
F_acq_time	= 2.18365952[s]
F_angle	= 45[deg]
F_atn	= 0.3[dB]
F_pulse	= 4.875[us]
Irr_mode	= Off
Tri_mode	= Off
Dante_presat	= FALSE
Initial_wait	= 1[s]
Recvr_gain	= 30
Relaxation_delay	= 4[s]
Repetition_time	= 6.18365952[s]
Temp_get	= 17.1[dC]

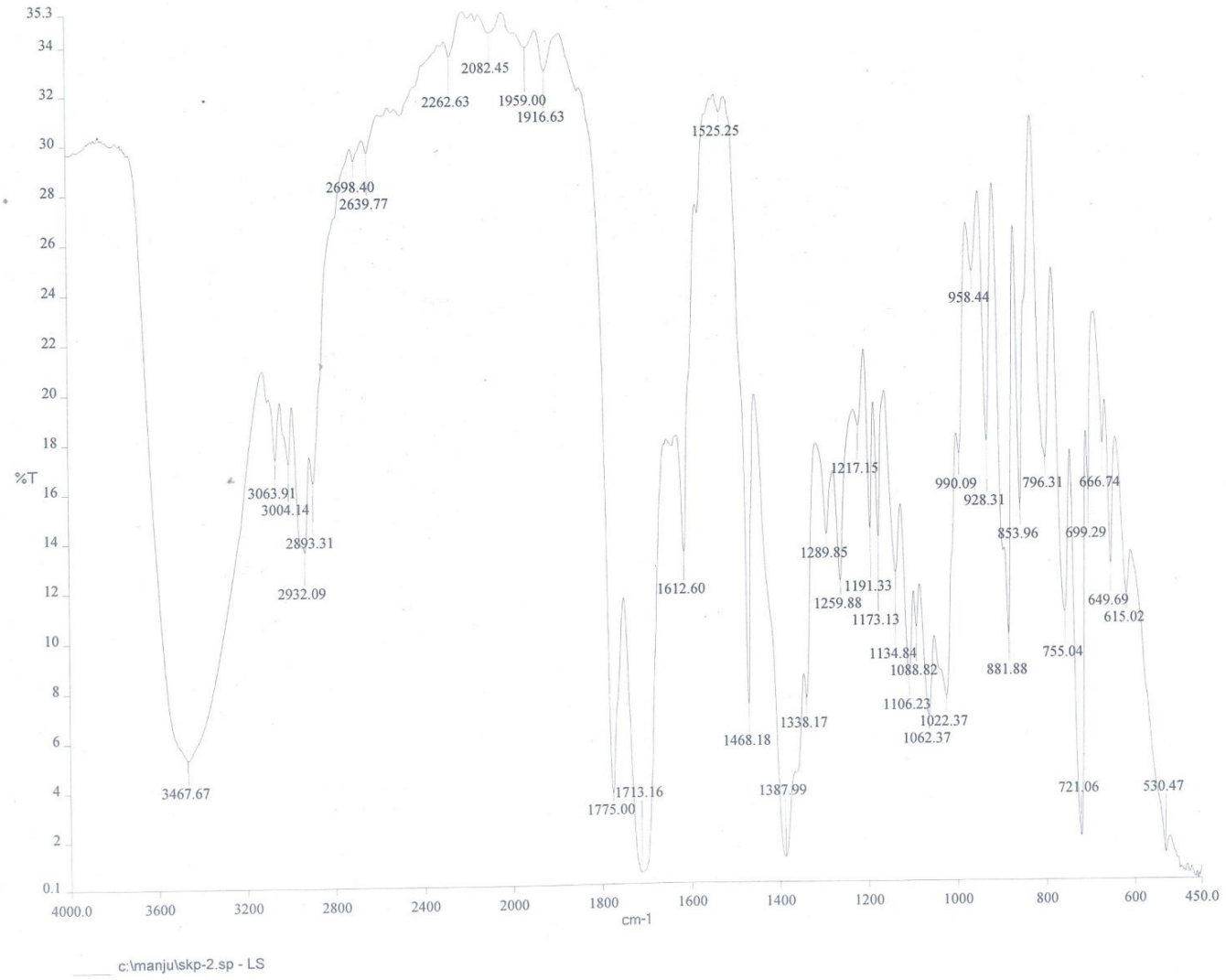

abundance
X: parts per Million : 13C
168.5987
134.1979
131.5092
123.4143
77.0000
60.8961
55.7951
49.6548
46.3940
---- PROCESSING PARAMETERS ----
dc_balance : 0 : PRLST
sexp_auto : 2
trapezoid3 : 0[%] : 80[%] : 100[%]
fft : 1
zerophase
dc_correct
ppm
thresh : 5[%] : 1
peak_pict : 0[Hz] : 0.1[ppm] : Peaks : 0
auto_reference : 5[%]
Filename = SKP-2-LS_CARBON-4.jdf
Author = delta
Experiment = single_pulse_dec
Sample_id = SKP-2-LS
Solvent = CHLOROFORM-D
Creation_time = 6-MAY-2013 23:44:50
Revision_time = 3-JUL-2013 22:51:36
Current_time = 3-JUL-2013 22:52:13
Comment = PROTON
Data_format = 1D COMPLEX
Dim_size = 26214
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = JCS 400
Spectrometer = CNM-JCS400
Field_strength = 9.389766[T] (400[MHz])
X_acq_duration = 1.04333312[s]
X_domain = 13C
X_freq = 100.52530333[MHz]
X_offset = 100[ppm]
