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Graphical Abstract

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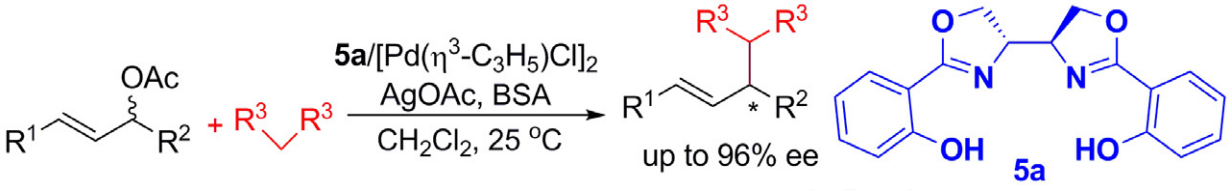

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ABSTRACT

A new class of highly stable O,N,N,O-tetradentate bioxazoline ligands were synthesized from L-tartaric acid. Exploration of those ligands in Pd-catalyzed asymmetric allylic alkylation yielded alkylated product up to 96% ee. Necessity of additional chelation to obtain high enantioselectivity was also demonstrated. Structural modifications of this ligand might result in identification of a novel privileged chiral ligand from an inexpensive chiral pool.

1. Introduction

Enantioselective synthesis of physiologically active pharmacophores/natural products is a need of the decade.[1] Asymmetric catalysis is emerging as the method of choice to synthesize enantiomerically pure pharmacophores/natural products.[2] Organic chemists play a pivotal role in the design and the synthesis of novel chiral ligands to facilitate metal mediated asymmetric transformations.[3] It is desirable if a chiral ligand can be synthesized from an inexpensive chiral pool like tartaric acid[4] or natural amino acids.[5]

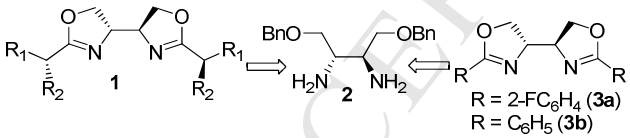

Figure 1. Bioxazoline from tartaric acid.

In our lab, we developed novel bioxazolines by fusing tartaric acid derived diamine **2** with optically active acids e.g. Naproxen (Figure 1). It was demonstrated that although ligand **1** forms only 5-membered chelate with metal, it catalyzed Henry reaction,[6a] alkyne addition to imines,[6b] enantioselective fluorination and allylic alkylation with very good efficiency and enantioselectivities up to 93%.[6c] Whereas bioxazolines **3** which form similar coordination did not show such promising enantioselectivity. In our continuing efforts in synthesizing novel ligands from chiral pool, we wish to report here a novel O,N,N,O-tetradentate ligand from tartaric acid and its application in asymmetric allylic alkylation (AAA).

Tartaric acid derived diamine **2** could be exploited to synthesize novel chiral ligands by combining with acids which have additional chelation moieties (Figure 2). Lee *et al.*[7] synthesized and demonstrated the usefulness of P,N,N,P-ligand **4** in asymmetric allylic alkylation and asymmetric transfer hydrogenation of aromatic ketones. To the best of our knowledge there is no report in the literature to synthesize O,N,N,O-tertradentate bioxazoline ligand **5** from diamine **2**. Since the coordinating atoms in tetradentate bioxazoline **5a** are similar to salen ligands, which would accommodate various metals, thus may provide opportunities to evaluate its efficiency in various asymmetric transformations. Since it has the potential to become a privileged ligand such as salen from an inexpensive chiral pool, we dedicated our efforts in synthesizing ligand **5a** and demonstrated its efficiency in catalyzing asymmetric allylic alkylation.[8]

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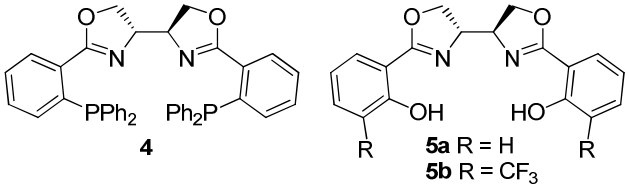
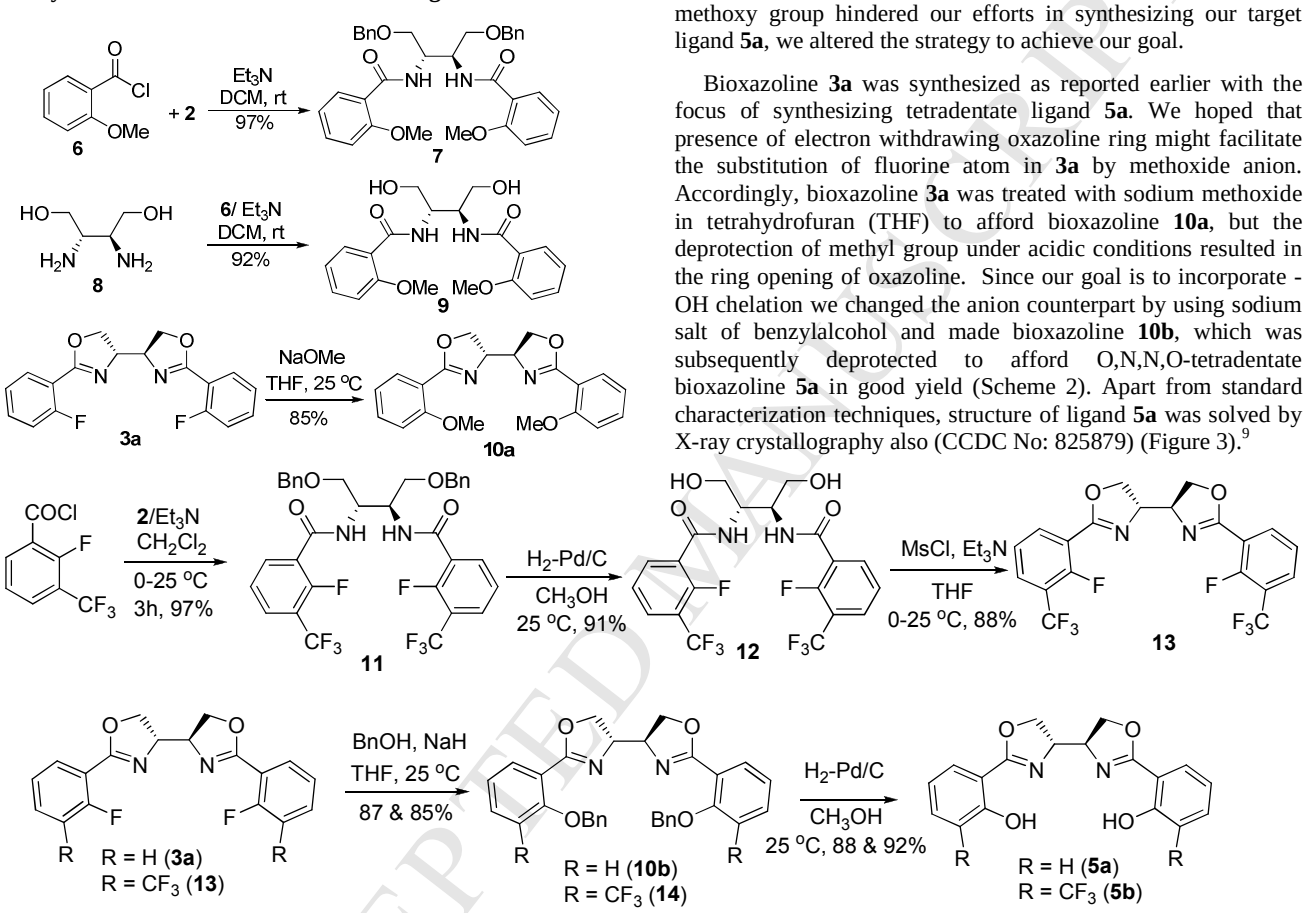


Figure 2. Tetradentate ligands derived from tataric acid

2. Results and discussion

2.1 Synthesis of tetradentate bioxazoline ligands



Scheme 2. Synthesis of novel O,N,NO-tetradentate ligand **5a**

2.2. Evaluation of Bioxazoline and Salen Ligands on Asymmetric Allylic Alkylation

Enantioselective formation of carbon-carbon and carbon-hetero atom bonds can be achieved by using palladium catalyzed asymmetric allylic substitution reactions. Bis(oxazoline)s, P,N-ligands and P,N,N,P-ligands have been extensively used for above said purposes. Nevertheless there is always room for improvement in case of substrate selectivity especially for unsymmetrical allylic acetates.[10] Since bisphosphine-bis(oxazoline) **4** was explored well with AAA, first we decided to evaluate the potential of tetradentate-bioxazoline **5a** in catalyzing AAA. Moreover, there is no literature precedence of using O,N,N,O-tetradentate ligands in allylic substitution reactions and to the best of our knowledge this is first time O,N,N,O-tetradentate bioxazoline ligands are being explored.

Scheme 1. Attempts to synthesize O,N,N,O-tetradentate ligand

Initial efforts were made to synthesize O,N,N,O-tetradentate ligand **5a** by reacting 2-methoxy benzoylchloride (**6**) with diamine **2** to afford diamide **7** in 97% yield. Our attempts to deprotect benzyl groups were not successful (H_2-Pd/C at 1 atm as well as high pressure, BCl_3, and HI, $FeCl_3$), and only very little conversion into diol **9** was observed under these reaction conditions (Scheme 1). By employing a modified synthetic pathway, diol **9** was synthesized efficiently by reacting diamine **8** with 2-methoxy benzoylchloride (**6**). However due to presence of electron releasing *o*-methoxy group, cyclization of diol **9** into corresponding bioxazoline **10a** did not materialize. Since *o*-methoxy group hindered our efforts in synthesizing our target ligand **5a**, we altered the strategy to achieve our goal.

Bioxazoline **3a** was synthesized as reported earlier with the focus of synthesizing tetradentate ligand **5a**. We hoped that presence of electron withdrawing oxazoline ring might facilitate the substitution of fluorine atom in **3a** by methoxide anion. Accordingly, bioxazoline **3a** was treated with sodium methoxide in tetrahydrofuran (THF) to afford bioxazoline **10a**, but the deprotection of methyl group under acidic conditions resulted in the ring opening of oxazoline. Since our goal is to incorporate -OH chelation we changed the anion counterpart by using sodium salt of benzylalcohol and made bioxazoline **10b**, which was subsequently deprotected to afford O,N,N,O-tetradentate bioxazoline **5a** in good yield (Scheme 2). Apart from standard characterization techniques, structure of ligand **5a** was solved by X-ray crystallography also (CCDC No: 825879) (Figure 3).[9]

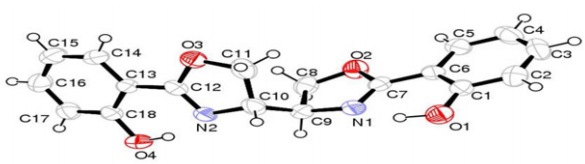
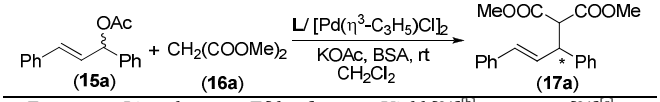


Figure 3. ORTEP drawing of the molecular structure of ligand **5a**

To evaluate the efficiency of ligand **5a** as a chiral ligand in Pd-catalyzed allylic substitutions, the traditional reaction between *rac*-(*E*)-1,3-diphenyl-2-propen-1-yl acetate (**15a**) and dimethyl malonate (**16a**) was examined. Dimethyl malonate (**16a**) was treated with allylic substrate **15a** in the presence of $[(\eta^3\text{-}C_3H_5)PdCl]_2$ (5 mol %) and ligand **5a** (10 mol %) at 25 °C and the results are summarized in Table 1. As seen from table 1, ligand **5a** exhibited modest increase in efficiency in catalyzing allylic substitution reaction with 81% ee in 79% yield (Table 1, entry 1). It is prudent to compare the catalytic efficiency of newly

developed O,N,N,O-ligand **5a** with similar chelating ligands i.e salen.[11] Hence we synthesized various salen ligands (**18** & **19**) (Figure 4) as reported earlier and gauged their ability in catalyzing AAA (Table 1, entries 2-5). The best performing salen ligands **18a** and **19a** in other asymmetric transformations failed to induce very good asymmetric induction (Table 1, entries 2 & 4). Poor enantioselectivity (22 & 36% ee) was observed using salen ligands **18a** and **19a** under the identical reaction conditions. Since tetradentate ligand **5a** does not contain any bulky substituents as in salen ligands **18a** and **19a**, it is necessary to screen salen ligands with no steric substituents. To simulate the similar steric environment of ligand **5a**, salen ligands **18b** and **19b** were evaluated for their efficiency in the formation of **17a**. Both salen ligands **18b** and **19b** neither catalyzed the reaction efficiently nor improved the asymmetric induction in AAA. Only low yields and moderate enantioselectivities were obtained using ligand **18b** and **19b** (Table 1, entries 3 & 5).

Table 1. Catalytic efficiency of tetradentate Bioxazoline ligands over bidentate Bioxazoline and Salen ligands in Pd-catalyzed asymmetric allylic alkylation (AAA) reaction.[a]



Entry	Ligand	*T* [days]	Yield [%][b]	ee [%][c]
1	**5a**	3	79	81 (*R*)
2	**18a**	3	69	22 (*R*)
3	**18b**	3	34	28 (*R*)
4	**19a**	2	92	36 (*S*)
5	**19b**	2	28	40 (*S*)
6	**3a**	6	52	49 (*R*)
7	**3b**	6	80	64 (*R*)
8	**10a**	3	73	38 (*R*)
9	**5b**	3	57	53 (*R*)

[a] Reaction conditions: ligand (10 mol %), $[(\eta^3\text{-}C_3H_5)PdCl]_2$ (5 mol %), **15a** (0.2 mmol), $CH_2(COOMe)_2$ (0.6 mmol), BSA (0.6 mmol) in 1 mL of Dichloromethane at 25 °C.
[b] Isolated yield.
[c] Determined by chiralpak AD-H column.

It is clear from these results that in case of AAA performance of our ligand **5a** is superior to salen ligands. It is necessary to prove the importance of additional chelation i.e phenoxy groups beyond reasonable doubt. Evaluating bioxazlines **3a**, **3b** and **10a** in allylic substation will give a clear indication about the need of additional chelation. Under the reaction conditions neither bioxazolines **3a** nor **3b** performed better than tetradentate ligand **5a** in inducing enantioselectivity (Table 1, entries 6 & 7). Only moderate enantioselectivity was obtained when bidentate bioxazolines **3a** and **3b** were used. These experiments indicate the need of additional chelation moiety in these types of bioxazolines to effect Pd-catalyzed allylic substitution. The substantially improved enantioselectivity obtained support that our ligand **5a** is better than the parent ligand **3** in which reaction took 6 days to complete (Table 1, entries 6 & 7).

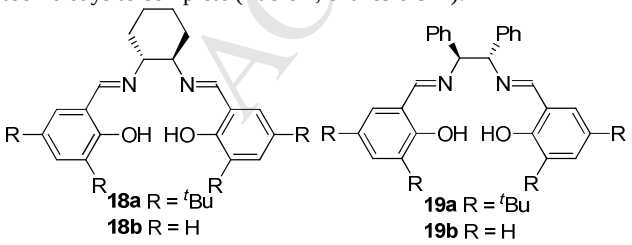


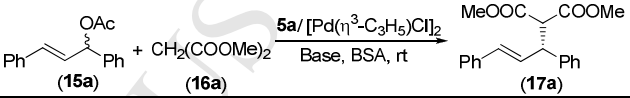
Figure 4. Structures of salen ligands

Recently Ooi and his co-workers found enhanced enantioselectivity and yield by phenolic –OH in case of Pd-catalyzed AAA using ion-paired ligand.[12] Although we observed the similar effects it is necessary to prove the need of free –OH, hence we screened ligand **10a** where the phenolic –OH protected with methyl which showed only 38% enantioselectivity (Table 1, entry 8). This experiment clearly showed the importance of additional chelation to enhance the reactivity as well as enantioselectivity. Thus we have identified a novel O,N,N,O-tetradentate ligand **5a** for asymmetric allylic alkylation reaction.

In case of Salen-complexes it is proven that presence of trifluoromethyl group at the ortho position increases the enantioselectivity considerably for asymmetric epoxidation.[13] In an attempt to optimize the structure of tetradentate ligand **5a**, we accomplished the synthesis of ligand **5b** by choosing the respective benzoic acid derivative. Screening of ligand **5b** in allylic substitution afforded the product **17a** in moderate yield and enantioselectivity (Table 1, entry 9). Presence of CF_3- group at ortho position did not bring in the desired effect.

2.3. Effect of Solvents and Additives on AAA

Table 2. Solvent and additive effect on enantioselectivity.[a]



Entry	Solvent	Base	*t* [days]	Yield [%][b]	ee [%][c]
1	Dichloroethane	KOAc	3	70	82
2	Chloroform	KOAc	3	48	81
3	THF	KOAc	3	51	48
4	Diethylether	KOAc	3	49	54
5	TBME	KOAc	3	57	56
6	Dioxane	KOAc	4	traces	nd
7	Acetonitrile	KOAc	4	88	64
8	Toluene	KOAc	3	traces	nd
9	Benzene	KOAc	3	53	71
10	Dichloromethane	LiOAc	3	83	84
11	Dichloromethane	NaOAc	3	78	77
12	Dichloromethane	AgOAc	4	70	92

[a] Reaction conditions: **5a** (10 mol%), $[(\eta^3\text{-}C_3H_5)PdCl]_2$ (5 mol%), **15a** (0.2 mmol), $CH_2(COOMe)_2$ (0.6 mmol), BSA (0.6 mmol) in 1 mL of solvent at 25 °C.
[b] Isolated yield.
[c] Determined by chiralpak AD-H column.

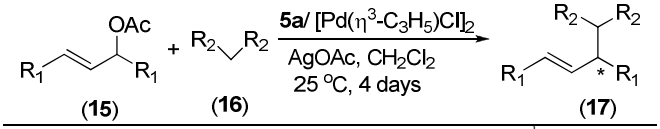
To improve the enantioselectivity further the role of solvents was investigated by performing the reaction in various solvents using the $[Pd(\eta\text{-}C_3H_5)Cl]_2$/**5a** in the presence of BSA and KOAc. It was observed that the choice of the solvent affected both the yield and the enantioselectivity. Among the chlorinated solvents dichloromethane was found to be most suitable solvent in mediating the reaction in the presence of KOAc to afford allylic alkylation product **17a** in 79% yield and with 81% ee (Table 1, entry 1). Neither dichloroethane nor chloroform as the reaction medium affected the yield or enantioselectivity favourably (Table 2, entries 1-2). Ethereal solvents such as THF, diethylether and *tert*-butyl methyl ether (TBME) failed to play an optimal role in terms of both yield (49-57%) and enantioselectivity (48-56%) (Table 2, entries 3-5). Only trace amount of product was formed when dioxane was used as the solvent (Table 2, entry 6) even after extending the reaction duration for 4 days. In acetonitrile, allylic substitution proceeded smoothly and came to completion in 4 days. Although the product isolated had 88% yield, only a moderate asymmetric induction was observed (64% ee) (Table 2, entry 7). No betterment of yield or enantioselectivity was noticed when toluene or benzene was used as reaction medium (Table 2, entries 8 & 9). With these findings, we concluded that dichloromethane is the most suitable solvent for ligand **5a** in catalyzing allylic substitution. Hence identification of a befitting base was carried out in dichloromethane (Table 2, entries 10-12).

Among the bases screened AgOAc was found as the most apt base in conjunction with N,O-bis(trimethylsilyl)acetamide. Allylic substitution product **17a** was obtained in 70% yield and very good enantioselectivity (92% ee).

2.4. Substrate Scope of AAA

With this optimized reaction conditions, the scope of catalytic asymmetric allylic alkylation (AAA) was demonstrated by the treatment of various allylic acetates with several carbon nucleophiles in the presence of 10 mol % of the ligand **5a** and 5 mol % of Pd in dichloromethane at room temperature. Aromatic allylic acetates with electron withdrawing substituents such as F, Cl and Br underwent allylic alkylation smoothly with very good enantioselectivity (87-96% ee, Table 3, entries 1-5). Whereas electron releasing groups in the aromatic ring such as -CH_3, and -OMe as well as napthyl-allylic acetates provided the corresponding alkylated product with enantiomeric excess in the range of 69-84% (Table 3, entries 6, 7 and 8). The above discussed reactions were carried out using dimethyl malonate as a nucleophile.

