RECENT ADVANCES TOWARDS THE DEVELOPMENT OF ENANTIO- AND DIASTEREOSELECTIVE PALLADIUM CATALYZED NITROGEN ARYLATION REACTIONS

by

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Bachelor of Science, Chemistry,

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Abstract

RECENT ADVANCES TOWARDS THE DEVELOPMENT OF ENANTIO- AND DIASTEREOSELECTIVE PALLADIUM CATALYZED NITROGEN ARYLATION REACTIONS

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A non-commercially available ligand, (*R)*-2(Dicyclohexylphosphino)-2'-methoxy-1,1'-binaphthyl), (*R*)-Cy_2MOP, has been synthesized and demonstrated to be very effective in the palladium catalyzed intramolecular desymmetrization of di-nitrogen malonamides. Additionally an enantio- and diastereoselective Buchwald-Hartwig reaction has been developed through the desymmetrization of 2-(2-bromobenzyl)-N^1,N^3-bis(2-(*tert*-butyl)phenyl)-2-methylmalonamide using palladium/Cy_2MOP as the catalyst system to produce *N*,1-bis(2-(*tert*-butyl)phenyl)-3-methyl-2-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide in excellent yield, with high enantio- and diastereoselectivity (99 %, 88 % *ee*). This serves as the first example of its kind whereby an enantio- and diastereoselective Buchwald-Hartwig reaction occurs in a single step from the preferential N-arylation of prochiral di-nitrogen malonamides. Application of the palladium/Cy_2MOP catalyst system in the intramolecular desymmetrization reaction also resulted in the formation of six membered ring benzomorpholinone and seven membered ring benzodiazepineone heterocycles. Furthermore several synthetic routes towards the synthesis of five membered ring oxindoles are thoroughly discussed. Lastly the synthesis of a precatalyst was also attempted using Cy_2MOP and Pd(II)Me_2TMEDA.

Acknowledgements

I would like to start off by thanking my supervisor Dr. Russell Viirre for giving me the opportunity to work in his lab. He is a phenomenal supervisor and this project would not have been possible if not for his guidance and expertise. Not only was he an outstanding mentor and teacher, he also inspired me to pursue my graduate studies in synthetic organic chemistry.

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1 Introduction

1.1 Stereochemistry

Stereochemistry is a branch of chemistry that deals with the three dimensional structure of molecules.[1] Stereoisomers are isomers that have the same connectivity but differ in their three dimensional orientation.[1]

1.1.1 Chirality

A molecule is said to be chiral if it is nonsuperimposable on its mirror image.[2] An example of a chiral molecule is shown in figure 1.

Figure 1: The two enantiomers of 2-bromobutane

A molecule can possess three different types of stereogenic elements: a chiral centre, chiral axis or chiral plane.

1.1.1.1 Central chirality

The presence of a tetrahedral carbon atom attached to four different groups usually makes a molecule chiral.[1] The carbon atom which is attached to the four different groups is called a chiral carbon or a chiral centre.[1] An example of a molecule that exhibits this type of chirality is shown in figure 1.

1.1.1.2 Axial Chirality

Axial chirality results from the non planar arrangement of four groups in pairs about a chiral axis.[3] A chiral axis can be generated due to restricted rotation around a single bond, pi bonds or rings and is usually observed in allenes, biphenyls and binaphthyls.[3] Some examples of axial chirality are shown in figure 2.

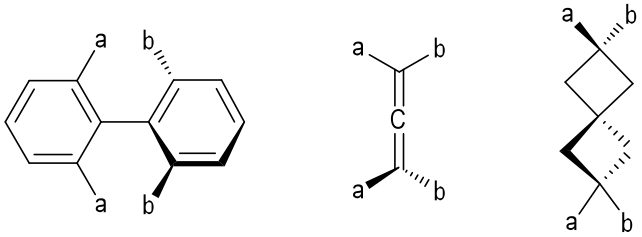


Figure 2: Axial Chirality

1.1.1.3 Planar Chirality

Planar chirality results from the arrangement of out of plane groups with respect to a plane.[3] The most common class of molecules that possess chiral planes are bridged aromatic molecules[3] in which a linker-chain, extending above or below the chiral plane, restricts rotation in the molecule. An example of a molecule exhibiting planar chirality is shown in figure 3.

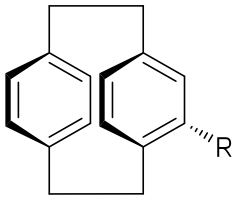


Figure 3: Planar Chirality

1.1.2 Stereoisomerism

Stereoisomers are isomers that have the same molecular formula and sequence of bonded atoms but differ in the three dimensional orientation of their atoms in space.[1] Stereoisomers can be subdivided into two classes: enantiomers and diastereomers.

1.1.2.1 Enantiomers

Enantiomers are a pair of stereoisomers that are nonsuperimposable mirror images.[1] An example of a pair of enantiomers is shown in figure 1. The chemical properties of enantiomers are identical when reacting with achiral molecules and differ when reacting with chiral molecules,

i.e. a reaction that forms enantiomers from achiral starting material will form a racemic mixture of enantiomers unless there is some chiral influence on the reaction (for example a chiral catalyst).[1] The physical properties of enantiomers are identical except for the direction in which they rotate plane polarized light.[1]

1.1.2.2 Diastereomers

Diastereomers are a special type of stereoisomer that are not mirror images of each other but differ in their spatial arrangement of atoms.[1] Diastereomers often have different chemical reactions and different physical properties.[1] Furthermore some reactions produce only one diastereomer and not the other and some reactions only occur with one diastereomer and not the other.[1] Diastereomers can be divided into two categories: cis-trans stereoisomers, i.e. the stereoisomers differ in the placement of groups on one side or the other of a double bond (see figure 4), and stereoisomers with multiple stereogenic elements, i.e. two chiral centers, a chiral center and a chiral axis, a chiral centre and a chiral plane, etc. (see figure 5).[1]

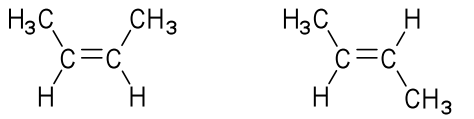
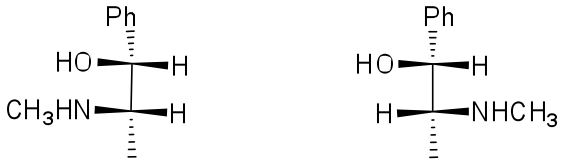


Figure 4: cis-trans isomers of 2-butene



(*R*,*S*)-configuration (*R*,*R*)-configuration

Figure 5: Diastereomers of ephedrine

1.1.3 Stereoselective Reactions

Stereoselective reactions can be broadly defined as reactions that favor the production of one enantiomer or diastereomer over another.[2] Stereoselective reactions include enantioselective reactions and diastereoselective reactions. The enantiomeric excess is a measure of how much of an excess of one enantiomer is in a mixture of enantiomers and is calculated using the equation shown in figure 6 (presuming, in this case, that the (*R*)-enantiomer is the major product).

$$ee = \frac{[(R)-(S)]}{[(R)+(S)]} \times 100\%$$

Figure 6: Equation for calculating enantiomeric excess

1.2 The Buchwald – Hartwig Reaction

The Buchwald-Hartwig reaction is a palladium catalyzed cross-coupling reaction of an aryl halide with a nitrogen nucleophile resulting in the formation of a new carbon-nitrogen bond.[4-12] This reaction is a very useful synthetic tool for the construction of arylamines. A general Buchwald-Hartwig reaction is shown in figure 6.

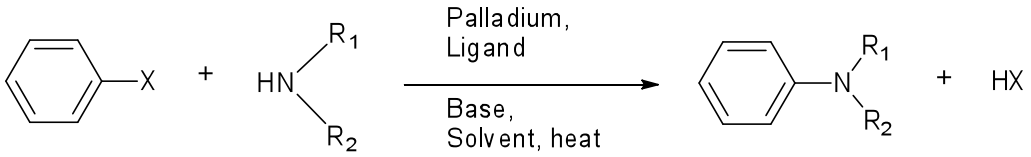
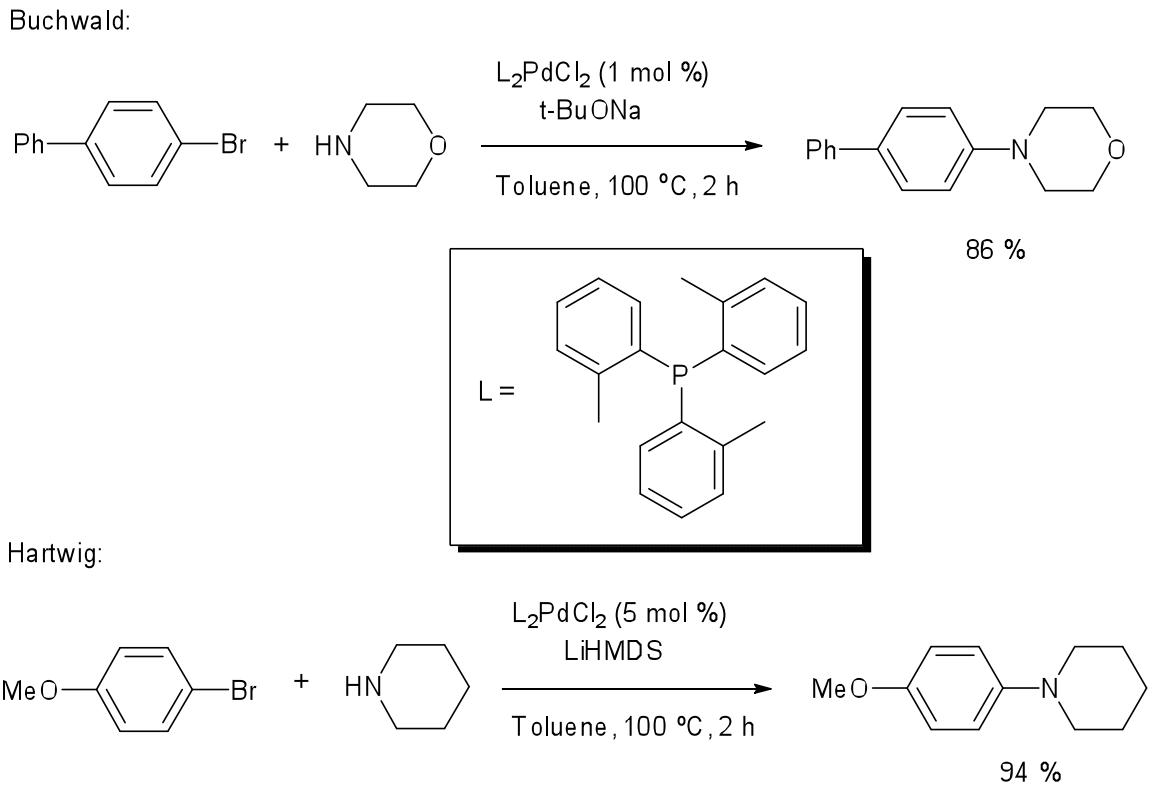


Figure 7: A General Buchwald-Hartwig reaction

In 1995 both Buchwald and Hartwig independently reported the intermolecular coupling of aryl halides with secondary amines using a small amount of palladium, a base and P(*o*-Tol)$_3$ as a ligand (scheme 1).[13,14]

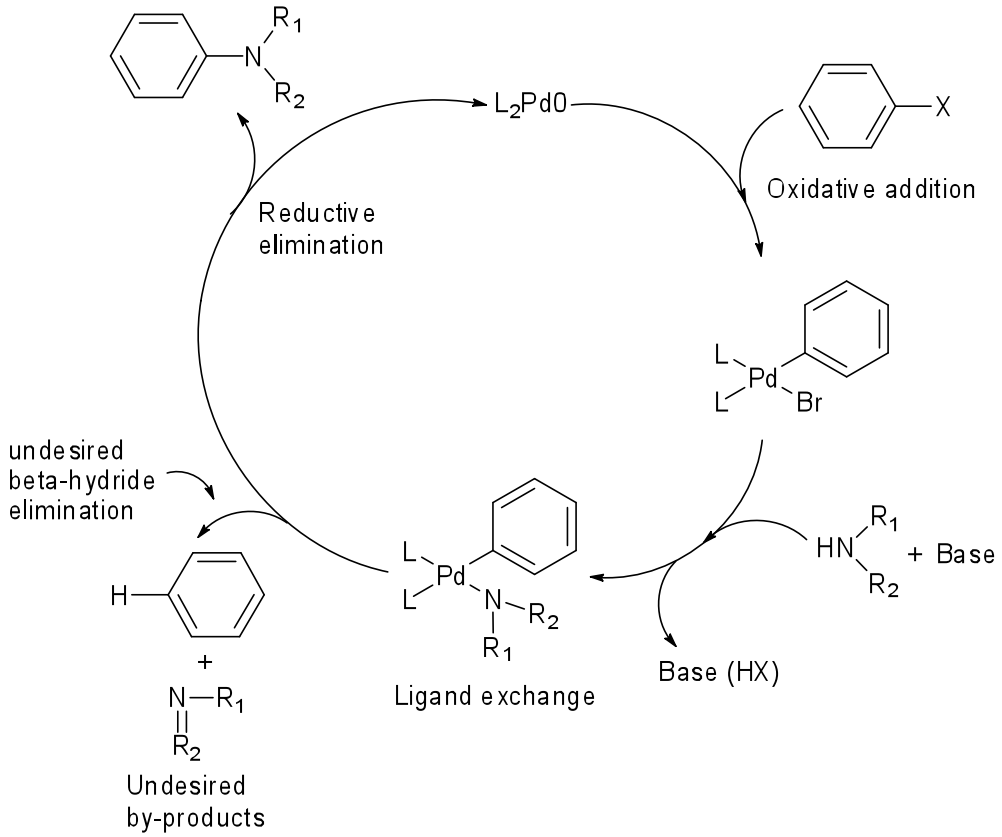


Scheme 1: Intermolecular coupling of aryl halides with secondary amines

1.2.1 Mechanism of the Buchwald – Hartwig Reaction

The mechanism of the Buchwald-Hartwig reaction has been extensively studied and is well understood.[15-20] A general mechanism of the Buchwald-Hartwig reaction is shown in scheme 2. Upon formation of the active palladium(0) complex, palladium inserts into the carbon halogen bond in a step called oxidative addition. Palladium then coordinates to the nitrogen atom of the amine and ligand exchange occurs with bromine, a base is also added to alleviate the positive

charge generated on nitrogen. The last step of the cycle is a reductive elimination which produces the coupled product and regenerates the catalyst thus enabling the cycle to repeat.

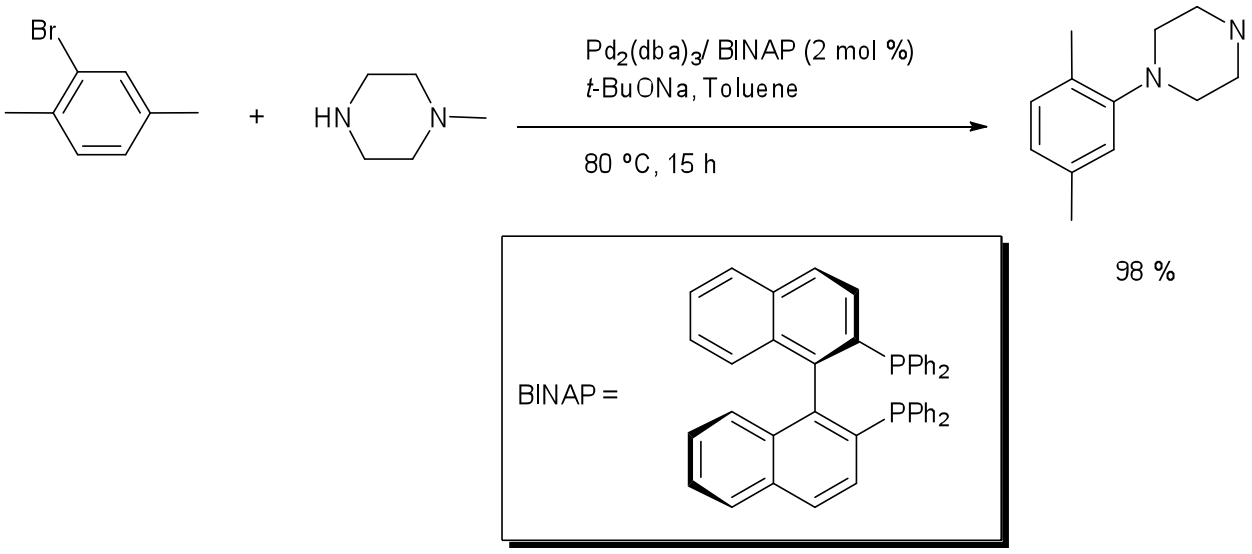


Scheme 2: General mechanism of the Buchwald-Hartwig reaction

1.2.2 Chiral Bisphosphine Ligands in the Buchwald-Hartwig Reaction

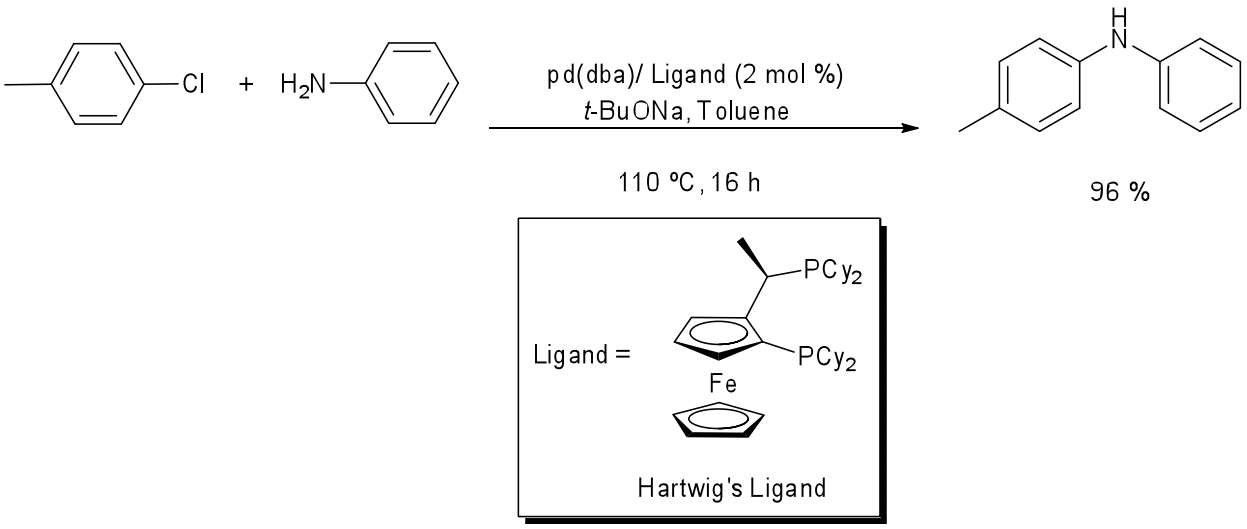
In these early experiments, especially when P(*o*-Tol)$_3$ was used as a ligand both Buchwald and Hartwig reported a significant amount of by-products arising from β-hydride elimination (scheme 2, bottom left). Soon after in 1996 Buchwald demonstrated that the amount of by-products could be substantially reduced by employing $Pd_2(dba)_3$ (tris(dibenzylideneacetone)dipalladium(0))/BINAP as the catalyst system (scheme 3a).[21] Similarly in 1998, Hartwig also reported a reduction in β-hydride elimination products by using a ferrocene based racemic, chiral, bulky, electron-rich phosphine ligand (scheme 3b).[22]

Buchwald:



Scheme 3a: Incorporation of chiral bisphosphine ligands in the Buchwald-Hartwig reaction

Hartwig:

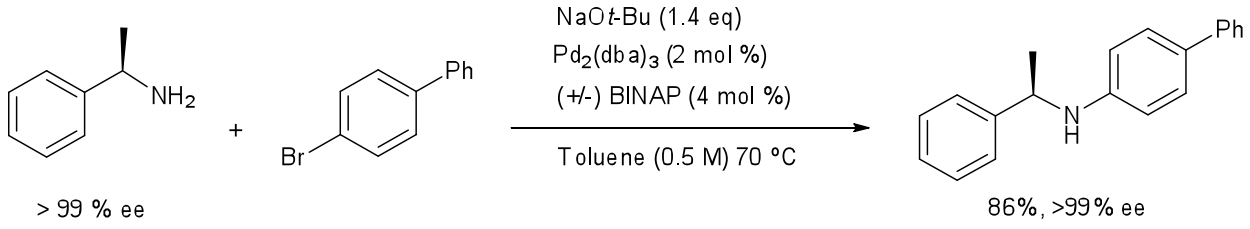


Scheme 3b: Incorporation of chiral bisphosphine ligands in the Buchwald/Hartwig reaction

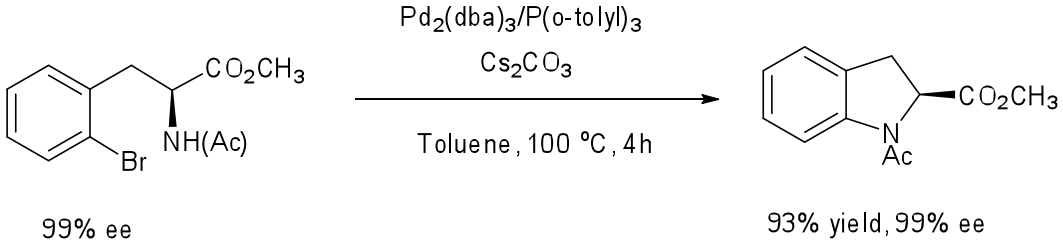
Although many of the ligands used in these transformations are chiral, only a few groups have tried to exploit the chirality of the ligand to develop an enantioselective variant of the Buchwald-Hartwig reaction.

1.2.3 Retention of Chirality in Buchwald-Hartwig Reactions

Palladium-catalyzed intermolecular and intramolecular coupling of amines with aryl halides has proven to be an efficient method for the synthesis of various aniline derivatives.[23] In a paper written by Wagaw *et al*. enantiomerically enriched aniline derivatives were prepared by coupling aryl bromides with enantiomerically enriched amines (scheme 4a).[23] The authors also report the intramolecular coupling of amines with aryl halides as shown in scheme 4b.



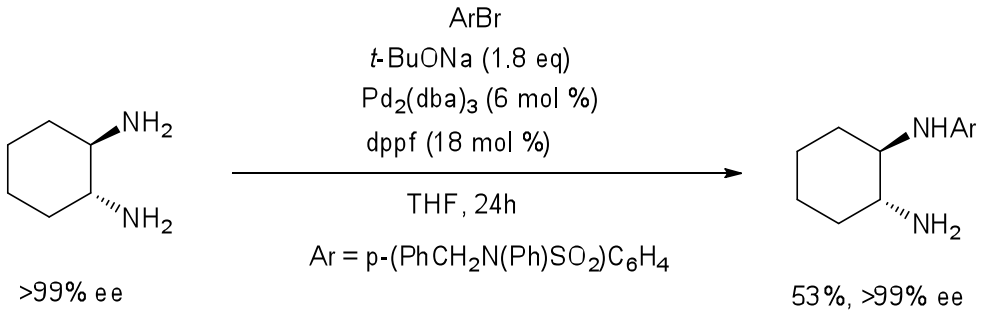
Scheme 4a: intermolecular coupling of an amine with an aryl halide



Scheme 4b: intramolecular coupling of an amine with an aryl halide

It is important to note that a new chiral centre is not formed in the products of the above reactions, the original stereochemistry is retained.

In a paper written by Frost & Mendonca, palladium catalyzed arylation of amines is used to selectively prepare various mono-N-arylated, enantiopure diamine ligands.[24] The catalytic cross-coupling of enantiopure amines with aryl bromides using Pd(0)/dppf (dppf=1,1'-bis(diphenylphosphino)ferrocene) or Pd(0)/BINAP (2,2'-Bis(*N*-diphenylphosphinoamino-1,1'-binaphthyl) produces products in moderate yields with no loss of enantiopurity.[24] The use of BINAP as a ligand resulted in a considerable increase in yield.[24] An example of the cross-coupling of (1*R*,2*R*)-(−)-1,2-diaminocyclohexane with an aryl bromide is shown in scheme 5.

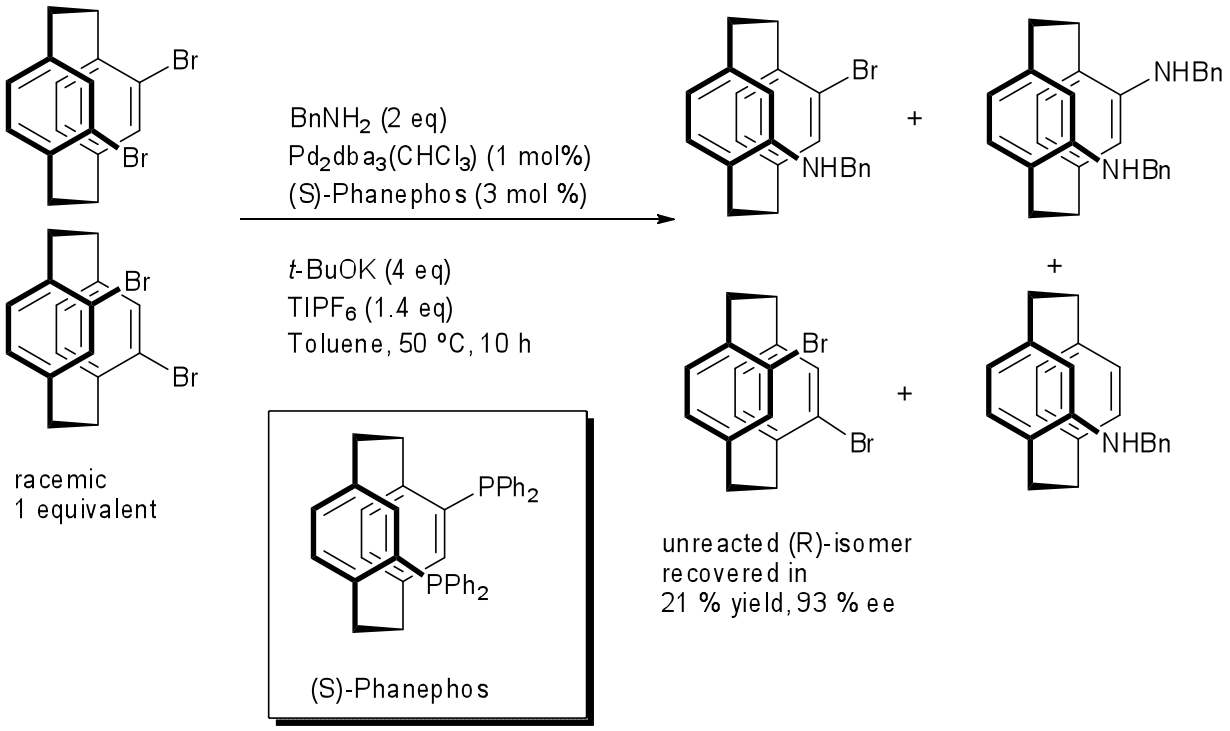


Scheme 5: Enantiopure mono-N-arylation of (1*R*,2*R*)-(−)-1,2-diaminocyclohexane

1.2.4 Enantioselective Buchwald-Hartwig Reactions

1.2.4.1 Kinetic Resolution

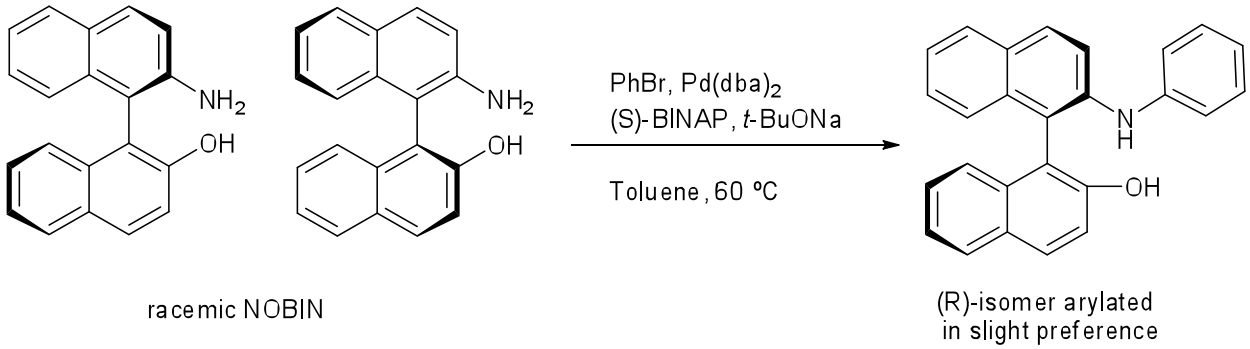
The first example of an enantioselective Buchwald-Hartwig reaction was reported by Rossen and Pye in which the authors demonstrated kinetic resolution of planar chiral bromides (scheme 6).[25]



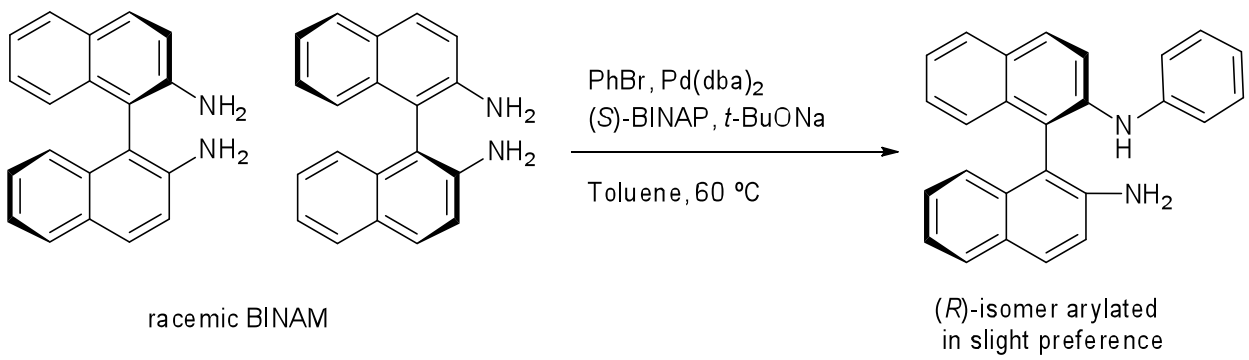
Scheme 6: Kinetic resolution of racemic planar chiral bromides

The catalyst system employed in these reactions was palladium/(*S*)-PHANEPHOS. Although the cross-coupling reaction produced a variety of products, i.e. mono-aminated, di-aminated, de-brominated, mono-aminated de-brominated, no efforts were made to recover these products. The authors were interested in the unreacted di-bromide starting material and when they determined the enantiomeric excess (*ee*) of this starting material they discovered that a kinetic resolution had taken place. The (*R*)-dibromide proved to be a poorer substrate for the (*S*)-PHANEPHOS palladium catalyst complex with the (*S*) isomer of the dibromide reacting 3-4 times faster. Addition of the halide scavenger $TlPF_6$ resulted in an increase in selectivity with the (*S*)-dibromide reacting 10-13 times faster than the (*R*) isomer. When the reaction was pushed to 79 % conversion this led to a 21 % recovery of the (*R*)-dibromide with a 93 % *ee*.