X_points = 32768
X_prescans = 4
X_resolution = 0.95846665[Hz]
X_sweep = 31.40703518[kHz]
Irr_domain = 1H
Irr_freq = 399.78219838[MHz]
Irr_offset = 5[ppm]
Clipped = PRLST
Mod_return = 1
Scans = 16
Total_scans = 16
X_90_width = 8.375[us]
X_acq_time = 1.04333312[s]
X_angle = 30[deg]
X_atn = 4.3[dB]
X_pulse = 2.79166667[us]
Irr_atn_dec = 21.734[dB]
Irr_atn_noe = 21.734[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recvr_gain = 60
Relaxation_delay = 2[s]
Repetition_time = 3.04333312[s]
Temp_get = 17.1[dC]



JEOL

```
---- PROCESSING PARAMETERS ----
dc_balance : 0 : FALSE
sexp_auto : 2
trapezoid% : 0[%] : 80[%] : 100[%]
fft : 1
#achinephase
dc_correct
thresh_ : 5[%] : 1
peak_pick : 0[Hz] : 0.1[ppm] : Peaks : 0
ppm
```

Filename	: SKP-2-VS_DEPT135-3.jd
Author	: delta
Experiment	: dept.ex2
Sample_id	: SKP-2-VS
Solvent	: CHLOROFORM-D
Creation_time	: 6-MAY-2013 23:58:03
Revision_time	: 6-MAY-2013 20:42:44
Current_time	: 3-JUL-2013 22:53:50
Comment	: ROONAM
Data_format	: 1D COMPLEX
Dim_size	: 26214
Dim_title	: 13C
Dim_units	: [ppm]
Dimensions	: X
Site	: DCS 400
Spectrometer	: GNM-DCS400
Field_strength	: 9.389766[T] (400[MHz]