Table 3. Alkylation of racemic allylic acetates in the optimized reaction conditions. Structural effects on the enantioselectivity.[a]

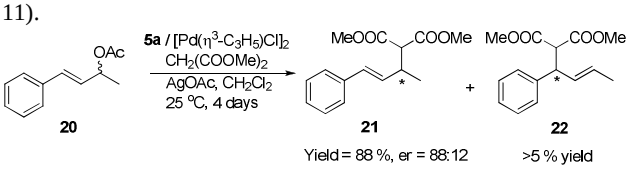


(**15**) (**16**) (**17**)

Entry	R_1	Product	R_2	Yield [%][b]	ee [%]
1	4-FC_6H_4	**17b**	CO_2Me	79	93
2	3-ClC_6H_4	**17c**	CO_2Me	81	90
3	4-ClC_6H_4	**17d**	CO_2Me	87	93
4	3-BrC_6H_4	**17e**	CO_2Me	79	96
5	4-BrC_6H_4	**17f**	CO_2Me	83	87
6	4-MeC_6H_4	**17g**	CO_2Me	79	84
7	4-$MeOC_6H_4$	**17h**	CO_2Me	78	69
8	2-Napthyl	**17i**	CO_2Me	86	79
9	4-ClC_6H_4	**17j**	CO_2Et	84	70
10	4-ClC_6H_4	**17k**	COMe	87	82
11	4-ClC_6H_4	**17l**	CN	77	78

[a] Reaction conditions: **5a** (10 mol%), [(η^3-C_3H_5)PdCl]$_2$ (5 mol%), **15** (0.2 mmol), **16** (0.6 mmol), BSA (0.6 mmol) in 1 mL of CH_2Cl_2 at 25 °C.
[b] Isolated yield.

Apart from the scope of various allylic acetates in asymmetric alkylation we also found the reactivity and selectivity using various carbon nucleophiles for AAA reaction under our optimized reaction conditions. Since the reactivity of 4-ClC_6H_4 (**15d**) was very fast in the previous experiments we chose **15d** as allylic substrate for the evaluation of various carbon nucleophiles such as diethyl malonate (**16b**), acetyl acetone (**16c**) and malononitrile (**16d**) in AAA. Under the identical reaction conditions treatment of **15d** with diethyl malonate (**16b**) afforded the corresponding alkylated product **17j** in very good yield with moderate enatioselectivity (70% ee, Table 3, entry 9). Allylic alkylation using acetyl acetone (**16c**) or malononitrile (**16d**) instead of using malonate ester was also found suitable nucleophiles for our catalytic system yielded the corresponding alkylated product (**17k** and **17l**) in very good yields and with good enantiomeric excess (78-82% ee, Table 3, entries 10 and 11).



20 **21** **22**

Yield = 88 %, er = 88:12 >5 % yield

Scheme 3. AAA of unsymmetrical allylic acetate

Although the allylic alkylation using symmetrical substrates was explored well in the literature, alkylation of unsymmetrical allylic substrates is less explored.[14] Especially the substrate bearing two different terminal groups such as phenyl and methyl **20** showed only 43% ee using chiral ferrocenyl phosphine-thioether ligands reported by Chan et al.[14e] All other reports including the well explored bis(oxazoline)[14g] ligands catalyzed allylic substitution with poor enantioselectivity. Hence we chose substrate **20** as a model substrate to explore the potentiality of our catalytic system for unsymmetrical allylic acetates. In this case we observed predominant nucleophilic attack at the least hindered carbon with extended conjugation to afford **21** with 76% enantioselectivity (Scheme 3). To the best of our knowledge there is no literature precedence to achieve this level of enantioselectivity while using **20** as a substrate for AAA. This promising result indicates that this tetradentate ligand might be the ideal choice to effect allylic substitution reaction in case of unsymmetrical allylic acetates, which is under investigation in our lab.

3. Conclusion

In conclusion we developed a novel tetradentate bioxazoline from tartaric acid and it was utilized successfully for AAA. Easy synthesis of this ligand paves the way to optimize its structure to increase its application in various mechanistically different asymmetric transformations. We are confident that structural optimization of tetradentate ligand **5a** might lead to the development of a novel privileged ligand for asymmetric catalysis.

4. Experimental section

4.1 General Information

Tetrahydrofuran (THF) was distilled prior to use under argon atmosphere over sodium benzophenone ketyl radical. Triethylamine (Et_3N) and diisopropylethylamine (DIPEA) were distillated under normal pressure and stored over potassium hydroxide. Dichloromethane (DCM) was stirred with calcium hydride and distilled before use. Petroleum ether (PE) and ethyl acetate (EA) were purified prior to use by distillation. The ligand precursor (2*S*,3*S*)-1,4-bis(benzyloxy)butane-2,3-diamine (**2**),[15] (2*S*,3*S*)-2,3-diaminobutane-1,4-diol (**8**),[16] Bioxazoline ligands (**3**)[4a-4d] and SALEN ligands (**18** & **19**)[17] were prepared according to the published procedures. All other chemicals were purchased from Aldrich and used as received without further purification.

^{1}H, ^{13}C NMR and DEPT-135 data were recorded with a Bruker AVANCE AV500 (500 MHz and 125.7 MHz) spectrometer with tetramethylsilane (TMS) as an internal standard. All ^{1}H NMR spectra were reported in delta (δ) units, parts per million (ppm) downfield from the internal standard. Coupling constants were reported in Hertz (Hz). High resolution mass spectra (HRMS) were measured under the condition of electro spray ionization (ESI) accurate masses were reported for the molecular ion ($[M]^+$ and $[M+1]^+$). IR spectra were recorded on PERKIN ELMER FT-IR instrument. Optical rotations were measured on a RUDOLPH AUTOPOL II, Automatic Polarimeter with a sodium lamp and are reported as follows: $[\alpha]_\lambda^{T\,°C}$ (*c* = g/100 mL, solvent). Column chromatography was carried out using 230-400 mesh silica gel (Merck) in PE and EA. Thin layer chromatography (TLC) was performed on commercially available pre-coated aluminium-backed plates (0.25 mm silica gel with fluorescent indicator UV254). Visualization was accomplished with UV light and phosphomolybdic acid stain, followed by heating.

4.2 Experimental procedure for the preparation of tetradentate bioxazoline 5a and 5b:

*4.2.1. (4S,4'S)-2,2'-bis(2-(benzyloxy)phenyl)-4,4',5,5'-tetrahydro-4,4'-bioxazole (**10b**).* To a solution of benzyl alcohol (1.5 mL, 15 mmol) and NaH (638 mg (60%), 20 mmol) in 25 mL of dry THF was added (4S,4'S)-2,2'-bis(2-fluorophenyl)-4,4',5,5'-tetrahydro-4,4'-bioxazole (**3a**) (1.64 g, 5 mmol) at room temperature. The resultant mixture was stirred at rt for 12h. After completion, the reaction was quenched with water and it was extracted with EtOAc and washed with water dried over Na_2SO_4 and concentrated under reduced pressure to afford crude compound. The purification of the crude compound by column chromatography over silica gel using 1:1 EtOAc-hexane to yield the pure title compound **10b** (2.19 g, 87%) as a colorless solid; mp: 125-127 °C; R_f = 0.4 (PE/EtOAc, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.70 (dd, *J* = 7.5, 1.5 Hz, 2H, ArH), 7.47 (d, *J* = 7.5 Hz, 4H, ArH), 7.40-7.33 (m, 6H, ArH), 7.30-7.27 (m, 2H, ArH), 7.00-7.95 (m, 4H, ArH), 5.17 (s, 4H, CH_2-Ph), 4.88 (dd, *J* = 7.5, 7.5 Hz, 2H, CH), 4.36-4.30 (m, 4H, CH_2-OBn) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 164.5, 157.4, 136.8, 132.3, 131.2, 128.4, 127.7, 126.9, 120.7,117.8, 113.6, 70.6, 68.9, 68.3 ppm; FTIR (KBr): 3364, 3067, 2932, 2884, 1736, 1644, 1531, 1452, 1300, 1229, 1103, 1049, 755 cm^{-1}; ESI-MS (m/z): 505 $(M+H)^+$; HRMS (ESI) calcd. for $[C_{32}H_{29}N_2O_4]^+$ requires 505.2127, found 505.2132; $[\alpha]_D^{25}$ -36.60 (*c* 1.00, $CHCl_3$).

*4.2.2. 2,2'-((4S,4'S)-4,4',5,5'-tetrahydro-4,4'-bioxazole-2,2'-diyl)diphenol (**5a**).* To a solution of compound **10b** (1.51 g, 3 mmol) in methanol (20 mL) were added 10% Pd/C (0.7 g) under H_2 atmosphere. The reaction mixture was stirred for 8 hours at 25 °C. The catalyst was removed by filtration over Celite, and the filtrate was concentrated under reduced pressure to remove all volatile materials. The white solid residue was purified by flash column chromatography using EtOAc and hexanes to give **5a** with the yield of 88% (855 mg) as a colorless solid; mp: 155 °C; R_f = 0.5 (PE/EtOAc, 4:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 11.74 (s, 2H, OH), 7.64 (dd, *J* = 7.9, 1.7 Hz, 2H, ArH), 7.35 (dt, *J* = 7.3, 1.7 Hz, 2H, ArH), 6.95 (dd, *J* = 8.3, 1.1 Hz 2H, ArH), 6.85 (dt, *J* = 7.6, 1.1 Hz, 2H, ArH), 4.81-4.76 (m, 2H, CH), 4.47-4.43 (m, 2H, CH_2), 4.39-4.35 (m, 2H, CH_2) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 167.1, 159.8, 133.7, 128.3, 118.7, 116.7, 110.0, 68.2, 67.5 ppm; FTIR (Neat): 3020, 2950, 2930, 2868, 1650, 1541, 1390, 1264, 1210, 1099, 1030, 851, 697 cm^{-1}; ESI-MS (m/z): 725 $(M+H)^+$; HRMS (ESI) calcd. for $[C_{18}H_{17}N_2O_4]^+$ requires 325.1188, found 325.1179; $[\alpha]_D^{25}$ +40.58 (*c* 1.00, CH_2Cl_2).

*4.2.3. N,N'-((2S,3S)-1,4-bis(benzyloxy)butane-2,3-diyl)bis(2-fluoro-3-(trifluoromethyl)benzamide) (**11**).* To a stirred solution of diamine **2** (1.5 g, 5 mmol) and Et_3N (1.71 mL, 10 mmol) in anhydrous CH_2Cl_2 (50 mL) was added 2-fluoro-3-(trifluoromethyl)benzoyl chloride (2.265 g, 10 mmol) at 0 °C under argon atmosphere. The solution was further stirred for 6 h at room temperature. Completion of the reaction was ascertained by TLC and quenched by addition of water and diluted with CH_2Cl_2. The organic phase was washed successively with 2% aqueous HCl solution, saturated $NaHCO_3$, and brine solution and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography (20% EtOAc in hexanes on silica gel) yielded title compound **11** with 97% (3.3 g) as a colorless solid; mp: 147-148 °C; R_f = 0.4 (PE/EtOAc, 4:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09 (t, *J* = 8.0 Hz, 2H, ArH), 7.70 (t, *J* = 8.0 Hz, 2H, ArH), 7.44 (t, *J* = 8.0 Hz, 2H, ArH), 7.34-7.26 (m, 12H, ArH and NH), 4.73-4.72 (m, 2H, CH), 4.50 (s, 4H, CH_2-Ph), 3.70-3.62 (m, 4H, CH_2) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 162.2, 156.5 (d, *J* = 258.9 Hz), 137.2, 135.6, 130.1 (d, *J* = 3.7 Hz), 128.4, 127.9 (d, *J* = 2.5 Hz), 124.3 (d, *J* = 3.7 Hz), 123.2, 123.1 (d, *J* = 11.3 Hz), 121.1, 118.9 (m), 73.5, 68.5, 50.9 ppm; FTIR (KBr): 3285, 3087, 2923, 1650, 1641, 1557, 1466, 1455, 1324, 1161, 1023, 919, 750 cm^{-1}; ESI-MS (m/z): 725 $(M+H)^+$; HRMS (ESI) calcd. for $[C_{34}H_{29}N_2O_6F_8]^+$ requires 681.2000, found 681.1991; $[\alpha]_D^{25}$ -45.80 (*c* 1.00, $CHCl_3$).

*4.2.4. N,N'-((2S,3S)-1,4-dihydroxybutane-2,3-diyl)bis(2-fluoro-3-(trifluoromethyl)benzamide) (**12**).* To a solution of compound **11** (2.72 g, 4 mmol) in methanol (20 mL) were added 10% Pd/C (0.5 g) under H_2 atmosphere. The reaction mixture was stirred for 12 hours at 25 °C. The catalyst was removed by filtration over Celite, and the filtrate was concentrated under reduced pressure to remove all volatile materials. The white solid residue was purified by flash column chromatography using CH_2Cl_2 and CH_3OH to give **12** with the yield of 91% (1.82 g) as a colorless solid; mp: 183-184 °C; R_f = 0.3 (CH_2Cl_2/CH_3OH, 19:1); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.23 (d, *J* = 8.0 Hz, 2H, NH), 7.90 (q, *J* = 6.5 Hz, 4H, ArH), 7.48 (t, *J* = 7.5 Hz, 2H, ArH), 4.83 (t, *J* = 6.0 Hz, 2H, OH), 4.36-4.30 (m, 2H, CH), 3.59-3.56 (m, 4H, CH_2) ppm; ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 163.3, 156.4 (d, *J* = 257.6 Hz), 135.1, 129.4 (d, *J* = 5.0 Hz), 126.5 (m), 125.3 (d, *J* = 3.7 Hz), 124.0, 121.8, 119.6, 117.6 (m), 61.1, 52.4 ppm; FTIR (KBr): 3281, 3084, 2930, 2888, 1642, 1546, 1465, 1317, 1239, 1154, 1136, 1081, 1019, 832 cm^{-1}; ESI-MS (m/z): 725 $(M+H)^+$; HRMS (ESI) calcd. for $[C_{20}H_{17}N_2O_4F_8]^+$ requires 501.1061, found 501.1047; $[\alpha]_D^{25}$ +3.60 (*c* 0.50, $CHCl_3$: CH_3OH (1:1)).

*4.2.5. (4S,4'S)-2,2'-bis(2-fluoro-3-(trifluoromethyl)phenyl)-4,4',5,5'-tetrahydro-4,4'-bioxazole (**13**).* To a solution of **12** (1.5 g, 3 mmol) in 20 mL of dry THF was added dry Et_3N (2.8 mL, 20 mmol) and MsCl (0.7 mL, 9 mmol) at 0 °C. After stirring at room temperature for 2 days, the volatiles were removed under vacuum to give a yellow solid. The residue was then extracted with DCM and washed with brine and it was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Crude product was purified by column chromatography (1:1 hexane and EtOAc) yielded title compound in 88% (1.2 g) yield as a colorless solid, mp: 80-81 °C; R_f = 0.4 (PE/EtOAc, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.03 (dt, *J* = 7.3, 1.1 Hz, 2H, ArH), 7.72 (dt, *J* = 7.3, 1.1 Hz, 2H, ArH), 7.28 (t, *J* = 7.2 Hz, 2H, ArH), 4.86-4.82 (m, 2H, CH), 4.53-4.47 (m, 4H, CH_2) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 161.2 (d, *J* = 3.7 Hz), 158.3 (d, *J* = 267.7 Hz), 134.8, 129.9 (t, *J* = 5.0 Hz), 125.4, 123.7 (d, *J* = 2.5 Hz), 123.2, 121.1, 119.7 (d, *J* = 12.57 Hz), 119.4 (m), 117.4 (d, *J* = 11.3 Hz), 69.1, 69.0 ppm; FTIR (KBr): 2902, 1638, 1612, 1462, 1375, 1314, 1210, 1144, 1079, 971, 748 cm^{-1}; ESI-MS (m/z): 725 $(M+H)^+$; HRMS (ESI) calcd. for $[C_{20}H_{13}N_2O_2F_8]^+$ requires 465.0849, found 465.0865; $[\alpha]_D^{25}$ -38.00 (*c* 0.50, $CHCl_3$).

*4.2.6.(4S,4'S)-2,2'-bis(2-(benzyloxy)-3-(trifluoromethyl)phenyl)-4,4',5,5'-tetrahydro-4,4'-bioxazole (**14**).* Prepared according to the procedure outlined for **10b** by using **13** (928 mg, 2 mmol), benzyl alcohol (0.62 mL, 6 mmol) and NaH (255 mg (60%), 8 mmol) in 20 mL of dry THF yielded the title compound **14** as a colorless solid (1.08 g, 85%), mp: 102-103 °C; R_f = 0.6 (PE/EtOAc, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 8.0, 1.5 Hz, 2H, ArH), 7.69 (dd, *J* = 8.0, 1.5 Hz, 2H, ArH), 7.45-7.43 (m, 4H, ArH), 7.37-7.30 (m, 6H, ArH), 7.12 (t, *J* = 8.0 Hz, 2H, ArH), 5.01-4.89 (m, 4H, CH_2), 4.68-4.64 (m, 2H, CH), 4.50-4.47 (m, 2H, CH_2), 4.39-4.35 (m, 2H, CH_2) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 136.6, 135.3, 130.0 (q, *J* = 5.0 Hz), 128.3, 128.0, 127.9, 125.7, 125.4, 124.3, 123.5, 123.4, 122.1, 69.3, 69.0 ppm; FTIR (KBr): 3060, 3029, 2950, 2920, 2858, 1392, 1264, 1210, 1099, 1040, 859, 697 cm^{-1}; ESI-MS (m/z): 505 $(M+H)^+$; HRMS (ESI) calcd. for

$[C_{34}H_{27}N_2O_4F_6]^+$ requires 641.1875, found 641.1878; $[\alpha]_D^{25}$ -68.40 (*c* 0.50, $CHCl_3$).

*4.2.7. 6,6'-((4S,4'S)-4,4',5,5'-tetrahydro-4,4'-bioxazole-2,2'-diyl)bis(2-(trifluoromethyl)phenol) (**5b**).* Prepared according to the procedure outlined for **5a** by using **14** (960 mg, 1.5 mmol) in methanol (15 mL) were added 10% Pd/C (400 mg) under H_2 atmosphere yielded the title compound **5b** as a colorless solid (634 mg, 92%); mp: 178 °C; R_f = 0.3 (PE/EtOAc, 4:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 12.57 (s, 2H, OH), 7.81 (dd, *J* = 7.8, 1.4 Hz, 2H, ArH), 7.62 (dt, *J* = 7.6, 1.0 Hz, 2H, ArH), 6.90 (t, *J* = 7.7 Hz, 2H, ArH), 4.78-4.74 (m, 2H, CH), 4.55-4.47 (m, 4H, CH_2) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 166.8, 157.9, 132.1, 131.0 (q, *J* = 5.0 Hz), 124.4, 122.3, 118.0, 111.2, 68.7, 67.5 ppm; FTIR (KBr): 3029, 2966, 2931, 2858, 1643, 1541, 1392, 1264, 1210, 1099, 1030, 851, 697 cm^{-1}; ESI-MS (m/z): 725 $(M+H)^+$; HRMS (ESI) calcd. for $[C_{20}H_{15}N_2O_6F_6]^+$ requires 461.0936, found 461.0925; $[\alpha]_D^{25}$ +49.20 (*c* 1.00, $CHCl_3$).

*4.2.8. (4S,4'S)-2,2'-bis(2-methoxyphenyl)-4,4',5,5'-tetrahydro-4,4'-bioxazole. (**10a**).* To a stirred solution of **3a** (656 mg, 2 mmol) in 10 mL of dry THF was added sodium methoxide (162 mg, 3 mmol) at room temperature. The resultant mixture was stirred at rt for 8h. After completion, the reaction was quenched with water and it was extracted with EtOAc and washed with water dried over Na_2SO_4 and concentrated under reduced pressure to afford crude compound. The purification of the crude compound by column chromatography over silica gel using 1:1 EtOAc-hexane to yield the pure title compound **10a** (598 mg, 85%) as a colorless solid; mp: 156 °C; R_f = 0.2 (PE/EtOAc, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.69 (dd, *J* = 8.0, 2.0 Hz, 2H, ArH), 7.62 (dt, *J* = 2.0, 8.0 Hz, 2H, ArH), 6.96 (t, *J* = 8.0 Hz 2H, ArH), 4.90-4.85 (m, 2H, CH), 4.42-4.33 (m, 4H, CH_2), 3.83 (s, 6H, OCH_3) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 164.3, 158.4, 132.4, 131.2, 120.2, 117.1, 111.6, 69.1, 68.3, 55.9, 29.7 ppm; FTIR (KBr): 2978, 2864, 1650, 1570, 1392, 1265, 1217, 1099, 1030, 858 cm^{-1}; $[\alpha]_D^{25}$ -57.32 (*c* 1.00, CH_2Cl_2).