Another early example illustrating an enatioselective intermolecular Buchwald-Hartwig reaction via kinetic resolution was reported by Kocovsky *et al*.[26] The authors demonstrated partial kinetic resolution of racemic axially chiral amines using palladium/(*S*)-BINAP as the catalyst system. When the amino alcohol NOBIN (scheme 7a) was used as a coupling partner with bromobenzene, preferential arylation of the (*R*)-enantiomer resulted in a 27 % *ee* at 35 % conversion and an 11 % *ee* at 60 % conversion (scheme 7a). Similarly the cross-coupling reaction of a binaphthyl diamine BINAM (scheme 7b) with bromobenzene also resulted in preferential arylation of the (*R*)-enantiomer with 17 % *ee* at 45 % conversion and 10 % *ee* at 70 % conversion for the monoarylated product (scheme 7b). In these reactions the (*R*)-amino alcohol/diamine is a better substrate for the palladium/(*S*)-BINAP catalyst complex.

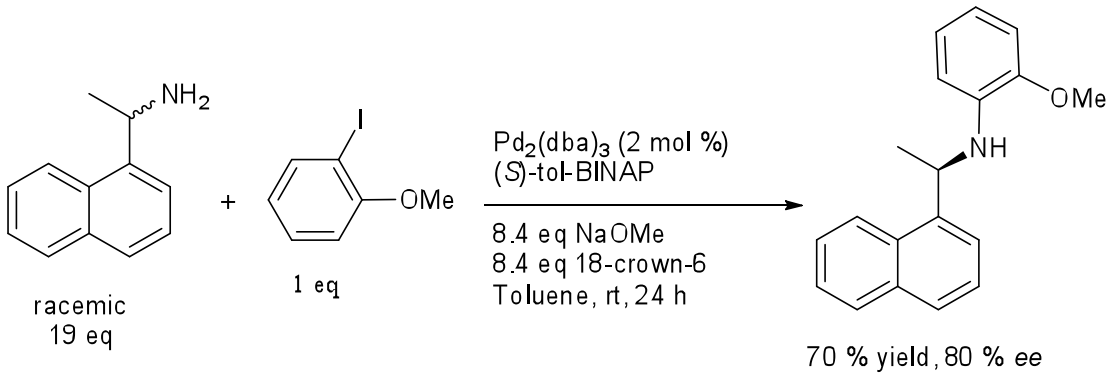


Scheme 7a: Kinetic resolution of a racemic axially chiral amino alcohol



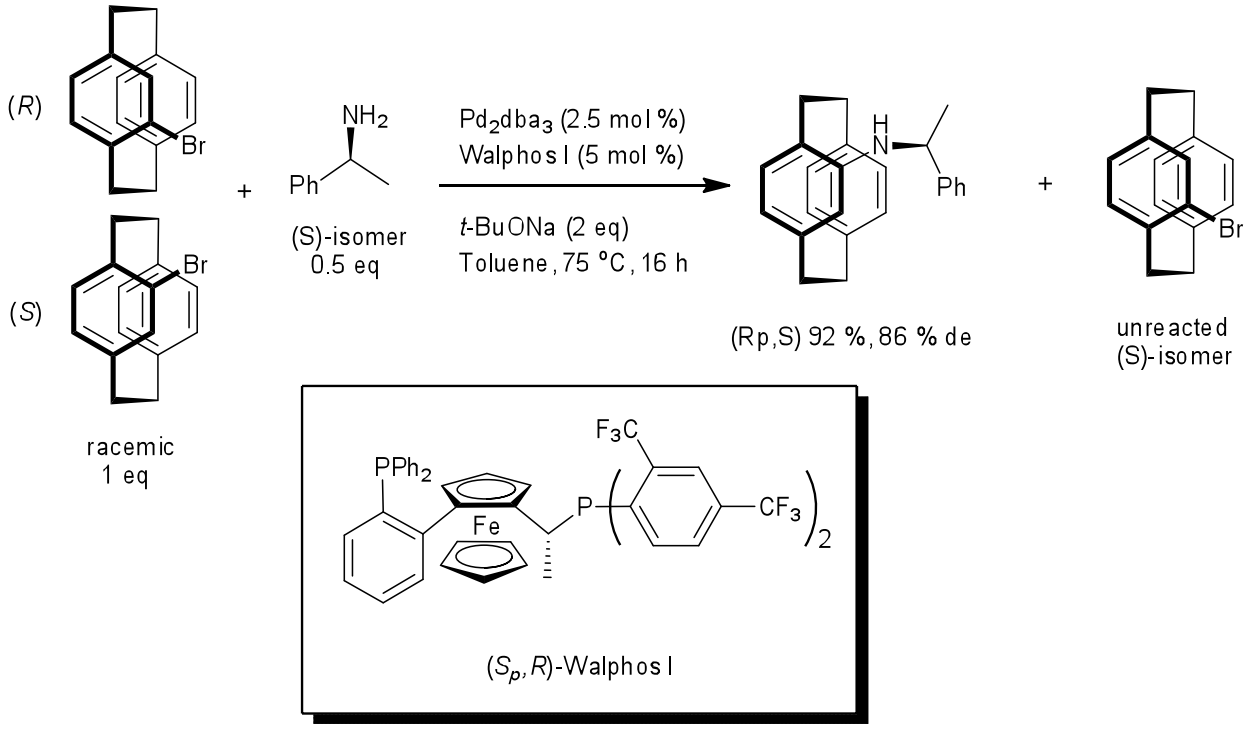
Scheme 7b: Kinetic resolution of a racemic axially chiral diamine

A more recent example of an enantioselective Buchwald-Hartwig reaction involving kinetic resolution of amines was reported by Ohta *et al*.[27] The authors employed palladium/(*S*)-Tol-BINAP as the catalyst system for the kinetic resolution of 1-(1-napthyl)ethylamine which furnished the arylated product in good yield and relatively high selectivity, 70 % yield and 80 % *ee* respectively (scheme 8). Although the selectivity of the reaction is good it should be noted that 19 equivalents of racemic amine and 8.4 equivalents of a crown ether additive were required.



Scheme 8: Kinetic resolution of optically active aniline derivatives

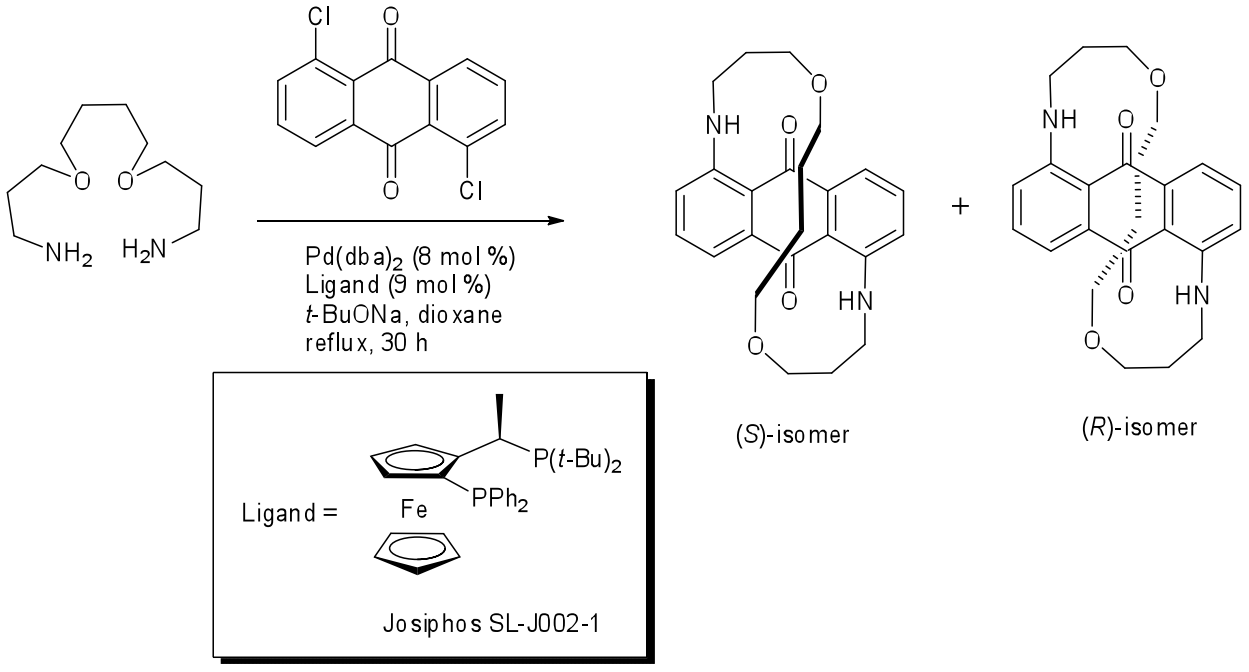
In 2005 Bräse *et al*. reported the first example of a diastereoselective Buchwald-Hartwig reaction through coupling of racemic [2.2]paracyclophane bromide with (*S*)-1-phenylethylamine.[28] The catalyst system employed was palladium/(S_p,*R*)-Walphos 1 which furnished the desired product in excellent yield and diastereoselectivity, 92 % yield, 86 % *de* (scheme 9). Additionally since the authors use half an equivalent of amine relative to the racemic [2.2]paracyclophane bromide a kinetic resolution also takes place when (*S*)-1-phenylethylamine is used resulting in the excess diastereomer with configuration (R_p,*S*) and the excess (*S*)-enantiomer of [2.2]paracyclophane bromide, making the reaction enantioselective as well as diastereoselective (scheme 9).



Scheme 9: Enantio- and diastereoselective Buchwald-Hartwig reaction

1.2.4.2 Chiral plane Formation

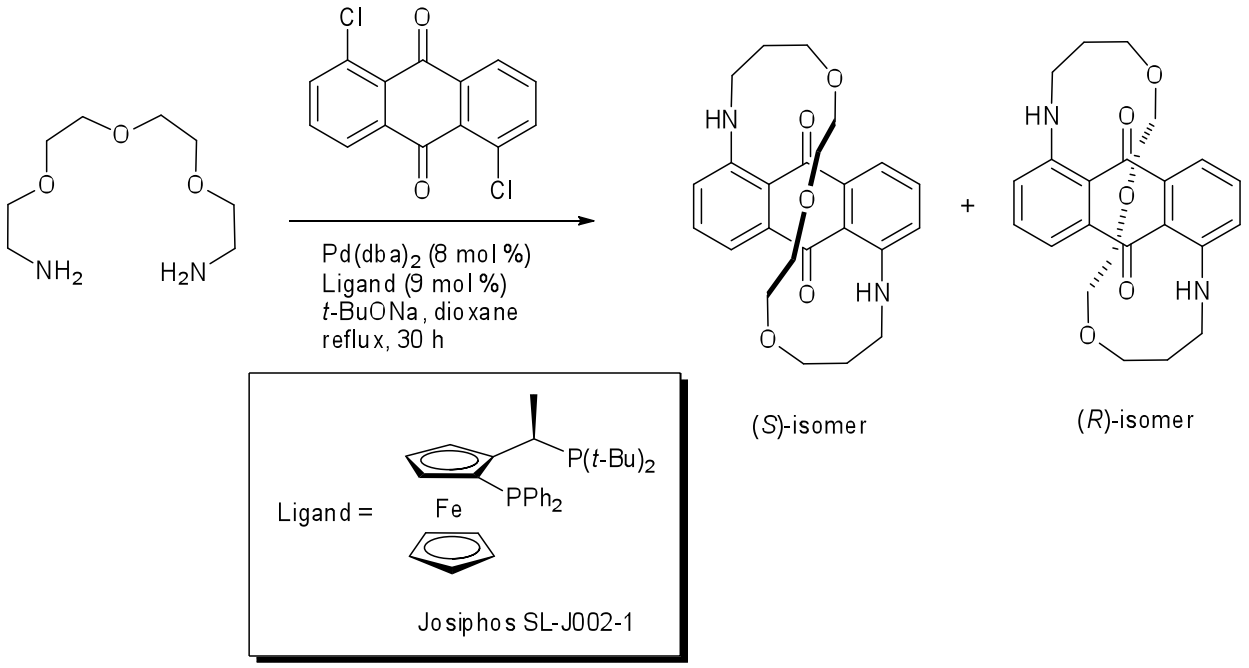
A more recent example of an enantioselective Buchwald-Hartwig reaction involving planar chirality was reported by Ranyuk *et al*. where the authors were successful in coupling 1,5-dichloroanthraquinone with dioxadiamine to produce an azamacrocycle (scheme 10a).[29] Palladium/Josiphos SL-J002-1 was the catalyst system used and the corresponding azamacrocycle was obtained in 31 % yield and 60 % *ee*. Recrystallization of the mixture of enantiomers from dichloromethane/petroleum ether resulted in an enantiopure azamacrocycle in 19 % yield.



Scheme 10a: Azamacrocycle synthesis via enantioselective Buchwald-Hartwig amination

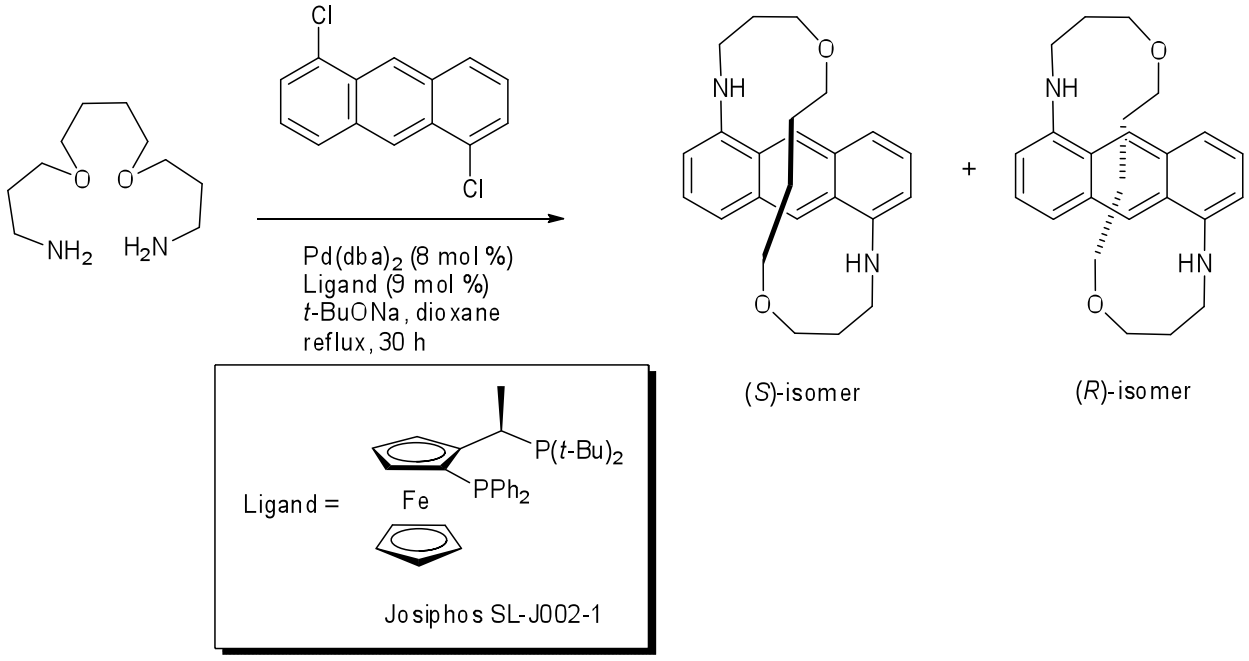
The authors followed up on this work and again were successful in coupling 1,5-dichloroanthraquinone with trioxadiamine using Palladium/Josiphos SL-J002-1 to produce the

corresponding azamacrocycles in 27 % yield and 58 % *ee* (scheme 10b).[29] However in this case the azamacrocycle could not be recrystallized to enantiopurity but rather 88 % *ee* in 11 % yield.



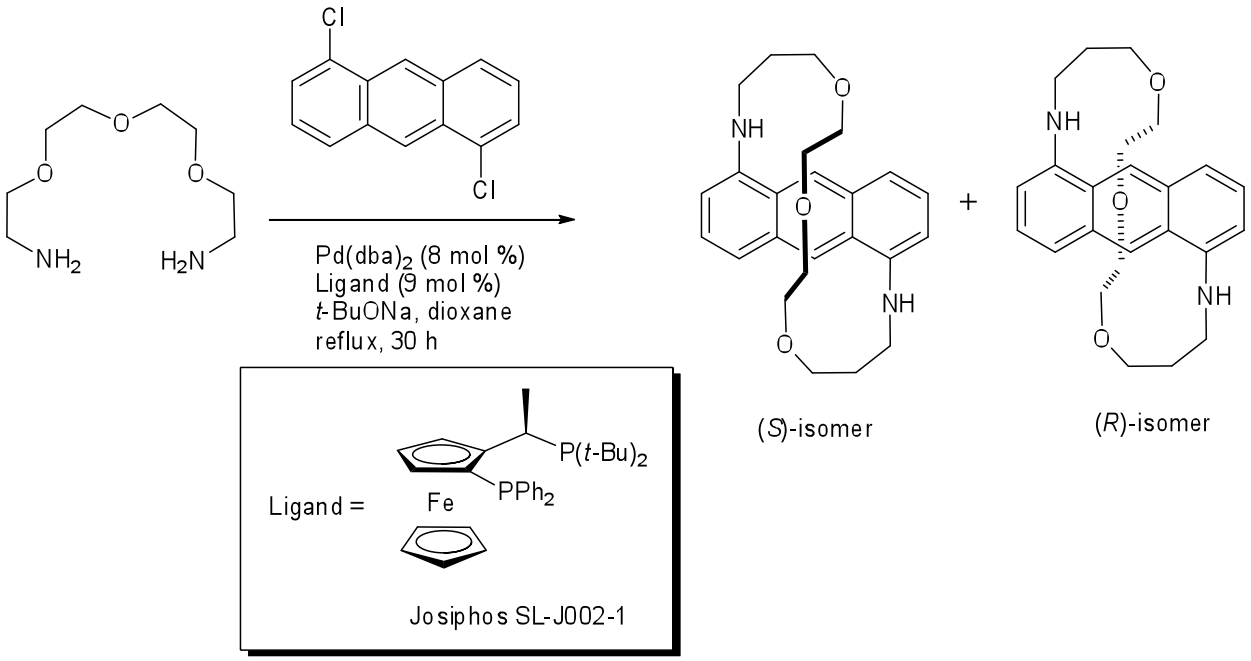
Scheme 10b: Azamacrocycle synthesis via enantioselective Buchwald-Hartwig amination

Next the authors investigated the coupling of 1,5-dichloroanthracene with dioxadiamine. Again palladium/Josiphos SL-J002-1 was the ideal catalyst system furnishing the azamacrocycle in 30 % yield, 34 % *ee* (scheme 11a).[29] In this case however recrystallization of the azamacrocycle could not be achieved to increase enantiopurity.



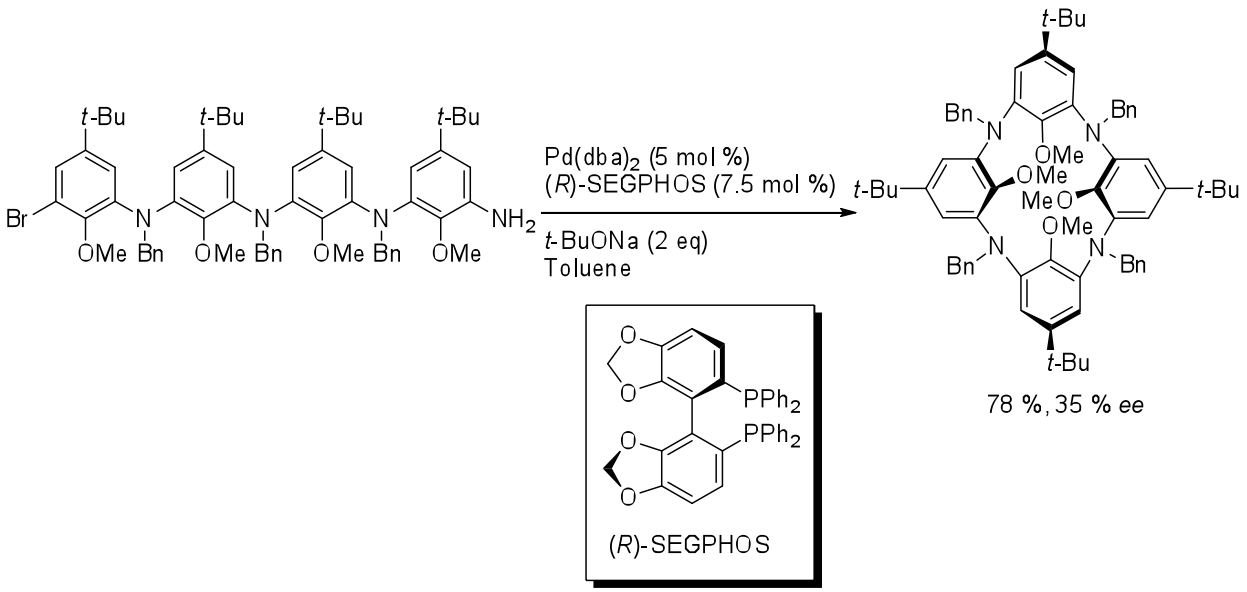
Scheme 11a: Azamacrocycle synthesis via enantioselective Buchwald-Hartwig amination

Lastly the authors successfully coupled 1,5-dichloroanthracene with trioxadiamine using palladium/Josiphos SL-J002-1 to produce the corresponding azamacrocycle in 29 % yield, 45 % *ee* (scheme 11b).[29] This azamacrocycle also could not be recrystallized to enantiopurity.



Scheme 11b: Azamacrocycle synthesis via enantioselective Buchwald-Hartwig amination

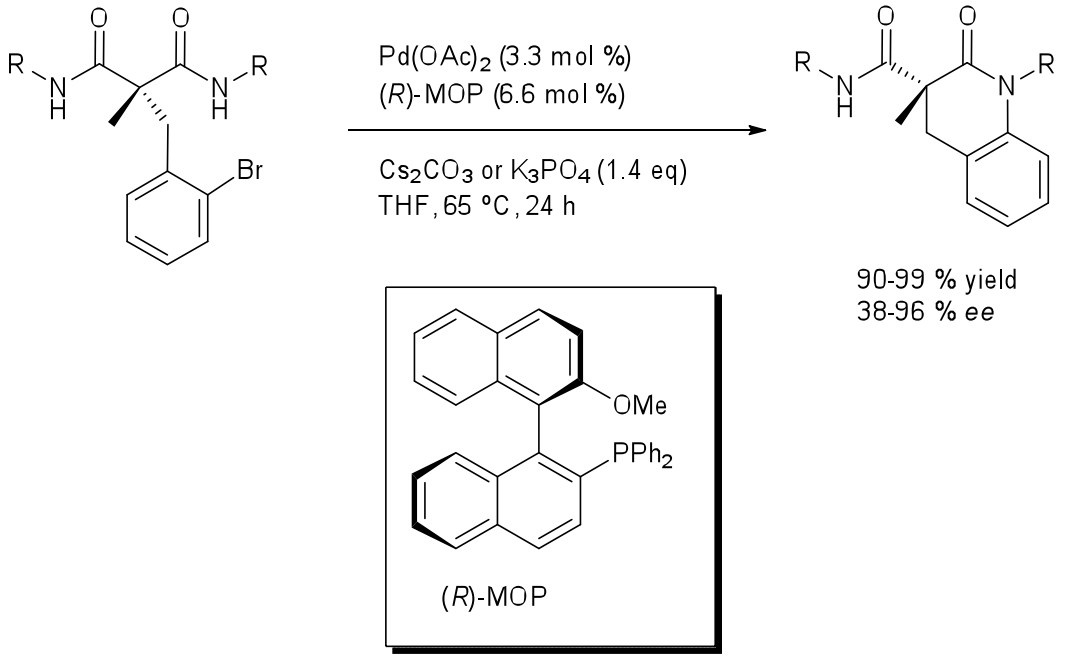
Another interesting example reported by Ishibashi *et al*. involves the synthesis of chiral azacalix[4]arene via enantioselective intramolecular Buchwald-Hartwig amination.[30] When palladium/(*R*)-SEGPHOS was used as the catalyst system the product was obtained in 78 % yield and 35 % *ee* (scheme 12). More importantly these enantiomerically enriched compounds were obtained in enantiopure form through multiple recrystallizations due to preferential crystallization of the racemic product.



Scheme 12: Synthesis of chiral azacalix[4]arene

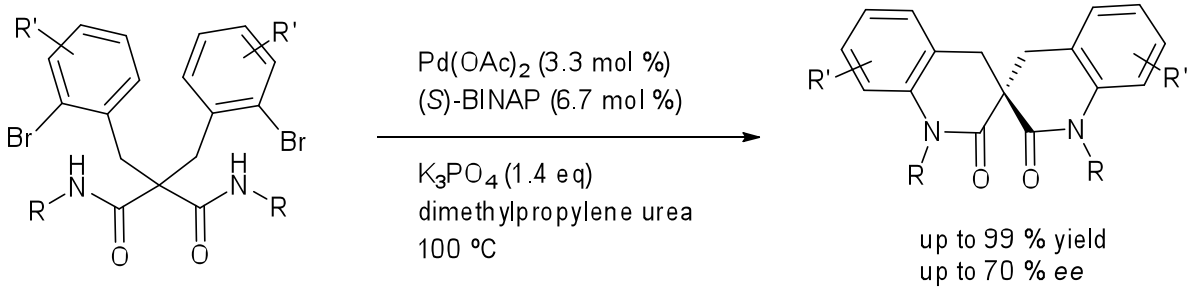
1.2.4.3 Chiral Centre Formation

In 2009 Porosa and Viirre reported an enantioselective intramolecular Buchwald-Hartwig reaction via desymmetrization of di-nitrogen malonamides.[31,32] The chiral catalyst employed in these reactions was palladium/(*R*)-MOP which furnished various six-membered quinolinone heterocycles in excellent yield, 90-99 %, with moderate to high enantiomeric excess, 38-96 % *ee* (scheme 13). Additionally the six-membered quinolinone heterocycle containing a 4-chloro-2-methylbenzyl substituent was obtained in enantiopure form by preferential recrystallization of the racemate, leaving behind the enantiopure mother liquor.[32]



Scheme 13: Desymmetrization of malonamide derivatives via an enantioselective intramolecular Buchwald-Hartwig reaction

Also in 2009 Sasai *et al*. reported a similar enantioselective intramolecular Buchwald-Hartwig reaction to produce spirobi(3,4-dihydro-2-quinolone) derivatives via double cyclization of various malonamides (scheme 14).[33] The catalyst system employed in these reactions was palladium/(*S*)-BINAP.