X_acq_duration	: 1.043333312[s]
X_domain	: 13C
X_freq	: 100.52530333[MHz]
X_offset	: 100[ppm]
X_points	: 32768
X_prescans	: 4
X_resolution	: 0.95846665[Hz]
X_sweep	: 31.40703518[kHz]
Irr_domain	: 1H
Irr_freq	: 399.78219838[MHz]
Irr_offset	: 5[ppm]
Clipped	: FALSE
Mod_return	: 1
Scans	: 16
Total_scans	: 16
X_acq_time	: 1.043333312[s]
X_atn	: 4.3[dB]
X_pulse	: 8.375[us]
Irr_atn	: 0.3[dB]
Irr_atn_dec	: 21.734[dB]
Irr_noise	: WALTZ
Irr_pulse	: 9.75[us]
Decoupling	: TRUE
Initial_wait	: 1[s]
J_constant	: 140[Hz]
Rcvr_gain	: 60
Relaxation_delay	: 2[s]
Selection_angle	: 135[deg]
Selection_pulse	: 14.625[us]
Temp_get	: 16.8[dC]


%T
cm-1
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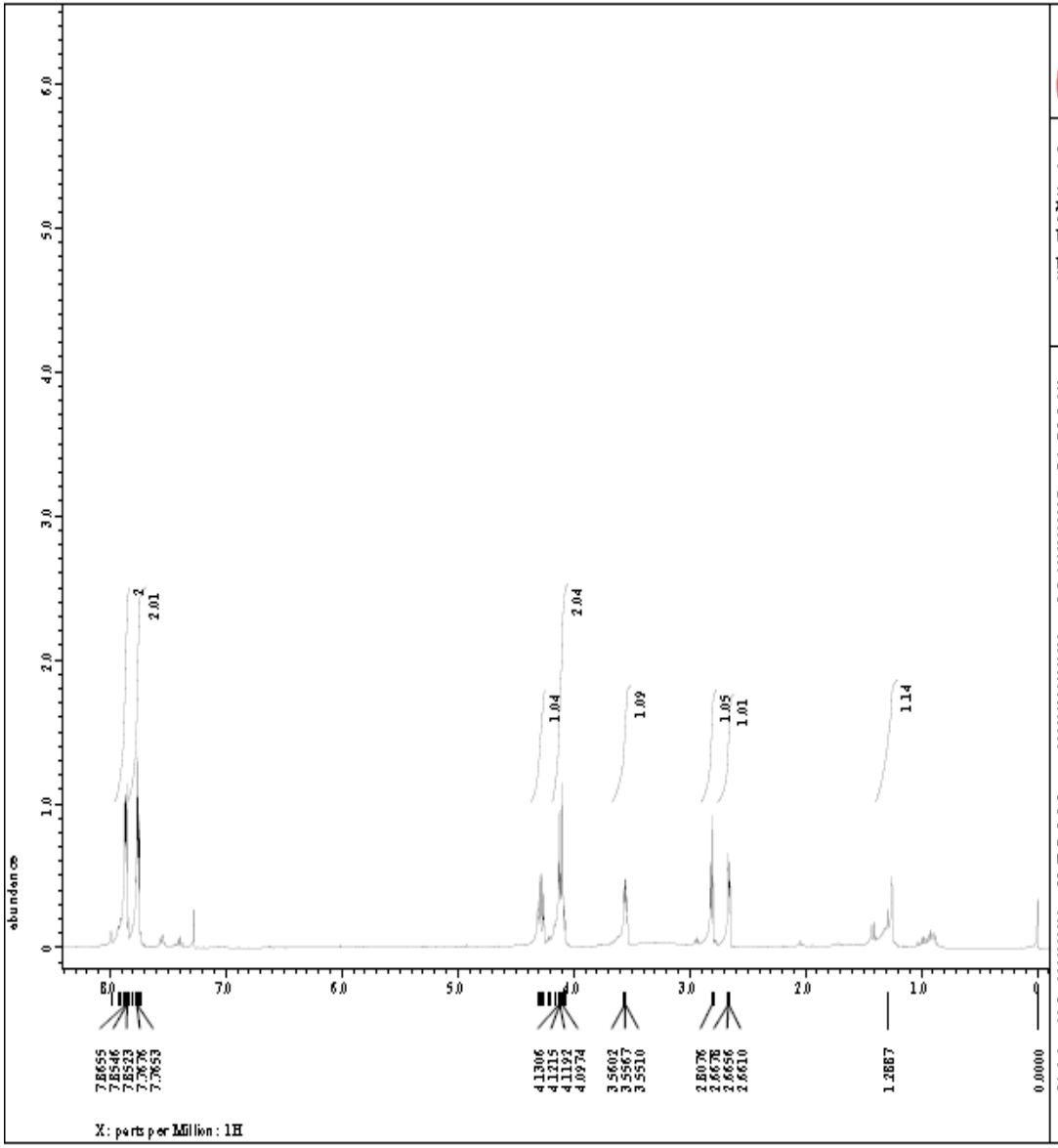
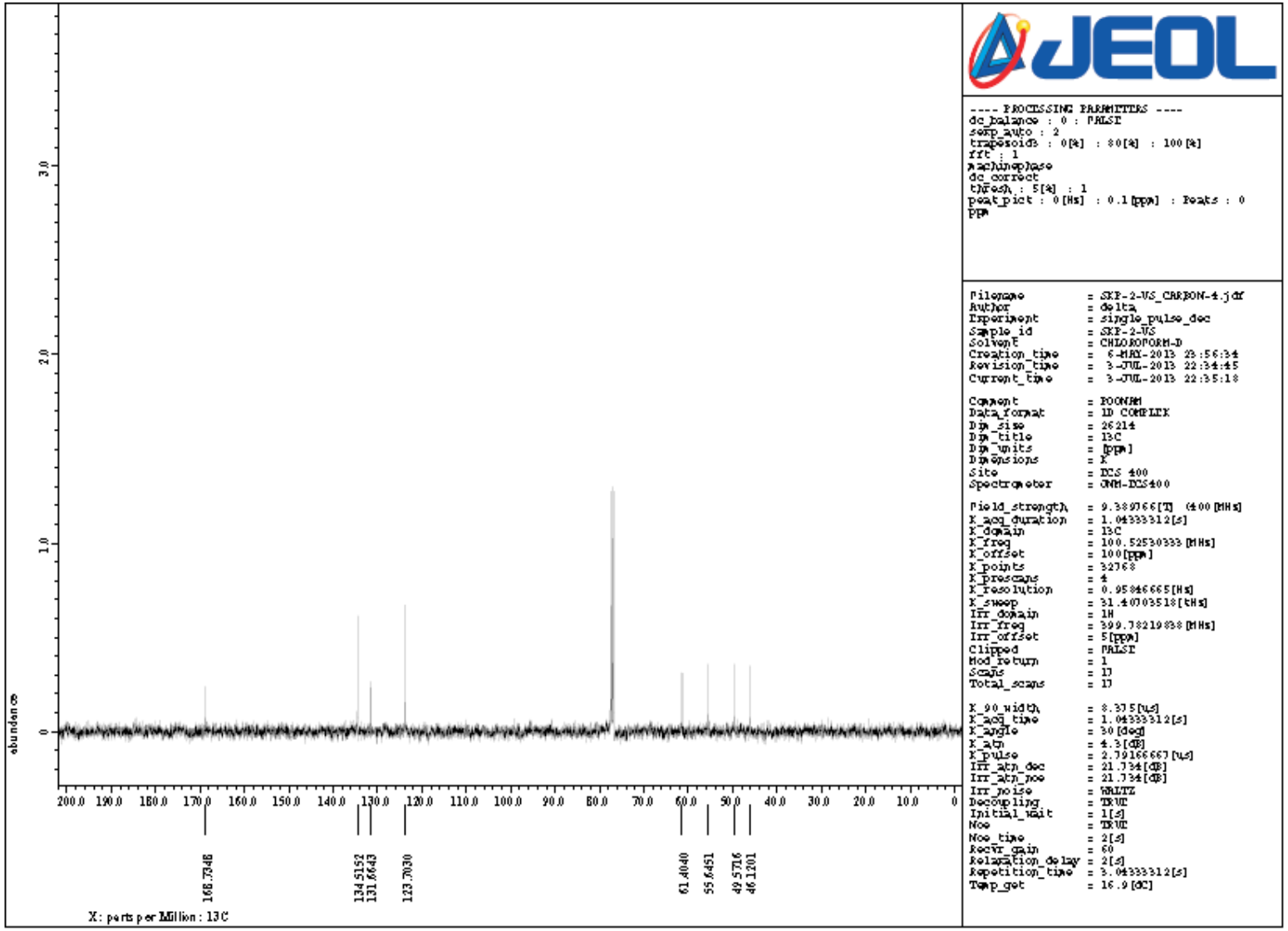
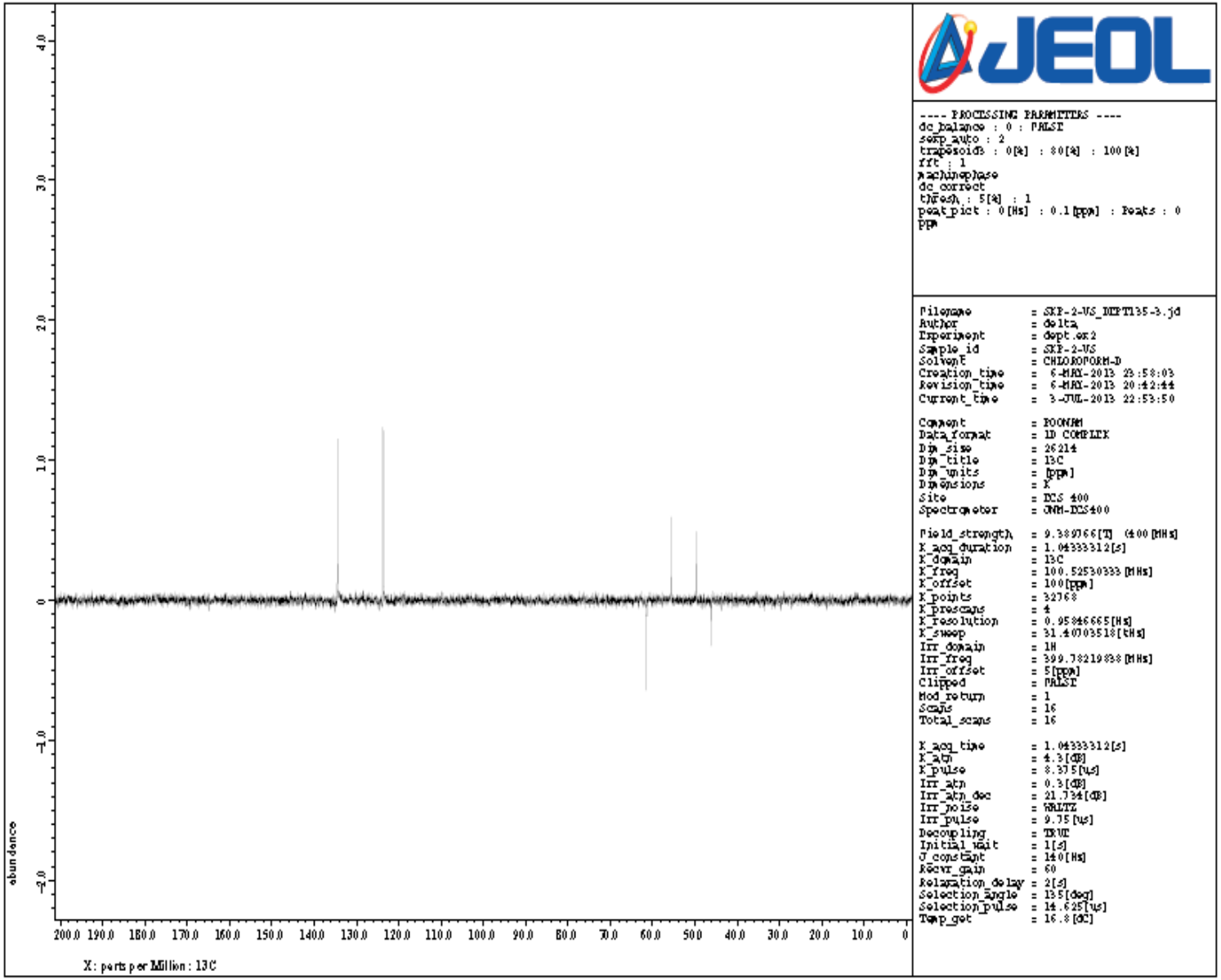
2262.63
1959.00
1916.63
2698.40
2639.77
1525.25
3063.91
3004.14
2893.31
2932.09
1217.15
990.09
928.31
796.31
666.74
853.96
699.29
1289.85
1612.60
1191.33
1259.88
1173.13
649.69
615.02
1134.84
1088.82
755.04
881.88
1106.23
1022.37
1062.37
1338.17
1468.18
3467.67
1713.16
1775.00
1387.99
721.06
530.47