4.3 The catalytic asymmetric allylic alkylation reaction:

4.3.1. General procedure. To a stirring solution of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (1.8 mg, 0.005 mmol) in CH_2Cl_2 was added ligand **5a** (6.4 mg, 0.02 mmol) under inert atmosphere. After 2 hours, *rac*-(*E*)-1,3-diphenyl-2-propen-1-yl acetate (**15a**) (50 mg, 0.198 mmol) was added and the solution was stirred for 30 min. N,O-Bis(trimethylsilyl)acetamide (0.145 ml, 0.594 mmol), dimethyl malonate (0.09 ml, 0.594 mmol) and AgOAc (0.007 mmol) were then added at 25 °C and solution was stirred further till the reaction is completed. The solvent was evaporated in vacuo and column chromatography on silica gel (hexane–EtOAc 4 : 1) of the residue yielded the pure product **17a** of 70%.

*4.3.2. (E)-dimethyl 2-(1,3-diphenylallyl)malonate. (**17a**).* Prepared according to the general procedure using (*E*)-1,3-diphenyl-2-propen-1-yl acetate (50 mg, 0.198 mmol) and dimethyl malonate (0.07 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (44 mg, 70% yield); The ee was determined by HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 17.1 min, minor enantiomer tr = 22.7 min; 92% ee. Configuration assignment: The absolute stereochemistry was assigned as (*R*) by comparison of the retention times in HPLC reported in the literature[13f, 18]; ^{1}H NMR (500 MHz): δ 7.35-7.21 (m, 10H, ArH), 6.50 (d, *J* = 15.7 Hz, 1H, ═CH), 6.35 (dd, *J* = 15.7, 8.1 Hz, 1H, ═CH), 4.29 (dd, *J* = 10.7, 8.5 Hz, 1H, CH), 3.98 (d, *J* = 10.8 Hz, 1H, CH), 3.73 (s, 3H, CH_3), 3.54 (s, 3H, CH_3) ppm; ^{13}C NMR (500 MHz, $CDCl_3$): δ 168.2, 167.7, 140.1, 136.8, 131.8, 129.1, 128.7, 128.4, 127.8, 127.5, 127.1, 126.3, 57.6, 52.6, 52.4, 49.2 ppm; FTIR (KBr): 3654, 3473, 3028, 2952, 1953, 1739, 1599, 1494, 1452, 1435, 1027, 967, 766, 699 cm^{-1}.

*4.3.3. (E)-dimethyl 2-(1,3-bis(4-fluorophenyl)allyl)malonate. (**17b**).* Prepared according to the general procedure using (*E*)-1,3-bis(4-fluorophenyl)-2-propen-1-yl acetate (57 mg, 0.198 mmol) and dimethyl malonate (0.07 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (56 mg, 79% yield); The ee was determined by HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 11.6 min, minor enantiomer tr = 18.0 min; 93% ee; ^{1}H NMR (500 MHz): δ 7.29-7.23 (m, 4H, ArH), 7.03-6.94 (m, 4H, ArH), 6.41 (d, *J* = 15.6 Hz, 1H, ═CH), 6.21 (dd, *J* = 15.5, 8.5 Hz, 1H, ═CH), 4.26-4.22 (m, 1H, CH), 3.88 (d, *J* = 11.0 Hz, 1H, CH) 3.70 (s, 3H, CH_3), 3.53 (s, 3H, CH_3) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 168.0, 167.3, 163.0 (d, *J* = 64.1 Hz), 161.1 (d, *J* = 64.1 Hz), 135.8 (d, *J* = 3.7 Hz), 132.8 (d, *J* = 3.7 Hz), 130.8, 129.4 (d, *J* = 8.7 Hz), 128.5, 127.8 (d, *J* = 7.5 Hz), 115.6 (d, *J* = 21.3 Hz), 115.4 (d, *J* = 21.3 Hz), 57.6, 52.6, 52.5, 48.2 ppm; FTIR (KBr): 3643, 3005, 2956, 1746, 1755, 1601, 1509, 1436, 1338, 1159, 1025, 971, 847 cm^{-1}; ESI-MS (m/z): 383 $(M+Na)^+$; HRMS (ESI) calcd. for $[C_{20}H_{18}O_4F_2Na]^+$ requires 383.1071, found 383.1074.

*4.3.4. (E)-dimethyl 2-(1,3-bis(3-chlorophenyl)allyl)malonate. (**17c**).* Prepared according to the general procedure using (*E*)-1,3-bis(3-chlorophenyl)-2-propen-1-yl acetate (63 mg, 0.198 mmol) and dimethyl malonate (0.07 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (63 mg, 81% yield); The ee was determined by HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 7.4 min, minor enantiomer tr = 9.5 min; 90% ee; ^{1}H NMR (500 MHz): δ 7.33-7.29 (m, 2H, ArH), 7.28-7.27 (m, 1H, ArH), 7.25-7.18 (m, 5H, ArH), 6.44 (d, *J* = 15.5 Hz, 1H, ═CH), 6.32 (dd, *J* = 15.5, 9.0 Hz, 1H, ═CH), 4.26 (dd, *J* = 11.0, 9.0 Hz, 1H, CH), 3.94 (d, *J* = 10.5 Hz, 1H, CH), 3.73 (s, 3H, CH_3), 3.58 (s, 3H, CH_3) ppm; ^{13}C NMR (500 MHz, $CDCl_3$): δ 167.9, 167.5, 141.9, 138.4, 134.6, 134.5, 131.2, 130.1, 129.8, 128.1, 127.7, 126.3, 126.1, 124.7, 57.2, 52.8, 52.6, 48.7 ppm; FTIR (KBr): 3668, 3470, 2950, 2920, 1917, 1739, 1596, 1489, 1452, 1435, 1027, 955, 766 cm^{-1}.

*4.3.5. (E)-dimethyl 2-(1,3-bis(4-chlorophenyl)allyl)malonate. (**17d**).* Prepared according to the general procedure using (*E*)-1,3-bis(4-chlorophenyl)-2-propen-1-yl acetate (63 mg, 0.198 mmol) and dimethyl malonate (0.07 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (67 mg, 87% yield); The ee was determined by HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 15.6 min, minor enantiomer tr = 24.6 min; 93% ee; ^{1}H NMR (500 MHz): δ 7.30-7.27 (m, 2H, ArH), 7.25-7.20 (m, 6H, ArH), 6.39 (d, *J* = 16.0 Hz, 1H, ═CH), 6.25 (dd, *J* = 16.0, 9.0 Hz, 1H, ═CH), 4.23 (dd, *J* = 11.0, 9.0 Hz, 1H, CH), 3.89 (d, *J* = 10.5 Hz, 1H, CH), 3.70 (s, 3H, CH_3), 3.54 (s, 3H, CH_3) ppm; ^{13}C NMR (500 MHz, $CDCl_3$): δ 167.9, 167.5, 138.5, 135.0, 133.4, 133.1, 131.0, 129.3, 129.2, 128.9, 128.7, 127.6, 57.3, 52.7, 52.6, 48.4 ppm; FTIR (KBr): 3665, 3462, 2953, 1899, 1754, 1594, 1488, 1159, 1013, 827 cm^{-1}.

*4.3.6. (E)-dimethyl 2-(1,3-bis(3-bromophenyl)allyl)malonate. (**17e**).* Prepared according to the general procedure using (*E*)-1,3-bis(3-bromophenyl)-2-propen-1-yl acetate (81 mg, 0.198 mmol) and dimethyl malonate (0.07 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (75 mg, 79% yield); The ee was determined by

HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 7.4 min, minor enantiomer tr = 9.5 min; 96% ee; ^{1}H NMR (500 MHz): δ 7.49-7.45 (m, 2H, ArH), 7.41-7.35 (m, 2H, ArH), 7.25-7.20 (m, 3H, ArH), 7.18-7.15 (m, 1H, ArH), 6.42 (d, *J* = 16.0 Hz, 1H, ═CH), 6.31 (dd, *J* = 15.5, 8.5 Hz, 1H, ═CH), 4.24 (dd, *J* = 10.5, 8.5 Hz, 1H, CH), 3.93 (d, *J* = 10.5 Hz, 1H, CH), 3.74 (s, 3H, CH_3), 3.59 (s, 3H, CH_3) ppm; ^{13}C NMR (500 MHz, $CDCl_3$): δ 167.8, 167.4, 142.2, 138.7, 131.1, 131.0, 130.7, 130.5, 130.4, 130.1, 129.9, 129.2, 126.5, 125.2, 122.8, 122.7, 57.2, 52.8, 52.6, 48.6 ppm; FTIR (KBr): 3486, 3455, 3028, 2956, 1953, 1759, 1610, 1434, 1072, 967, 826, 766 cm^{-1}.

*4.3.7. (E)-dimethyl 2-(1,3-bis(4-bromophenyl)allyl)malonate. **(17f)**.* Prepared according to the general procedure using (*E*)-1,3-bis(3-bromophenyl)-2-propen-1-yl acetate (81 mg, 0.198 mmol) and dimethyl malonate (0.07 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (79 mg, 83% yield); The ee was determined by HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 16.4 min, minor enantiomer tr = 24.4 min; 87% ee; ^{1}H NMR (500 MHz): δ 7.48-7.45 (m, 2H, ArH), 7.43-7.40 (m, 2H, ArH), 7.20-7.17 (m, 4H, ArH), 6.41 (d, *J* = 15.5 Hz, 1H, ═CH), 6.29 (dd, *J* = 16.0, 8.5 Hz, 1H, ═CH), 4.24 (dd, *J* = 11.0, 8.5 Hz, 1H, CH), 3.91 (d, *J* = 10.5 Hz, 1H, CH), 3.72 (s, 3H, CH_3), 3.57 (s, 3H, CH_3) ppm; ^{13}C NMR (500 MHz, $CDCl_3$): δ 167.9, 167.5, 138.9, 135.5, 131.9, 131.6, 131.1, 129.6, 129.2, 127.9, 121.5, 121.2, 57.2, 52.7, 52.6, 48.4 ppm; FTIR (KBr): 3462, 3026, 2952, 1738, 1487, 1434, 1312, 1254, 1160, 1072, 968, 824 cm^{-1}.

*4.3.8. (E)-dimethyl 2-(1,3-dip-tolylallyl)malonate. **(17g)**.* Prepared according to the general procedure using (*E*)-1,3-bis(4-methylphenyl)-2-propen-1-yl acetate (55 mg, 0.198 mmol) and dimethyl malonate (0.07 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (55 mg, 79% yield); The ee was determined by HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 24.6 min, minor enantiomer tr = 35.1 min; 84% ee; ^{1}H NMR (500 MHz): δ 7.23-7.18 (m, 4H, ArH), 7.14-7.08 (m, 4H, ArH), 6.50 (d, *J* = 15.5 Hz, 1H, ═CH), 6.27 (dd, *J* = 16.0, 8.5 Hz, 1H, ═CH), 4.23 (dd, *J* = 11.0, 8.5 Hz, 1H, CH), 3.94 (d, *J* = 11.0 Hz, 1H, CH), 3.71 (s, 3H, CH_3), 3.55 (s, 3H, CH_3), 2.33 (s, 6H, CH_3) ppm; ^{13}C NMR (500 MHz, $CDCl_3$): δ 168.3, 167.8, 137.3, 137.2, 136.6, 134.1, 131.4, 129.3, 129.1, 128.2, 127.7, 126.2, 57.7, 52.5, 52.4, 48.8, 21.1, 21.0 ppm; FTIR (KBr): 3463, 3024, 2952, 1759, 1513, 1434, 1312, 1256, 1159, 1021, 968, 818, 781 cm^{-1}.

*4.3.9. (E)-dimethyl 2-(1,3-bis(4-methoxyphenyl)allyl)malonate. **(17h)**.* Prepared according to the general procedure using (*E*)-1,3-bis(4-methoxylphenyl)-2-propen-1-yl acetate (61 mg, 0.198 mmol) and dimethyl malonate (0.07 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (59 mg, 78% yield); The ee was determined by HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 19.9 min, minor enantiomer tr = 32.5 min; 69% ee; ^{1}H NMR (500 MHz): δ 7.24-7.19 (m, 4H, ArH), 6.85-6.78 (m, 4H, ArH), 6.38 (d, *J* = 15.5 Hz, 1H, ═CH), 6.16 (dd, *J* = 15.5, 8.5 Hz, 1H, ═CH), 4.19 (dd, *J* = 10.5, 8.5 Hz, 1H, CH), 3.88 (d, *J* = 11.0 Hz, 1H, CH), 3.78 (s, 3H, CH_3), 3.77 (s, 3H, CH_3), 3.69 (s, 3H, CH_3), 3.52 (s, 3H, CH_3) ppm; ^{13}C NMR (500 MHz, $CDCl_3$): δ 168.3, 167.9, 159.1, 158.5, 132.4, 130.9, 129.7, 128.8, 127.5, 127.1, 114.0, 113.8, 57.9, 55.3, 55.2, 52.5, 52.4, 48.4 ppm; FTIR (KBr): 3491, 2954, 2837, 1755, 1738, 1608, 1512, 1463, 1302, 1250, 1176, 1033, 968, 832, 813 cm^{-1}; ESI-MS (m/z): 407 $(M+Na)^+$; HRMS (ESI) calcd. for $[C_{22}H_{24}O_6Na]^+$ requires 407.1471, found 407.1466.

*4.3.10. (E)-dimethyl 2-(1,3-di(naphthalen-2-yl)allyl)malonate. **(17i)**.* Prepared according to the general procedure using (*E*)-1,3-bis(naphthalene-2-yl)-2-propen-1-yl acetate (69 mg, 0.198 mmol) and dimethyl malonate (0.07 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (72 mg, 86% yield); Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 20.5 min, minor enantiomer tr = 27.4 min; 79% ee; ^{1}H NMR (500 MHz): δ 7.86-7.75 (m, 7H, ArH), 7.70 (S, 1H, ArH), 7.57-7.55 (m, 1H, ArH), 7.52-7.43 (m, 5H, ArH), 6.71 (d, *J* = 15.5 Hz, 1H, ═CH), 6.57 (dd, *J* = 15.5, 8.5 Hz, 1H, ═CH), 4.56-4.52 (m, 1H, CH), 4.16 (d, *J* = 10.5 Hz, 1H, CH), 3.76 (s, 3H, CH_3), 3.52 (s, 3H, CH_3) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 168.2, 167.8, 137.6, 134.2, 133.6, 133.5, 132.9, 132.6, 132.2, 129.3, 128.5, 128.1, 127.9, 127.8, 127.7, 127.6, 126.5, 126.3, 126.2, 126.1, 126.1, 125.8, 123.5, 57.6, 53.4, 52.6, 49.3 ppm; FTIR (KBr): 3454, 3049, 2951, 1743, 1723, 1432, 1317, 1261, 1157, 1025, 979, 970, 820, 749 cm^{-1}.

*4.3.11. (E)-diethyl 2-(1,3-bis(4-chlorophenyl)allyl)malonate. **(17j)**.* Prepared according to the general procedure using (*E*)-1,3-bis(4-chlorophenyl)-2-propen-1-yl acetate (63 mg, 0.198 mmol) and diethyl malonate (0.09 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (70 mg, 84% yield); The ee was determined by HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 14.3 min, minor enantiomer tr = 22.8 min; 70% ee; ^{1}H NMR (500 MHz): δ 7.30-7.21 (m, 8H, ArH), 6.40 (dd, *J* = 15.7, 0.4 Hz, 1H, ═CH), 6.28 (dd, *J* = 15.75, 8.5 Hz, 1H, ═CH), 4.25-4.15 (m, 3H, CH_2 and CH), 4.00 (m, 2H, CH_2), 3.86 (d, *J* = 10.7 Hz, 1H, CH), 1.2 (t, *J* = 7.1 Hz 3H, CH_3), 1.05 (t, *J* = 7.1 Hz 3H, CH_3) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 167.5, 167.1, 138.7, 135.1, 133.3, 133.0, 130.9, 129.5, 129.4, 128.8, 128.7, 127.5, 61.7, 61.5, 57.5, 48.4, 14.1, 13.8 ppm; FTIR (KBr): 3462, 2982, 1751, 1733, 1491, 1369, 1305, 1253, 1174, 1093, 1032, 969, 829 cm^{-1}.

*4.3.12. (E)-3-(1,3-bis(4-chlorophenyl)allyl)pentane-2,4-dione. **(17k)**.* Prepared according to the general procedure using (*E*)-1,3-bis(4-chlorophenyl)-2-propen-1-yl acetate (63 mg, 0.198 mmol) and acetyl acetone (0.06 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (62 mg, 87% yield); The ee was determined by HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 32.0 min, minor enantiomer tr = 22.5 min; 82% ee; ^{1}H NMR (500 MHz): δ 7.31-7.28 (m, 2H, ArH), 7.25-7.22 (m, 2H, ArH), 7.20-7.16 (m, 4H, ArH), 6.35 (d, *J* = 16.0 Hz, 1H, ═CH), 6.11 (dd, *J* = 16.0, 8.2 Hz, 1H, ═CH), 4.34-4.26 (m, 2H, 2CH), 2.23 (s, 3H, CH_3), 1.94 (s, 3H, CH_3) ppm; ^{13}C NMR (500 MHz, $CDCl_3$): δ 202.3, 202.1, 138.4, 134.8, 133.6, 133.2, 130.9, 129.3, 129.3, 129.2, 128.7, 127.6, 74.4, 48.2, 29.9, 29.6 ppm; FTIR (KBr): 3402, 2978, 2320, 2138, 1641, 1465, 1381, 1301, 1161, 1128, 950, 815 cm^{-1}.

*4.3.13. (E)-2-(1,3-bis(4-chlorophenyl)allyl)malononitrile. **(17l)**.* Prepared according to the general procedure using (*E*)-1,3-bis(4-chlorophenyl)-2-propen-1-yl acetate (63 mg, 0.198 mmol) and malononitrile (0.04 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (49 mg, 77% yield); The ee was determined by HPLC with a Chiralpak AD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 15.2 min, minor enantiomer tr = 16.3 min; 78% ee; ^{1}H NMR (500 MHz): δ 7.44-7.41 (m, 2H, ArH), 7.35-7.30 (m, 6H, ArH), 6.65 (d, *J* = 15.8 Hz,

1H, =CH), 6.39 (dd, *J* = 15.8, 7.5 Hz, 1H, =CH), 4.11-4.07 (m, 2H, 2CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 135.2, 135.0, 134.7, 134.6, 133.7, 130.0, 129.1, 129.0, 128.0, 123.9, 111.4, 111.3, 49.1, 30.1 ppm; FTIR (KBr): 3443, 2907, 2256, 1902, 1728, 1594, 1492, 1413, 1249, 1093, 1014, 969, 826 cm^{-1}; ESI-MS (m/z): 349 $(M+Na)^+$; HRMS (ESI) calcd. for $[C_{18}H_{12}Cl_2N_2Na]^+$ requires 349.0276, found 349.0274.

*4.3.14. (E)-dimethyl 2-(4-phenylbut-3-en-2-yl)malonate. (**21**).* Prepared according to the general procedure using (*E*)-4-phenylbut-3-en-2-yl acetate (37 mg, 0.198 mmol) and dimethyl malonote (0.09 mL, 0.594 mmol), while the reaction time was 4 days. The desired product was obtained as colorless oil (45 mg, 88% yield); The ee was determined by HPLC with a Chiralcel OD-H column (90:10 hexanes:isopropanol, 0.8 mL/min, 254 nm); major enantiomer tr = 23.0 min, minor enantiomer tr = 20.8 min; 76% ee; ^{1}H NMR (500 MHz): δ 7.34-7.19 (m, 5H, ArH), 6.45 (d, *J* = 15.5, 1H, =CH), 6.12 (dd, *J* = 16.0, 8.5 Hz, 1H, =CH), 3.75 (s, 3H, CH_3), 3.67 (s, 3H, CH_3), 3.40 (d, *J* = 9.0, 1H, CH), 3.16-3.09 (m, 1H, CH), 1.19 (d, *J* = 6.5, 3H, CH_3) ppm; FTIR (KBr): 3463, 2954, 1754, 1738, 1435, 1246, 1158, 1022, 968, 748, 694 cm^{-1}.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org.