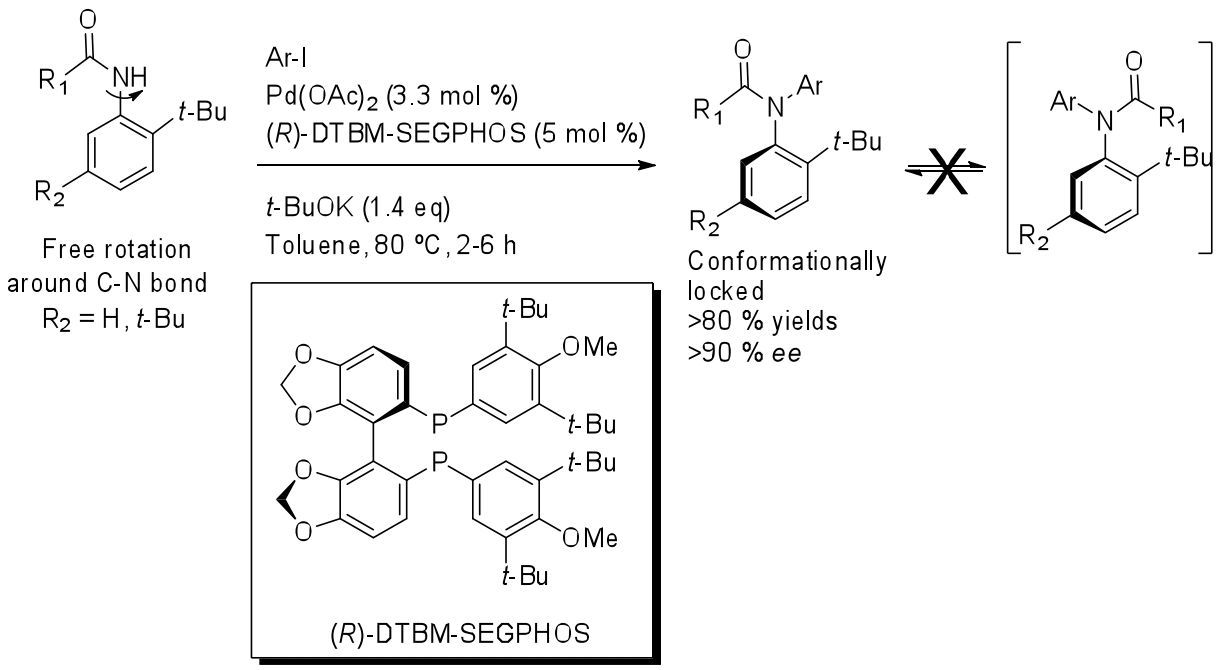


Scheme 14: Synthesis of C_2-symmetric spirobilactams via an enantioselective intramolecular Buchwald-Hartwig reaction

Furthermore the dimethyl, diethyl and dibenzyl derivatives were obtained in enantiopure form through a single recrystallization. Interestingly when the authors used palladium/(*R*)-MOP as the catalyst system, which worked well for Porosa and Viirre, the resulting spirobilactam was isolated as a racemic mixture in 69 % yield.

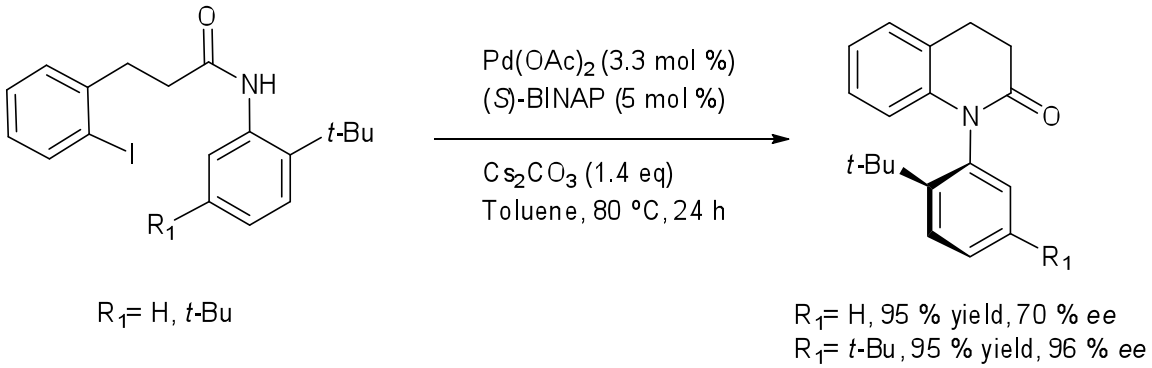
1.2.4.4 Chiral Axis Formation

In 2005 Taguchi *et al*. demonstrated a very impressive intermolecular enantioselective Buchwald-Hartwig reaction by N-arylation of bulky achiral *t*-butyl anilide derivatives (scheme 15).[34] There is free rotation around the C-N bond in the starting material of the reaction shown in scheme 15 however upon arylation at the nitrogen atom the rotation becomes locked in the product thus forming a chiral axis. The authors employed palladium/(*R*)-DTBM-SEGPHOS as a catalyst system which furnished the coupled products in high yields and enantioselectivity, >80 % yield and >90 % *ee* (scheme 15).



Scheme 15: Enantioselective intermolecular nitrogen arylation of *t*-butylanilides

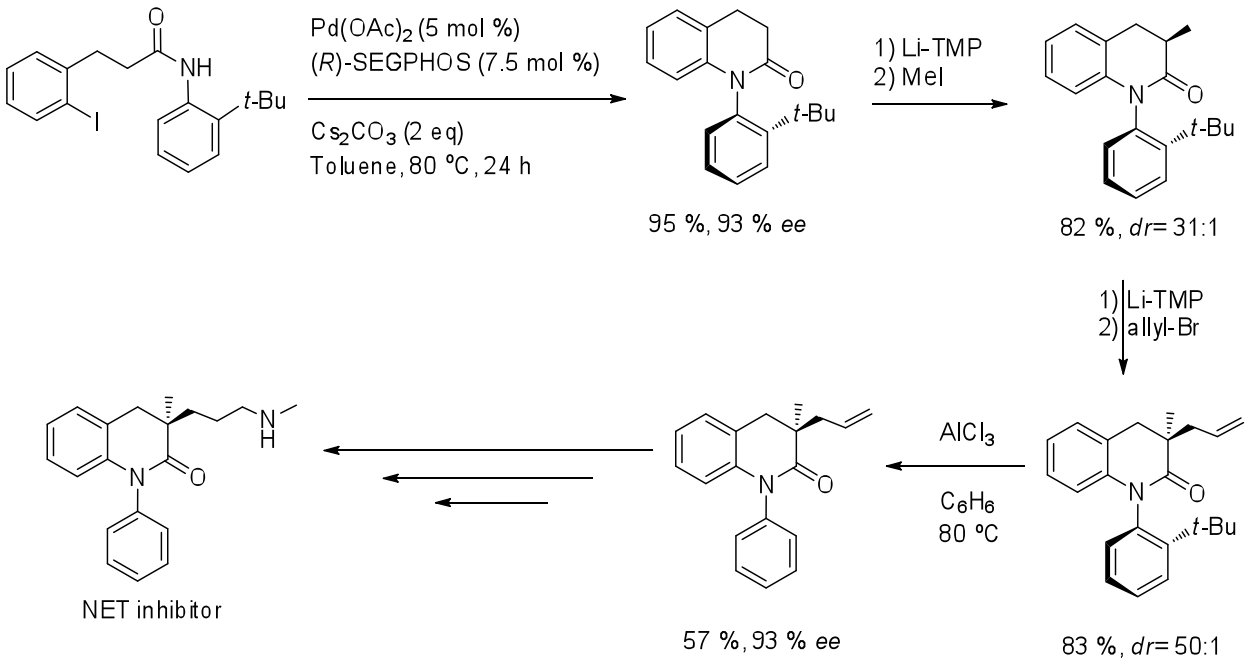
The authors also successfully applied this chemistry to intramolecular systems resulting in the formation of six-membered ring lactams.[34-37] Interestingly the palladium/(*R*)-DTBM-SEGPHOS catalyst complex was not ideal for the intramolecular N-arylation reaction, resulting in racemic lactam product in low, 12 %, yield. Instead palladium/(*S*)-BINAP proved to be the optimal catalyst system resulting in the highest enantioselectivity, 70 % *ee*, and good yield, 95 %, for the formation of lactam product (scheme 16). When 2,5-bis-*t*-butylanilide was used as the substrate for N-arylation using palladium/(*S*)-BINAP as the catalyst system the corresponding lactam was obtained in high yield, 95 %, with a remarkable increase in enantioselectivity, 96 % *ee* (scheme 16).



Scheme 16: Enantioselective intramolecular nitrogen arylation of *t*-butylanilides

Additionally the anilide products from the intermolecular N-arylation reactions and lactam products from the intramolecular N-arylation reactions have been applied to asymmetric enolate chemistry.[34-37] The chiral axis of these products is what dictates the chirality at the α-carbon because attack of alkyl halides to either the anilide or lactam enolate preferentially occurs from the opposite face of the *ortho*-*t*-butyl group. These highly diastereoselective reactions were used in the synthesis of a key intermediate for a norepinephrine transporter (NET) inhibitor. The first step in the synthesis of the NET inhibitor involves an intramolecular asymmetric N-arylation reaction using palladium/(*R*)-SEGPHOS as the catalyst complex. This yields the desired lactam product in excellent yield and enantioselectivity, 95 % yield and 93 % *ee* (scheme 17). Subsequent α-methylation of the *t*-butyl lactam product proceeded in high yield, 82 %, with high diastereoselectivity, *dr* = 31:1. Construction of the quaternary α-carbon atom was achieved by α-allylation which again resulted in remarkably high diastereoselectivity, *dr* = 50:1, and good yield, 86 %. The final steps toward the NET inhibitor was removal of the ortho-*t*-butyl group of lactam product via a retro-Friedel-Crafts reaction followed by *anti*-Markovnikov hydration and

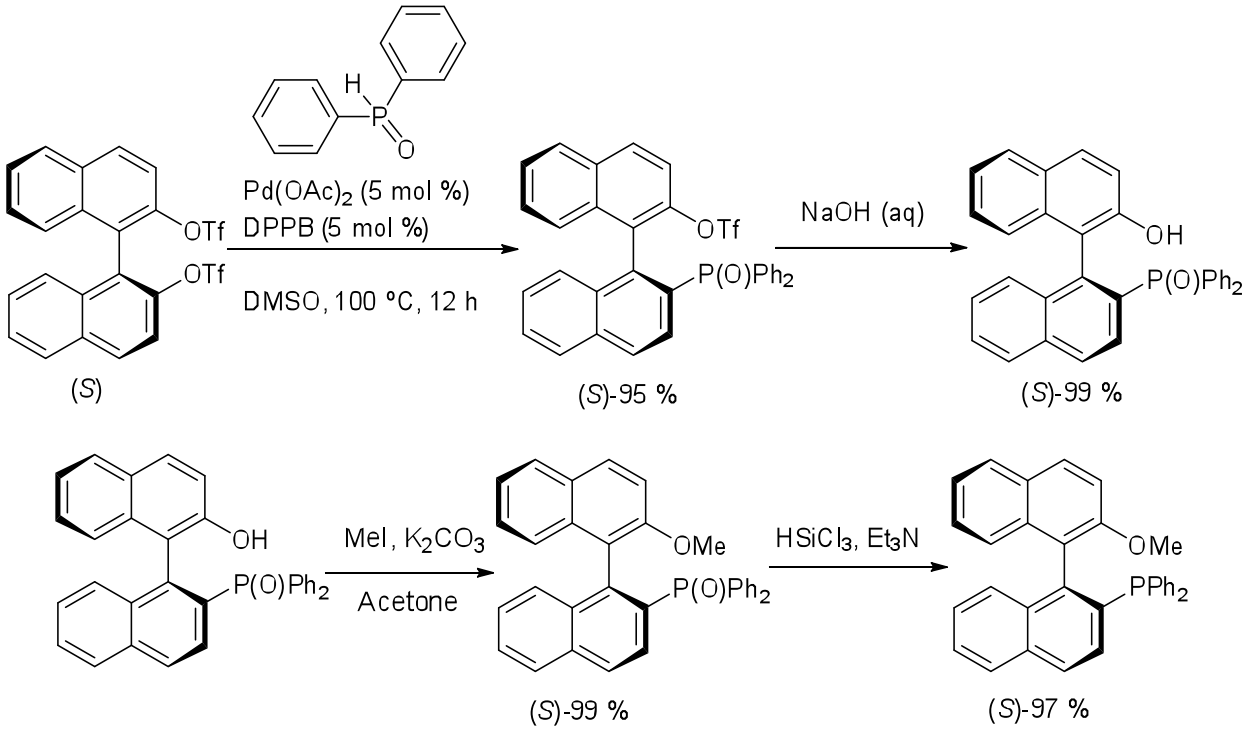
installation of the amine to furnish the product in moderate yield, 57 %, but more importantly with retention of chirality, 93 % *ee*, from the original starting lactam.



Scheme 17: Atropisomeric lactam chemistry as a chiral auxiliary in the synthesis of key intermediates for a NET inhibitor

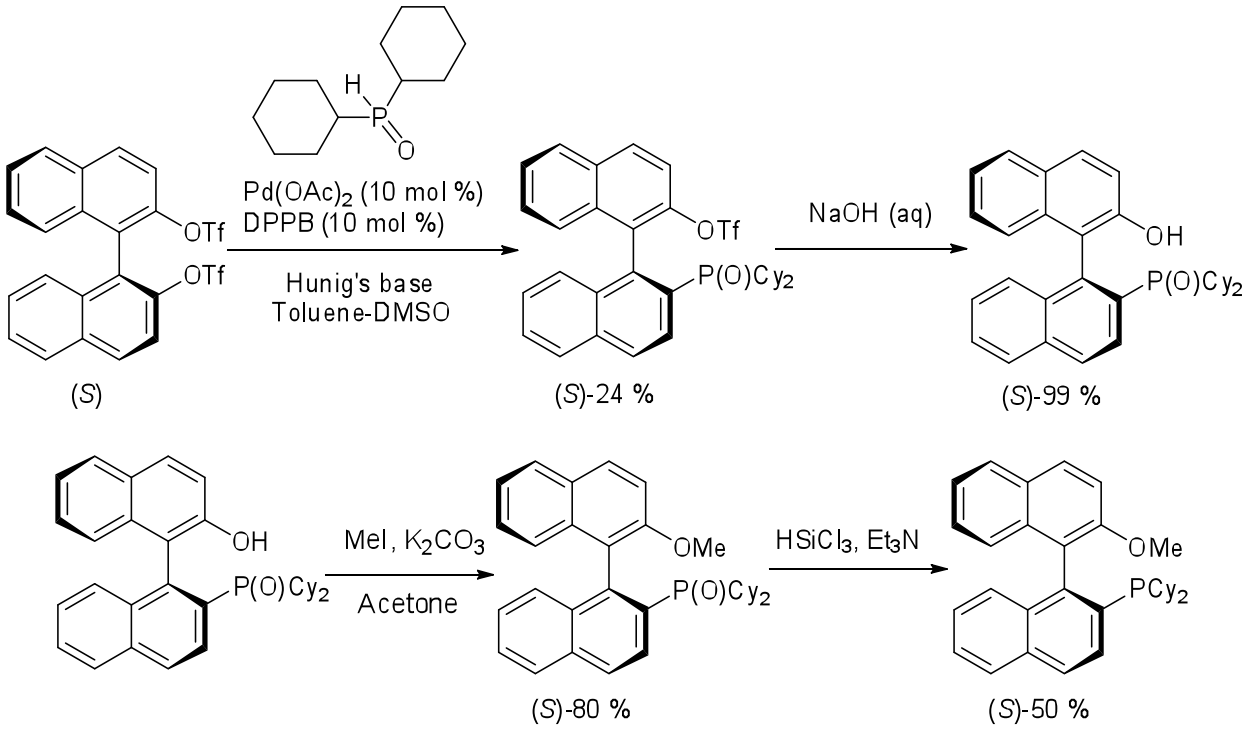
1.3 Synthesis of MOP and MOP Type Ligands

In 1993 Hayashi *et al*. reported the synthesis of enantiopure 2-(Diarylphosphino)-1,1'-binaphthyl ligands for use in asymmetric transition metal catalyzed reactions (scheme 18).[38] The first step in the synthesis involved the monophosphinylation of the ditriflate with diphenylphosphine oxide using palladium/dppb as the catalyst system. Next hydrolysis of the monotriflate was accomplished using aqueous NaOH in 1,4-dioxane and methanol. The phenolic hydroxyl moiety was then alkylated by treatment with iodomethane and K_2CO_3 to produce the corresponding phosphine oxide. Reduction of the phosphine oxide was achieved using trichlorosilane and triethylamine to obtain the free phosphine.



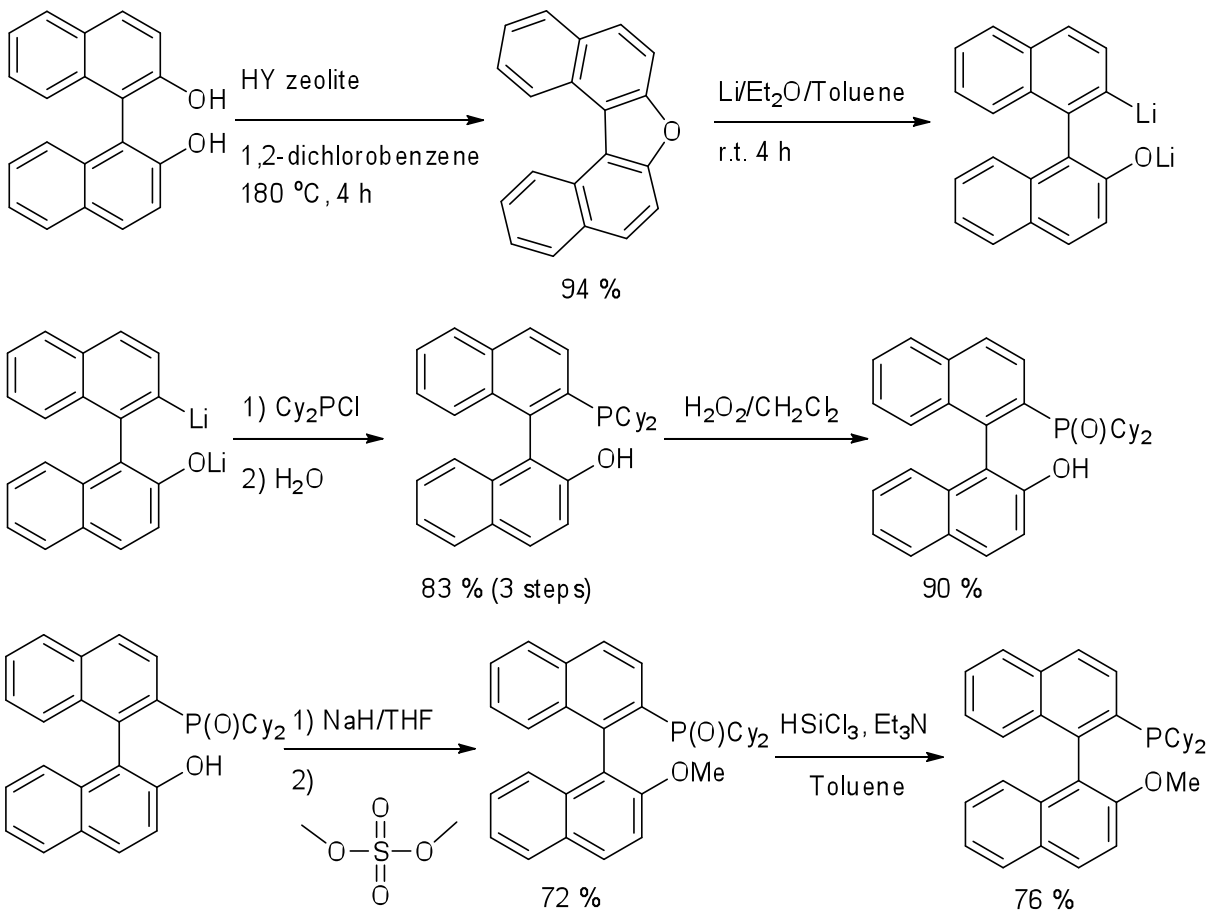
Scheme 18: Hayashi's Synthesis of (*S*)-MOP

In 2002 Buchwald *et al*. reported the synthesis of novel, enantiopure 2-alkoxy-2'-dialkylphosphino-1,1'-binaphthyl ligands which are used in palladium-catalyzed asymmetric arylation reactions of enolates.[39] The synthetic protocol used to access these ligands was similar to that reported by Hayashi *et al*. in the preparation of enantiopure 2-(diarylphosphino)-1,1'-binaphthyls (scheme 19).[38,39]



Scheme 19: Buchwald's Synthesis of (*S*)-Cy_2MOP

About five years later Zhang and his group reported the synthesis of racemic 2-alkoxy-2'-dialkylphosphino-1,1'-binaphthyl ligands and demonstrated their utility in intermolecular palladium catalyzed carbon-nitrogen bond forming reactions.[40] The synthetic route towards the synthesis of these ligands differs from that reported by Hayashi and Buchwald (scheme 20). The first step in the synthesis involved dehydration of 1,1'-bi(2-binaphthol) using an HY zeolite to form a dinaphthofuran ring. Next reductive opening of the dinaphthofuran ring was accomplished with lithium metal to form the dilithium salt which reacted with chlorodicyclohexyl phosphine to produce racemic 2-dicyclohexylphosphino-2'-hydroxybinaphthyl. This compound was oxidized using hydrogen peroxide followed by treatment with sodium hydride to form a soluble sodium salt which was then alkylated using dimethyl sulfate. Lastly the alkylated phosphine oxide was reduced to the free phosphine using trichlorosilane and triethylamine.



Scheme 20: Zhang's Synthesis of racemic Cy_2MOP

In 2004 Buchwald et al. reported the coupling of thiols with aryl halides using palladium/dippf as a catalyst system.[41] The substrate scope of the reaction was quite broad making it possible to couple various aryl bromides/chlorides with aliphatic and aromatic thiols. More importantly this catalyst system was also useful for accessing tertiary phosphines via coupling of aryl bromides/chlorides with secondary phosphines (figure 8).

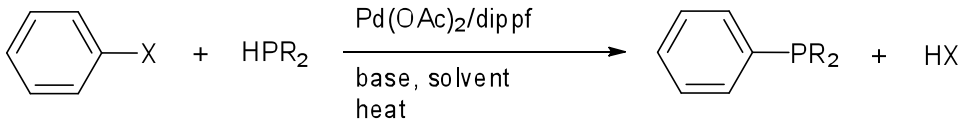
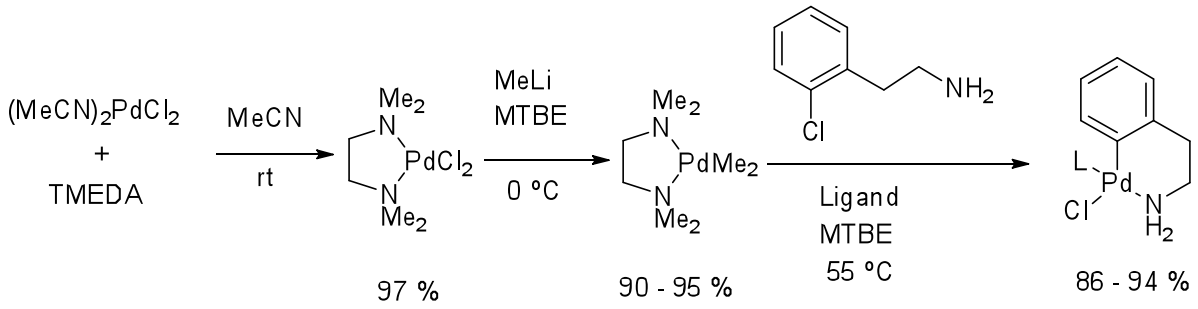


Figure 8: Coupling of aryl halides with secondary phosphines

1.4 Synthesis of Palladium Precatalysts for C-N Cross-coupling Reactions

In 2008 Buchwald *et al*. reported the synthesis of a new class of palladium precatalysts and demonstrated their utility in carbon-nitrogen cross-coupling reactions.[42,43] The synthetic outline for the synthesis of these palladium precatalysts is shown in scheme 21. The precatalysts are easily activated by treatment with base to produce indoline and the active Pd(0) catalyst (Figure 9).



Scheme 21: Synthesis of Palladium Precatalysts

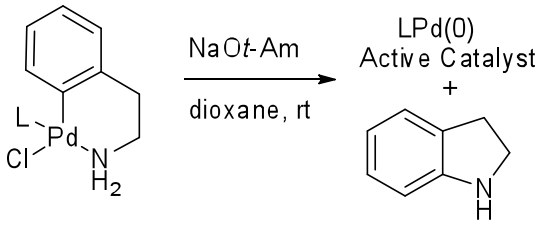
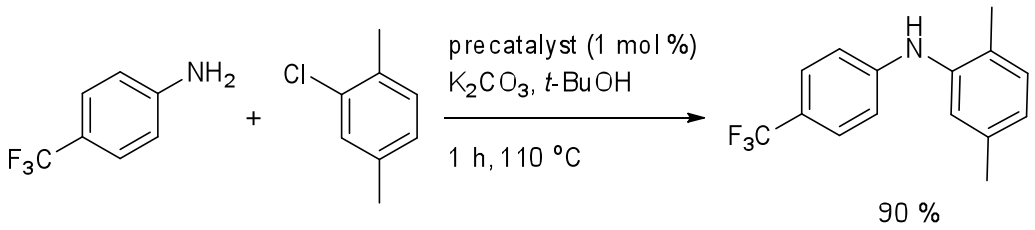


Figure 9: Precatalyst Activation

Products of cross-coupling reactions were obtained in high yield using low catalyst loadings with short reaction times thus implying that these precatalysts act as highly reactive palladium sources in C-N cross-coupling reactions. Even electron deficient anilines, which are usually difficult coupling partners in C-N cross-couplings due to their low nucleophilicity, were coupled with unactivated aryl chlorides in high yields (scheme 22).



Scheme 22: Coupling of electron deficient anilines with unactivated aryl chlorides

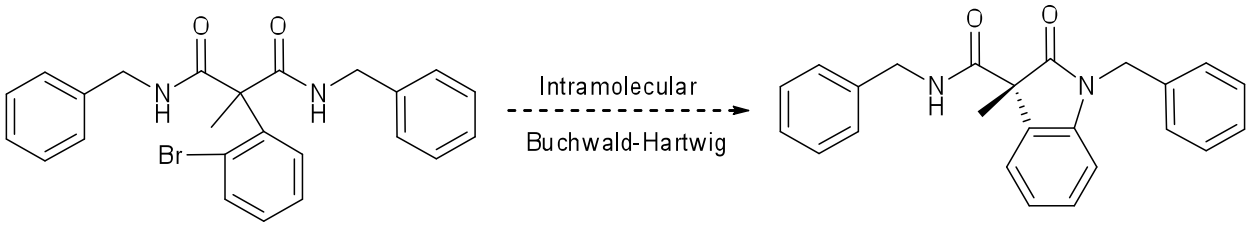
1.5 Research Goals and Objectives

This thesis paper entails the synthesis of (*R)*-2(Dicyclohexylphosphino)-2'-methoxy-1,1'-binaphthyl), (*R*)-Cy_2MOP, which appears to be a very efficient ligand for the palladium catalyzed intramolecular desymmetrization of di-nitrogen malonamides. Additionally an enantio- and diastereoselective Buchwald-Hartwig reaction has been developed through the desymmetrization of 2-(2-bromobenzyl)-N^1,N^3-bis(2-(*tert*-butyl)phenyl)-2-methylmalonamide using palladium/Cy_2MOP as the catalyst system to produce (3*R*,S_a)-*N*,1-bis(2-(*tert*-butyl)phenyl)-3-methyl-2-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide in excellent yield, with high enantio- and diastereoselectivity (99 %, 88 % *ee*). The absolute configuration of the formed diastereomer was determined by x-ray crystallography. The Cy_2MOP/Palladium catalyst system has also been effective in the cyclization of six membered ring benzomorpholinone and seven membered ring benzodiazepineone heterocycles. Furthermore various synthetic routes towards the synthesis of five membered ring oxindoles have been explored and each method is thoroughly discussed. Lastly the synthesis of a precatalyst was also attempted using Cy_2MOP and Pd(II)Me_2TMEDA.

2 Results and Discussion:

2.1 Towards the Synthesis of 5 membered ring Oxindole Heterocycles

In order to extend the work carried out by Porosa in 2009[31,32] to include smaller ring sizes an intramolecular Buchwald-Hartwig reaction was envisioned which would furnish five-membered ring oxindole heterocycles (Figure 10).