c:\manju\skp-2.sp - LS

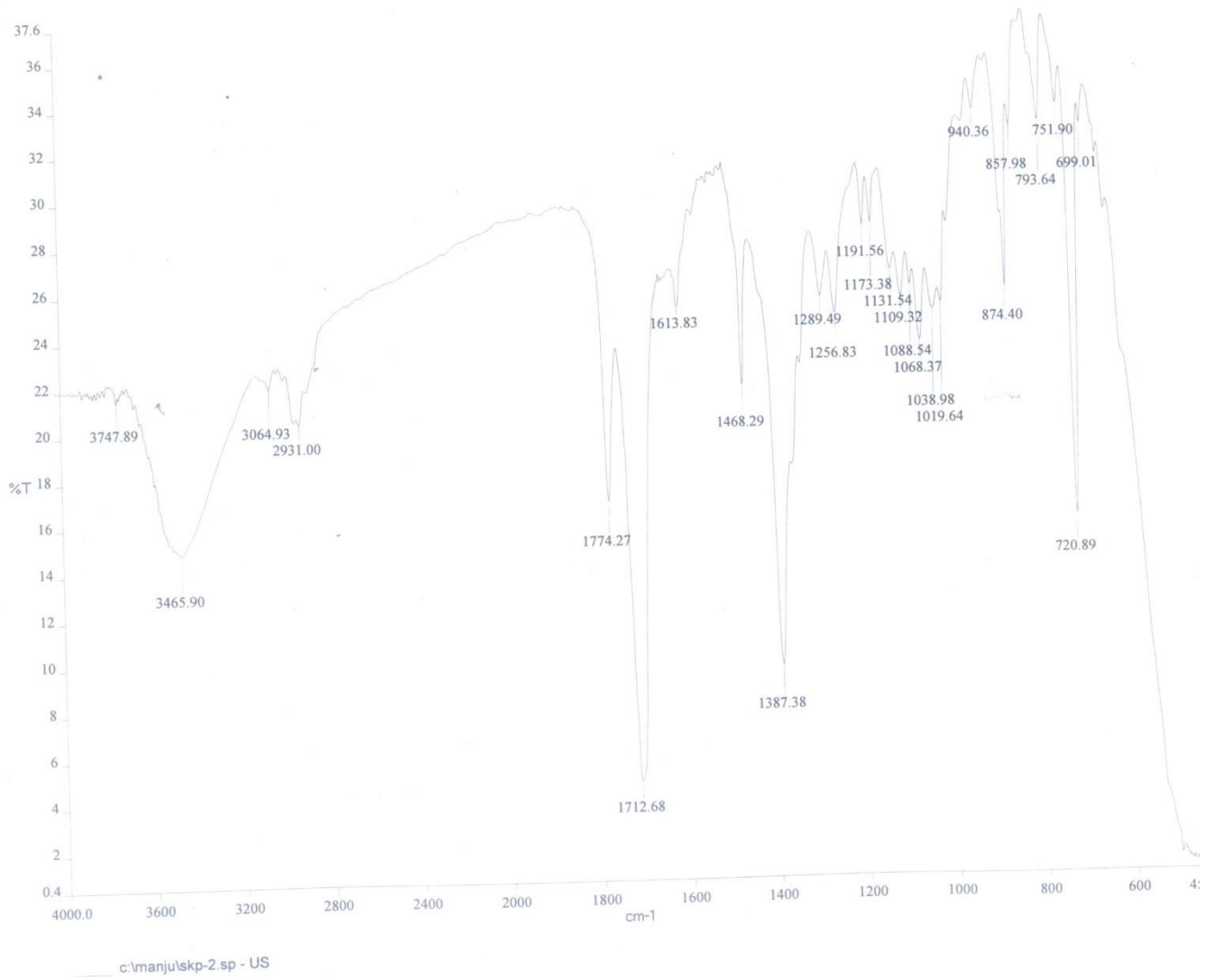


```
---- PROCESSING PARAMETERS ----
dc_balance : 0 : FALSE
sexp_auto : 0.2
trapezoid3 : 0[%] : 80[%] : 100[%]
fft : 1
machinephase
dc_correct
ppm
thresh : 5[%] : 1
peak_pick : 0[Hz] : 0.1[ppm] : Both : 0[
auto_reference : 5[%]
```

```
Filename          = SKP-2_US_PROTON-4.jdf
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = SKP-2_US
Solvent           = CHLOROFORM-D
Creation_time     =  6-MAY-2013 02:20:28
Revision_time     =  3-JUL-2013 22:30:03
Current_time      =  3-JUL-2013 22:30:41

Comment           = SKP-2_US
Data_format       = 1D COMPLEX
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = DCS 400
Spectrometer      = GNM-DCS400

Field_strength    = 9.389766[T]  (400[MHz]
X_acq_duration    = 2.18365952[s]
X_domain          = 1H
X_freq            = 399.78219838[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 1
X_resolution      = 0.45794685[Hz]
X_sweep           = 7.5030012[kHz]
Irr_domain        = 1H
Irr_freq          = 399.78219838[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 399.78219838[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 200