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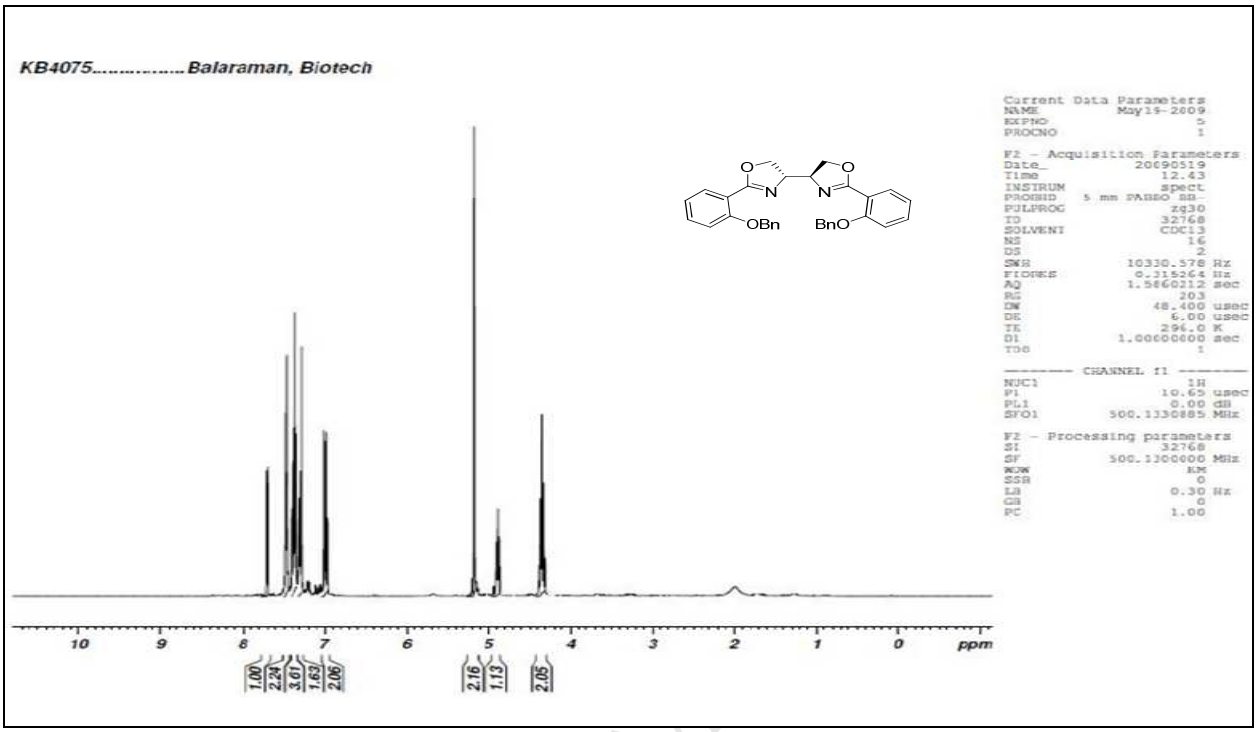
Supporting Information

Novel O,N,N,O-tetradentate ligand from tartaric acid

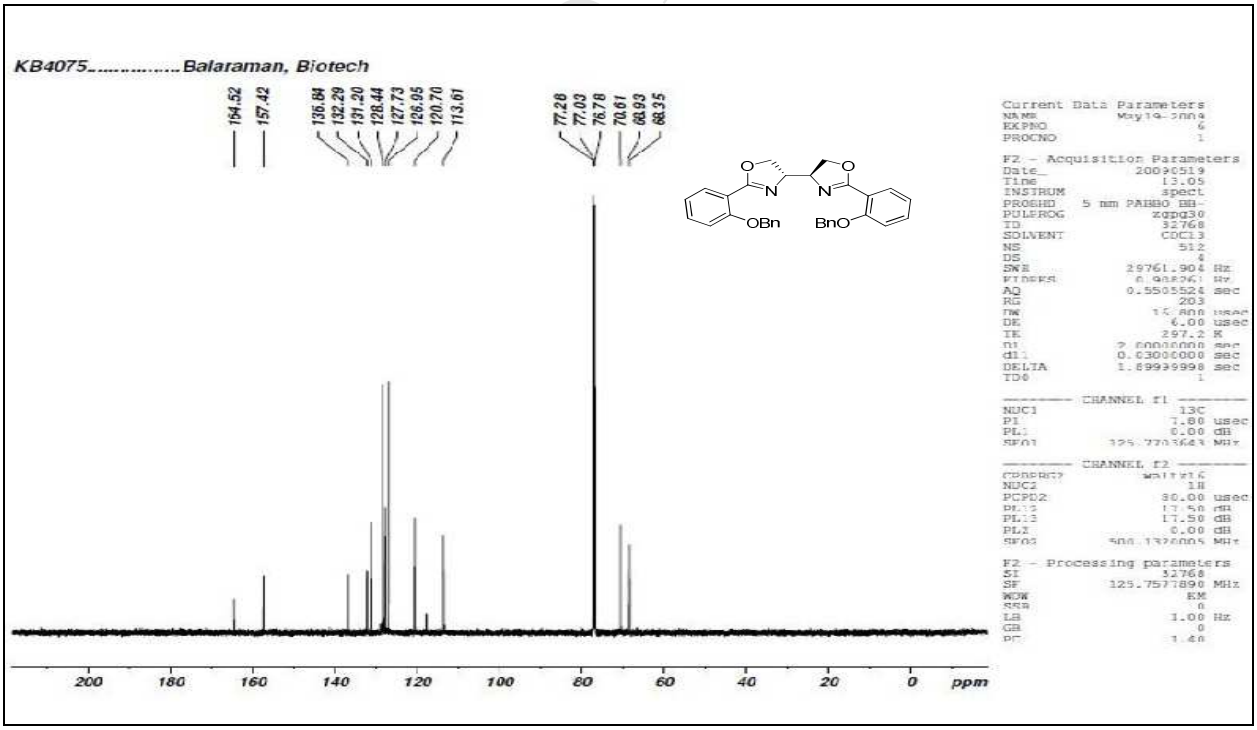
Kaluvu Balaraman, Ravichandran Vasanthan and Venkitasamy Kesavan*