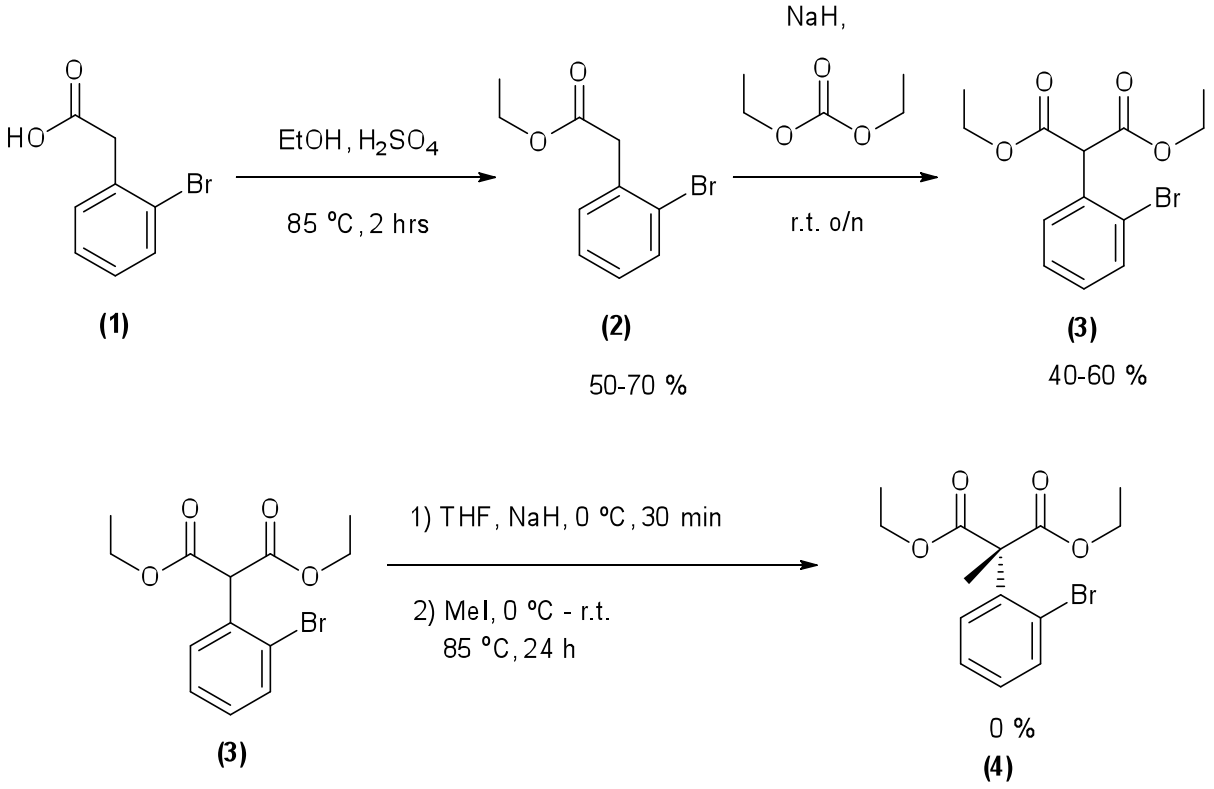


(10) **(11)**

Figure 10: Desymmetrization of di-nitrogen malonamides to form oxindole heterocycles

The initial synthetic protocol towards the synthesis of oxindole heterocycles is shown in scheme 23. The first step entailed a Fischer esterification reaction between compound **1** (2-(2-bromophenyl) acetic acid) and ethanol using a Dean-Stark apparatus. The reaction was catalyzed by H_2SO_4, heated to 85 ^oC and refluxed for two hours. Under these reaction conditions the desired ethyl ester **2** (ethyl 2-(2-bromophenyl)acetate) was obtained in 50 – 70 % yield. Next an ethoxycarbonylation reaction was carried out by deprotonation of **2** in diethyl carbonate using NaH. The reaction was left stirring overnight at room temperature and compound **3** (diethyl 2-(2-bromophenyl)malonate) was obtained in 40 – 60 % yield. Methylation of **3** at the α-carbon was attempted by deprotonation of **3** in THF using NaH followed by the addition of iodomethane. The reaction was heated to 85 ^oC and refluxed overnight. The reaction was checked by TLC and showed no disappearance of the starting material, thus another half equivalent of sodium hydride and iodomethane were added to the reaction mixture and the reaction was refluxed overnight. The reaction was checked by TLC and again showed no disappearance of the starting material.

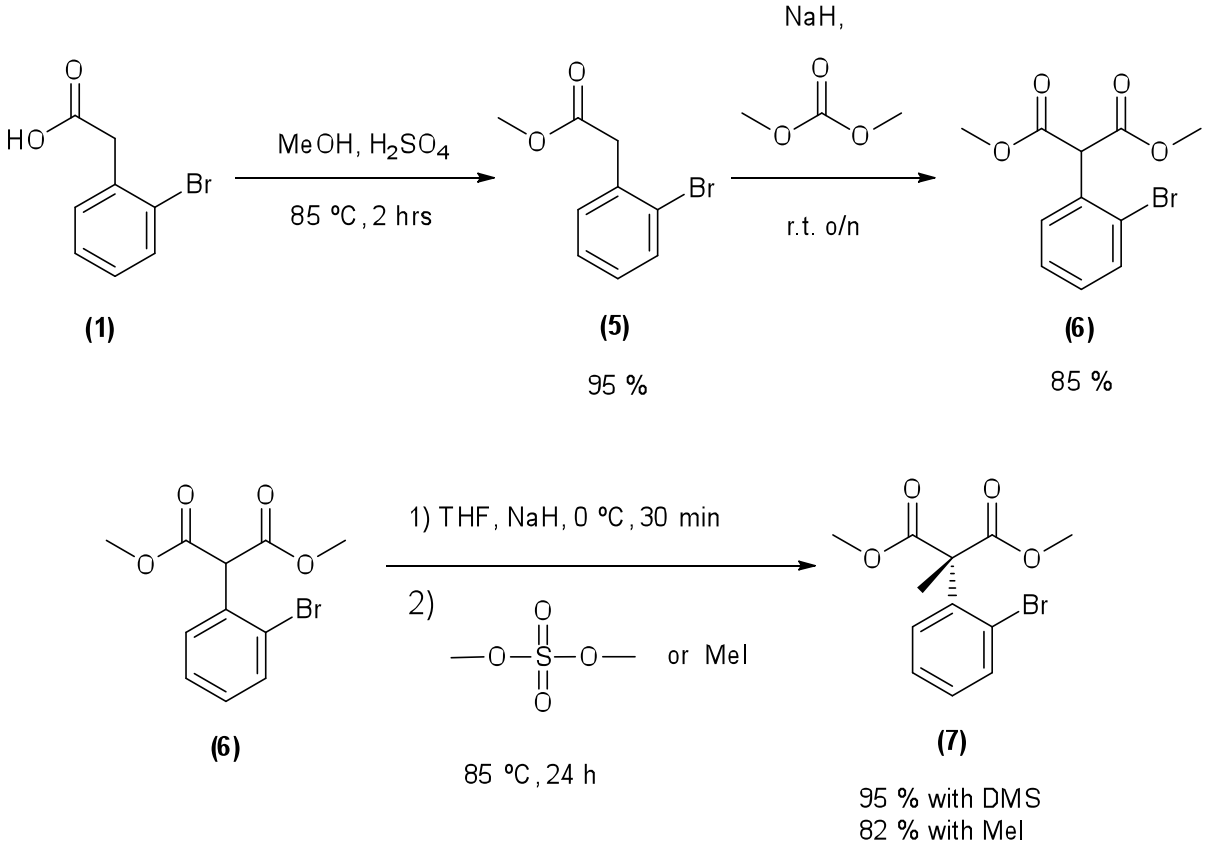
This methylation procedure was repeated twice more however the desired compound **4** (diethyl 2-(2-bromophenyl)-2-methylmalonate) was not obtained, in each case TLC of the reaction mixture showed unreacted starting material.



Scheme 23: Initial synthetic protocol for the synthesis of oxindole precursors

An improved synthetic protocol was established for these three steps and is shown in scheme 24. The first step entailed a Fischer esterification reaction between **1** and methanol. The reaction was catalyzed by H_2SO_4, heated to 85 ^oC and refluxed for two hours. The reaction worked exceptionally well and furnished the desired product **5** (methyl 2-(2-bromophenyl)acetate) in 95 % yield. Next a methoxycarbonylation reaction was carried out by deprotonation of **5** in dimethyl carbonate using NaH. The reaction was left stirring overnight at room temperature and compound **6** (dimethyl 2-(2-bromophenyl)malonate) was obtained in 85 % yield. Methylation of **6** at the α-carbon was accomplished by deprotonation of **6** in THF using NaH followed by the

addition of either iodomethane or dimethylsulfate. The reaction was heated to 85 ^{o}C and refluxed overnight. Compound **7** (dimethyl 2-(2-bromophenyl)-2-methylmalonate) was obtained in good yield, 82 and 95 %, when using iodomethane or dimethylsulfate respectively.



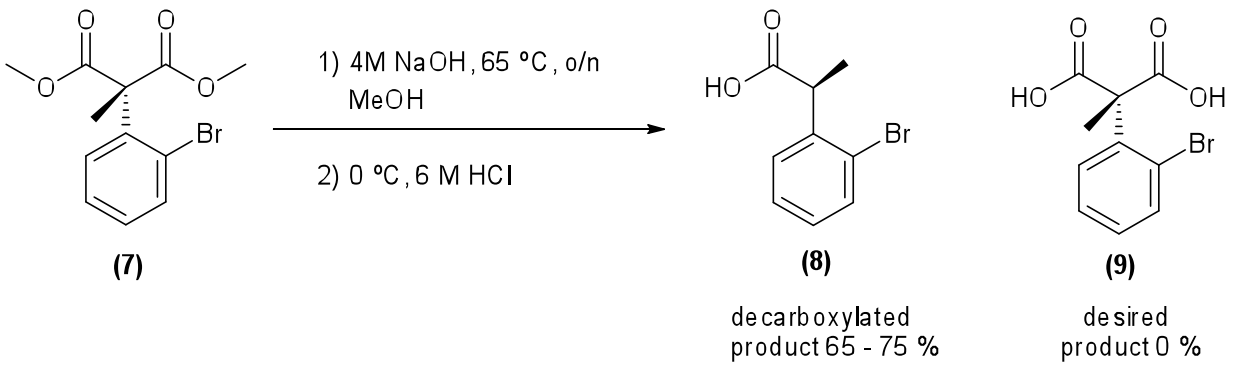
Scheme 24: An Improved Synthetic Protocol for the Synthesis of Oxindole Precursors

Thus there is a distinct increase in yield for the Fischer esterification reaction when using methanol as opposed to ethanol. This is likely due to the decreased steric bulk of a methyl group compared to an ethyl group thus making it a better nucleophile. Interestingly the methoxycarbonylation reaction shows a similar trend with a dramatic increase in yield when using dimethyl esters as opposed to diethyl esters. The most striking comparison is observed with the methylation reaction whereby alkylation at the α-position was never accomplished using

compound **3** as the starting material, however when compound **6** was used as the starting material the desired α-methylated product was obtained in high yield.

2.1.1 Decarboxylation of 2-(2-bromophenyl)-2-methylmalonic acid

Synthesis of 2-(2-bromophenyl)-2-methylmalonic has proven to be quite tricky due to the propensity of this compound to undergo rapid decarboxylation. Base catalyzed ester hydrolysis of dimethyl 2-(2-bromophenyl)-2-methylmalonate followed by subsequent acidification resulted in 65 % yield of racemic 2-(2-bromophenyl)propanoic acid **(8)** and 0 % of the desired 2-(2-bromophenyl)-2-methylmalonic acid **(9)** (scheme 25). The reaction was repeated twice more using 2.2 equivalents of 2 M NaOH followed by acidification with 2 M HCl resulting in 75 % and 67 % yield of racemic **8** respectively. In each case the desired compound **9** was not obtained.



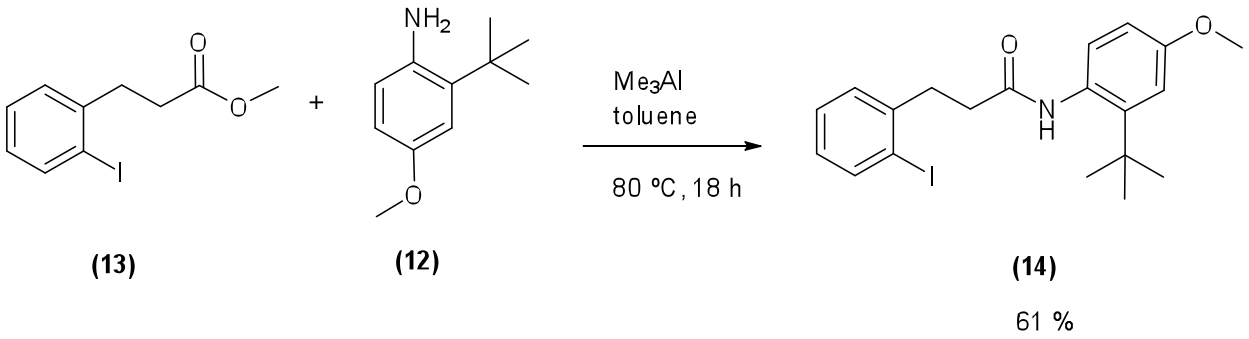
Scheme 25: Decarboxylation of 2-(2-bromophenyl)-2-methylmalonic acid

2.1.2 Alternate synthetic route towards N^1,N^2-dibenzyl-2-methyl-2-phenylmalonamide

2.1.2.1 N^1,N^2-dibenzyl-2-methyl-2-phenylmalonamide Synthesis using trimethyl aluminum

Since the production of **9** was not working via the base catalyzed ester hydrolysis route due to rapid decarboxylation of the desired product, an alternate approach towards the synthesis of **10** (N^1,N^2-dibenzyl-2-methyl-2-phenylmalonamide) was explored. In 2010 Taguchi *et al*. reported a reaction between **12** (2-*t*-butyl-4-methoxyaniline) and **13** (3-(2-iodophenyl)propanoate) to

produce **14** (*N*-(2-*t*-butyl-4-methoxyphenyl)-3-(2-iodophenyl)propanamide) using Me_3Al (scheme 26).[37]



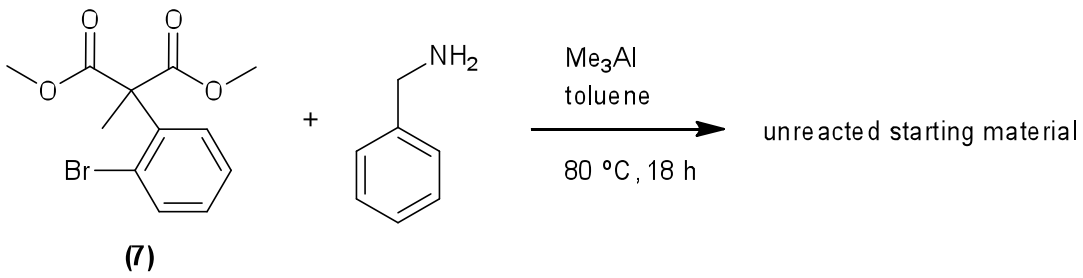
(13) **(12)** **(14)**

61 %

Scheme 26: Amide bond formation using Me_3Al

The reaction required an atmosphere of argon and entailed dissolving **13** in toluene followed by the addition of Me_3Al on ice. After stirring for 20 minutes at 0 ^oC **12** was added and the reaction was stirred at 80 ^oC for 18 h. After an aqueous work-up followed by purification via column chromatography the desired compound was obtained in 61 % yield.

Application of this method towards the synthesis of **10** seemed very appealing since compound **9** was not required as the starting material. Thus under an atmosphere of argon, benzylamine was dissolved in toluene followed by the addition of Me_3Al on ice (scheme 27). After stirring for 20 minutes at 0 ^oC compound **7** was added and the reaction was stirred at 80 ^oC for 18 h. The reaction was then checked by TLC and showed no disappearance of the starting material, therefore another half equivalent of Me_3Al was added to the reaction and the mixture was stirred overnight at 80 ^oC. Once again the reaction was checked by TLC and still there appeared to be no disappearance of starting material. After a quick mini work-up ^1H-NMR confirmed that there was only starting material in the reaction mixture.

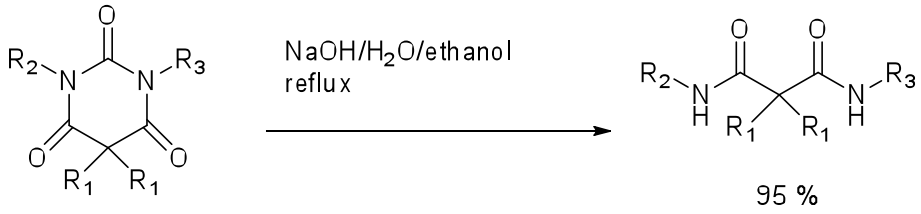


(7)

Scheme 27: Me_3Al approach to diamide bond formation

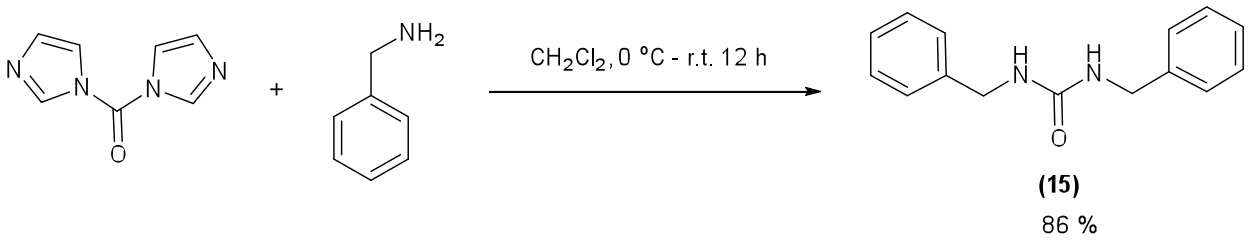
2.1.2.2 Decarbonylation of Barbituric acids

In 2000 Jursic reported a versatile and convenient procedure for the preparation of *N*,*N*'-2,2-tetrasubstituted malonamides by decarbonylation of tetrasubstituted barbituric acids (scheme 28).[44]



Scheme 28: decarbonylation of tetrasubstituted barbituric acids

Since the synthesis of **10** proved to be problematic, decarbonylation of tetrasubstituted barbituric acids appeared to be a reasonable method for obtaining this compound. The first step towards the synthesis of tetrasubstituted barbituric acids was to synthesize **15** (dibenzylurea) which was accomplished by reacting benzylamine with 1,1'-carbonyldiimidazole in DCM at room temperature for 12 hours. The reaction worked extremely well and compound **15** was obtained in 86 % yield (scheme 29).

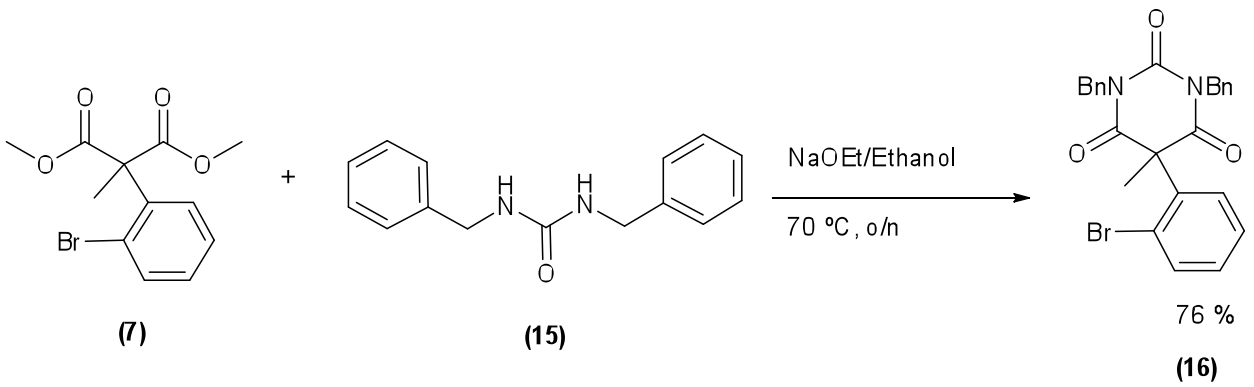


(15)

86 %

Scheme 29: Synthesis of dibenzylurea

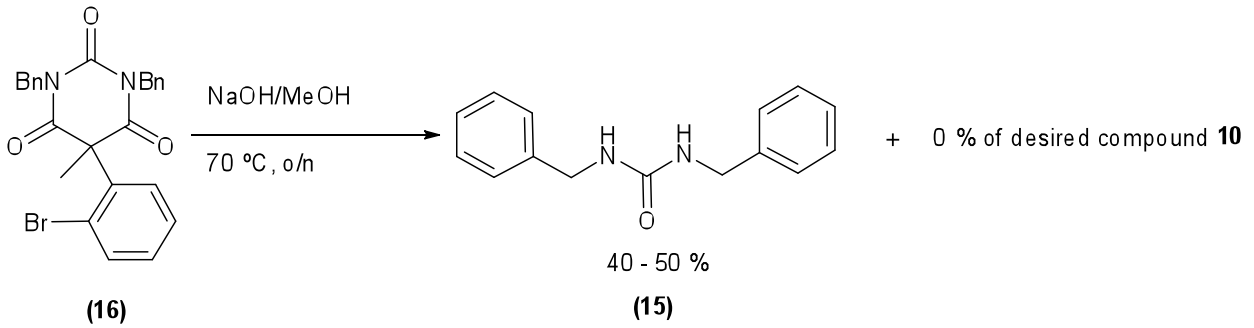
The next step was to synthesize the corresponding barbituric acids. The first attempt towards the synthesis of these compounds was based on a literature procedure reported by Bose *et al*. in which the authors reacted various carbodiimides with substituted malonic acids to obtain the desired barbiturates.[45] Thus compounds **7** and **15** were dissolved in a solution of NaOEt/ethanol and the reaction mixture was heated to 70 ^{o}C (scheme 30). After refluxing overnight the reaction was checked by TLC and showed complete disappearance of the starting material. Furthermore the appearance of a broad streak on the TLC plate became evident. After an acidic work-up, ^{1}H-NMR of the crude product looked encouraging however it was clear that the compound needed to be purified in order to determine if it was indeed the desired barbituric acid. The sample would always appear as a broad streak on the TLC plate regardless of the various different solvents and solvent conditions used in attempt to see distinct spots on the TLC plate. Thus column chromatography was carried out using 60 % EtOAc: 40 % Hexanes, and the broad streak was isolated in 76 % yield, however ^{1}H-NMR of this sample still showed that the compound was not pure.



(7) (15) (16)

Scheme 30: Synthesis of a tetrasubstituted barbituric acid

Nevertheless a reaction was set up to decarbonylate the putative barbituric acid based on the procedure reported by Jursic *et al*.[44] in which the crude compound **16** was dissolved in MeOH followed by the addition of 0.2 M NaOH, the reaction was heated to 70 ^{o}C and left refluxing overnight (scheme 31). The reaction was checked by TLC and showed that the broad streak was still present along with another spot that had an R_f corresponding to that of dibenzyl urea. An aqueous work-up followed by recrystallization of the organic phase resulted in 40 % recovery of dibenzylurea. Decarbonylation of the putative barbituric acid was repeated twice more resulting in 50 % and 40 % recovery of dibenzylurea respectively (scheme 31).

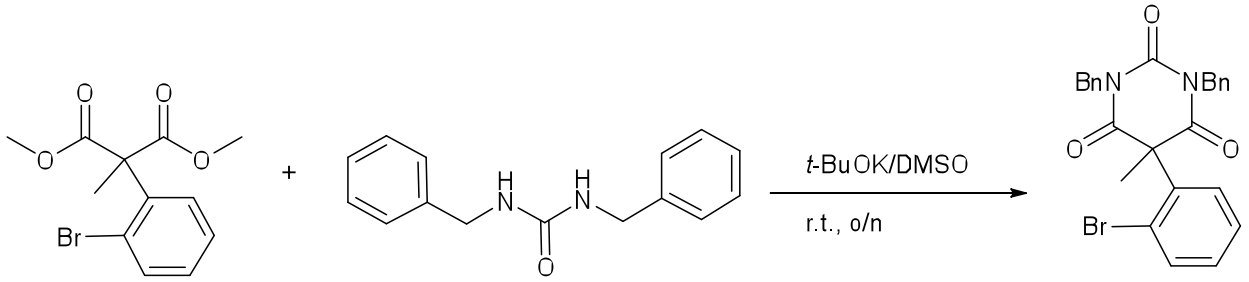


(16) (15)

Scheme 31: Decarbonylation of the putative Barbituric acid

Barbituric acid synthesis was also attempted using *t*-BuOK as a base instead of NaOEt, thus to a solution of *t*-BuOK in DMSO was added a solution of dibenzyl urea in DMSO at 0 ^{o}C. After 10

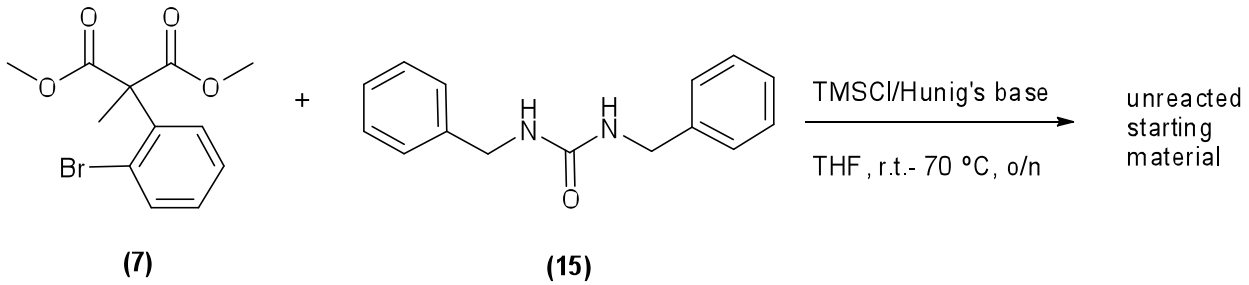
minutes of stirring, a solution of compound **7** in DMSO was added and the reaction was left stirring at room temperature overnight (scheme 32). The reaction was checked by TLC and again the appearance of a broad streak was evident. Once again the crude product was subjected to column chromatography however in this case the crude compound either decomposed or was strongly retained on the column because only 16 % of the crude product was recovered.



(7) **(15)** **(16)**

Scheme 32: Barbituric acid synthesis using *t*-BuOK and DMSO

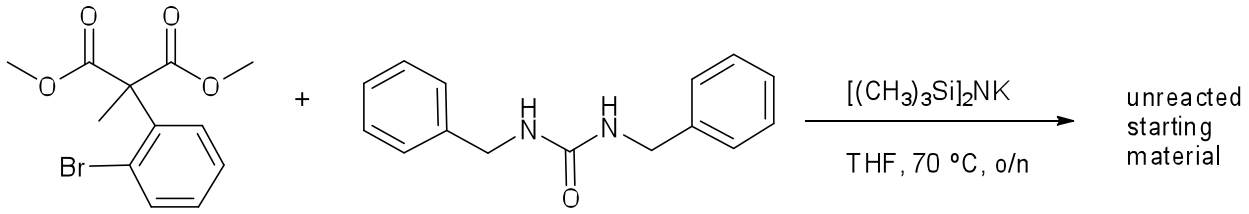
Another attempt towards the synthesis of barbituric acids was explored using TMSCl (scheme 33). In this procedure dibenzylurea, TMSCl and Hunig's base were stirred in a concentrated solution of THF for thirty minutes. Compound **7** was then added to the reaction mixture and the reaction was stirred at room temperature for two hours. After seeing no disappearance of starting material by TLC the reaction was heated to 70 ^{o}C and left refluxing overnight. The reaction was checked by TLC and again showed no disappearance of starting material.



(7) **(15)**

Scheme 33: Barbituric acid synthesis using TMSCl and Hunig's base

A similar reaction was set up using $[(CH_3)_3Si]_2NK$ (potassium bis(trimethylsilyl)amide) in which dibenzylurea and $[(CH_3)_3Si]_2NK$ were stirred in a concentrated solution of THF for thirty minutes. Compound **7** was then added to the reaction mixture and the reaction was stirred at room temperature for two hours (scheme 34). The reaction was monitored by TLC and showed no disappearance of starting material after two hours, therefore the reaction was heated to 70 ^oC and left refluxing overnight. Once again only starting material was visible after the reaction was checked by TLC.



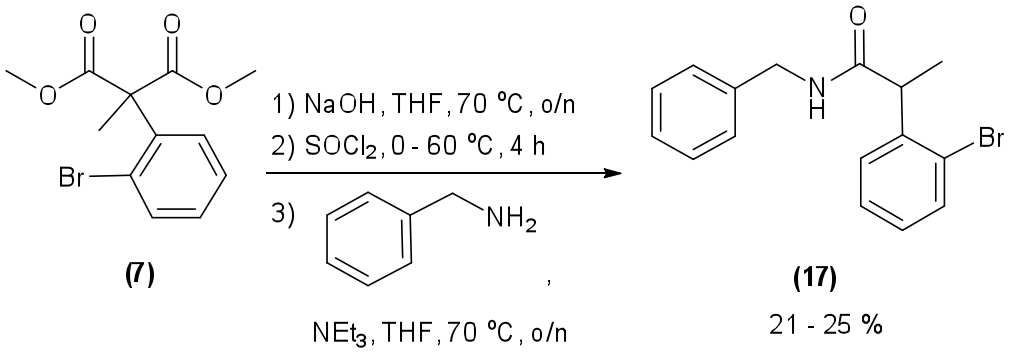
(7) **(15)**

Scheme 34: Barbituric acid synthesis using potassium bis(trimethylsilyl)amide

2.1.2.3 Base catalyzed ester hydrolysis followed by immediate activation with $SOCl_2$

Having had no success in synthesizing compound **10** using the Me_3Al protocol or through decarbonylation of barbituric acids, base catalyzed ester hydrolysis was reinvestigated. This time compound **7** was dissolved in THF upon addition of three equivalents of NaOH. The reaction was heated to 70 ^oC and left refluxing overnight in THF. The reaction mixture was evaporated to dryness (without acidification) cooled to 0 ^oC and transferred to ice cold $SOCl_2$ in THF. The reaction was stirred for four hours at 60 ^oC, evaporated to dryness, redissolved in THF and evaporated to dryness once again. This process of redissolving the crude product in THF and evaporating to dryness was repeated four more times to get rid of any excess $SOCl_2$. The crude product was redissolved in THF and treated with benzylamine and Et_3N. The reaction mixture was heated to 70 ^oC and left refluxing overnight (scheme 35). TLC of the crude reaction mixture

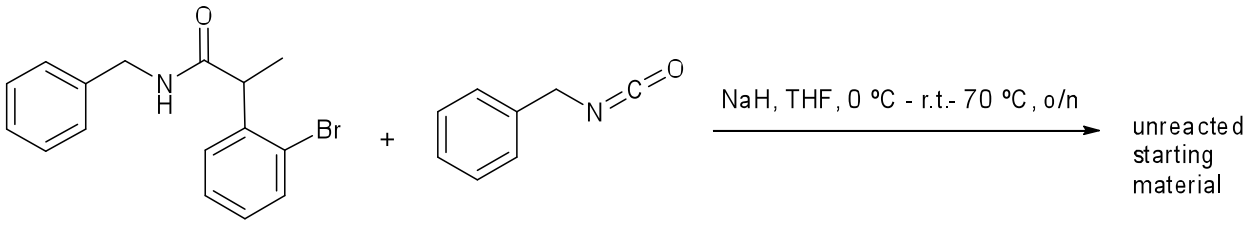
showed the appearance of a new spot which was isolated in 21 % yield and found to be the mono-substituted benzylamide. This reaction was repeated once more with freshly distilled $SOCl_2$ and once again the mono-substitued product was obtained in low 25 % yield. So even under these reaction conditions decarboxylation of compound **9** was still occurring.