Total_scans       = 200

X_90_width        = 9.75[us]
X_acq_time        = 2.18365952[s]
X_angle           = 45[deg]
X_atn             = 0.3[dB]
X_pulse           = 4.875[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 34
Relaxation_delay  = 4[s]
Repetition_time   = 6.18365952[s]
Temp_get          = 17[dC]
```


abundance
3.0
2.0
1.0
0
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
168.7348
134.5152
131.6643
123.7030
61.4040
55.6451
49.5716
46.1201
X: parts per Million : 13C
---- PROCESSING PARAMETERS ----
dc_balance : 0 : FALSE
sexp_auto : 2
trapezoids : 0[%] : 80[%] : 100[%]
fft : 1
machinephase
dc_correct
thresh : 5[%] : 1
peak_pick : 0[Hz] : 0.1[ppm] : Peaks : 0
PPM
Filename = SKP-2-VS_CARBON-4.jdf
Author = delta
Experiment = single_pulse_dec
Sample_id = SKP-2-VS
Solvent = CHLOROFORM-D
Creation_time = 6-MAY-2013 23:56:34
Revision_time = 3-JUL-2013 22:34:45
Current_time = 3-JUL-2013 22:35:18
Comment = ROONMR
Data_format = 1D COMPLEX
Dim_size = 26214
Dim_title = 13C
Dim_units = [ppm]
Dimensions = F
Site = DCS 400
Spectrometer = GNM-DCS400
Field_strength = 9.389766[T] (400[MHz]