Copies of ^{1}H NMR and ^{13}C NMR spectra

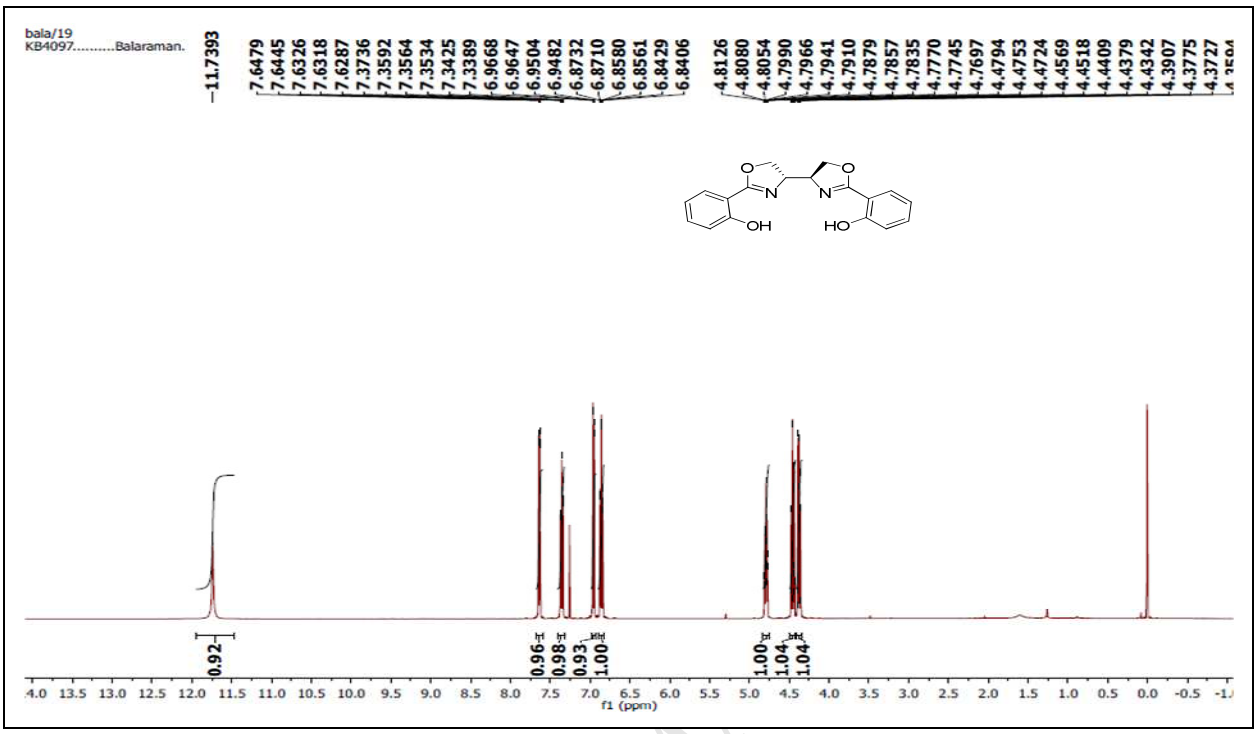
^{1}H NMR of **10b**



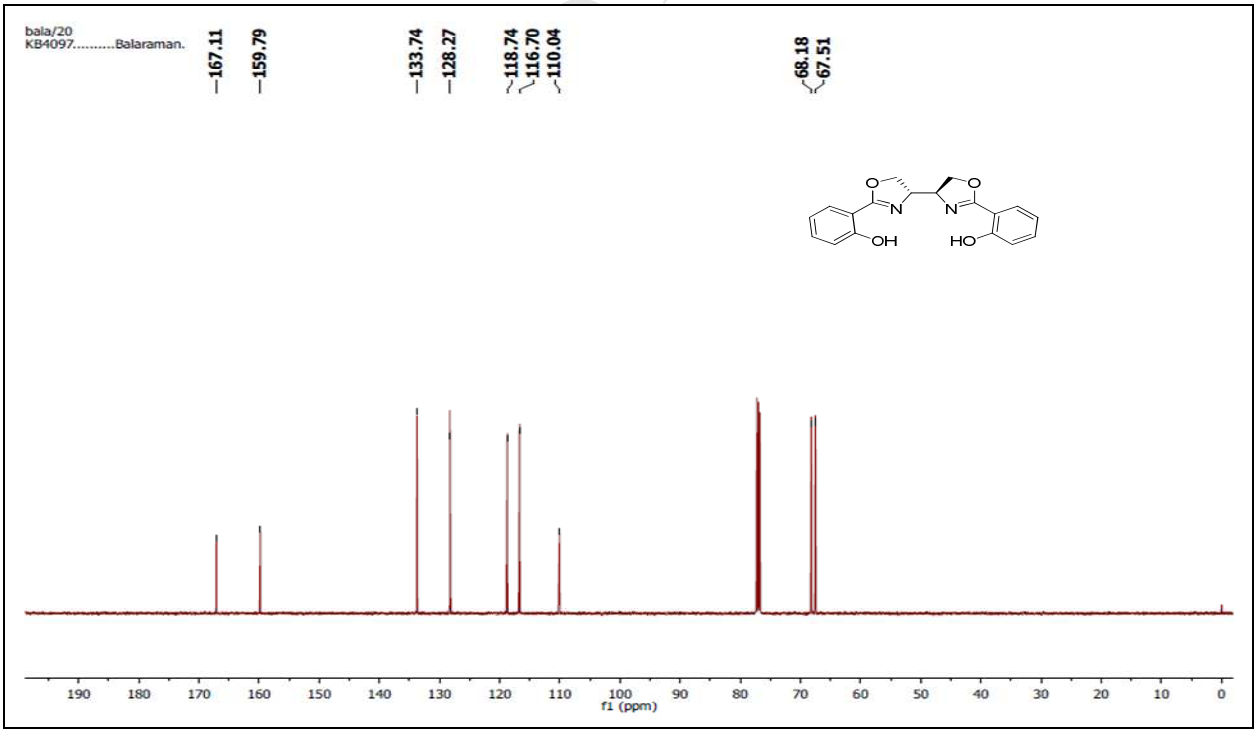
^{13}C NMR of **10b**



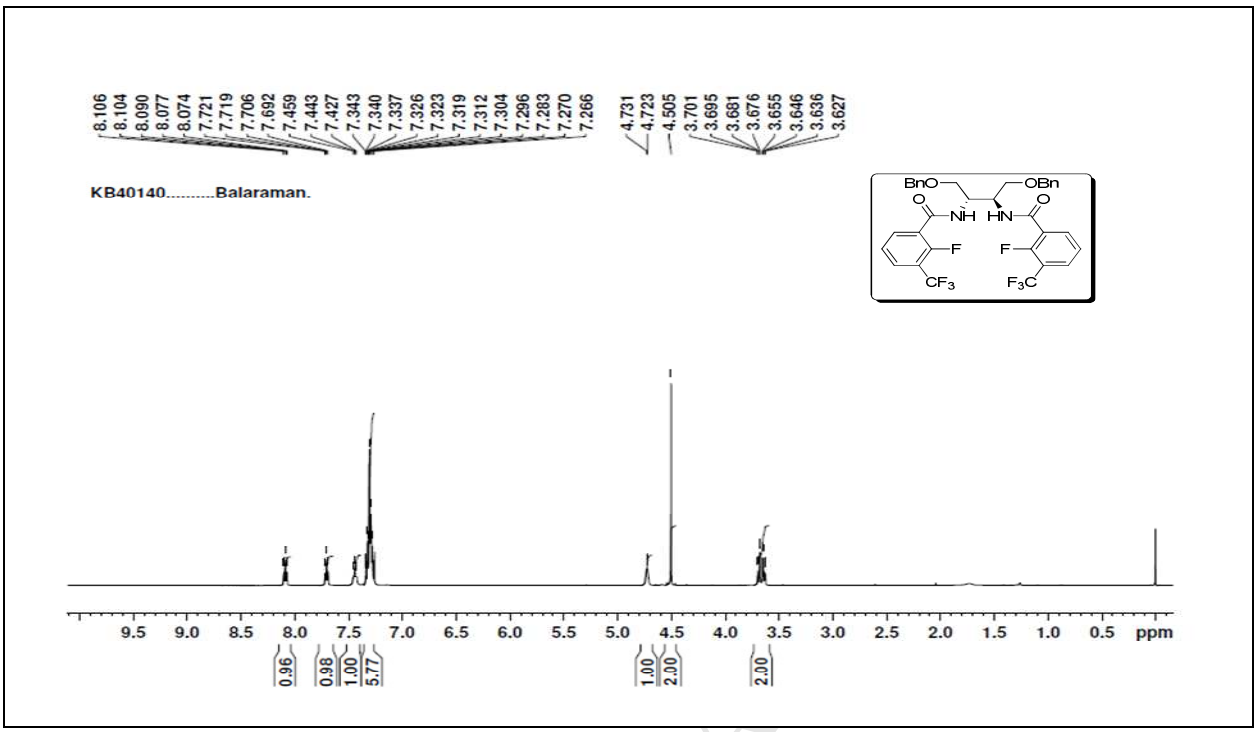
^{1}H NMR of **5a**



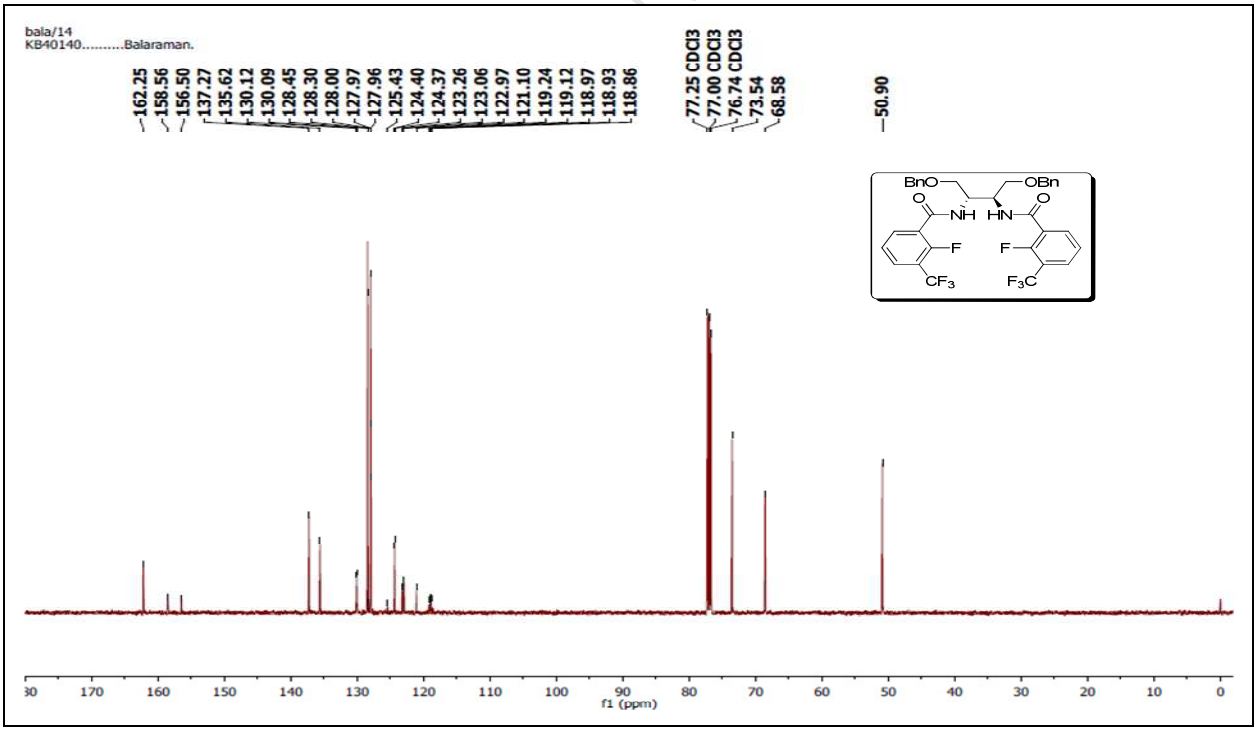
^{13}C NMR of **5a**



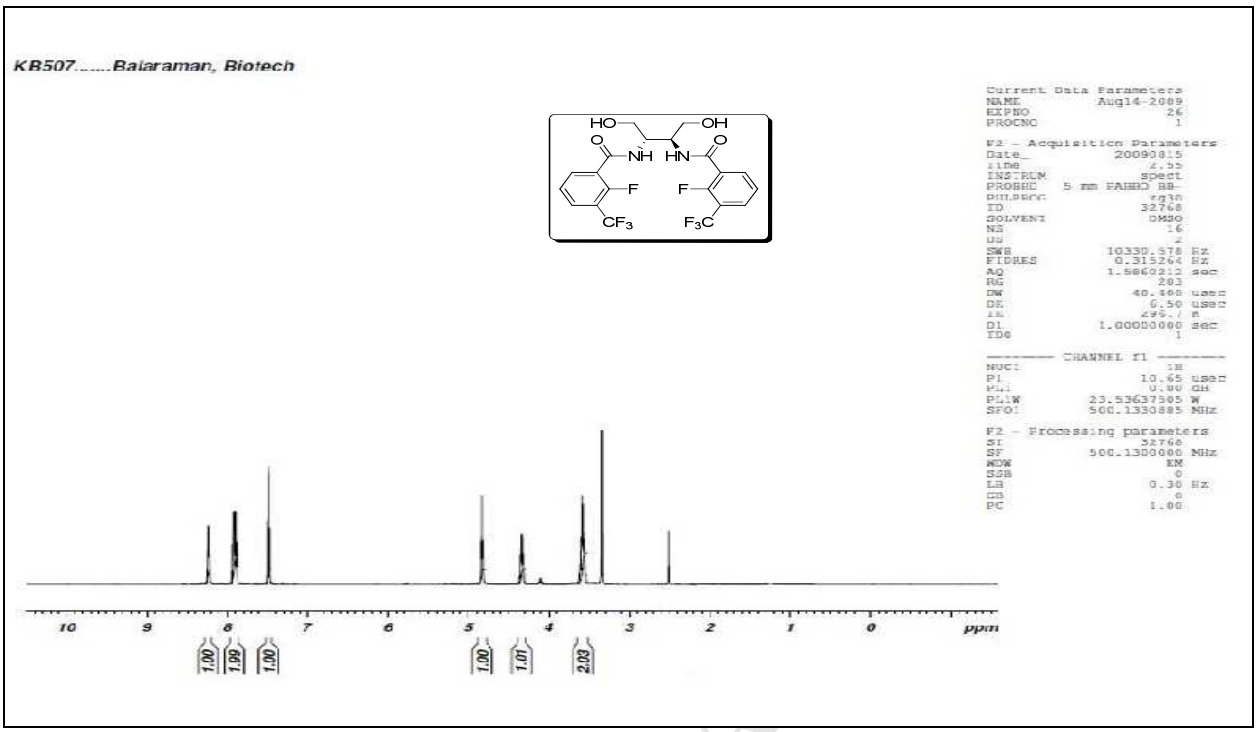
^{1}H NMR of **11**



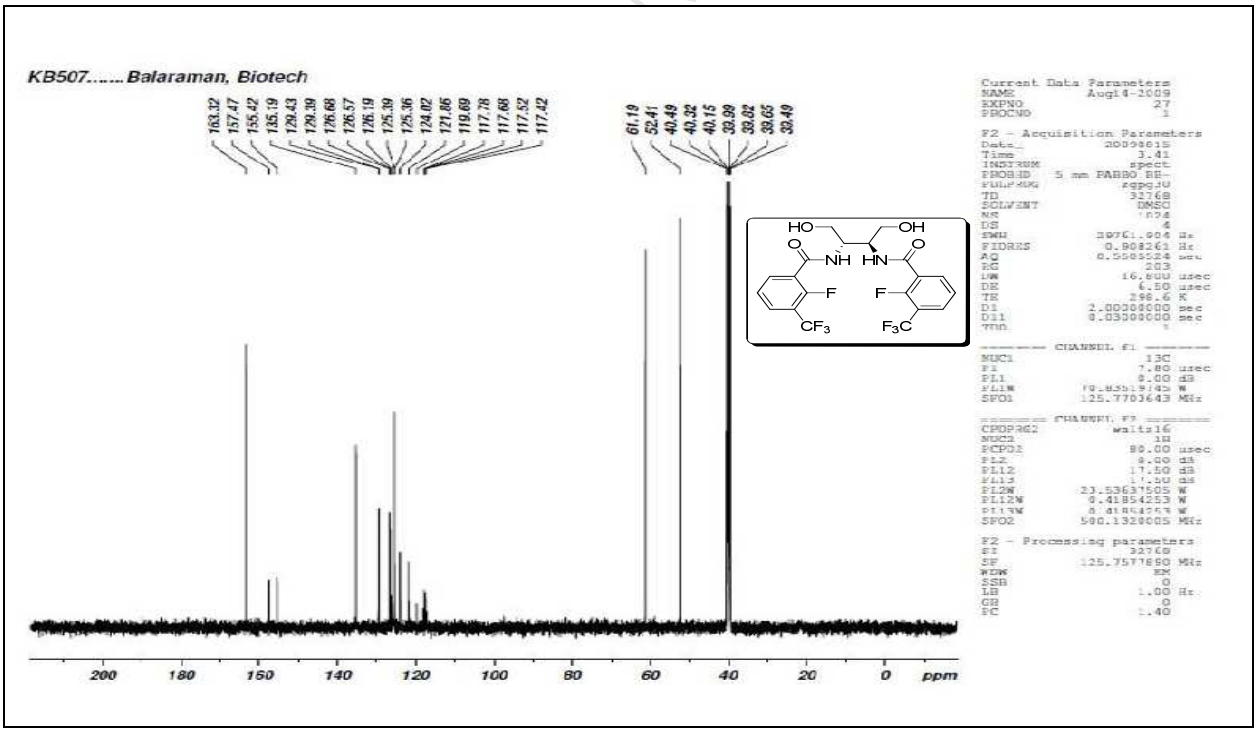
^{13}C NMR of **11**



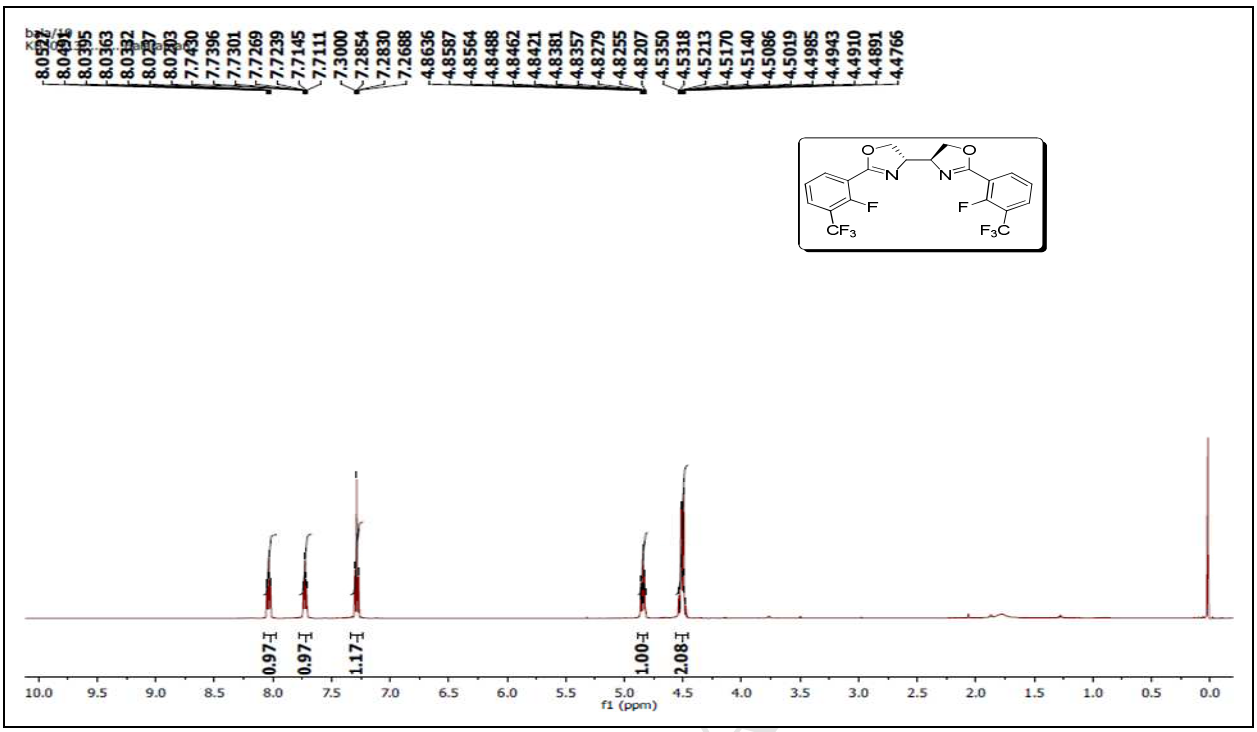
^{1}H NMR of **12**



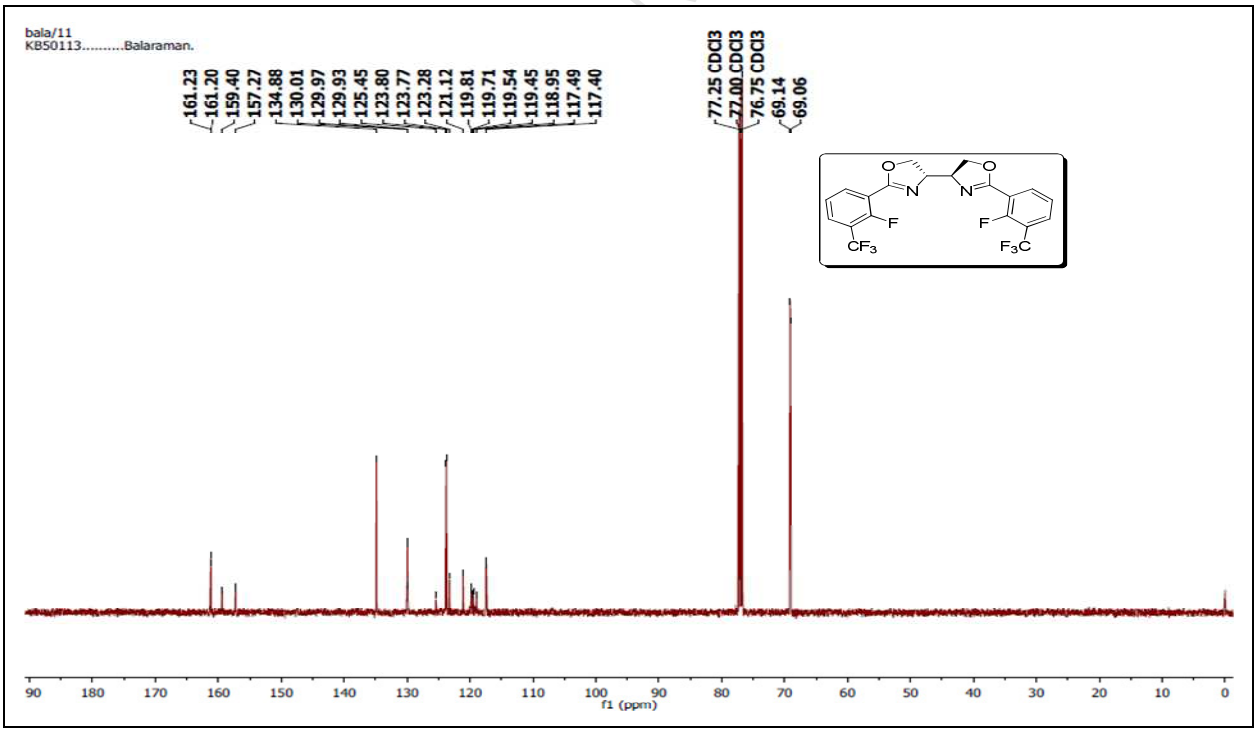
^{13}C NMR of **12**



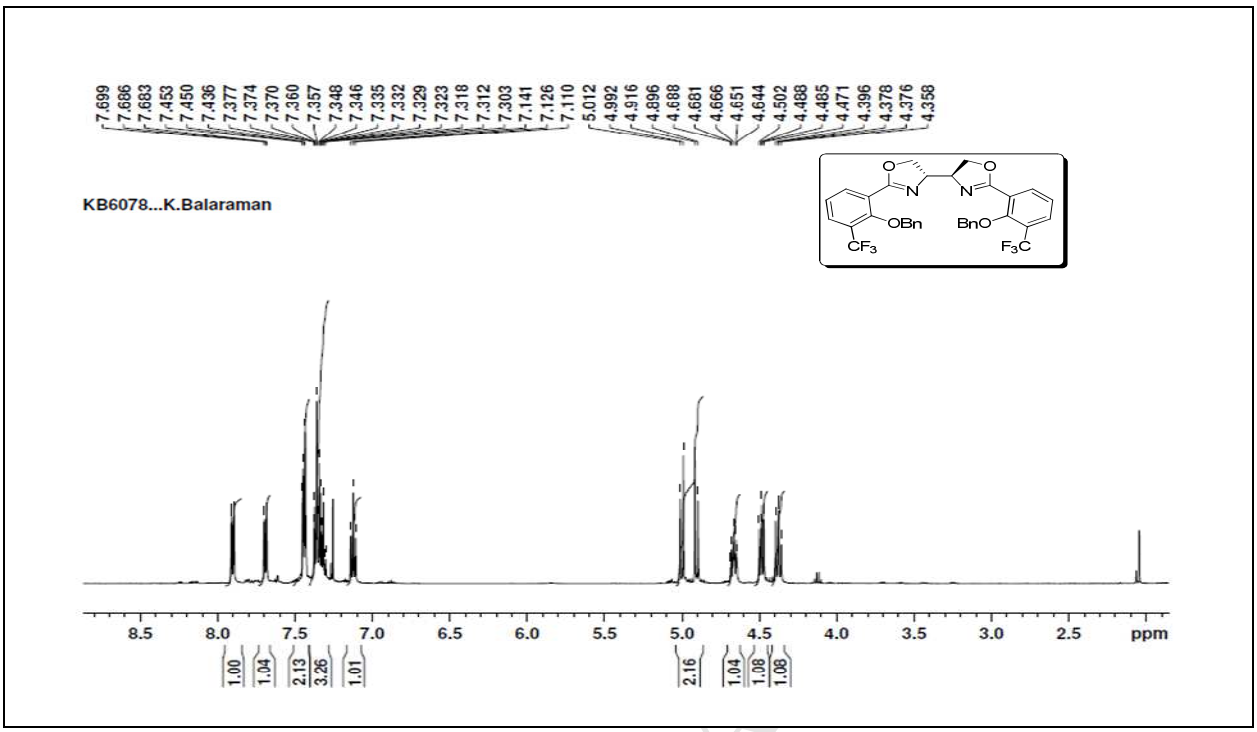
^{1}H NMR of **13**



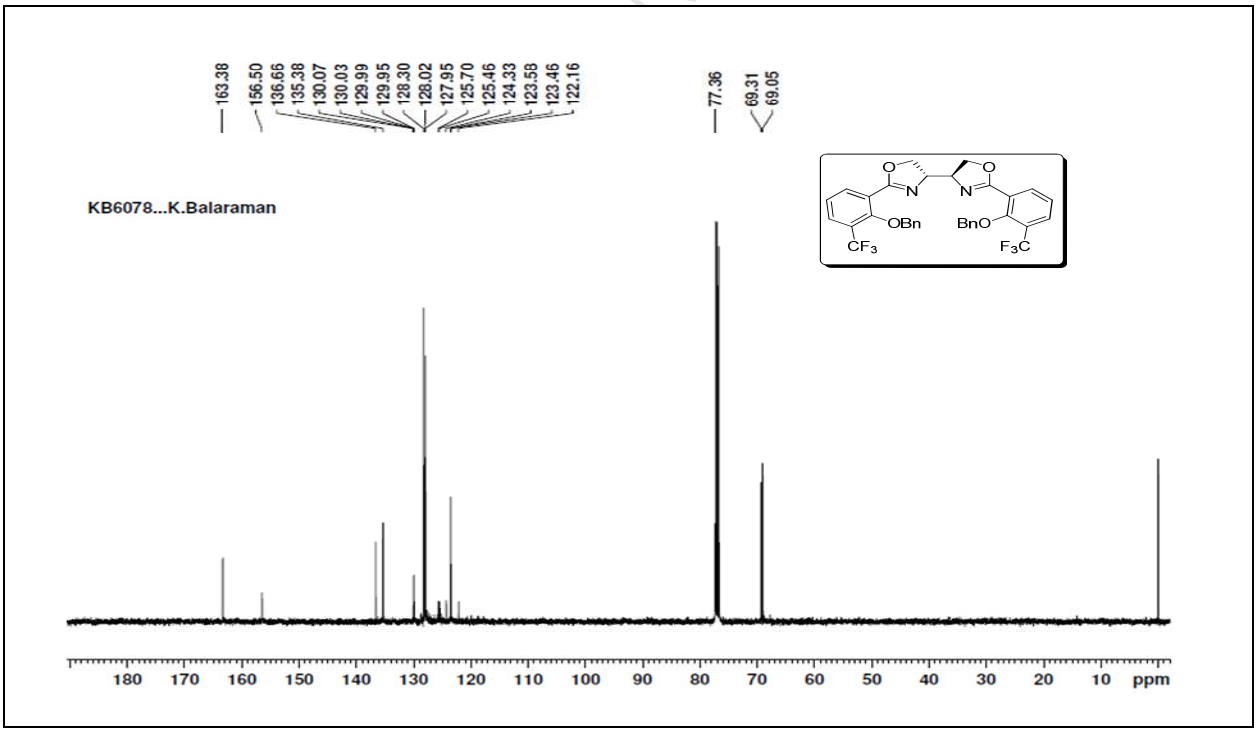
^{13}C NMR of **13**



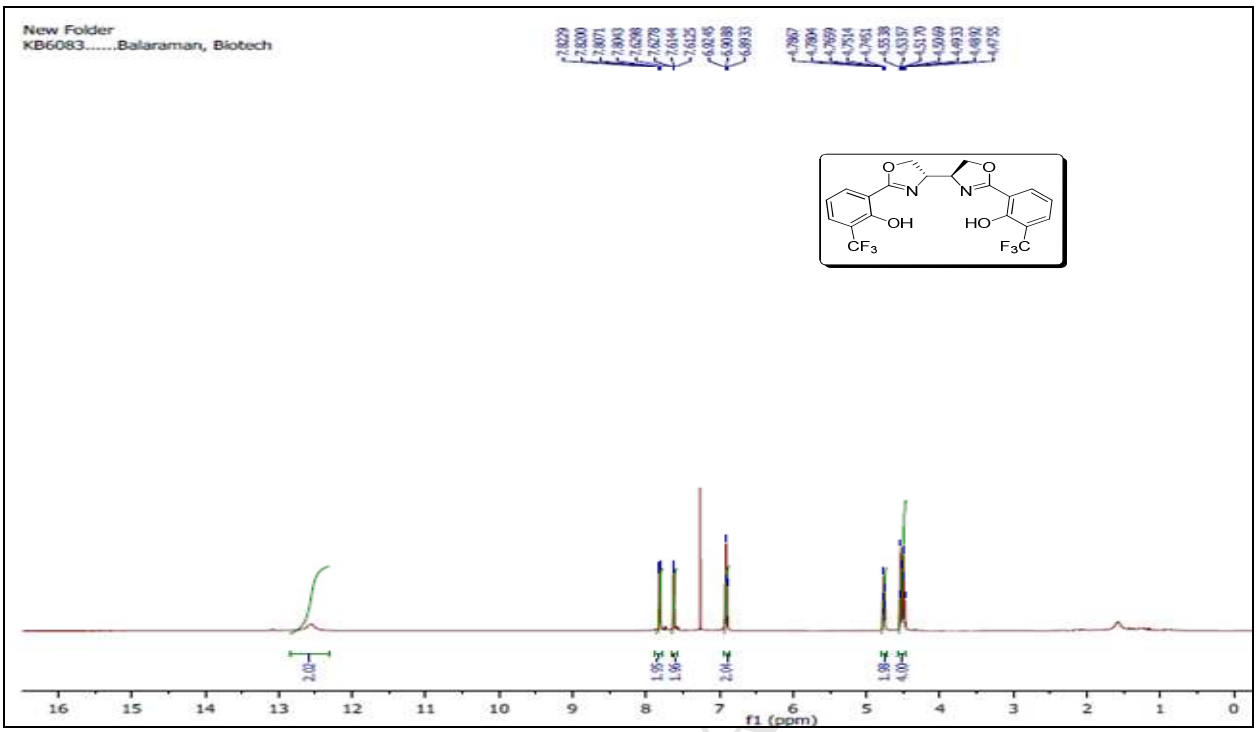
^{1}H NMR of **14**



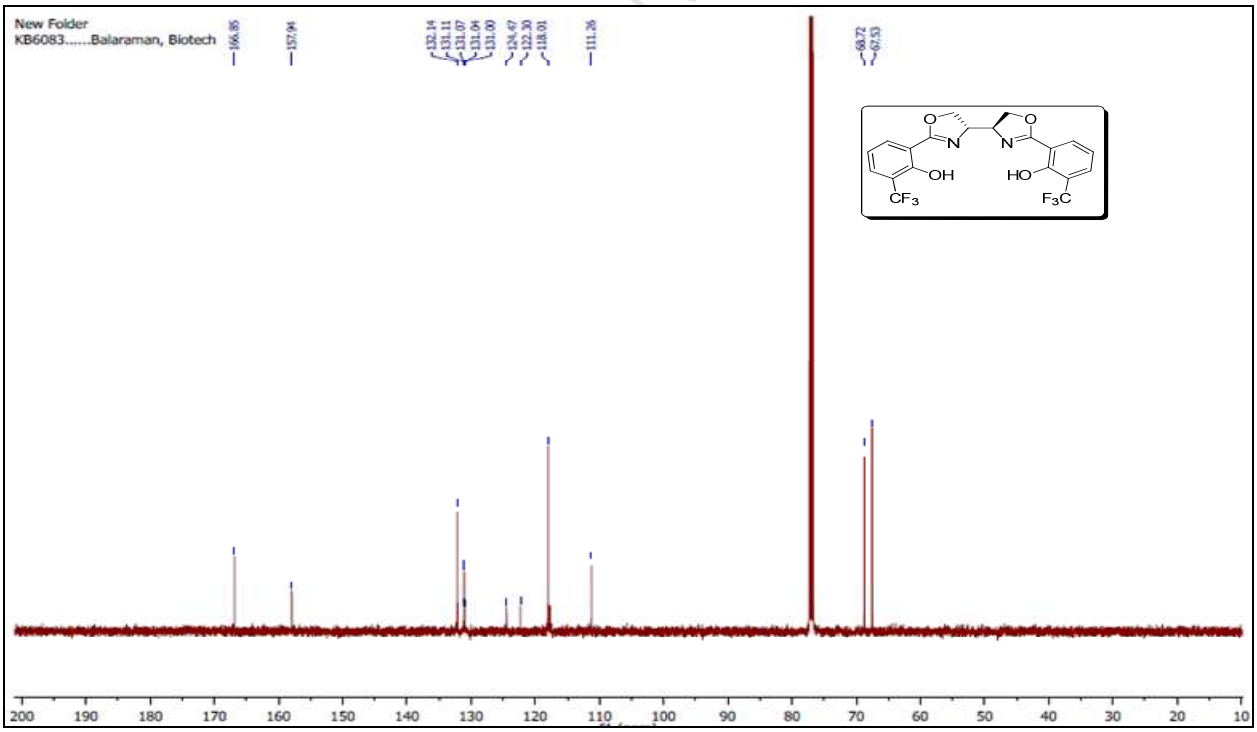
^{13}C NMR of **14**



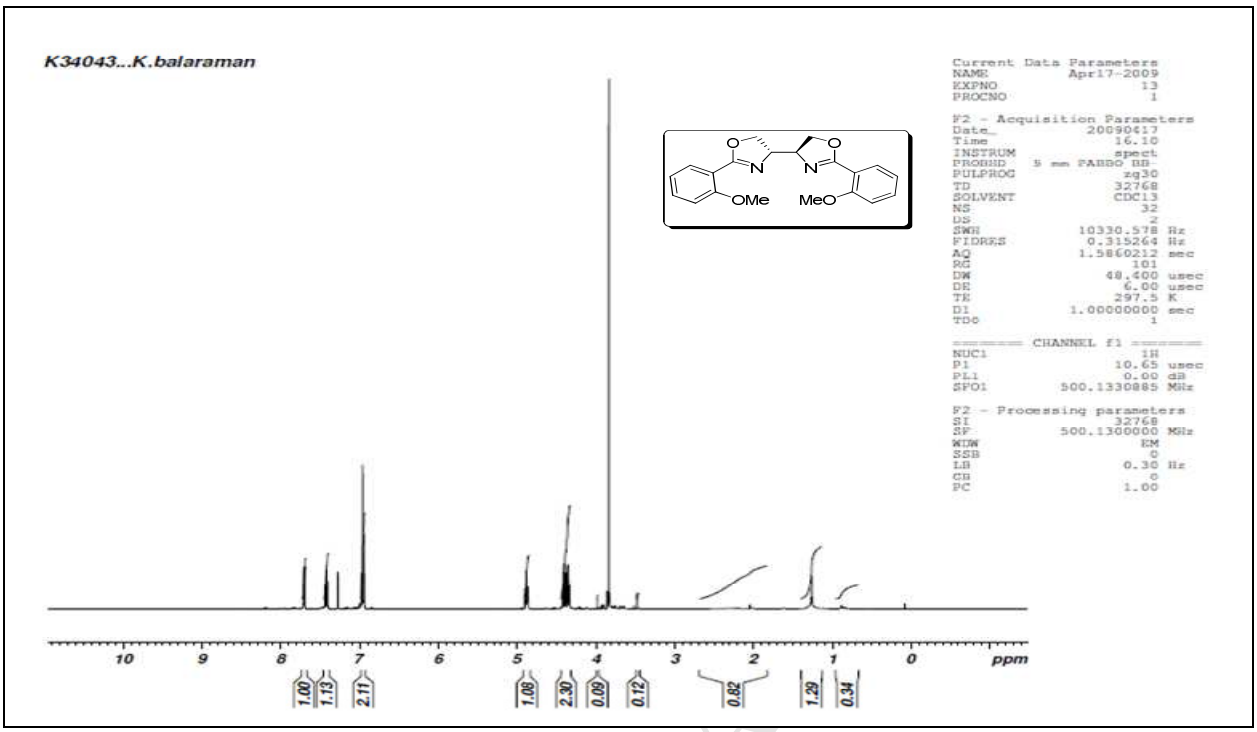
^{1}H NMR of **5b**



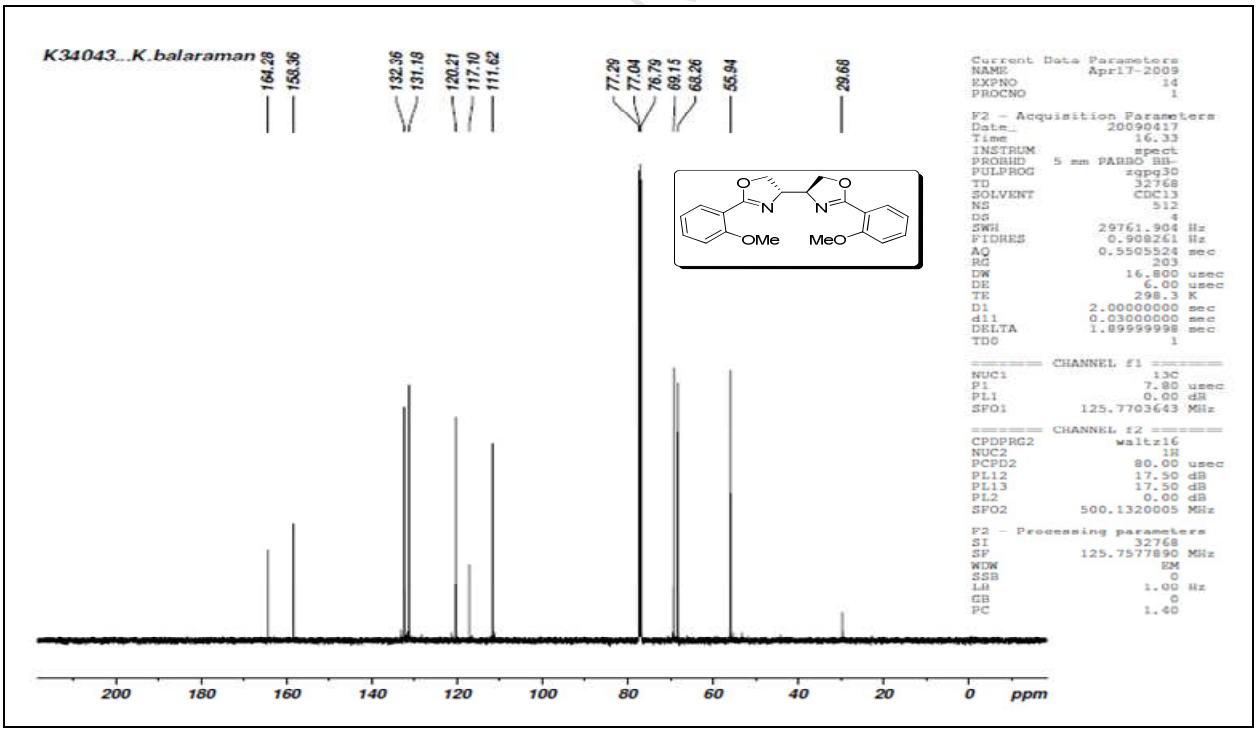
^{13}C NMR of **5b**



^{1}H NMR of **10a**

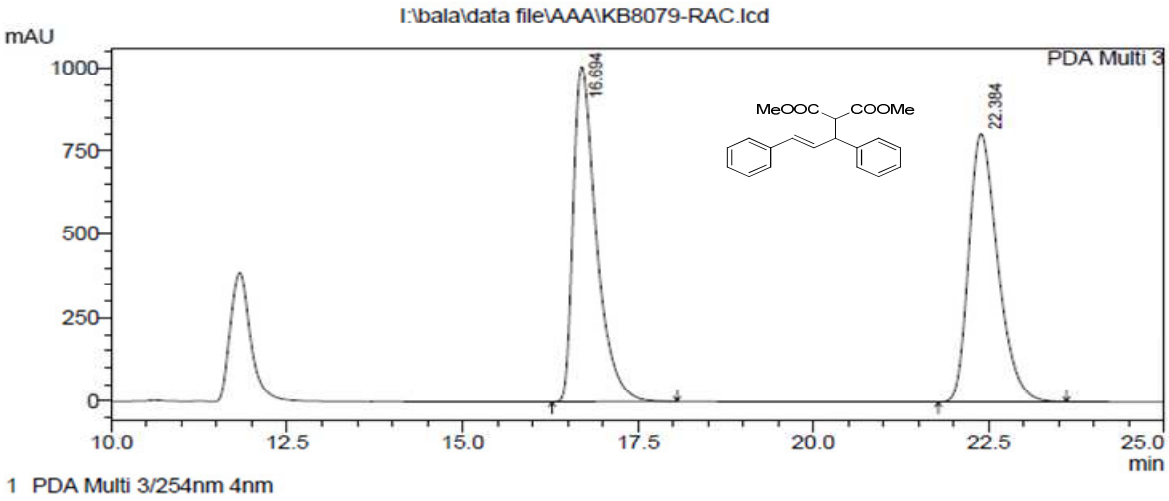


^{13}C NMR of **10a**



Copies of HPLC chromatograms

Racemic of 17a

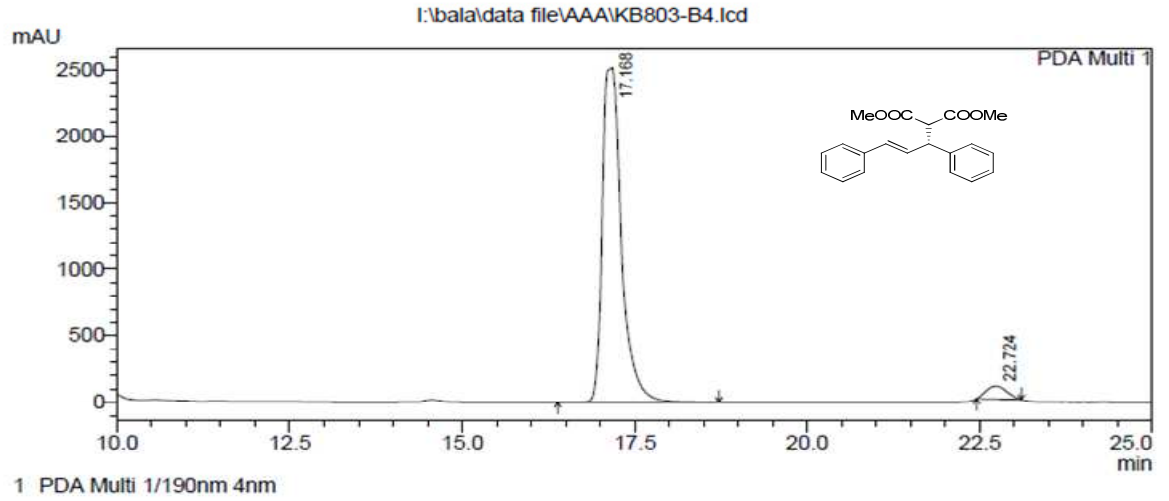