Scheme 35: Base catalyzed ester hydrolysis followed by immediate activation with $SOCl_2$

2.1.2.3.1 *N*^{1},*N*^{2}-dibenzyl-2-methyl-2-phenylmalonamide synthesis using benzyl isocyanate

With compound **17** (*N*-benzyl-2-(2-bromophenyl)propanamide) in hand, a reaction using benzyl isocyanate was envisioned which would afford **10**. Thus a solution of **17** in THF was added to a suspension of NaH in THF and the reaction was heated to 70 ^oC (scheme 36). The reaction was refluxed for one hour and cooled to room temperature, followed by the addition of benzyl isocyanate on ice. The reaction was stirred at room temperature and monitored by TLC. After two hours of stirring at room temperature, TLC of the reaction mixture showed no disappearance of starting material and no appearance of a new spot. Therefore the reaction was heated to 70 ^oC and left refluxing overnight. Once again TLC of the reaction mixture showed that no reaction had occurred.



(17)

Scheme 36: Attempted synthesis of compound 10 using benzyl isocyanate

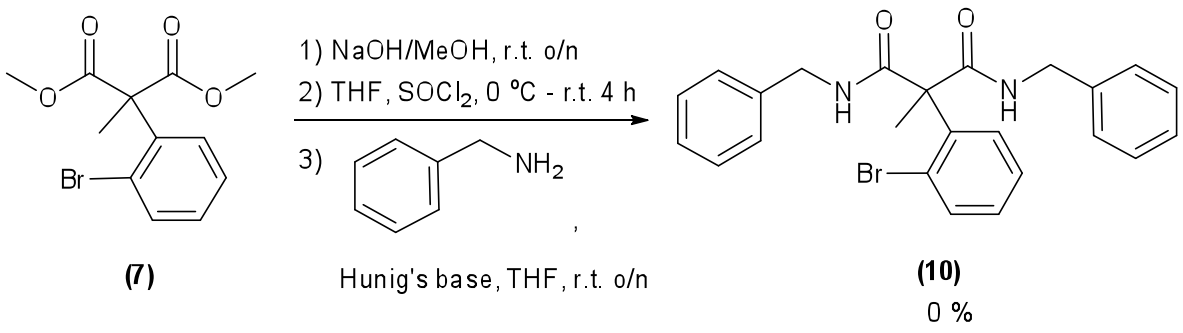
2.1.2.3.2 Temperature experiments on base catalyzed ester hydrolysis

A small scale heating experiment was performed on compound **7**. In this experiment compound **7** was dissolved in MeOH and treated with 3 eq of 4 M NaOH. The reaction was left stirring overnight at room temperature. After the reaction was evaporated to dryness ^{1}H-NMR showed complete disappearance of the ester signals of the starting material and peaks corresponding to a 3:1 ratio of the disodium salt to the decarboxylated compound. This experiment was taken one step further whereby this sample was redissolved in methanol, heated to 70 ^{o}C and left stirring overnight at this temperature. Interestingly ^{1}H-NMR of this sample revealed that the only product in the reaction after heating overnight at 70 ^{o}C was in fact the decarboxylated compound. Therefore heat was found to be the culprit for decarboxylation.

2.1.2.4 Base catalyzed ester hydrolysis re-revisited

Since the disodium salt of compound **7** could be obtained by treatment with NaOH/MeOH (1:3) and stirring overnight at room temperature, synthesis of compound **10** could potentially be achieved by treatment of the disodium salt with $SOCl_2$ followed by subsequent addition of benzylamine and Hunig's base. Thus compound **7** was dissolved in MeOH and treated with NaOH and the reaction was stirred overnight at room temperature (Scheme 37). The reaction mixture was checked by TLC and showed complete disappearance of the starting material. At this point the reaction was evaporated to dryness then re-dissolved in toluene and evaporated to

dryness once again. This process of re-dissolving in toluene and evaporating to dryness was repeated four more times to get rid of any remaining water. After keeping the product overnight under vacuum the disodium salt was dissolved in cold THF and transferred to ice cold $SOCl_2$. The reaction was stirred for four hours at room temperature then evaporated to dryness, re-dissolved in THF and evaporated to dryness once again. This process of re-dissolving in THF and evaporating to dryness was repeated four more times to get rid of any remaining $SOCl_2$. Next the crude product was dissolved in THF and treated with benzylamine and Hunig's base. The reaction was left stirring overnight at room temperature. TLC of the reaction mixture did not show the appearance of a new spot but rather unreacted benzylamine indicating that the amide bond forming reaction needs heat.

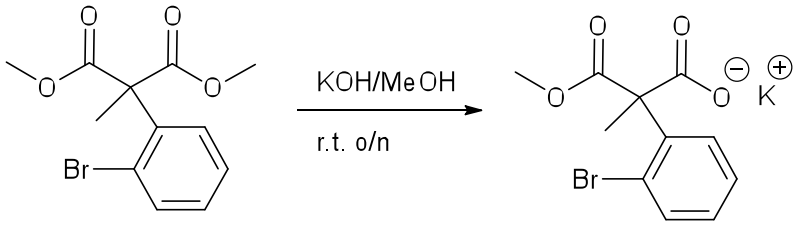


Scheme 37: Amide bond formation in the absence of heat

2.1.2.5 N^1,N^2-dibenzyl-2-methyl-2-phenylmalonamide synthesis using HBTU

It became evident that mild conditions were necessary for the synthesis of compound **10** and HBTU (2-(1H-benzotriazole-1-yl-1,1,3,3-tetramethyl uronium hexafluorophosphate) appeared to be a good candidate for promoting mild amide couplings. Having the disodium salt in hand a coupling reaction with benzylamine using HBTU was envisioned however even at low reaction concentrations, < 0.001 M, the disodium salt would not dissolve in DMF.

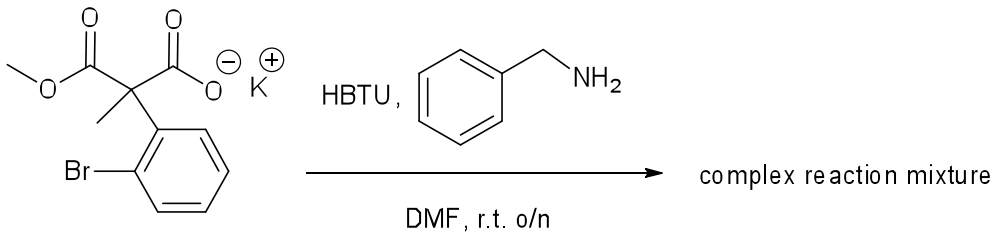
In order to increase the solubility of the starting material in DMF, a base catalyzed ester hydrolysis was set up using KOH instead of NaOH. Interestingly only one side of the molecule reacted resulting in a mono-potassium salt mono-ester compound (scheme 38).



(7) 85 % **(18)**

Scheme 38: Base-catalyzed ester hydrolysis using KOH

Nevertheless this compound was subjected to a coupling reaction using HBTU as the coupling agent (scheme 39). Thus the starting material was dissolved in DMF followed by the addition of HBTU and benzylamine. The reaction was stirred at room temperature overnight. TLC of the crude reaction mixture showed the appearance of several new spots however any attempt at purifying this compound via column chromatography was unsuccessful.



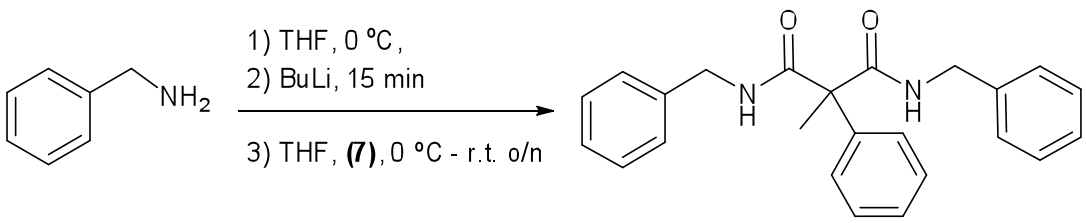
(18)

Scheme 39: HBTU coupling of mono-acid mono-ester with benzylamine

2.1.2.6 N^1,N^2-dibenzyl-2-methyl-2-phenylmalonamide synthesis using BuLi

The last procedure attempted for the synthesis of **10** entailed using BuLi to deprotonate benzylamine, thus creating an extremely strong nucleophile which should theoretically undergo di-substitution with compound **7**. In this method benzylamine was dissolved in dry THF and

cooled to 0 ^{o}C followed by the slow dropwise addition of BuLi under a stream of argon. The reaction was stirred for fifteen minutes at 0 ^{o}C before the addition of a solution of compound **7** in THF at 0 ^{o}C. The reaction was stirred overnight at room temperature. TLC of the crude reaction mixture at 40 % EtOAc:Hexanes showed many spots however it looked encouraging due to the appearance of a spot with a strikingly similar R_f to the six and seven membered ring precursor di-substituted benzylmalonamides. This spot was easily isolated by column chromatography eluting at 40 % EtOAc:Hexanes, however ^{1}H-NMR of this compound showed too much signal in the methylene region of the spectrum. Perhaps what happened was lithium exchange with bromide resulting in the compound shown in scheme 40. The reaction was repeated with the addition of BuLi at -78 ^{o}C instead of 0 ^{o}C and this also resulted in the isolation of a compound with peaks corresponding to **19** by ^{1}H-NMR.

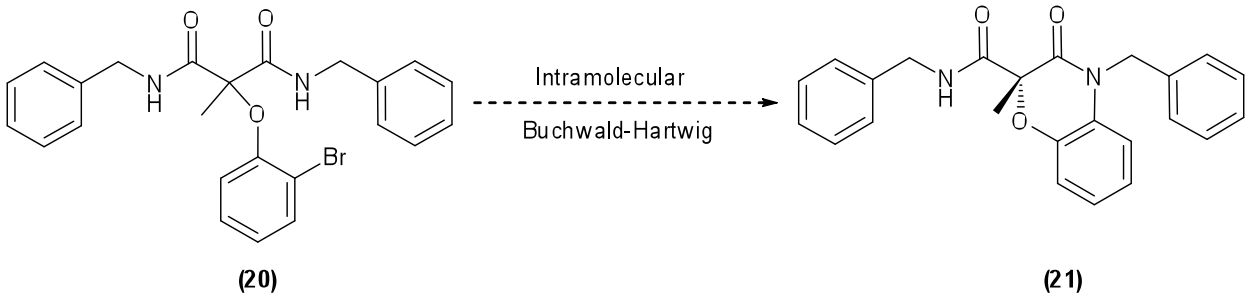


(19)

Scheme 40: Amide bond formation using Butyl-Lithium

2.2 Synthesis of six membered ring Benzomorpholinone Heterocycles

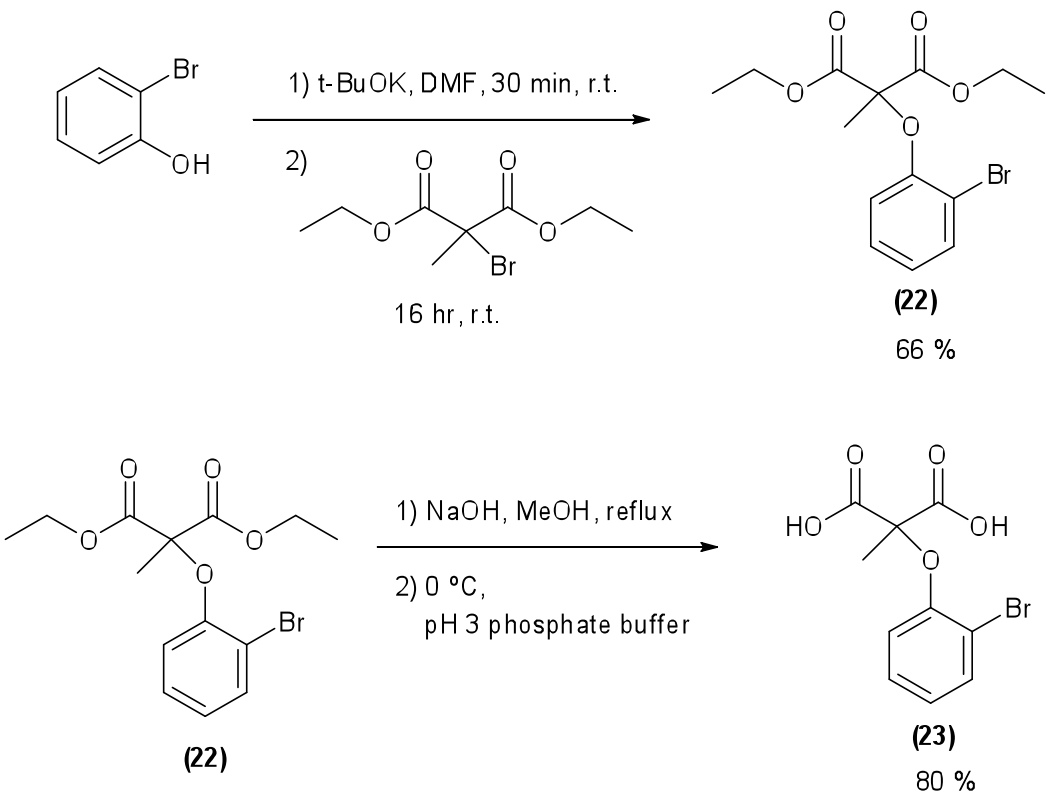
In order to further investigate the work carried out by Porosa in 2009[31,32] to include six membered rings with more than one heteroatom in the ring an intramolecular Buchwald-Hartwig reaction was envisioned which would furnish six-membered ring benzomorpholinone heterocycles (Figure 11).



(20) (21)

Figure 11: Desymmetrization of malonamides to form benzomorpholinone heterocycles

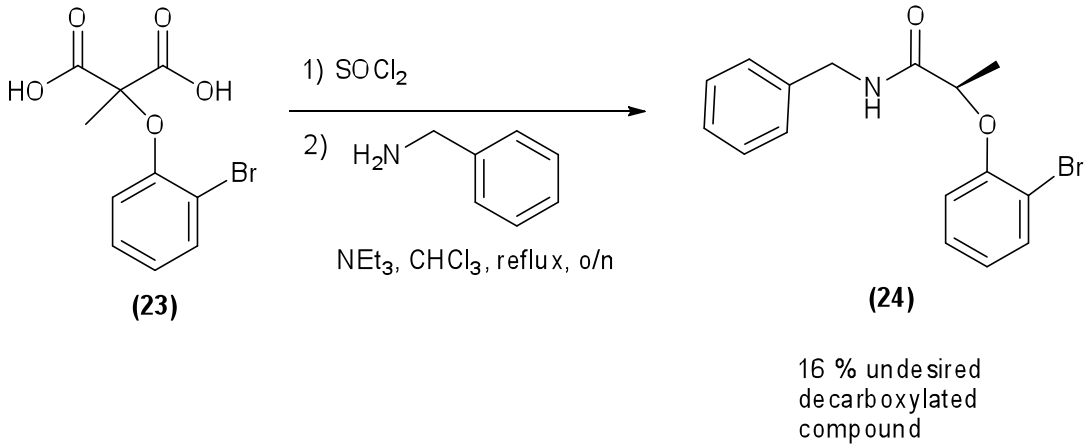
The synthesis of six membered ring benzomorpholinone heterocycles began with a substitution reaction between 2-bromophenol and diethyl 2-bromo-2-methylmalonate (scheme 41). The reaction worked reasonably well and the desired product **22** (diethyl 2-(2-bromophenoxy)-2-methylmalonate) was obtained in 66 % yield. The next step entailed base catalyzed ester hydrolysis of **22** followed by subsequent acidification with a pH 3 phosphate buffer which furnished compound **23** (2-(2-bromophenoxy)-2-methylmalonic acid) in 80 % yield (scheme 41).



Scheme 41: Towards the Synthesis of Benzomorpholinone Heterocycles

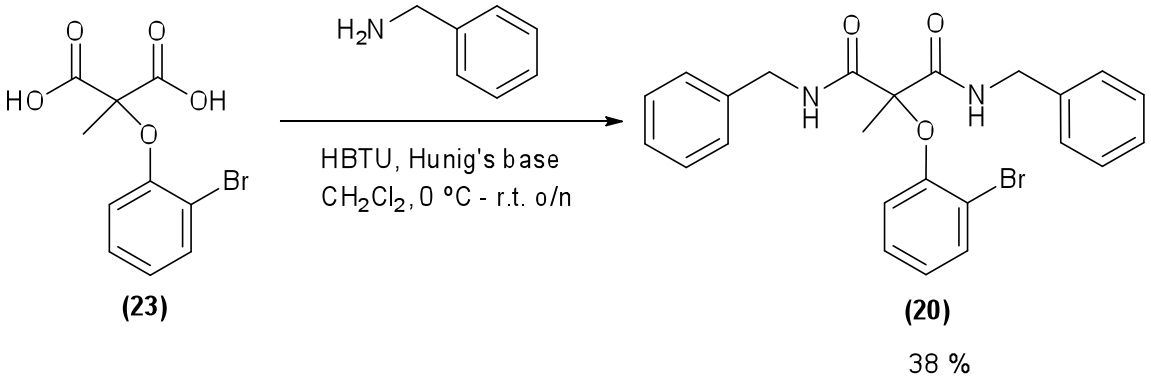
Initially the base catalyzed ester hydrolysis of **22** was followed by acidification with 6 M HCl which produced the corresponding di-acid **23** in 50 % yield. Thus the rationale for switching from 6 M HCl to a pH 3 phosphate buffer was that the buffer would be a less harsh way to protonate the di-sodium salt and ultimately lead to a decrease in decarboxylation.

Coupling of **23** with benzylamine to form **20** (N^1,N^3-dibenzyl-2-(2-bromophenoxy)-2-methylmalonamide) was originally attempted by activation of the di-carboxcylic acid with $SOCl_2$ followed by the addition of benzylamine but this route yielded only 16 % of compound **24** (*N*-benzyl-2-(2-bromophenoxy)propanamide) the undesired decarboxylated compound (scheme 42).



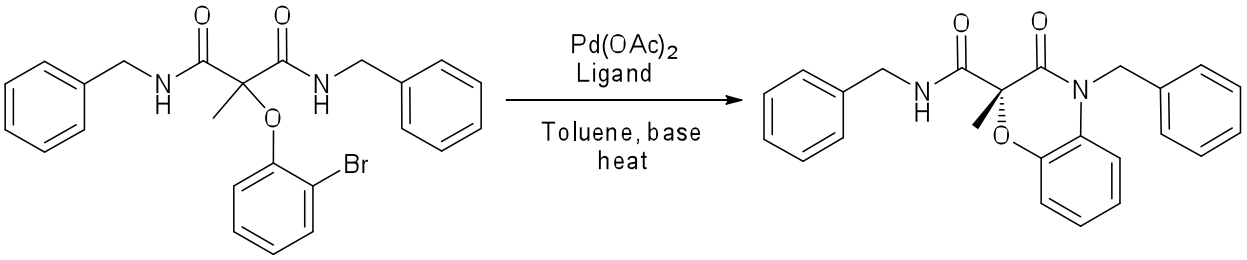
Scheme 42: Activation of di-acid using $SOCl_2$

Activation of **23** with HBTU proved superior to $SOCl_2$ and the desired diamide compound **20** was obtained in 38 % yield (scheme 43). One of the benefits of using HBTU over $SOCl_2$ is the ability to run reactions at room temperature, this is important because heat is a factor that increases the rate of decarboxylation.



Scheme 43: Activation of di-acid using HBTU

With the desired dibenzylamide in hand a series of cross coupling reactions were carried out to find optimal cyclization conditions (Table 1).



(20) **(21)**

Trial	Ligand	Base	Temp (°C)	Time (h)	Conversion* (%)	Isolated yield (%)	*ee* (%)
1	(+/-) BINAP	K_2CO_3	100	48	95	50	0
2	(*R*)-$Cy_2MOP{\cdot}BH_3$	K_2CO_3	100	48	25	nd	nd
3	(*R*)-Cy_2MOP	K_2CO_3	100	48	35	nd	nd
4	(*R*)-MOP	K_2CO_3	100	48	< 10	nd	nd
5	(*R*)-BINAP	K_2CO_3	100	48	100	88	20
6	(*R*)-Cy_2MOP	Cs_2CO_3	100	48	100	90	12
7	(*R*)-BINAP	Cs_2CO_3	100	48	100	99	12
8	(*R*)-MOP	Cs_2CO_3	100	48	100	98	3
9	(*R*)-BINAP	K_2CO_3	60	96	0	0	nd

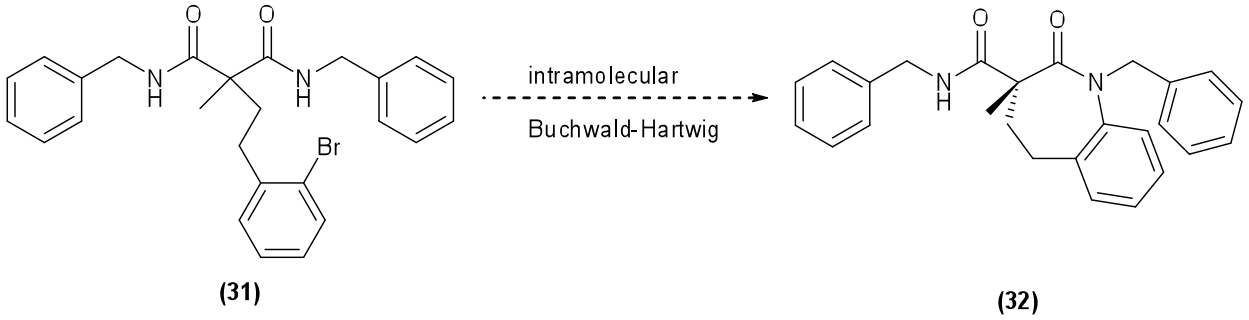
Table 1: Desymmetrization of di-nitrogen malonamides via an intramolecular Buchwald-Hartwig reaction to produce benzomorpholinone heterocycles (* ^{1}H-NMR Conversion determined from the disappearance of CH_2 signals in compound 20)

Initially compound **20** was cyclized using racemic BINAP as the ligand (Table 1, Trial 1). The reaction worked well showing 95 % conversion by ^{1}H-NMR however the cyclized product was only isolated in 50 % yield. The reason for the low isolated yield of the cyclized product is because the crude product was purified by preparative plate TLC. Although this seemed to be an appropriate method for purification, since this reaction was done on a small scale (0.05mmol, 25

mg), it proved to be inferior to purification via column chromatography. Next a series of reactions were set up in order to investigate the enantioselectivity of the desymmetrization reaction using chiral, enantiopure phosphine ligands. Application of (*R*)-Cy_2MOP·BH_3, (*R*)-Cy_2MOP and (*R*)-MOP using K_2CO_3 as a base all demonstrated low conversion , < 10 – 35 %, to the desired cyclized product by ^{1}H-NMR (Table 1, Trials 2,3,4). Cyclization of compound **20** using (*R*)-BINAP and K_2CO_3 resulted in 100 % conversion to cyclized product **21**. This compound was isolated in good yield, 88 %, however the enantioselectivity was low, 20 % *ee*, (Table 1, Trial 5). Interestingly application of (*R*)-Cy_2MOP, (*R*)-BINAP and (*R*)-MOP using Cs_2CO_3 as a base instead of K_2CO_3 resulted in 100 % conversion of compound **20** to compound **21** (Table 1, Trials 6,7,8). The crude product of these reactions was isolated in excellent yield, 90 – 99 %, however once again the enantioselectivity of the product was quite low, 3 – 12 % *ee*. It was thought that perhaps the high temperature of the cyclization reaction could be detrimental to the enantioselevtivity of the product thus a cross-coupling reaction was set-up using (*R*)-BINAP and K_2CO_3 at 60 ^{o}C instead of 100 ^{o}C (Table 1, Trial 9). After two days the reaction was monitored by ^{1}H-NMR and showed no conversion of **20** to compound **21**. Another catalyst loading of palladium and (*R*)-BINAP was added to the reaction mixture, since the catalyst tends to decompose after 2 days, and the reaction was left stirring for two more days. Even after four days however this reaction showed no conversion to compound **21** by ^{1}H-NMR indicating that the high temperature is key for this cyclization to occur.

2.3 Synthesis of Seven Membered Ring Benzodiazepinone Heterocycles

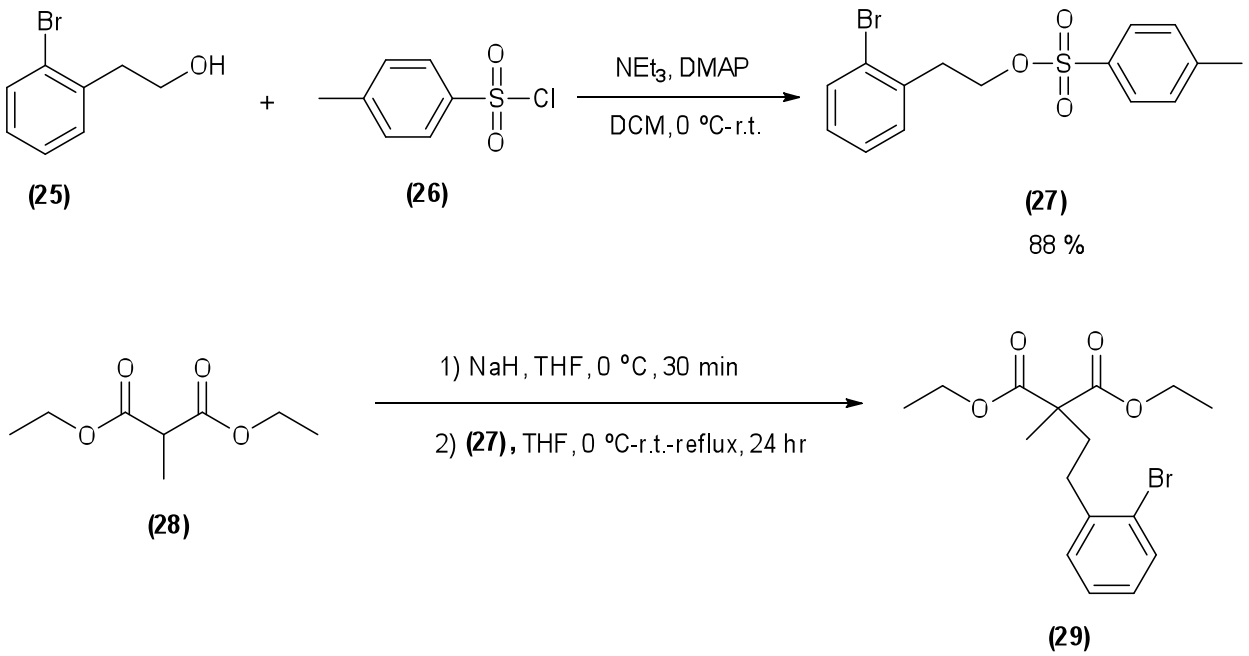
In order to extend the work carried out by Porosa in 2009[31,32] to include larger ring sizes an intramolecular Buchwald-Hartwig reaction was envisioned which would furnish seven-membered ring benzodiazepinone heterocycles (Figure 12).