F_acq_duration = 1.04333312[s]
F_domain = 13C
F_freq = 100.52530333[MHz]
F_offset = 100[ppm]
F_points = 32768
F_prescans = 4
F_resolution = 0.95846665[Hz]
F_sweep = 31.40703518[kHz]
Irr_domain = 1H
Irr_freq = 399.78219838[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 17
Total_scans = 17
F_90_width = 8.375[us]
F_acq_time = 1.04333312[s]
F_angle = 30[deg]
F_atn = 4.3[dB]
F_pulse = 2.79166667[us]
Irr_atn_dec = 21.734[dB]
Irr_atn_noe = 21.734[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recvr_gain = 60
Relaxation_delay = 2[s]
Repetition_time = 3.04333312[s]
Temp_get = 16.9[dC]


abundance
4.0
3.0
2.0
1.0
0
-1.0
-2.0
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
X: parts per Million : 13C
---- PROCESSING PARAMETERS ----
dc_balance : 0 : PRLST
samp_auto : 2
trapezoid3 : 0[%] : 80[%] : 100[%]
fft : 1
Machinephase
dc_correct
thresh : 5[%] : 1
peak_pick : 0[Hz] : 0.1[ppm] : Peaks : 0
PPM
Filename = SKF-2-VS_DEPT135-3.jd
Author = delta
Experiment = dept.ex2
Sample_id = SKF-2-VS
Solvent = CHLOROFORM-D
Creation_time = 6-MAY-2013 23:58:03
Revision_time = 6-MAY-2013 20:42:44