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.694	23110518	1006152	50.055	55.624
2	22.384	23059511	802700	49.945	44.376
Total		46170029	1808852	100.000	100.000

Table:2, Entry:12

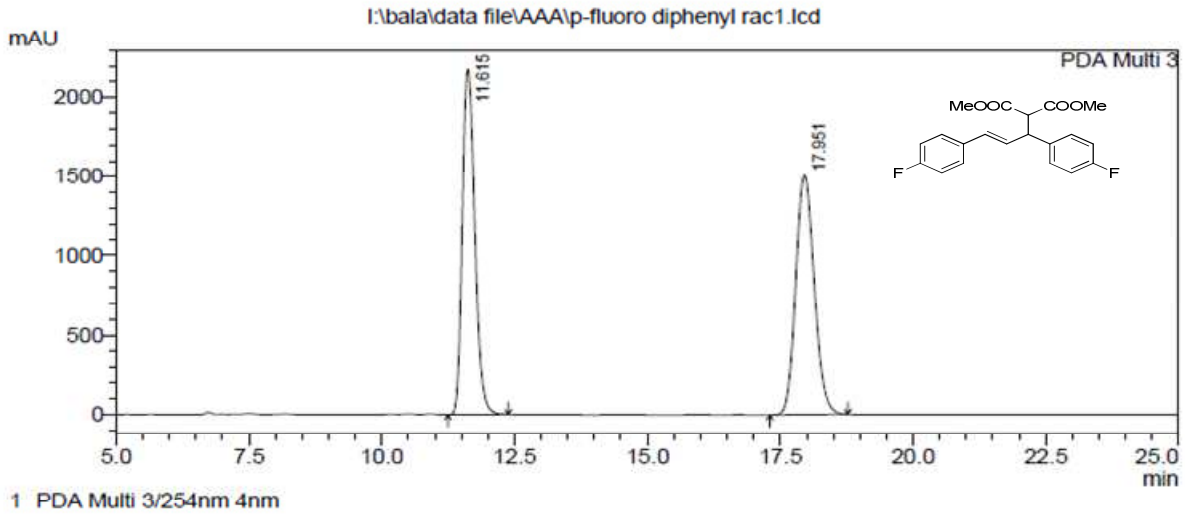


PeakTable

PDA Ch1 190nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.168	48474603	2521252	95.940	96.244
2	22.724	2051516	98391	4.060	3.756
Total		50526119	2619643	100.000	100.000

Racemic of 17b

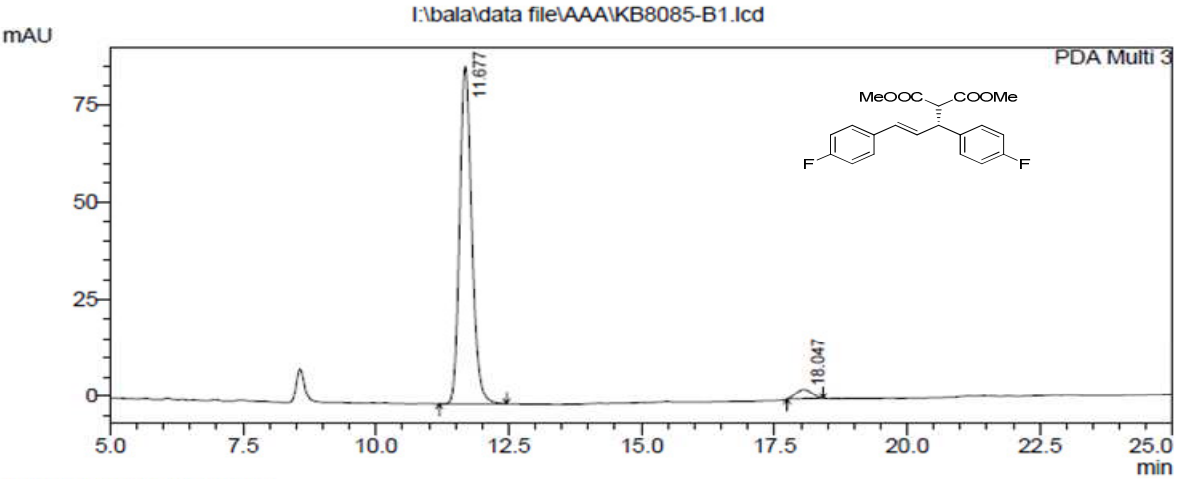


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.615	35475949	2180348	49.100	59.075
2	17.951	36777085	1510491	50.900	40.925
Total		72253034	3690839	100.000	100.000

Table:3, Entry:1

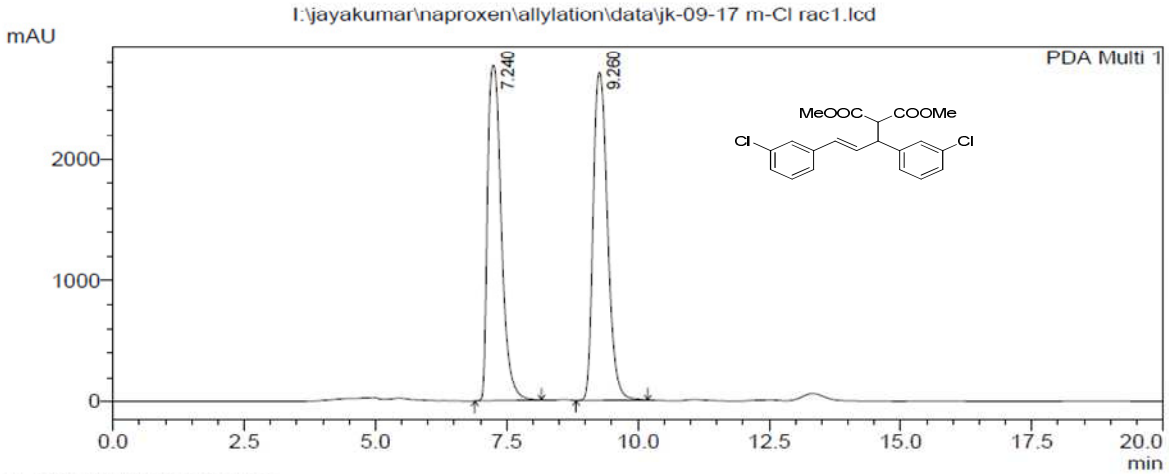


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.677	1377830	87029	96.298	97.195
2	18.047	52973	2512	3.702	2.805
Total		1430803	89541	100.000	100.000

Racemic of 17c

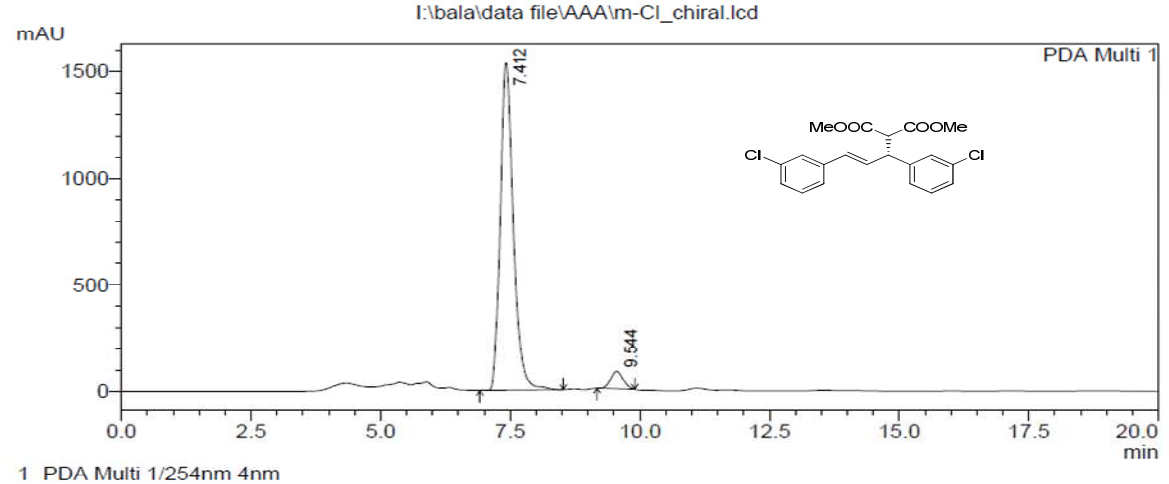


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.240	50721119	2771775	49.605	50.548
2	9.260	51529743	2711677	50.395	49.452
Total		102250862	5483452	100.000	100.000