(31) **(32)**

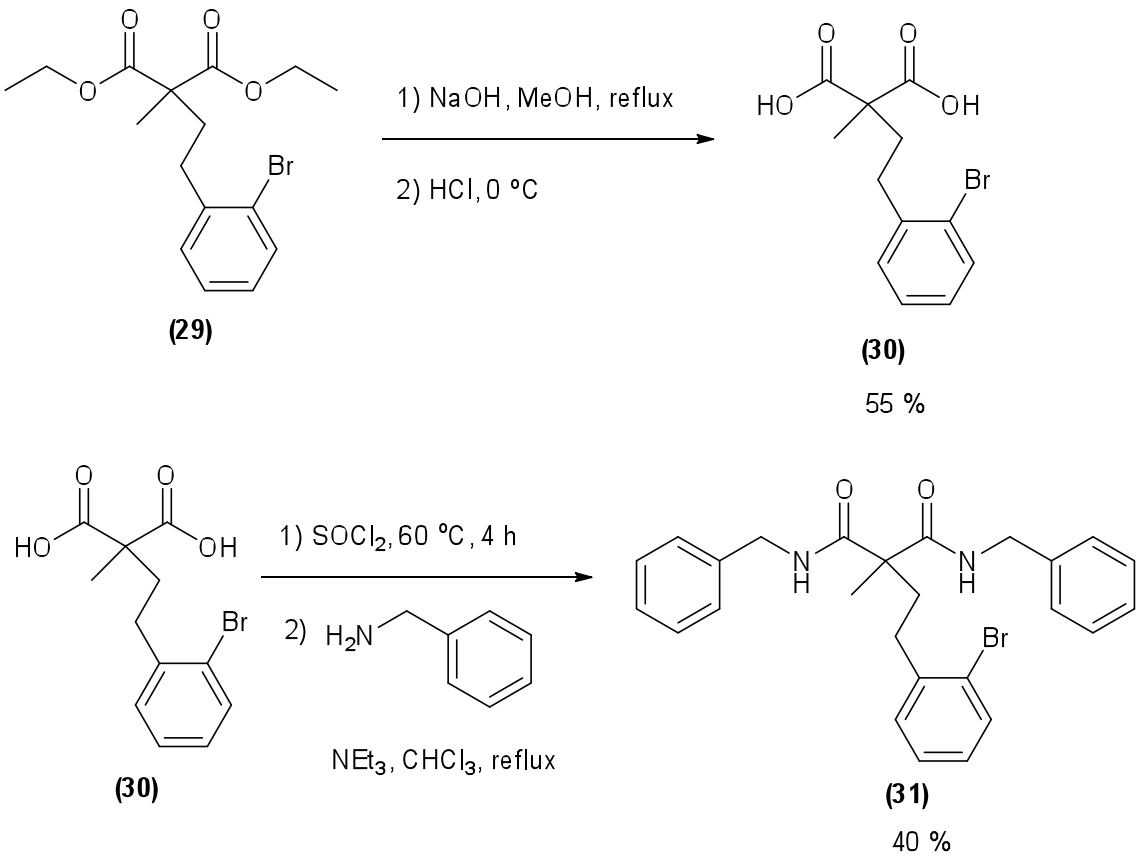
Figure 12: Desymmetrization of malonamides to form benzodiazepinone heterocycles

The first step towards the synthesis of benzodiazepinone heterocycles was a substitution reaction between **25** (2-bromophenethyl alcohol) and **26** (tosyl chloride) using triethylamine and DMAP which furnished the desired tosylate ester in 88 % yield (scheme 44). Next the tosylate ester was reacted with **28** to produce compound **29** (diethyl-2-(2-bromophenethyl)-2-methylmalonate) in 50 % yield (scheme 44).



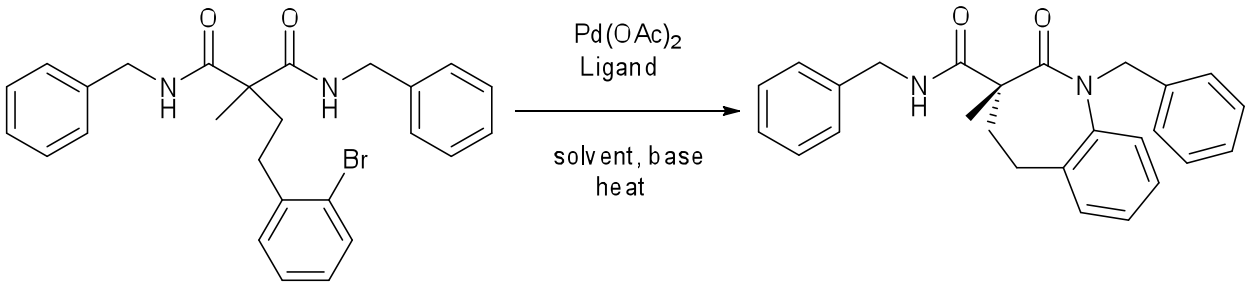
Scheme 44: Synthesis of benzodiazapineone precursors

The diethyl ester was then hydrolyzed using NaOH and acidified with HCl to produce **30** (2-(2-bromophenethyl)-2-methylmalonic acid) in 55 % yield (scheme 45). Activation of the dicarboxcylic acid with $SOCl_2$ and subsequent treatment with benzylamine provided the desired dibenzylmalonamide **31** in 40 % yield (scheme 45).



Scheme 45: Towards the Synthesis of benzodiazepinone heterocycles

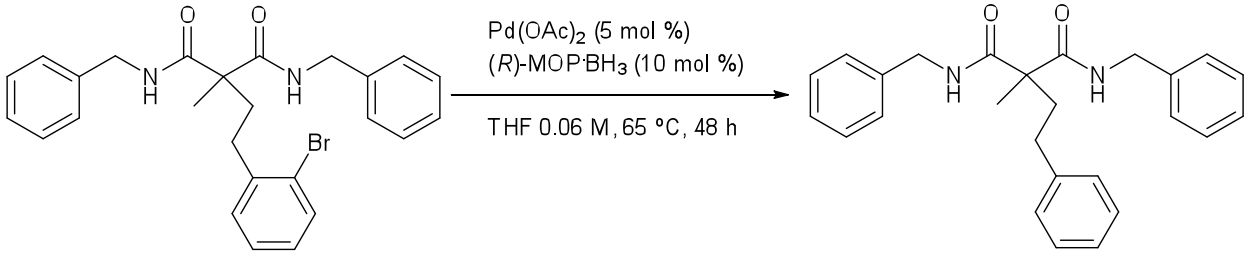
With the desired dibenzylmalonamide in hand a series of cross coupling reactions were carried out to find optimal cyclization conditions (Table 2). Initially the cyclization of **31** was attempted with racemic BINAP and (*R*)-MOP using K_3PO_4 as a base, in THF at 65 ^oC for twenty-four hours, however neither of these reactions showed any conversion to compound **31** by ^1H-NMR (Table 2, Trials 1,2). Cyclization of **31** was also attempted with (*R*)-MOP·BH_3 and K_3PO_4 in *t*-BuOH at 65 ^oC, nonetheless this reaction still showed no conversion to compound **32** by ^1H-NMR (Table 2, Trial 3). Interestingly when the cyclization of compound **31** was attempted with (*R*)-MOP·BH_3 using Cs_2CO_3, in THF at 65 ^oC for forty-eight hours, ^1H-NMR of the crude reaction showed a 50:50 mixture of the starting material and compound **33**, the debrominated compound (Table 2, Trial 4, scheme 46).



(31) (32)

Trial	Ligand	Solvent	Base	Temp (°C)	Time (h)	Conversion* (%)	Isolated yield (%)
1	(+/-) BINAP	THF	K_3PO_4	65	24	0	0
2	(*R*)-MOP	THF	K_3PO_4	65	24	0	0
3	(*R*)-MOP·BH_3	*t*-BuOH	K_3PO_4	65	24	0	0
4	(*R*)-MOP·BH_3	THF	Cs_2CO_3	65	48	0	0
5	(*R*)-MOP·BH_3	Toluene	Cs_2CO_3	100	48	75	nd
6	(*R*)-Cy_2MOP	Toluene	Cs_2CO_3	100	48	100	50

Table 2: Desymmetrization of di-nitrogen malonamides via an intramolecular Buchwald-Hartwig reaction to produce benzodiazepinone heterocycles (* ^{1}H-NMR Conversion determined from the disappearance of CH_2 signals in compound 31)



(31) (33)

50:50 mixture by ^{1}H-NMR of debrominated **33** to unreacted starting material **31**

Scheme 46: Debromination under cross-coupling conditions

Having had no success in the synthesis of benzodiazepinone heterocycles thus far, it was believed that perhaps higher temperatures were required for this cyclization to happen. Indeed when compound **31** was cyclized using (*R*)-MOP·BH_3 and Cs_2CO_3 in Toluene at 100 ^oC for forty-eight hours, ^{1}H-NMR showed a 75 % conversion of compound **31** to **32** (Table 2, Trial 5). Unfortunately the cyclized product could not be separated from the starting material because they appear to have a very similar R_f by TLC. Application of Cy_2MOP for the cyclization of compound **31** resulted in 100 % conversion to the desired benzodiazapineone heterocycle (Table 2, Trial 6). The crude product was isolated in 50 % yield because it was purified by preparative plate TLC which has proven not to be the optimal method of purification for these compounds. Nevertheless the seven-membered ring heterocycle has been synthesized and the isolated compound is being analyzed by chiral column HPLC to determine the enantiomeric excess.

2.4 Development of an enantio- and diastereoselective Buchwald-Hartwig reaction

To further expand the work carried out by Porosa in 2009[31,32] and develop an enantio- and diastereoselective Buchwald-Hartwig reaction a desymmetrization reaction was envisioned which would generate a chiral centre as well as a chiral axis due to locked rotation around the N-aryl bond (Figure 13).

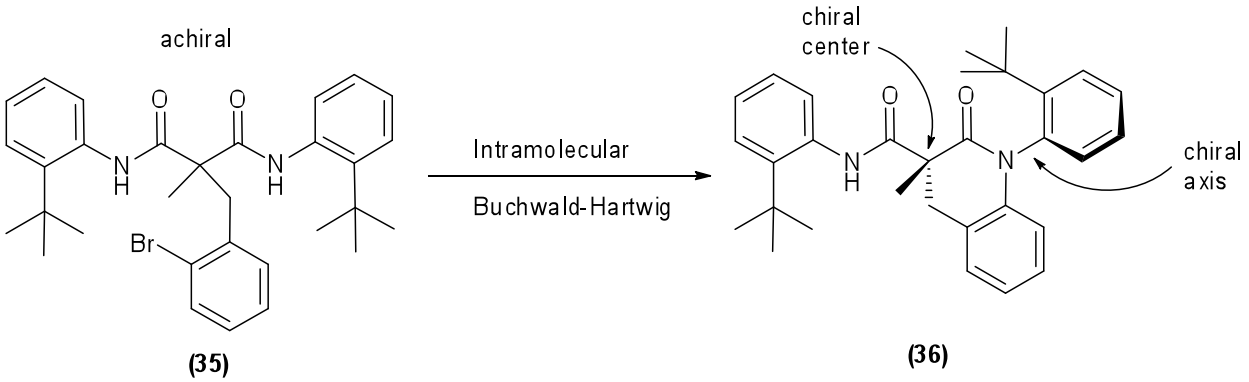
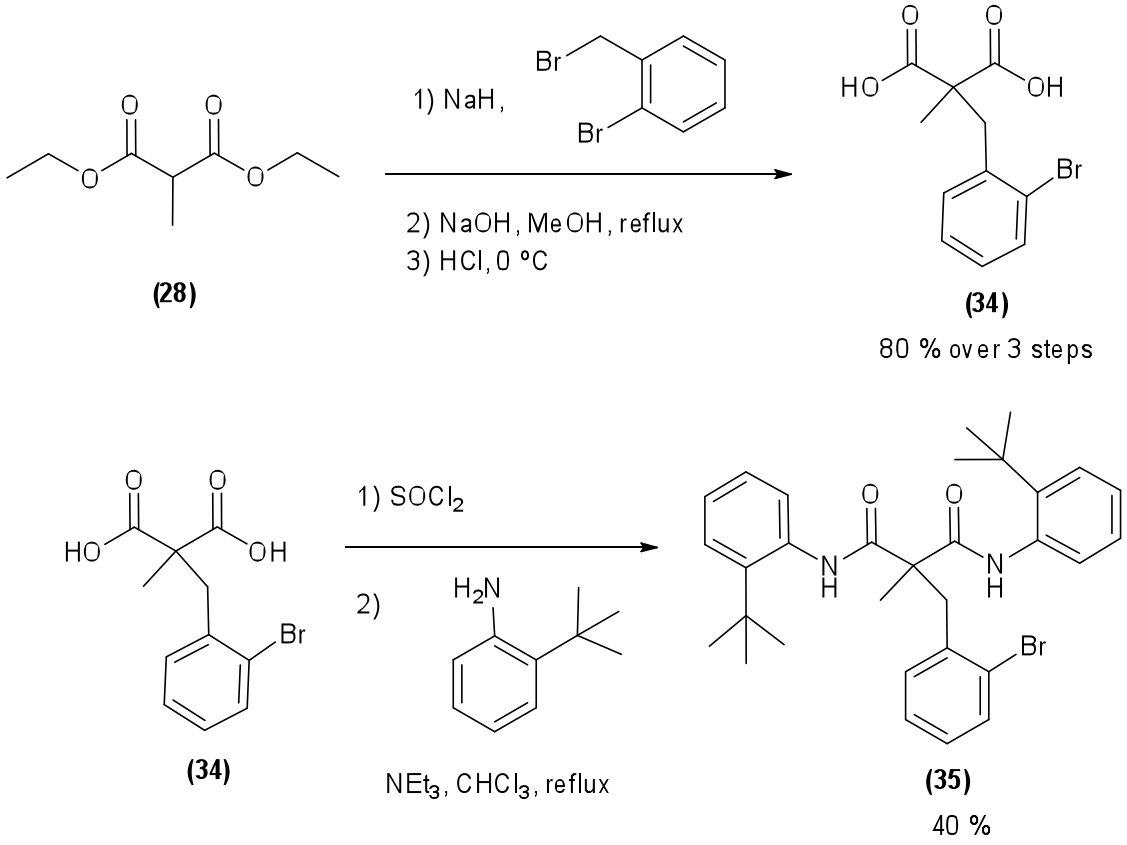


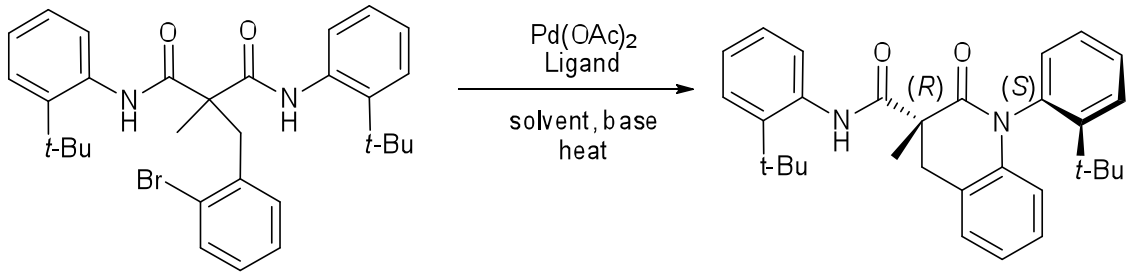
Figure 13: Development of an enantio- and diastereoselective Buchwald-Hartwig reaction

The synthesis of *t*-butyl substituted quinolinone began with a substitution reaction between compound **28** and 2-bromobenzylbromide followed by base catalyzed ester hydrolysis using NaOH and subsequent acidification with concentrated HCl. Activation of the dicarboxcylic acid was accomplished with $SOCl_2$ followed by the addition of *t*-butyl aniline to obtain the desired diamide compound (scheme 47).



Scheme 47: Towards the synthesis of *t*-butyl quinolinone

The steric bulk created by the *ortho t*-butyl group made the substitution reaction between the acyl chloride and *t*-butylaniline difficult resulting in unreacted starting material as well as the mono-substituted decarboxylated compound. Nevertheless with the di-*t*-butylphenyl amide in hand a series of cross coupling reactions were carried out to find optimal cyclization conditions (Table 3).



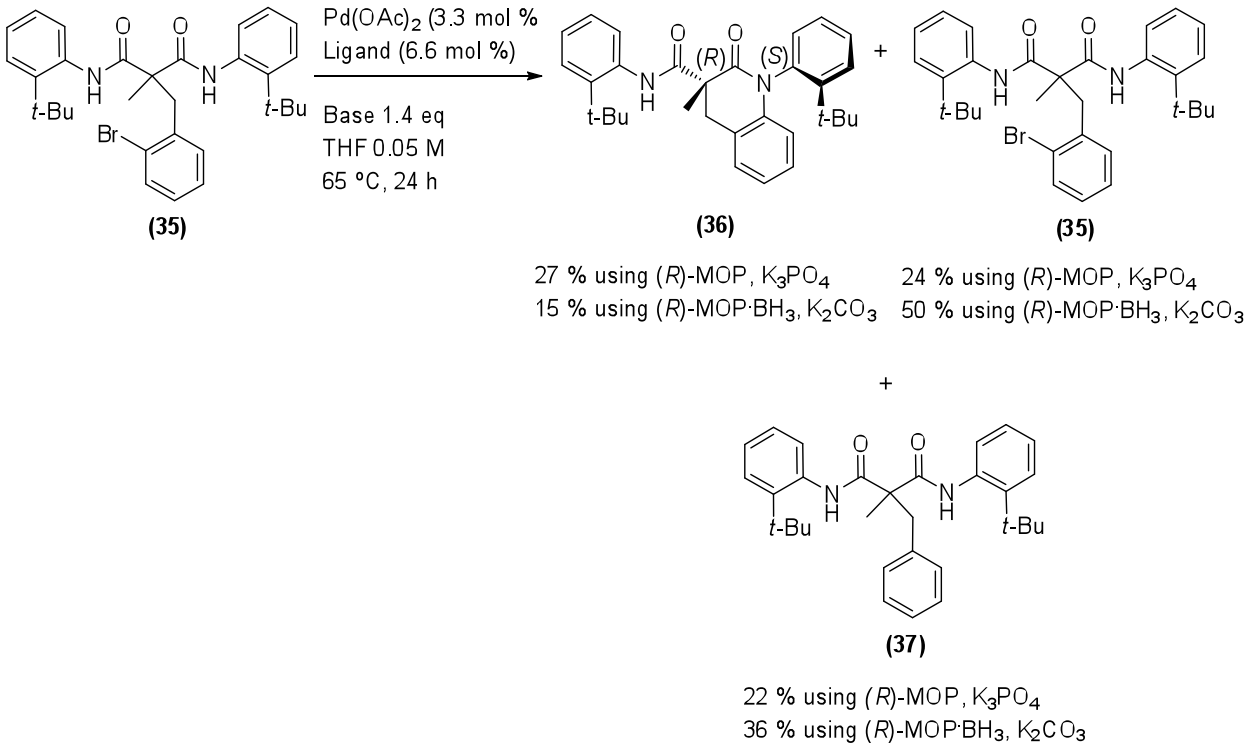
(35) **(36)**

Absolute stereochemistry (3*R*,S_a)

Trial	Ligand	Base	Solvent	Temp (^oC)	Time (h)	Conversion* (%)	Isolated Yield (%)
1	(*R*)-MOP	K_3PO_4	THF	65	24	27	22
2	(*R*)-MOP·BH3	K_2CO_3	THF	65	24	15	10
3	(*R*)-DTBM-SEGPHOS	K_2CO_3	Toluene	100	48	0	0
4	(*R*)-Cy_2MOP	K_2CO_3	Toluene	100	48	50	48
5	(*R*)-Cy_2MOP	Cs_2CO_3	Toluene	100	48	100	99
6	(+/-)-BINAP	Cs_2CO_3	Toluene	100	48	<10	nd
7	S-Phos precatalyst complex	Cs_2CO_3	Toluene	100	48	100	99

Table 3: Desymmetrization of di-nitrogen malonamides via an intramolecular Buchwald-Hartwig reaction to produce *t*-butyl substituted quinolinone (* ^{1}H-NMR Conversion determined from the disappearance of CH_2 signals in compound 35)

Initially the cyclization of **35** was carried out with (*R*)-MOP using K_3PO_4, in THF at 65 ^oC. Interestingly ^{1}H-NMR of the crude reaction mixture showed unreacted **35**, the debrominated compound **37**, but more importantly only one diastereomer of *t*-butyl substituted quinolinone **36** (Table 3, Trial 1, scheme 48). When the cyclization of **35** was done using (*R*)-MOP·BH_3 and K_2CO_3, with all other reaction parameters kept constant, the same three compounds **35, 36** and **37**, were obtained (Table 3, Trial 2, scheme 48).



Scheme 48: Initial cross-coupling experiments using (*R*)-MOP and (*R*)-MOP·BH_3

Cyclization of **35** using (*R*)-DTBM-SEGPHOS and K_2CO_3 in Toluene at 100 ^oC resulted in 100 % unreacted **35** (Table 3, Trial 3), this was an interesting result because even though the desired compound **36** was not produced neither was the undesired debrominated compound **37**, indicating that THF may have been the culprit for debromination of the starting material. Amazingly when the cyclization of **35** was carried out using (*R*)-Cy_2MOP and K_2CO_3 in Toluene at 100 ^oC, ^{1}H-NMR of the crude reaction showed 50 % conversion of **35** to **36** (Table 3, Trial 4). Furthermore when this same reaction was done using Cs_2CO_3 as a base instead of K_2CO_3, the reaction proceeded with 100 % conversion of **35** to **36** and the crude product was isolated in excellent, 99 %, yield (Table 3, Trial 5). The purified compound was recrystallized once from chloroform:cyclohexane (1:1) and analyzed by x-ray crystallography. The absolute configuration of compound **36** determined by x-ray crystallography is (*R*) at the chiral centre and (*S*) at the chiral axis (figure 14).

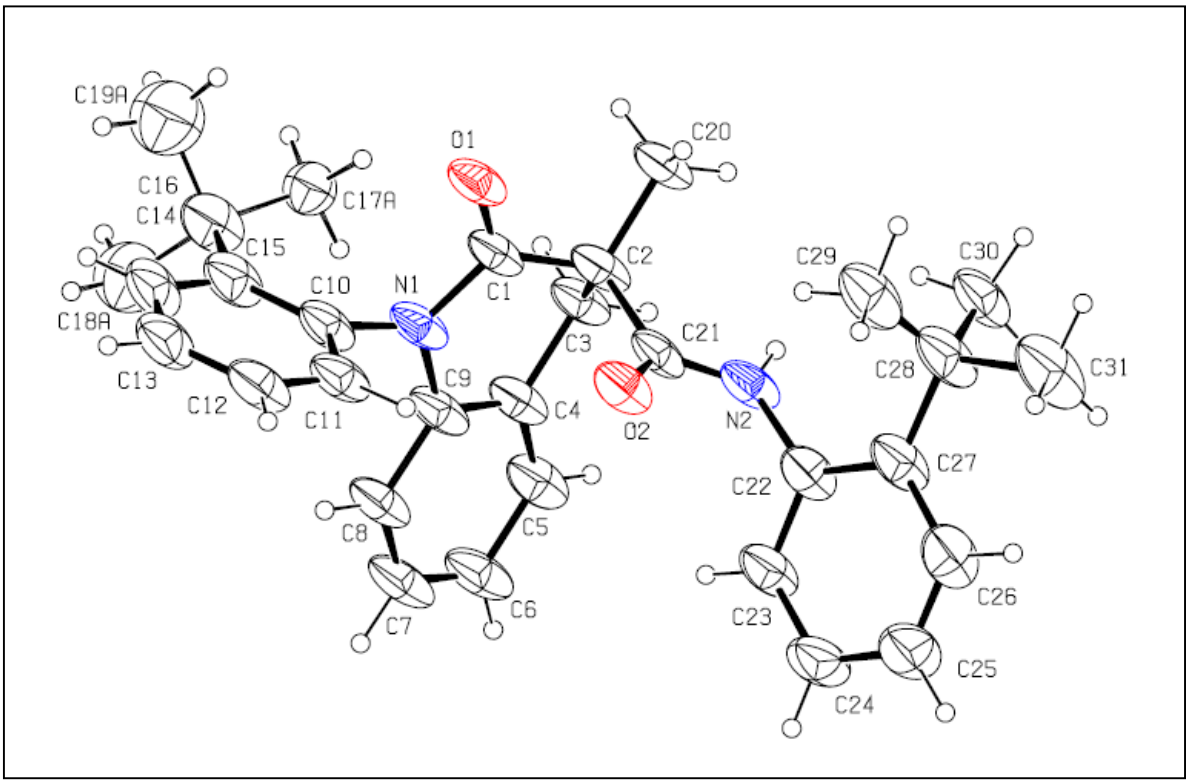
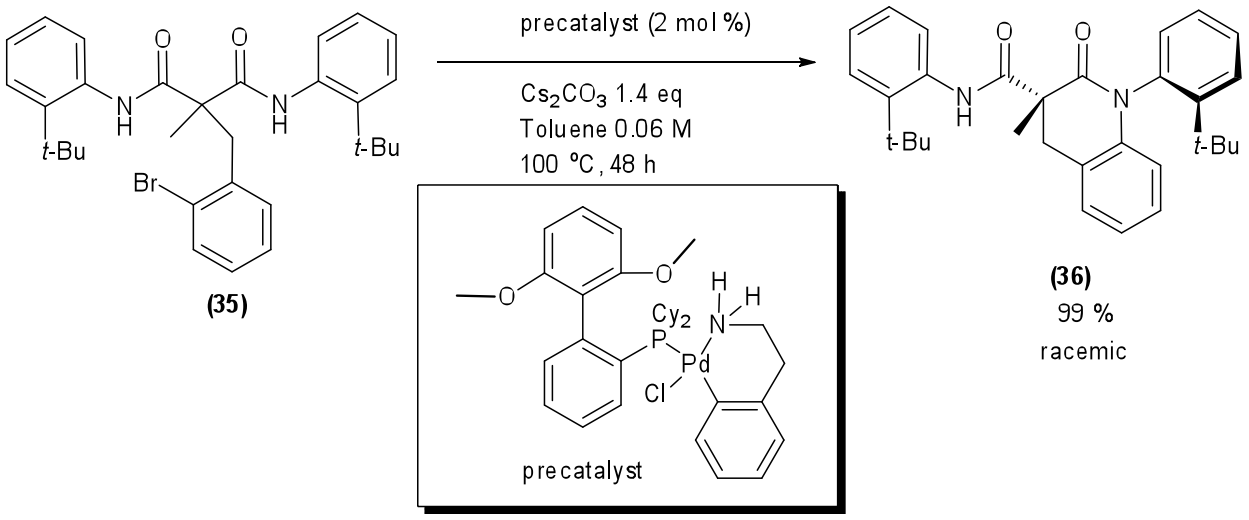


Figure 14: X-ray crystal structure of *t*-butylphenyl substituted quinolinone

In order to obtain racemic **36** a cross-coupling reaction was set up using racemic BINAP and Cs_2CO_3 in Toluene at 100 ^oC, however this reaction resulted in poor, < 10 % conversion, of compound **35** to **36** (Table 3, Trial 6). Nevertheless racemic **36** was obtained in 99 % yield using the achiral S-Phos precatalyst complex (Table 3, Trial 7, scheme 49).



Scheme 49: Synthesis of racemic *t*-butyl quinolinone using an S-PHOS precatalyst

Interestingly TLC of the crude reaction showed a single spot and ^{1}H-NMR analysis revealed only a single diastereomer was formed in this reaction. Furthermore it was proved by ^{1}H-NMR that the diastereomer formed in this reaction is the same diastereomer that is formed when the cyclization of **35** was carried out using (*R*)-Cy_2MOP. Thus the reaction appears to be diastereoselective even when using an achiral catalyst. Additionally chiral column HPLC analysis of the racemic compound illustrated two peaks in an equal ratio to one another, signifying that the two enantiomers are formed in equal amounts in the absence of a chiral catalyst (figure 15a). Amazingly, chiral column HPLC analysis of compound **36** cyclized with Cy_2MOP using Cs_2CO_3 or K_2CO_3 revealed a significant decrease in the peak with a retention time around 10.74 min (Figure 15b and c). The *ee* of compound **36** cyclized with Cy_2MOP using Cs_2CO_3 or K_2CO_3 was calculated to be 88 %. Although it is not certain that the crystal structure shown in figure 14 represents the major enantiomer formed in this reaction, there is a 94 % probability that it does since the *er* (enantiomeric ratio) of compound **36** cyclized with Cy_2MOP using Cs_2CO_3 or K_2CO_3 is 94:6. Nevertheless this serves as the first example of its kind whereby

an enantio- and diastereoselective Buchwald-Hartwig reaction occurs in a single step through preferential N-arylation of prochiral di-nitrogen malonamides.