Current_time = 3-JUL-2013 22:53:50
Comment = ROONMR
Data_format = 1D COMPLEX
Dim_size = 26214
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = ECS 400
Spectrometer = JNM-ECS400
Field_strength = 9.389766[T] (400[MHz]
X_acq_duration = 1.04333312[s]
X_domain = 13C
X_freq = 100.52530333[MHz]
X_offset = 100[ppm]
X_points = 32768
X_prescans = 4
X_resolution = 0.958466665[Hz]
X_sweep = 31.407035518[kHz]
Irr_domain = 1H
Irr_freq = 399.78219838[MHz]
Irr_offset = 5[ppm]
Clipped = PRLST
Mod_return = 1
Scans = 16
Total_scans = 16
X_acq_time = 1.04333312[s]
X_atn = 4.3[dB]
X_pulse = 8.375[us]
Irr_atn = 0.3[dB]
Irr_atn_dec = 21.734[dB]
Irr_noise = WALTZ
Irr_pulse = 9.75[us]
Decoupling = TRUE
Initial_wait = 1[s]
J_constant = 140[Hz]
Rcvr_gain = 60
Relaxation_delay = 2[s]
Selection_angle = 135[deg]
Selection_pulse = 14.625[us]
Temp_get = 16.8[dC]


%T
cm-1
3747.89
3465.90
3064.93
2931.00
1774.27
1712.68
1613.83
1468.29
1387.38
1289.49
1256.83
1191.56
1173.38
1131.54
1109.32
1088.54
1068.37
1038.98
1019.64
940.36
874.40
857.98
793.64
751.90
720.89
699.01
c:\manju\skp-2.sp - US

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