Table:3, Entry:2

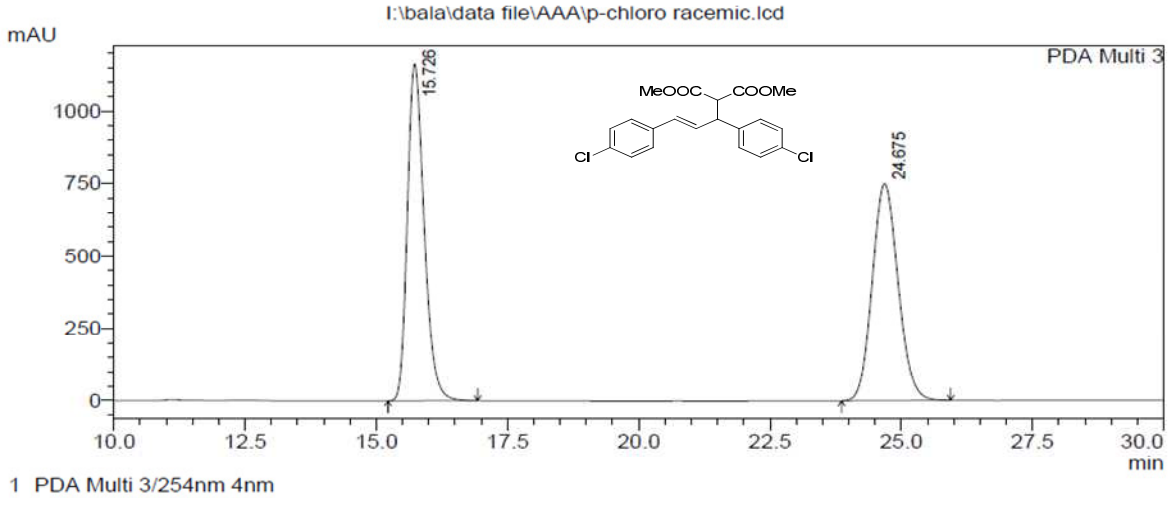


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.412	26902199	1540687	95.135	94.893
2	9.544	1375668	82915	4.865	5.107
Total		28277867	1623602	100.000	100.000

Racemic of 17d

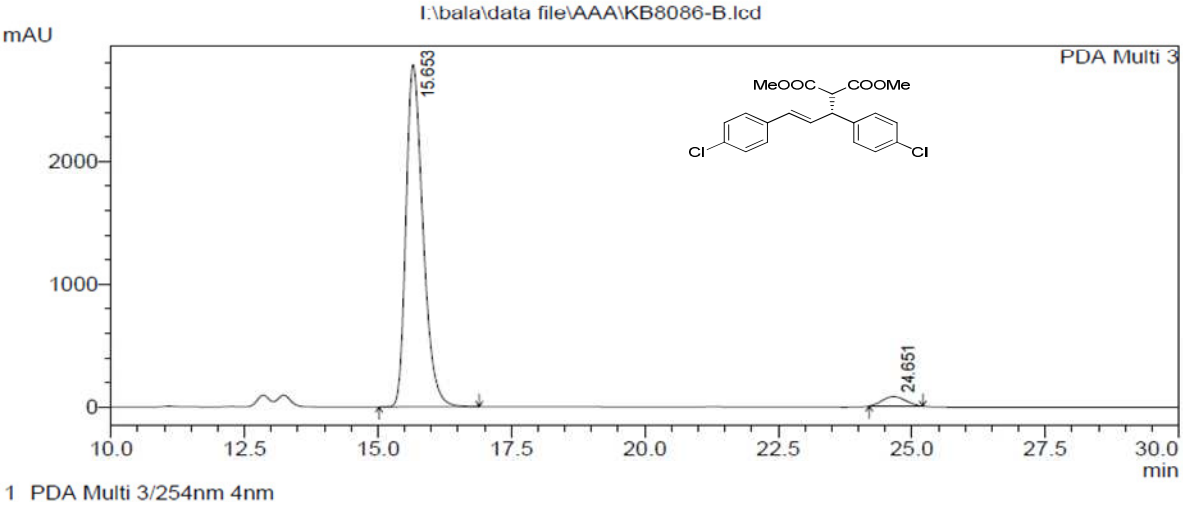


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.726	25950536	1164859	50.138	60.822
2	24.675	25807614	750331	49.862	39.178
Total		51758150	1915190	100.000	100.000

Table:3, Entry:3

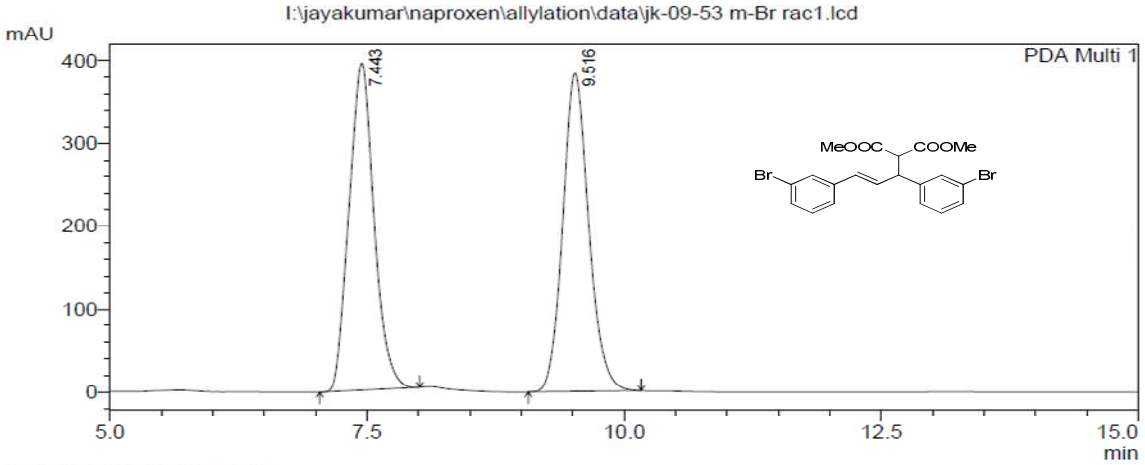


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.653	61833488	2785411	96.424	97.353
2	24.651	2292992	75731	3.576	2.647
Total		64126480	2861142	100.000	100.000

Racemic of 17e

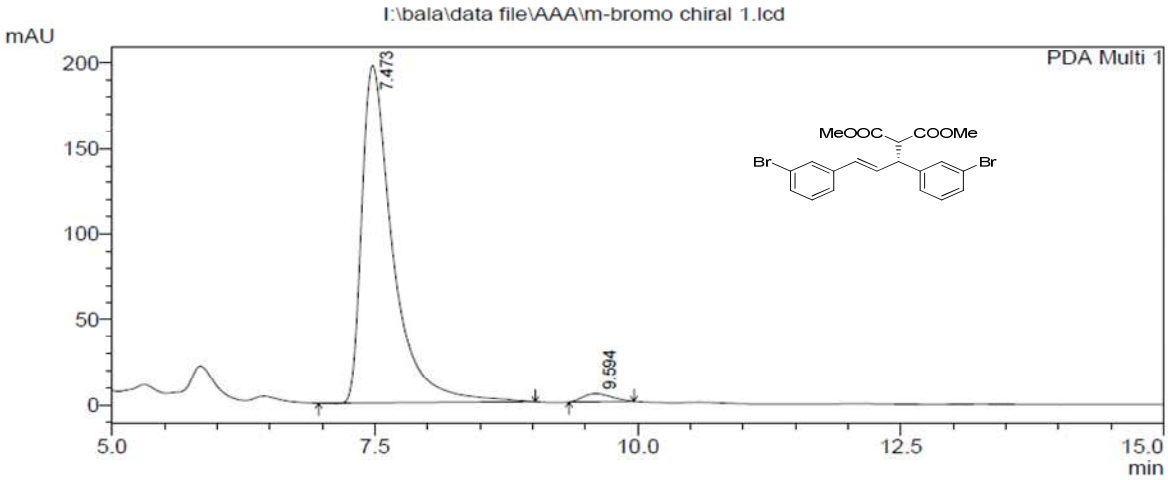


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.443	6655453	394780	49.656	50.690
2	9.516	6747644	384025	50.344	49.310
Total		13403098	778805	100.000	100.000

Table:3, Entry:4

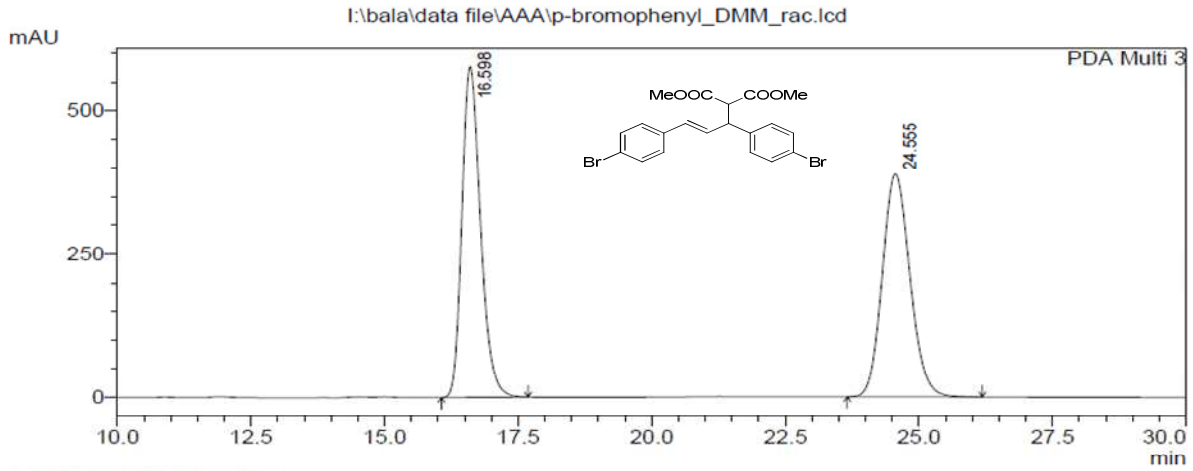


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.473	4036262	197245	97.858	97.674
2	9.594	88357	4696	2.142	2.326
Total		4124619	201941	100.000	100.000

Racemic of 17f

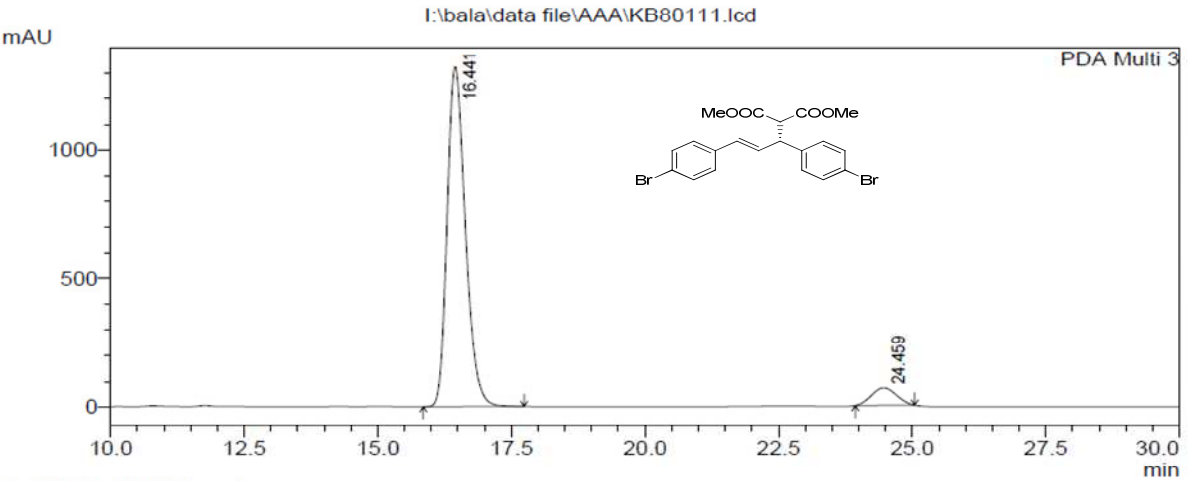


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.598	13951256	576975	49.883	59.734
2	24.555	14016865	388939	50.117	40.266
Total		27968121	965914	100.000	100.000

Table:3, Entry:5

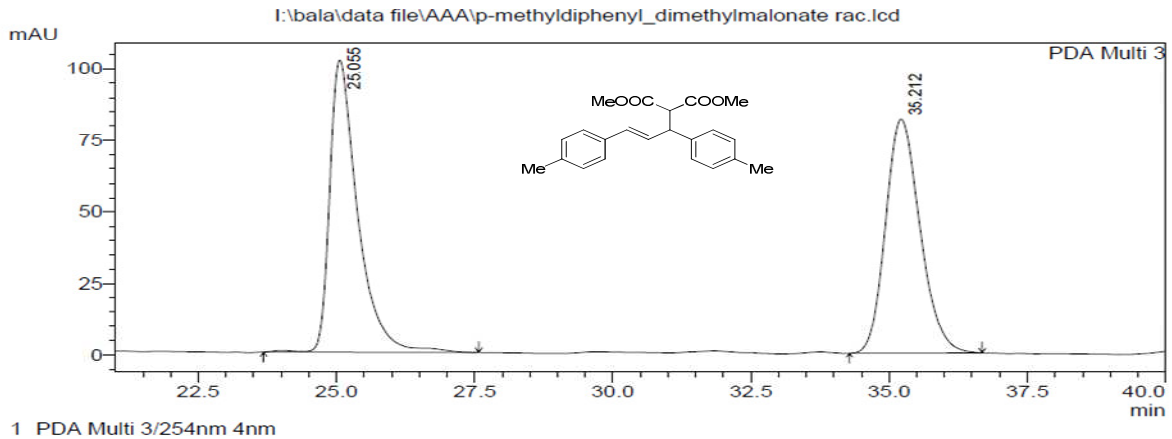


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.441	31461782	1324053	93.543	95.167
2	24.459	2171862	67240	6.457	4.833
Total		33633645	1391293	100.000	100.000

Racemic of 17g

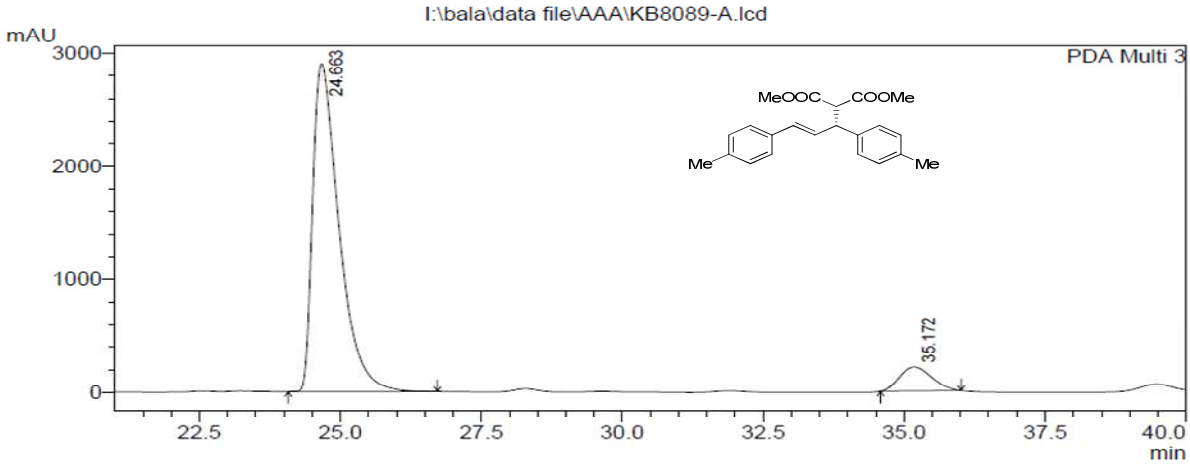


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.055	3599330	101933	50.383	55.536
2	35.212	3544664	81612	49.617	44.464
Total		7143994	183545	100.000	100.000

Table:3, Entry:6

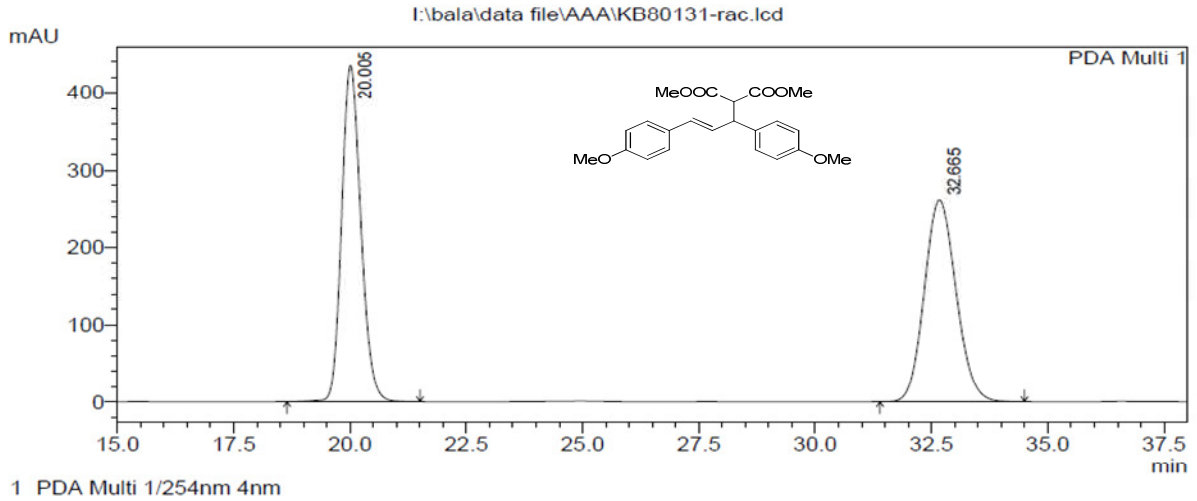


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.663	94314022	2901895	91.892	93.269
2	35.172	8322135	209418	8.108	6.731
Total		102636157	3111314	100.000	100.000

Racemic of 17h

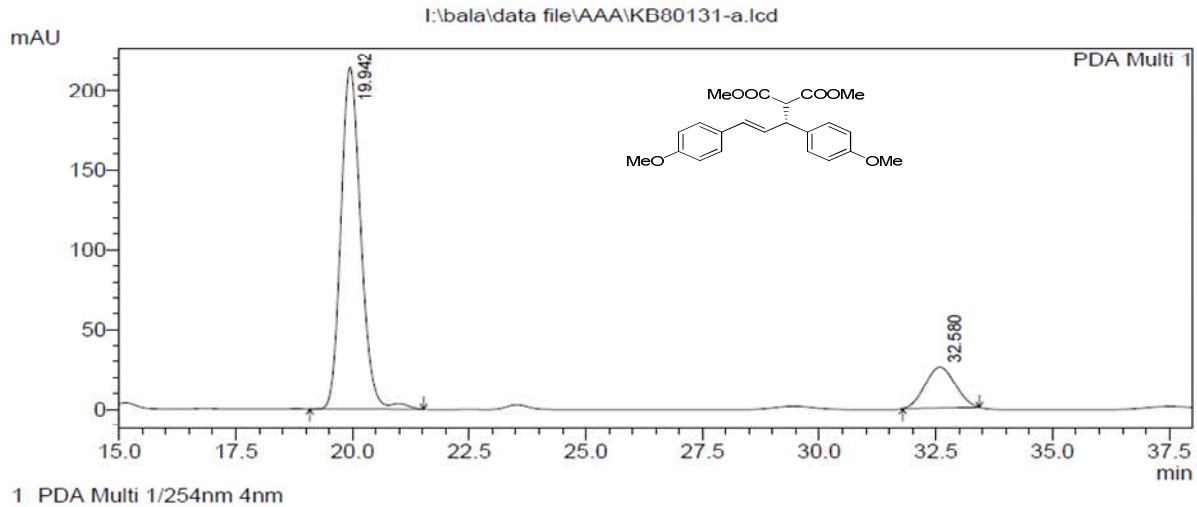


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.005	12527294	434838	50.189	62.469
2	32.665	12432830	261252	49.811	37.531
Total		24960124	696090	100.000	100.000