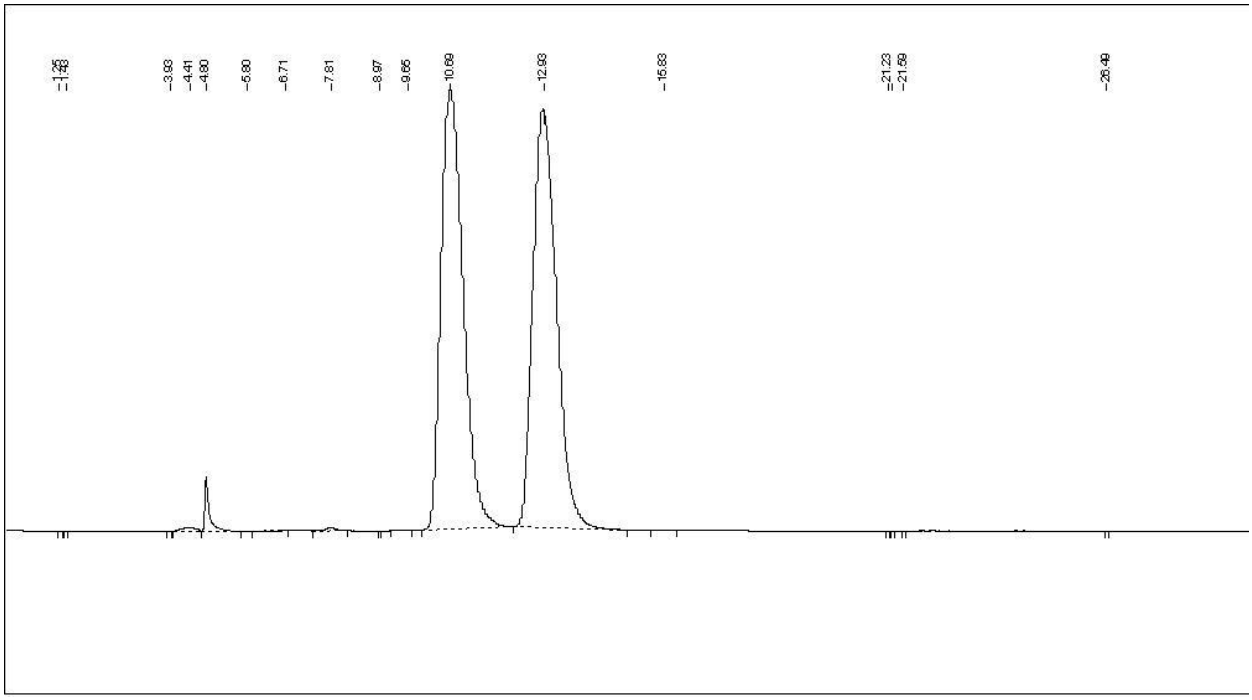


Figure 15a: HPLC chromatogram of racemic compound 36

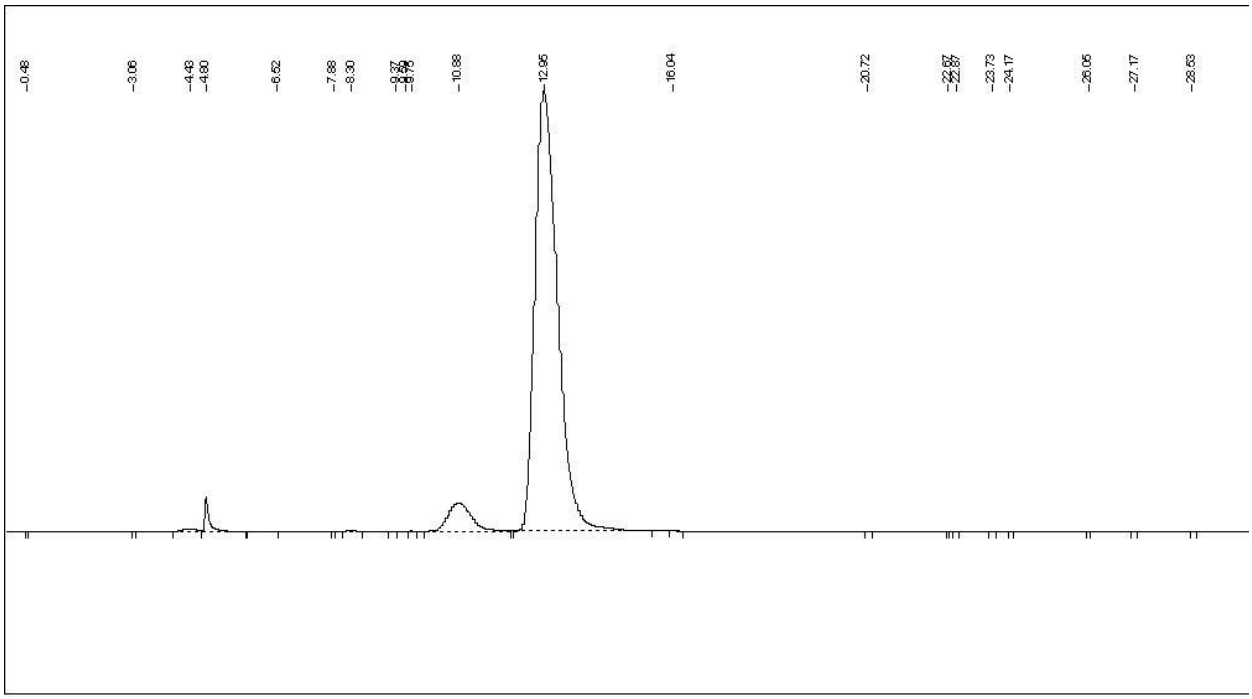


Figure 15b: HPLC chromatogram of compound 36 cyclized with Cy_2MOP using Cs_2CO_3 as a base

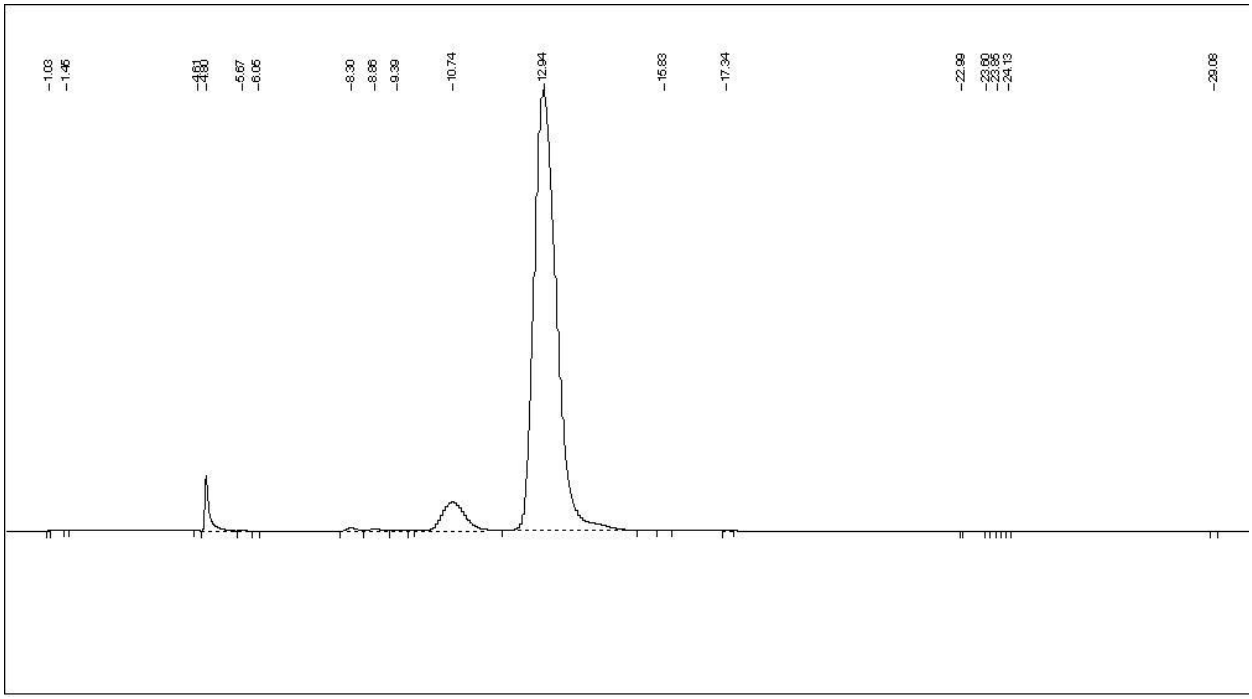
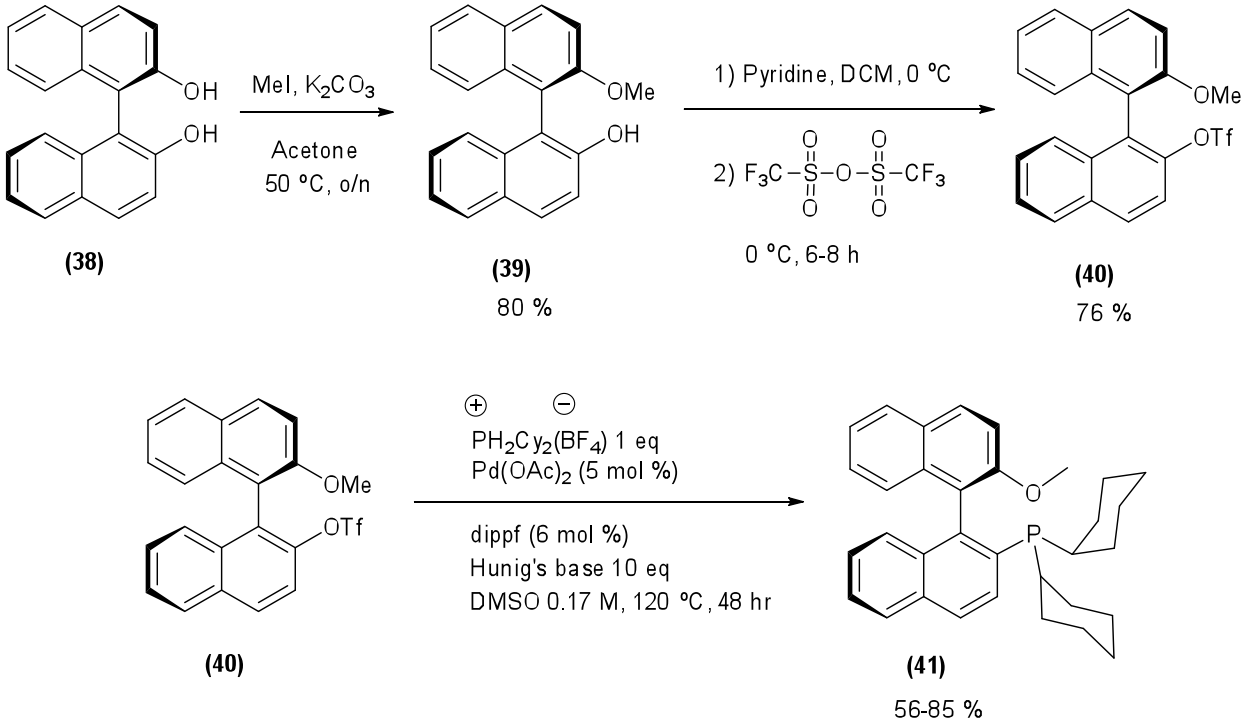


Figure 15c: HPLC chromatogram of compound 36 cyclized with Cy_2MOP using K_2CO_3 as a base

2.5 Synthesis of Cy_2MOP

In order to demonstrate the utility of chiral dialkylbiarylphosphines in the intramolecular desymmetrization of malonamides, a synthetic protocol was carried out to obtain the enantiopure, non-commercially available, ligand **41** ((*R)*-2(Dicyclohexylphosphino)-2'-methoxy-1,1'-binaphthyl) (Scheme 50).

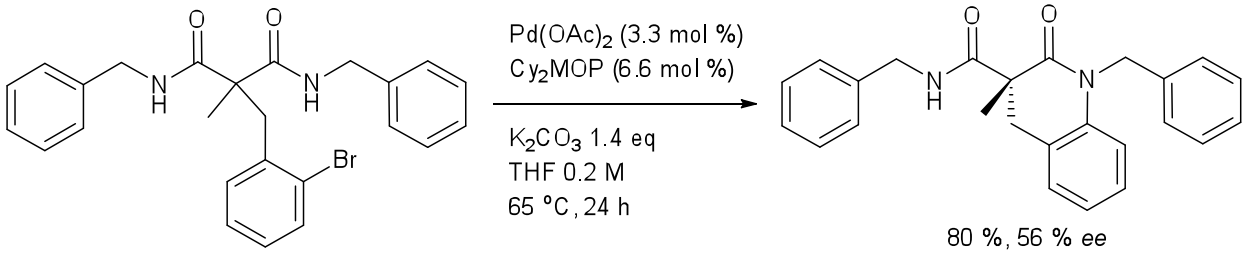


Scheme 50: Synthesis of (*R)*-2(Dicyclohexylphosphino)-2'-methoxy-1,1'-binaphthyl)

The first two steps towards the synthesis of **41** were performed by Bashar Alkhouri and entailed treating compound **38** (BINOL, commercially available in the enantiopure (*R*) form) with potassium carbonate in acetone followed by methylation, using iodomethane, which furnished **39** (Me-BINOL) in high yield (scheme 50).[46] Next compound **39** was deprotonated using pyridine and reacted with triflic anhydride to produce **40** (Me-BINOL-OTf) in good yield (scheme 50).[46] The final step was accomplished via a palladium catalyzed cross-coupling reaction between **40**

and dicyclohexylphosphonium tetrafluoroborate using palladium/dippf as the catalyst system (scheme 50). This catalyst system was employed due to the successful coupling of aryl bromides/chlorides with secondary phosphines reported by Buchwald and co-workers in 2004.[41] The reaction worked fairly well and the desired tertiary phosphine was obtained in moderate to high yield. Two factors which increased the yield of **41** were the use of ten equivalents of Hunig's base as opposed to six equivalents, in order to ensure complete deprotonation of dicyclohexylphosphonium tetrafluoroborate and keeping the reaction solvent, DMSO, under vacuum for one hour followed by purging with argon for another half hour before use.

Initially compound **41** was utilized in the desymmetrization of **45** in order to compare the yield and selectivity of this reaction with (*R*)-MOP (Scheme 51). Interestingly the *ee* of the desired product **46** was identical, 56 % *ee* when cyclized with Cy_2MOP or (*R*)-MOP[47], however the yield of compound **46** was somewhat lower, 80 % when cyclized with Cy_2MOP compared to quantitative when cyclized with (*R*)-MOP.[47]



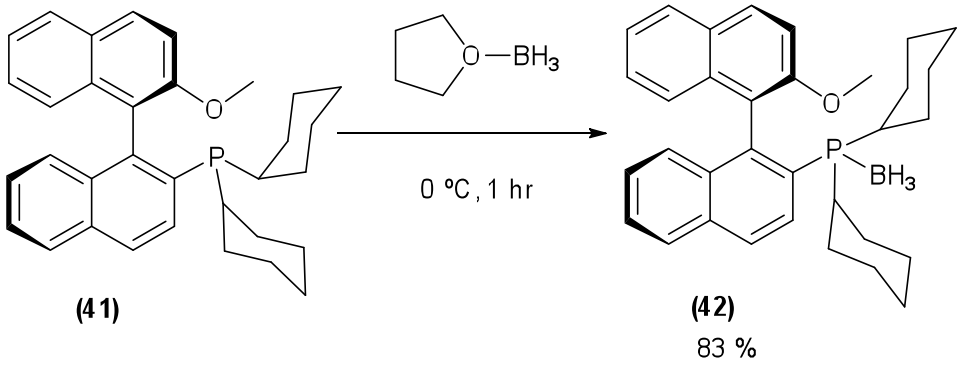
(45) **(46)**

Scheme 51: Intramolecular desymmetrization using Cy_2MOP

Nevertheless compound **41** was remarkably more air-stable than MOP and showed a substantial increase in activity for the intramolecular palladium catalyzed amidation reaction with other substrates i.e. compounds **20**, **31** and **35**. Both MOP and Cy_2MOP have an *ortho*-methoxy group that can act as a hemilabile coordination site with palladium, thus increasing electron density and stability of the palladium center. Replacement of the diphenylphosphino group of MOP with the

bulkier and more basic dicyclohexylphosphino group probably slows down the rate of oxidative addition and ligand exchange but at the same time speeds up the rate of reductive elimination and thus regeneration of the active catalyst due to the massive steric bulk surrounding palladium. Therefore the acceleration in rate of cross coupling can be attributed to the fact that regeneration of the active catalyst is in fact the rate determining step in this catalytic cycle.[19]

Furthermore complexation of Cy_2MOP with borane-THF resulted in the desired phosphine-borane complex which was easily purified by column chromatography is air-stable and crystalline (scheme 52, Figure 16).



Scheme 52: Synthesis of $Cy_2MOP{\cdot}BH_3$ via complexation with borane-THF

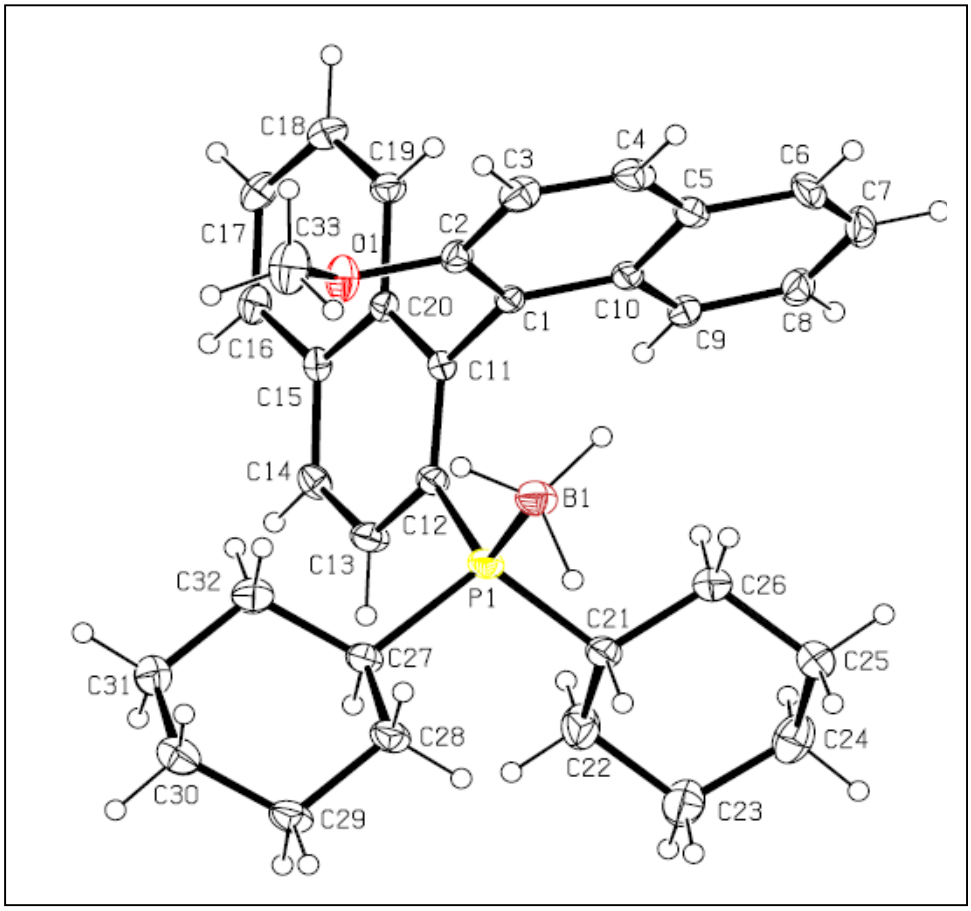


Figure 16: X-ray crystal structure of $Cy_2MOP{\cdot}BH_3$

2.6 Palladium Precatalyst Synthesis

With compound **41** in hand a palladium precatalyst complex was envisioned which would incorporate an element of chirality into the precatalyst complexes synthesiszed by Buchwald *et al*. in 2008[42-43] (Figure 17).

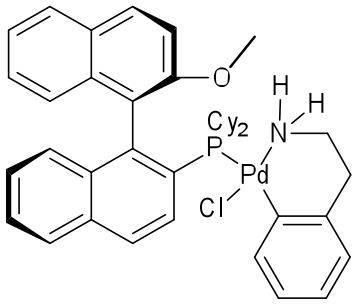
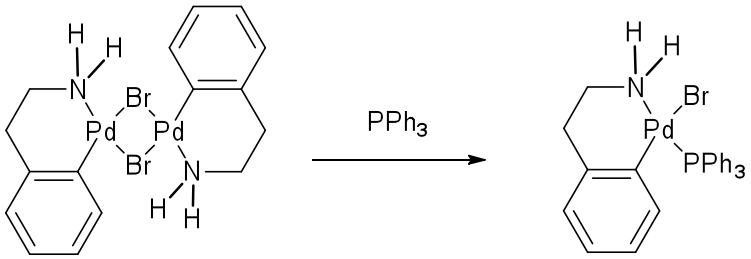


Figure 17: An axially chiral, enantiopure palladium precatalyst

2.6.1 Palladium Precatalyst Synthesis via orthopalladated complexes

Initially the synthetic protocol towards these precatalysts was based on a report by Vicente *et al* in 1997, whereby the authors treated orthopalladated complexes with tertiary phosphines to obtain the desired compound **44** (Figure 18).[48]

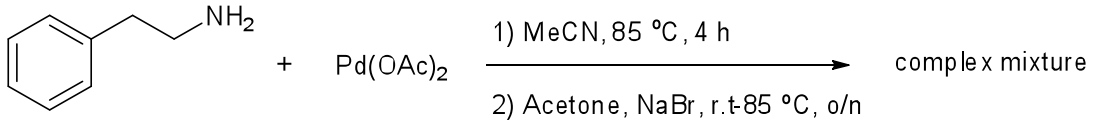


(43) **(44)**

Figure 18: Reaction of tertiary phosphines with orthopalladated complexes

Synthesis of compound **43** was attempted by dissolving $Pd(OAc)_2$ in acetonitrile followed by the addition of phenethylamine. The reaction was heated to 85 ^{o}C and left refluxing for four hours. Next the reaction mixture was filtered through a plug of $MgSO_4$, the solvent was removed and acetone was added followed by the addition of NaBr. The resulting suspension was heated to 85 ^{o}C and left stirring overnight at this temperature. After an aqueous work-up, ^{1}H-NMR analysis of the crude reaction showed a complex mixture of products. Furthermore TLC of the crude material at various different solvent conditions failed to show distinct spots, but rather a large

smear on the TLC plate (scheme 53). This reaction was repeated twice more however the result was the same.



Scheme 53: Attempted orthopalladation of (2-Phenylethyl)amine

2.6.2 Palladium Precatalyst Synthesis using Pd(II)Me_2TMEDA

Palladium precatalyst synthesis was also attempted following Buchwald's procedure which entailed reacting the desired phosphine ligand with Pd(II)Me_2TMEDA (figure 16).[42-43]

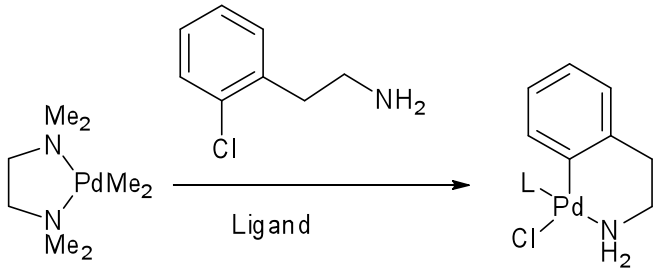
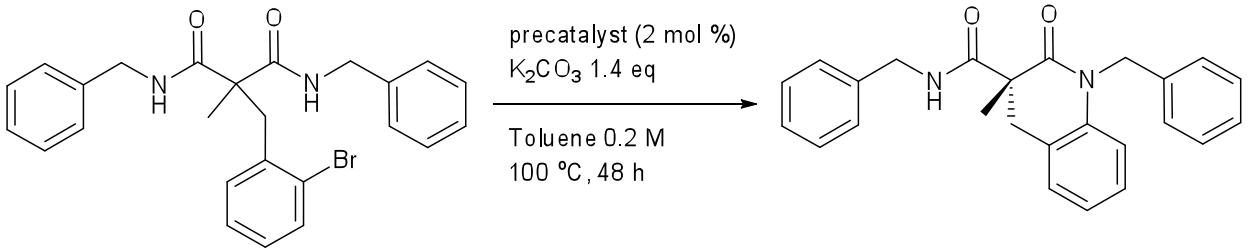


Figure 19: Buchwald's Palladium precatalyst synthesis using Pd(II)Me_2TMEDA

Thus in a nitrogen glove box, Pd(II)Me_2TMEDA was dissolved in MTBE followed by the addition of 2-chloro(phenylethyl)amine. Cy_2MOP was then added to the reaction and the mixture was heated to 55 ^oC outside the glove box. The reaction was left stirring at this temperature for two hours. Next the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure and the crude solid was redissolved in MTBE and precipitated out with hexanes. An off-white powder was obtained in 50 % yield however this compound did not appear to be the desired precatalyst by ^{1}H-NMR or ^{31}P-NMR. In fact there was no methyl peak corresponding to the methoxy group of Cy_2MOP in the proton spectrum. Furthermore there was

not enough signal in the alkyl region of the proton spectrum with respect to cyclohexyl groups of Cy_2MOP. Lastly the phosphorus signal for these precatalysts usually show up around δ 55 – 65, however in this case the phosphorus signal was visible at δ 36.0. Nevertheless a cross coupling reaction was set up to determine if this compound was able to catalyze the intramolecular cyclization reaction (scheme 54).



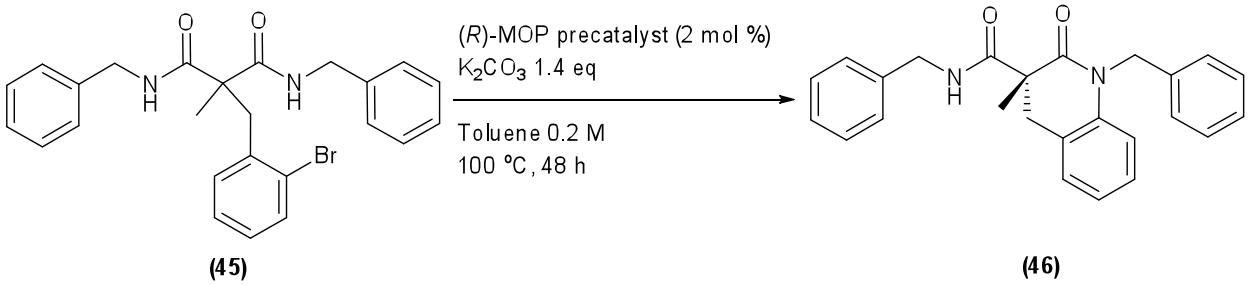
(45) (46)

Scheme 54: Cross coupling reaction using putative Cy_2MOP precatalyst

Therefore compound **45**, the putative precatalyst and K_2CO_3 were added to a Schlenk flask and the flask was evacuated and backfilled with argon. Toluene was added under a stream of argon, the reaction was sealed and heated to 100 ^oC. The reaction mixture was left stirring at 100 ^oC for two days. Analysis of the crude reaction by ^{1}H-NMR showed a 40 % conversion of compound **45** to **46**. Thus under these reaction conditions the assumed precatalyst was able to cyclize compound **45**. Efforts are underway to recrystallize the presumed precatalyst in order to determine its structure.

Precatalyst synthesis was also attempted with (*R*)-MOP instead of Cy_2MOP following Buchwald's procedure,[42-43] i.e. in a nitrogen glove box, Pd(II)Me_2TMEDA was dissolved in MTBE followed by the addition of 2-chloro(phenylethyl)amine. (*R*)-MOP was then added to the reaction and the mixture was heated to 55 ^oC outside the glove box. The reaction was left stirring at this temperature for two hours. Next the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure and the crude solid was redissolved in MTBE and

precipitated out with hexanes. An orange powder was obtained this time and analysis of this compound by ^{1}H-NMR and ^{31}P-NMR revealed the formation of at least three different MOP complexes. In the proton spectrum there were three separate methyl signals corresponding to the methoxy group of (*R*)-MOP in a 1:1:0.5 ratio. Furthermore ^{31}P-NMR showed two distinct phosphorus signals at δ 28.6 and -13.8 respectively, neither of which correspond to the precatalyst or the free phosphine. Since this reaction was done on a small scale (50 mg w.r.t. (*R*)-MOP) no attempt was made to purify the crude product. Nonetheless a cross coupling reaction was set up to determine if this crude material would be able to catalyze the cyclization of compound **45** to **46** (scheme 55).

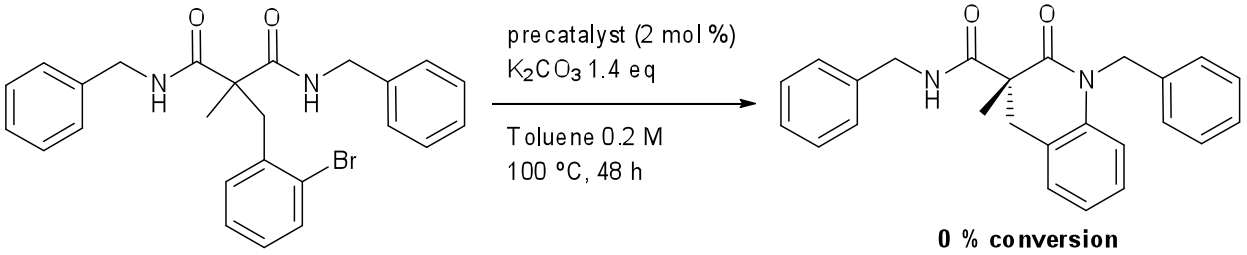


Scheme 55: Cross coupling reaction using putative (*R*)-MOP precatalyst

Thus compound **45**, the putative (*R*)-MOP precatalyst and K_2CO_3 were added to a Schlenk flask and the flask was evacuated and backfilled with argon. Toluene was added under a stream of argon, the reaction was sealed and heated to 100 ^{o}C. The reaction mixture was left stirring at 100 ^{o}C for two days. However analysis of the crude reaction by ^{1}H-NMR showed < 10 % conversion of compound **45** to **46**. Thus under these reaction conditions the assumed precatalyst was not effective in the cyclization of compound **45**.

Palladium precatalyst synthesis was attempted one last time with Cy_2MOP following Buchwald's procedure.[42-43] All the reaction parameters were kept constant and interestingly a

different result was obtained. Again an off-white powder was obtained in 50 % yield however ^{1}H-NMR of this compound looked more encouraging than the first time this reaction was attempted. There was indeed enough signal in the aliphatic region of the proton spectrum, corresponding to the cyclohexyl groups of Cy_2MOP, and these signals were in the appropriate region i.e. between δ 1-2, for the precatalyst complex. Oddly though there was no methyl signal for the methoxy group of Cy_2MOP. Also there was no phosphorus signal in the ^{31}P-NMR spectrum. Nevertheless a cross coupling reaction was carried out with this compound but unlike in the first case there was no conversion of compound **45** to **46** (scheme 56).