Table:3, Entry:7

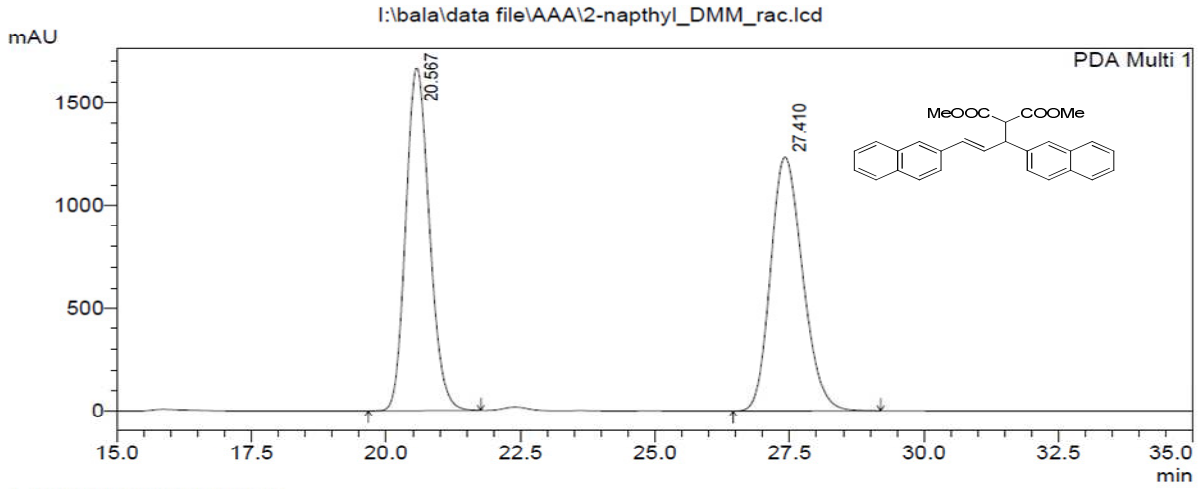


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.942	6344527	214264	84.677	89.341
2	32.580	1148066	25563	15.323	10.659
Total		7492593	239827	100.000	100.000

Racemic of 17i



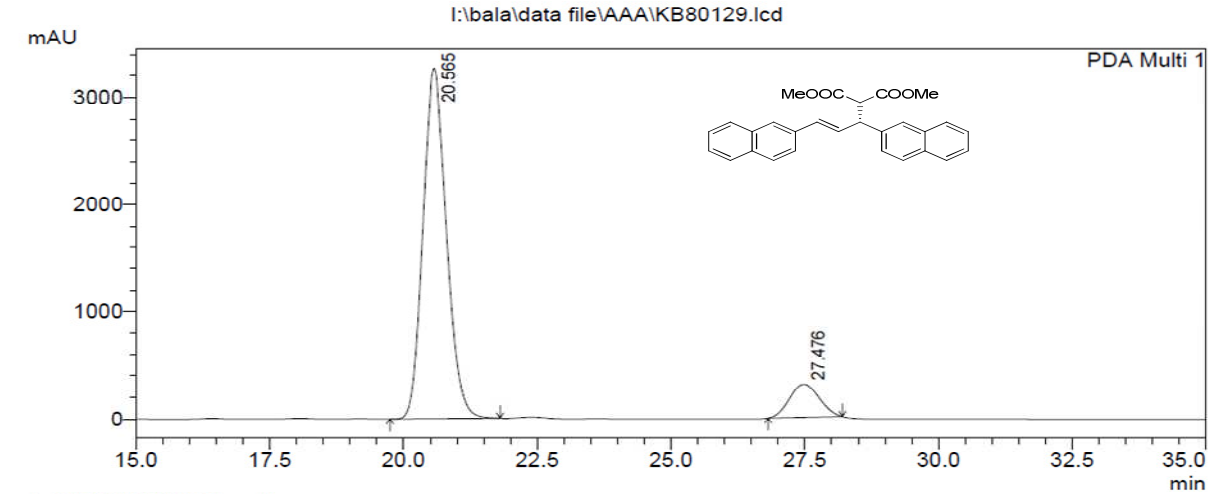
1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.567	51027487	1666306	49.863	57.437
2	27.410	51307388	1234819	50.137	42.563
Total		102334875	2901125	100.000	100.000

Table:3, Entry:8



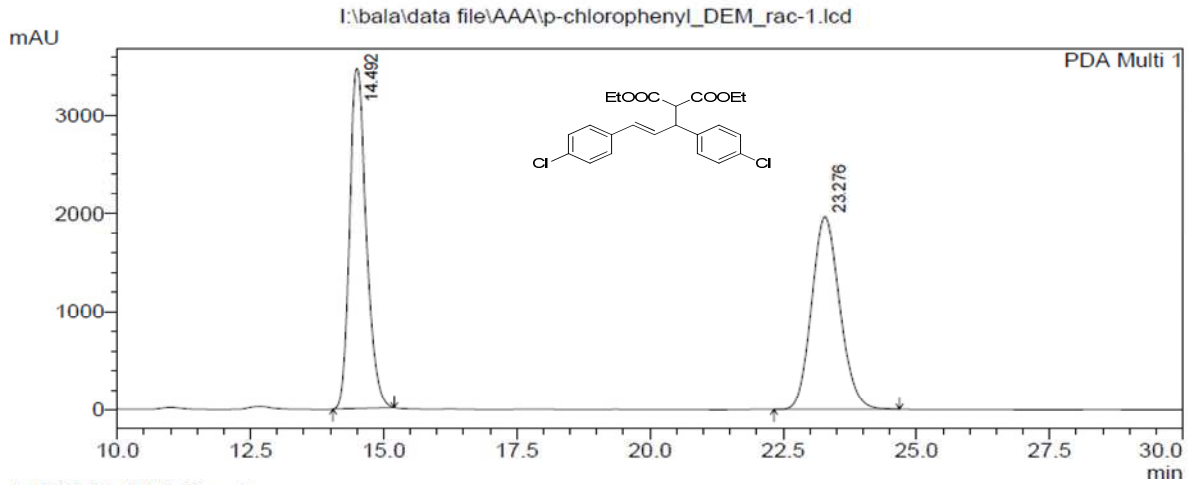
1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.565	98962367	3269441	89.367	91.451
2	27.476	11774609	305632	10.633	8.549
Total		110736976	3575073	100.000	100.000

Racemic of 17j

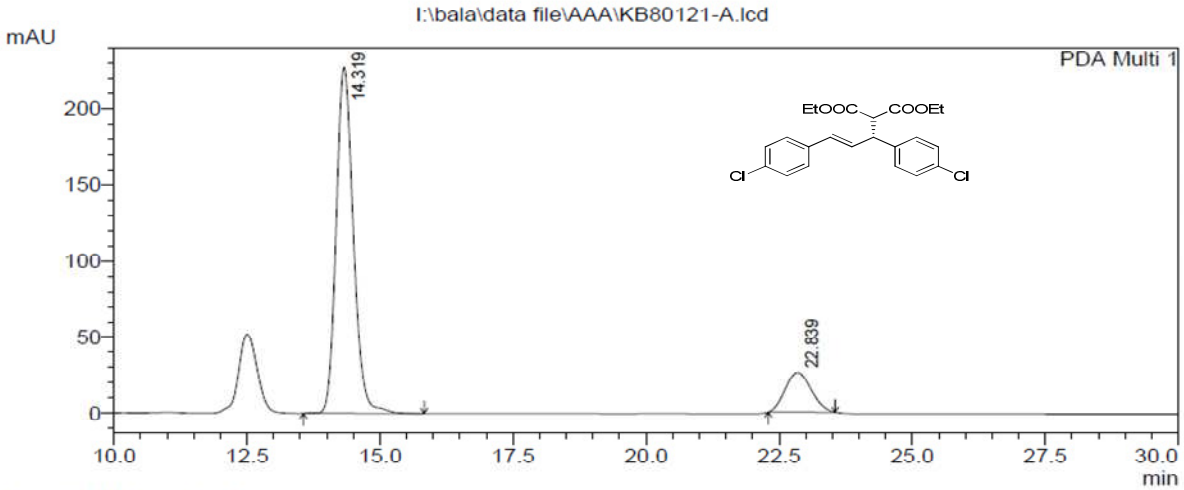


PeakTable

PDA Ch1 240nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.492	75508281	3472156	51.089	63.894
2	23.276	72290237	1962078	48.911	36.106
Total		147798518	5434235	100.000	100.000

Table:3, Entry:9

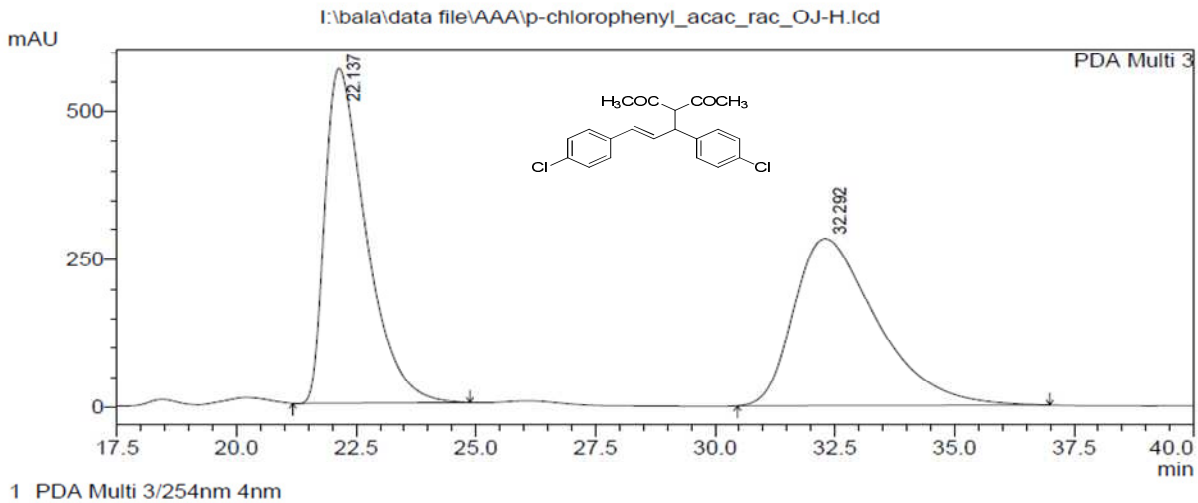


PeakTable

PDA Ch1 240nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.319	5109896	227489	85.244	89.754
2	22.839	884513	25968	14.756	10.246
Total		5994410	253457	100.000	100.000

Racemic of 17k

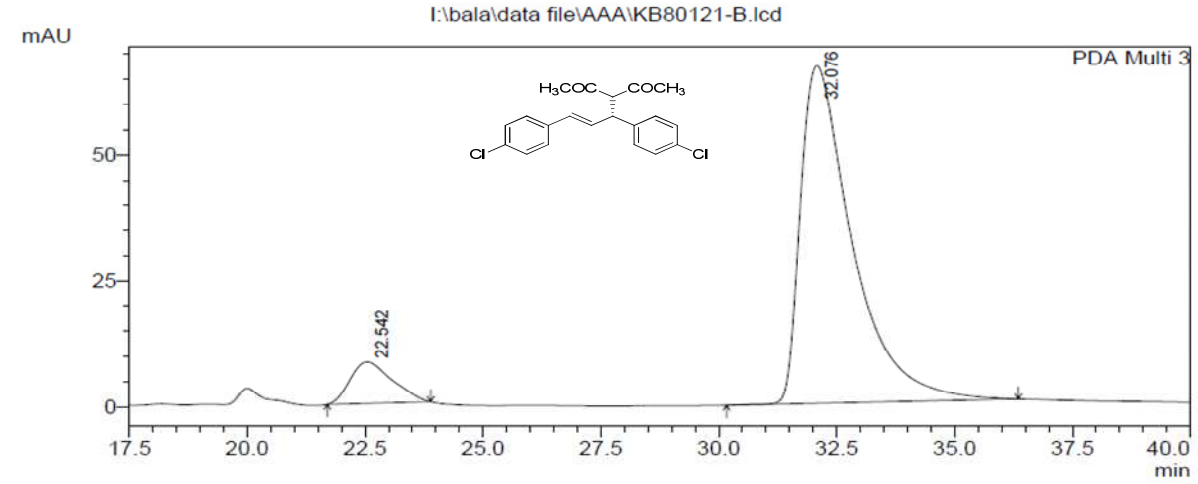


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.137	33987708	566814	49.814	66.748
2	32.292	34241697	282376	50.186	33.252
Total		68229405	849191	100.000	100.000

Table:3, Entry:10

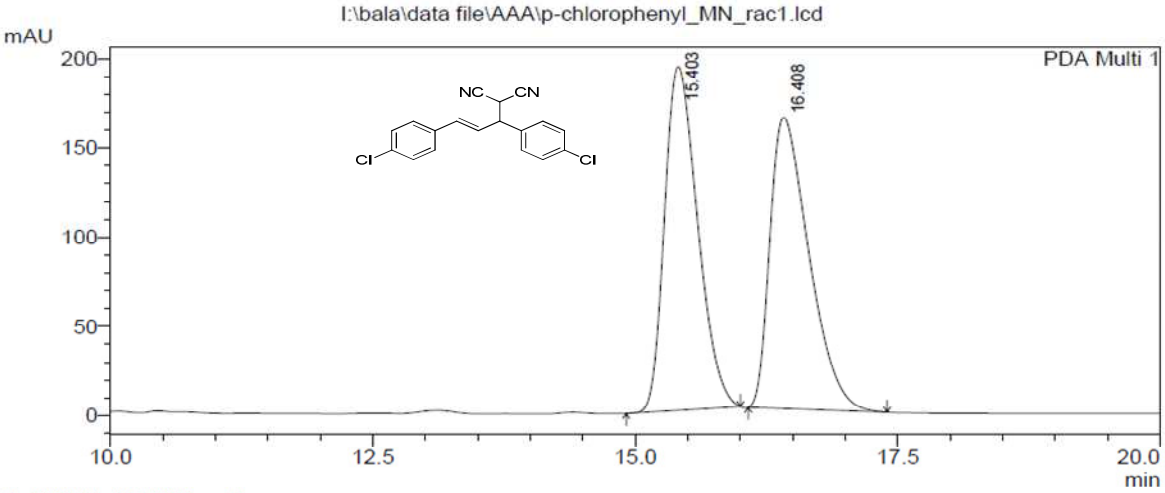


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.542	509577	8213	9.036	10.914
2	32.076	5129562	67041	90.964	89.086
Total		5639139	75254	100.000	100.000

Racemic of 17l

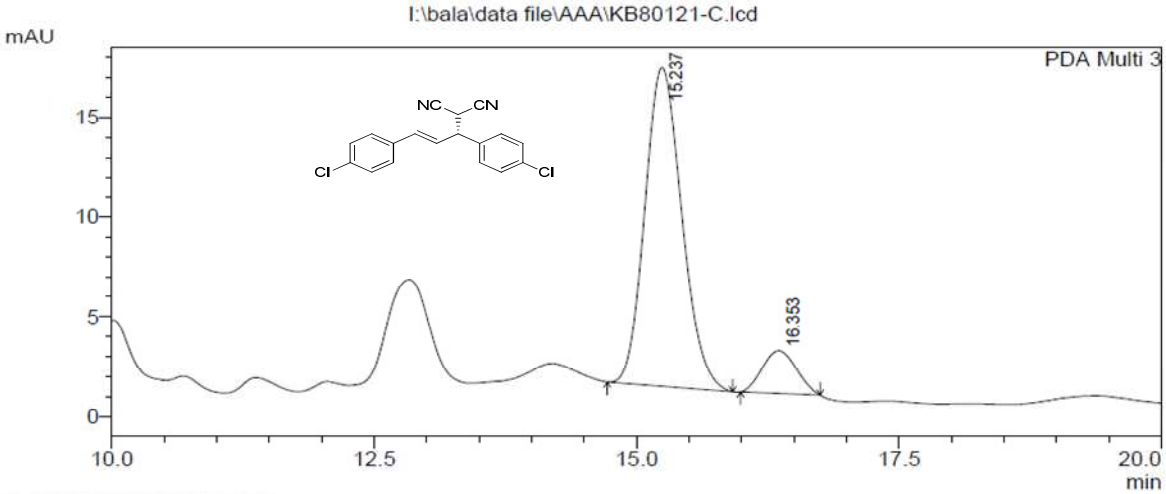


PeakTable

PDA Ch1 300nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.403	4217216	192598	49.955	54.139
2	16.408	4224753	163147	50.045	45.861
Total		8441969	355745	100.000	100.000

Table:3, Entry:11

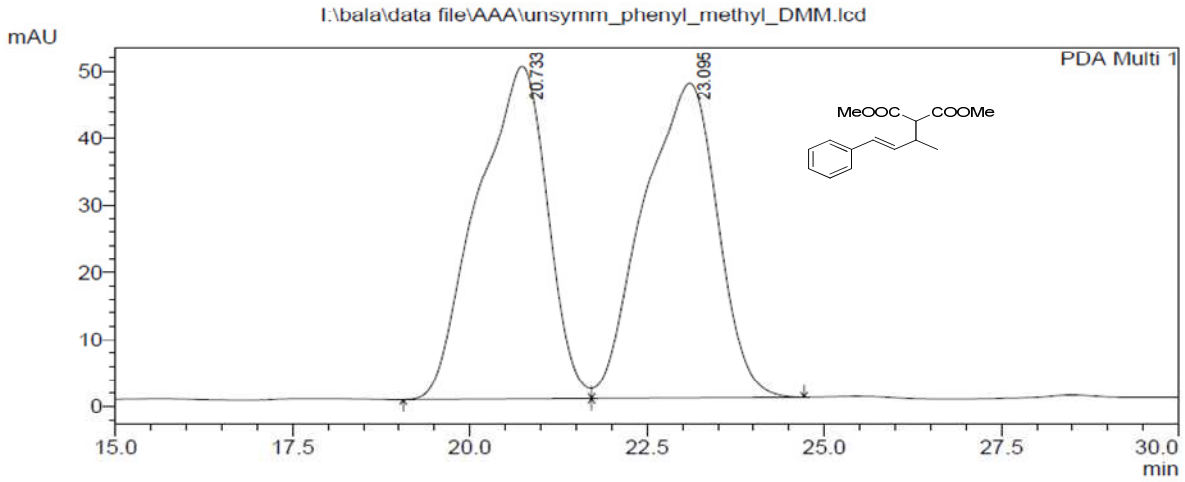


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.237	391229	16019	89.002	88.237
2	16.353	48346	2136	10.998	11.763
Total		439575	18154	100.000	100.000

Racemic of 21

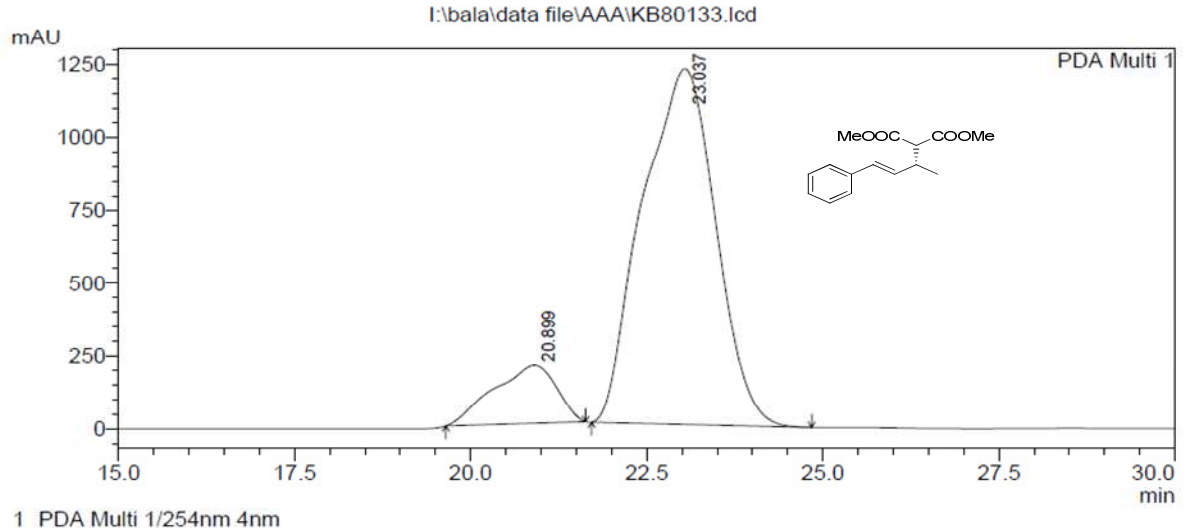


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.733	3401816	49602	49.923	51.361
2	23.095	3412297	46974	50.077	48.639
Total		6814113	96576	100.000	100.000

Compound 21



PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.899	12333302	197554	12.262	13.920
2	23.037	88245738	1221651	87.738	86.080
Total		100579040	1419205	100.000	100.000