(45) **(46)**

Scheme 56: Cross coupling reaction using another putative precatalyst

This suggests that there may not be a palladium atom present which consequently does not allow the reaction to occur. Efforts are also underway to recrystallize this compound in order to determine its structure.

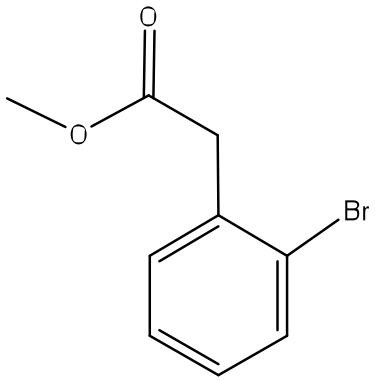
3 Experimental

3.1 General Considerations

All reagents unless otherwise noted were purchased from SIGMA-ALDRICH.

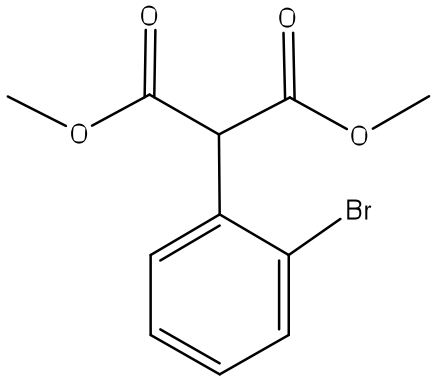
(*R*)-MOP was purchased from STREM CHEMICAL COMPANY. ^{1}H, ^{13}C, ^{11}B, and ^{31}P-NMR spectra were recorded on a 400 MHz Bruker Avance II-400 Spectrometer (Ryerson University). High-performance liquid chromatography (HPLC) analysis was performed with a 25 x 0.4 cm i.d. CHIRALCEL-OD-H column with a UV-detector.

3.2 Towards the Synthesis of Oxindole Heterocycles

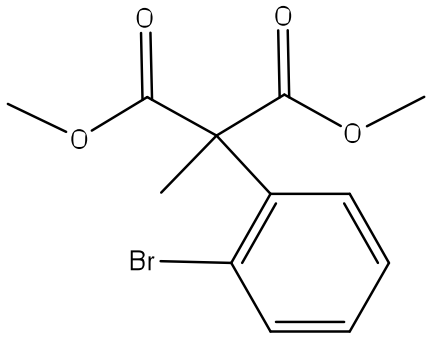


Methyl 2-(2-bromophenyl)acetate (5): 2-(2-bromophenyl)acetic acid (12.0 g, 55.8 mmol) was dissolved in methanol (200 mL). Several drops of H_2SO_4 were added and the mixture was heated to 85 ^{o}C and left refluxing for three hours. The reaction mixture was diluted with diethyl ether (600 mL) and extracted with 0.1 M HCl, saturated $NaHCO_3$, and brine. The organic phase was dried over Na_2SO_4 and evaporated under reduced pressure to afford methyl 2-(2-bromophenyl)acetate, compound **5** (12.1 g, 95 %) as an opaque oil. This compound was used without further purification. R_f = 0.45 (SiO_2, 5 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.55 (d, *J* = 7.9 Hz, 1H, C_6H_4), 7.29-7.23 (m, 2H, C_6H_4), 7.16-7.08 (m, 1H, C_6H_4), 3.79

(s, 2H, CH_2), 3.69 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 170.8, 134.2, 132.8, 131.5, 128.9, 127.5, 124.9, 52.1, 41.5.



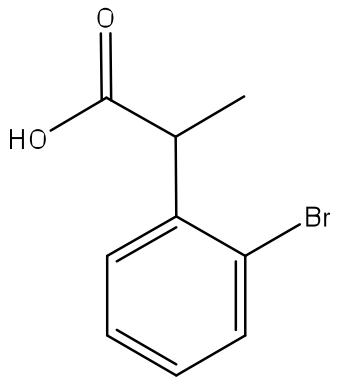
Dimethyl 2-(2-bromophenyl)malonate (6): To a solution of methyl 2-(2-bromophenyl)acetate, compound **5**, (5g, 21.8 mmol) in dimethyl carbonate (40 mL) was added sodium hydride (2.62 g, 65.4 mmol) at 0 ^{o}C. The mixture was left stirring overnight at room temperature. The reaction mixture was quenched with saturated ammonium chloride and extracted three times with ethyl acetate. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified via flash chromatography eluting with 5 % EtOAc:Hexanes to afford Dimethyl 2-(2-bromophenyl)malonate compound **6** in 85 % yield as a white solid. Melting point: 41-42 ^{o}C; R_f = 0.35 (SiO_2, 5 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.59 (dd, J_1 = 8.0 Hz, J_2 = 1.3 Hz, 1H, C_6H_4), 7.47 (dd, J_1 = 7.8 Hz, J_2 = 1.7 Hz, 1H, C_6H_4), 7.33 (td, J_1= 7.6 Hz, J_2 = 1.3, 1H, C_6H_4), 7.19 (td, J_1 = 7.9 Hz, J_2 = 1.7, 1H, C_6H_4), 3.78 (s, 6H, CH_3). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 168.1, 132.9, 132.7, 130.3, 129.8, 127.8, 125.0, 56.8, 53.0.



Dimethyl 2-(2-bromophenyl)-2-methylmalonate (7): Method A: A round bottom flask was charged with sodium hydride, 60 % dispersion in mineral oil, (194.9 mg, 4.87 mmol). The hydride was washed twice with anhydrous hexanes (5 mL) and suspended in anhydrous THF (6.7 mL). A solution of dimethyl 2-(2-bromophenyl)malonate, compound **6**, (1 g, 3.48 mmol) in THF (2 mL) was added to the rapidly stirring sodium hydride suspension at 0 ^{o}C. The reaction mixture was allowed to warm to room temperature. Once gas evolution had ceased, iodomethane (0.3 mL, 4.87 mmol) was added, the mixture was heated to 70 ^{o}C and left refluxing overnight. The reaction mixture was quenched with saturated ammonium chloride (10 mL) and extracted with ethyl acetate (3 x 20 mL). The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified via column chromatography eluting with 5 % EtOAc:Hexanes to afford dimethyl 2-(2-bromophenyl)-2-methylmalonate, compound **7** (856.7 mg, 82 %) as a colorless oil.

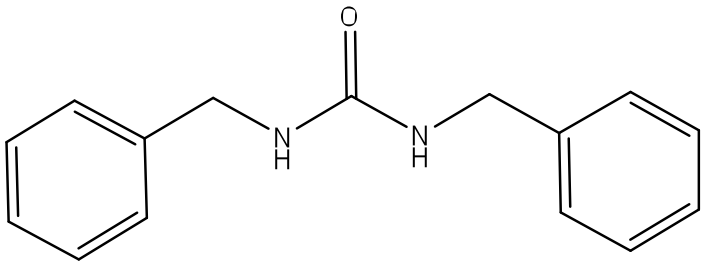
Dimethyl 2-(2-bromophenyl)-2-methylmalonate (7): Method B: A round bottom flask was charged with sodium hydride, 60 % dispersion in mineral oil (1.304 g, 32.6 mmol). The hydride was washed twice with anhydrous hexanes (10 mL) and suspended in anhydrous THF (43 mL). A solution of dimethyl 2-(2-bromophenyl)malonate, compound **6**, (6.547 g, 23.3 mmol) in THF (15.2 mL) was added to the rapidly stirring sodium hydride suspension at 0 ^{o}C. The reaction mixture was allowed to warm to room temperature, once gas evolution had ceased dimethyl

sulfate (3.09 mL, 32.6 mmol) was added, the reaction was heated to 70 ^{o}C and left refluxing overnight. The reaction mixture was quenched with saturated ammonium chloride and extracted three times with ethyl acetate. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified via column chromatography eluting with 5 % EtOAc:Hexanes to afford dimethyl 2-(2-bromophenyl)-2-methylmalonate, compound **7** (6.663 g, 95 %) as a colorless oil. R_f = 0.25 (SiO_2, 5 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.60 (dd, J_1 = 7.9 Hz, J_2 = 1.3 Hz, 1H, C_6H_4), 7.29 (td, J_1 = 7.7 Hz, J_2 = 1.4, 1H, C_6H_4), 7.16 (td, J_1= 7.8 Hz, J_2 = 1.6 Hz, 1H, C_6H_4), 7.11 (dd, J_1 = 7.8 Hz, J_2 = 1.6 Hz, 1H, C_6H_4), 3.77 (s, 6H, CH_3), 1.91 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 171.0, 139.0, 134.4, 128.8, 128.6, 127.4, 123.2, 61.1, 52.2, 21.3.

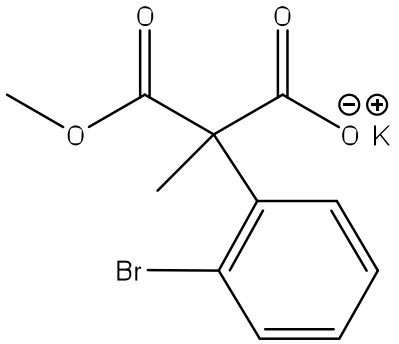


2-(2-bromophenyl)propanoic acid (8): Dimethyl 2-(2-bromophenyl)-2-methylmalonate, compound **7,** (619.3 mg, 2.057 mmol) was dissolved in methanol (2.5 mL) followed by the addition of 4 M NaOH (2.5 mL). The reaction was refluxed overnight. The reaction mixture was cooled to room temperature, diluted with water (10 mL) and extracted with ether (10 mL). The aqueous phase was acidified via slow dropwise addition of 6 M HCl and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and evaporated

under reduced pressure to afford 2-(2-bromophenyl)propanoic acid, compound **8** (417.8 mg, 75 %) as a white solid which did not require further purification. Melting point: 95-96 ^{o}C; ^{1}H-NMR ($(CD_2)_3O$, 400 MHz): δ 7.61 (dd, J_1 = 8.1 Hz, J_2 = 1.3 Hz, 1H, C_6H_4), 7.43-7.34 (m, 2H, C_6H_4), 7.22-7.16 (m, 1H, C_6H_4), 4.21 (q, J = 7.2 Hz, 1H, CH), 1.45 (d, J = 7.2 Hz, 3H, CH_3). ^{13}C-NMR ($(CD_2)_3O$, 400 MHz): δ 205.6, 174.0, 140.7, 132.8, 128.7, 128.0, 124.0, 44.3, 17.3.

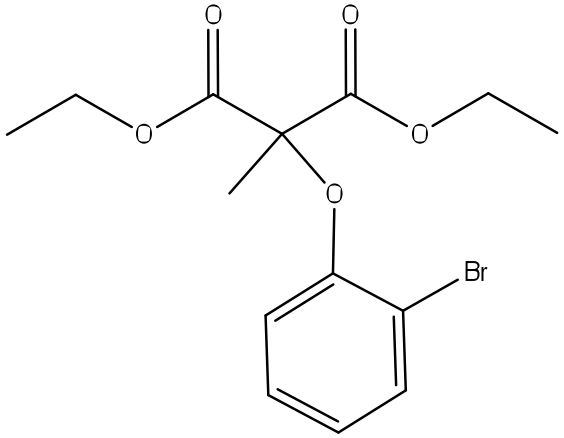


Dibenzylurea (15): Benzylamine (5.5 mL, 50 mmol) was dissolved in 104 mL of dichloromethane and cooled in an ice bath. Next 1,1'-carbonyldiimidazole (4.05 g, 25 mmol) was dissolved in 125 mL of dichloromethane and added dropwise to the ice cold benzylamine solution. The reaction was left stirring overnight at room temperature. The reaction mixture was diluted with dichloromethane and extracted three times with 0.1 M HCl. The crude product was dried over $MgSO_4$, filtered and evaporated under reduced pressure to afford dibenzylurea, compound **15**, (5.17 g, 86 %) as a white solid which was used without further purification. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.35-7.20 (m, 10H, C_6H_5), 4.76 (s, 2H, NH), 4.36 (d, J_1 = 5.8 Hz, 4H, CH_2).

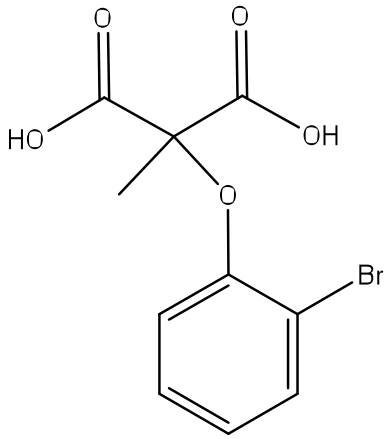


potassium 2-(2-bromophenyl)-3-methoxy-2-methyl-3-oxopropanoate (18): Dimethyl 2-(2-bromophenyl)-2-methylmalonate, compound **7,** (150 mg, 0.5 mmol) was dissolved in methanol (0.8 mL) followed by the addition of 4 M KOH (0.3 mL). The reaction was left stirring overnight at room temperature. The crude reaction mixture was evaporated to dryness under reduced pressure and stored under vacuum overnight to afford compound **18** (276.4 mg, 85 %) as a white solid which was used without further purification. ^{1}H-NMR (D_2O, 400 MHz): δ 7.65 (d, J = 8.2 Hz, 1H, C_6H_4), 7.39-7.34 (m, 2H, C_6H_4), 7.22-7.19 (m, 1H, C_6H_4), 3.70 (s, 3H, CH_3), 1.82 (s, 3H, CH_3).

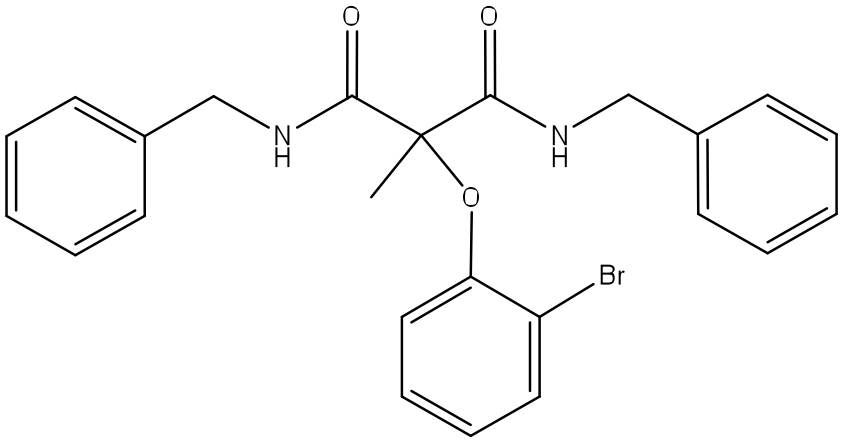
3.3 Towards the Synthesis of Benzomorpholinone Heterocycles



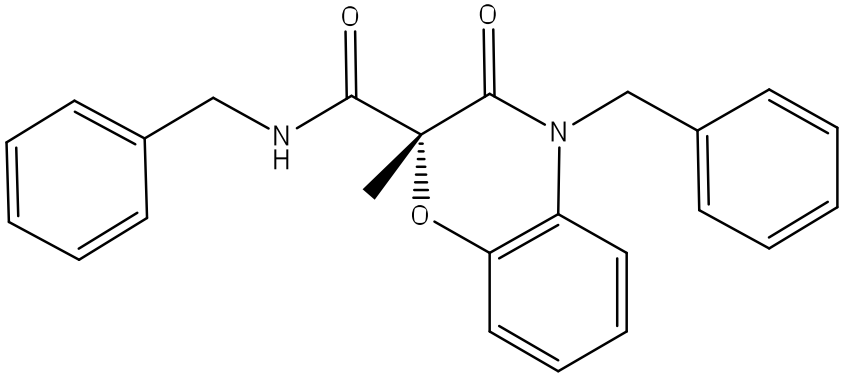
Diethyl 2-(2-bromophenoxy)-2-methylmalonate (22): Under an atmosphere of argon, 2-bromophenol (1.62 mL, 15.3 mmol) was dissolved in DMF (250 mL) followed by the addition of *t*-BuOK (1.545 g, 13.8 mmol). The reaction mixture was stirred for 30 minutes at room temperature before the addition of diethyl 2-bromo-2-methylmalonate (2.77 mL, 14.5 mmol) at room temperature. The reaction was left stirring for 16 hours at room temperature. The reaction was diluted with EtOAc (500 mL) washed with water (5 x 250 mL) and 1 M NaOH (100 mL). The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure to afford diethyl 2-(2-bromophenoxy)-2-methylmalonate **22** as an orange oil (3.277 g, 66 %) which was used without further purification. R_f = 0.80 (SiO_2, 25 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.55 (dd, J_1 = 7.9 Hz, J_2 = 1.6 Hz, 1H, C_6H_4), 7.21-7.15 (m, 1H, C_6H_4), 7.07 (dd, J_1 = 8.2 Hz, J_2 = 1.5 Hz, 1H, C_6H_4), 6.96-6.90 (m, 1H, C_6H_4), 4.29 (q, J = 7.1 Hz, 4H, CH_2), 1.73 (s, 3H, CH_3), 1.30-1.24 (m, 6H, CH_3). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 168.5, 151.9, 133.5, 128.0, 124.8, 120.7, 116.8, 83.9, 62.4, 20.3, 14.0.



2-(2-bromophenoxy)-2-methylmalonic acid (23): Diethyl 2-(2-bromophenoxy)-2-methylmalonate **22** (1.000 g, 2.70 mmol) was dissolved in methanol (8.1 mL) followed by the addition of 4 M NaOH (2.70 mL). The reaction was left stirring overnight at room temperature. The reaction mixture was diluted with water (20 mL) and extracted with ether (20 mL). The aqueous phase was acidified via slow dropwise addition of a pH 3 phosphate buffer and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phases were dried over $MgSO_4$, filtered and evaporated under reduced pressure to afford 2-(2-bromophenoxy)-2-methylmalonic acid **23** as an opaque solid (507.3 mg, 80 %) which was used without further purification. Melting point: 95-97 ^{o}C; ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.59 (dd, J_1 = 7.9 Hz, J_2 = 1.6 Hz, 1H, C_6H_4), 7.29-7.23 (m, 1H, C_6H_4), 7.19 (s, 2H, OH), 7.05-6.98 (m, 2H, C_6H_4), 1.78 (s, 3H, CH_3). ^{13}C-NMR ($(CD_2)_3O$, 400 MHz): δ 205.6, 169.2, 152.2, 133.4, 128.3, 124.2, 119.5, 115.1, 20.4.



***N*[1],*N* [3]-dibenzyl-2-(2-bromophenoxy)-2-methylmalonamide (20)**: 2-(2-bromophenoxy)-2-methylmalonic acid **23** (562.4 mg, 1.945 mmol) was dissolved in 48.7 mL of dry CH_2Cl_2 and cooled to 0 ^oC followed by the addition of benzylamine (0.47 mL, 4.279 mmol), Hunig's base (0.75 mL, 4.279 mmol) and HBTU (1.6228 g, 4.279 mmol) on ice. The reaction was left stirring at room temperature overnight. The reaction mixture was extracted with 1 M HCl (4 x 10 mL), the organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified via flash chromatography eluting at 40 % EtOAc:Hexanes to afford *N*[1],*N* [3]-dibenzyl-2-(2-bromophenoxy)-2-methylmalonamide, compound **20**, (340.8 mg, 38 %) as a white solid. Melting point: 122-124 ^oC; R_f = 0.45 (SiO_2, 25 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.55 (s, 2H, NH), 7.53-7.49 (m, 1H, C_6H_4), 7.34-7.22 (m, 10H, C_6H_5), 7.18-7.12 (m, 1H, C_6H_4), 7.05-7.03 (m, 1H, C_6H_4), 6.96-6.90 (m, 1H, C_6H_4), 4.51 (d, *J* = 5.8, 4H, CH_2), 1.78 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 169.2, 150.7, 137.5, 133.4, 128.8, 128.4, 127.7, 127.6, 124.7, 119.7, 115.2, 84.6, 43.8, 21.5.



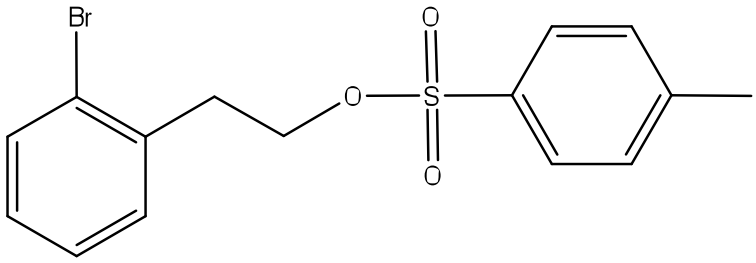
***N*,4-dibenzyl-2-methyl-3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazine-2-carboxamide (21)**:

3.3.1 General Procedure for the Synthesis of 21

A 10 mL Schlenk flask was charged with N^1,N^3-dibenzyl-2-(2-bromophenoxy)-2-methylmalonamide (**20)** (50 mg, 0.107 mmol), Cs_2CO_3 (1.4 eq), 5 mol % $Pd(OAc)_2$ and 10 mol % Ligand. The flask was evacuated and backfilled with argon a total of three times. Toluene (1.8 mL) was added via syringe under a stream of argon, the reaction was sealed and left stirring at 100 ^oC for 48 hours. The reaction mixture was cooled to room temperature, diluted with CH_2Cl_2 (10 mL) and filtered through a short plug of celite. The crude product was purified via column chromatography eluting at 25 % EtOAc:Hexanes to afford compound **21** as a white solid (88-99 % yield). Melting point: 105-110 ^oC; R_f = 0.40 (SiO_2, 25 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): 7.32-7.26 (m, 4H, Ar), 7.25-7.17 (m, 4H, Ar), 7.04-6.90 (m, 5H, Ar), 6.89-6.83 (m, 1H, Ar), 6.58-6.51 (m, 1H, NH), 5.41 (d, J = 16.1 Hz, 1H, CH_2), 4.92 (d, J = 16.1 Hz, 1H, CH_2), 4.52 (dd, J_1 = 15.0 Hz, J_2 = 6.6 Hz, 1H, CH_2), 4.30 (dd, J_1 = 15.0 Hz, J_2 = 5.2 Hz, 1H, CH_2), 1.93 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 168.4, 164.6, 143.4, 137.4, 135.9, 128.9, 128.7, 127.5, 127.4, 126.4, 124.3, 123.4, 117.3, 116.0, 81.8, 46.1, 43.5, 29.7, 22.7, 22.2. HPLC analysis of compound **21** isolated from Ligand = (*R*)-BINAP, Base = K_2CO_3. i.e. Table 1, entry 5; (Chiaralcel OD-H column, eluting with 0.65 mL/min 25 % *i*-PrOH:Hexanes), t_R minor = 17.3 min (peak area = 1018747.76), t_R major = 50.9 min (peak area = 1539462.16), *ee* = 20 %. HPLC

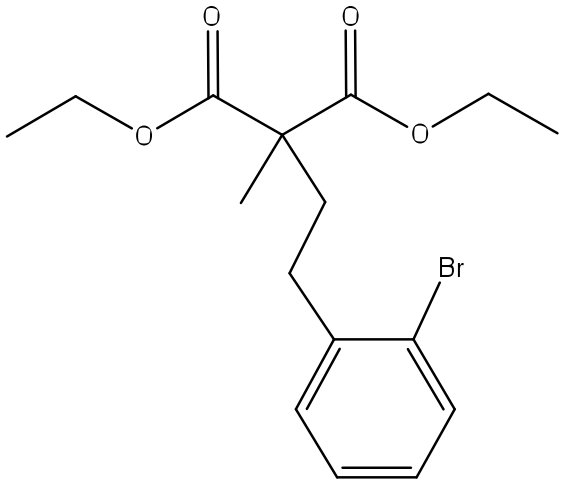
analysis of compound **21** isolated from Ligand = (*R*)-BINAP, Base = Cs_2CO_3. i.e. Table 1, entry 7; (Chiaralcel OD-H column, eluting with 0.65 mL/min 25 % *i*-PrOH:Hexanes), t_R major = 17.9 min (peak area = 2801143.53), t_R minor = 51.9 min (peak area = 2193959.25), *ee* = 12 %. HPLC analysis of compound **21** isolated from Ligand = (*R*)-MOP, Base = Cs_2CO_3. i.e. Table 1, entry 8; (Chiaralcel OD-H column, eluting with 0.65 mL/min 25 % *i*-PrOH:Hexanes), t_R minor = 17.9 min (peak area = 1265584.01), t_R major = 52.1 min (peak area = 1370314.47), *ee* = 3 %. HPLC analysis of compound **21** isolated from Ligand = (*R*)-Cy_2MOP, Base = Cs_2CO_3. i.e. Table 1, entry 6; (Chiaralcel OD-H column, eluting with 0.65 mL/min 20 % *i*-PrOH:Hexanes), t_R minor = 13.7 min (peak area = 6320578.20), t_R major = 38.1 min (peak area = 8088409.20), *ee* = 12 %.

3.4 Towards the Synthesis of Benzodiazepinone Heterocycles



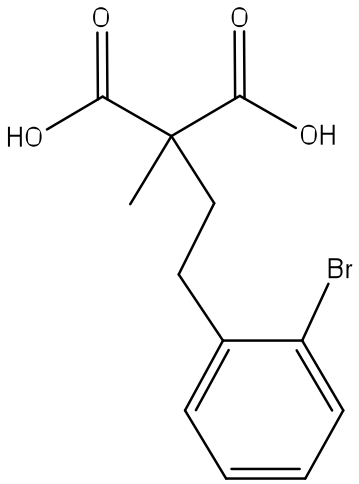
2-bromophenethyl 4-methylbenzenesulfonate (27): To a solution of 2-bromophenethyl alcohol (2.000 g, 9.95 mmol) in dry CH_2Cl_2 (4.1 mL) was added triethyamine (13.9 mL, 99.5 mmol) and DMAP (121.3 mg, 0.995 mmol) at 0 ^oC. A solution of tosyl chloride (2.086 g, 10.94 mmol) in dry CH_2Cl_2 (4.1 mL) was slowly added to the reaction mixture at 0 ^oC using an addition funnel. The reaction mixture was allowed to warm to room temperature and stirred for 3 hours. The reaction was treated with aqueous 1 M HCl (10 mL) and extracted with CH_2Cl_2 (3 x 30 mL) The

organic layer was washed with $NaHCO_3$ (15 mL) and water (15 mL). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography of the crude product eluting with 20 % EtOAc:Hexanes afforded compound **27** (1.547 g, 88 %) as a white solid. Melting point: 36-37 ^oC; R_f = 0.4 (SiO_2, 20 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.68 (d, *J* = 8.3 Hz, 2H, C_6H_4), 7.45 (d, *J* = 8.4 Hz, 1H, C_6H_4), 7.27 (d, *J* = 8.1 Hz, 1H, C_6H_4), 7.24-7.15 (m, 3H, C_6H_4), 7.11-7.05 (m, 1H, C_6H_4), 4.24 (t, *J* = 6.9 Hz, 2H, CH_2), 3.08 (t, *J* = 6.9 Hz, 2H, CH_2), 2.43 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 144.7, 135.5, 132.9, 132.7, 131.5, 129.8, 128.7, 127.8, 127.6, 124.4, 68.8, 35.7, 21.6.



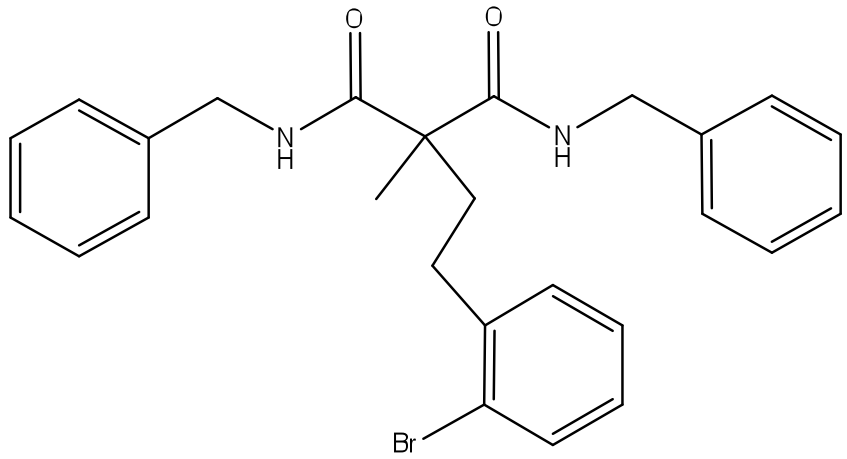
Diethyl 2-(2-bromophenethyl)-2-methylmalonate (29): A 250 ml three-necked round bottom flask equipped with an addition funnel, reflux condenser and attachment piece to an argon line was charged with sodium hydride, 60 % dispersion in mineral oil (750 mg, 18.7 mmol). The hydride was washed twice with anhydrous hexanes (10 mL) and suspended in anhydrous THF (17 mL). Diethyl methylmalonate (2.28 mL, 13.4 mmol) was added to the rapidly stirring sodium hydride suspension at 0 ^oC. The reaction mixture was allowed to warm to room temperature, once gas evolution had ceased a solution of compound **27**, (5.212 g, 14.67 mmol) in THF (7.3 mL) was added and the mixture was heated and left refluxing overnight. The reaction mixture

was quenched with saturated ammonium chloride and extracted three times with ethyl acetate. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified via column chromatography eluting with 5 % EtOAc:Hexanes to afford Diethyl 2-(2-bromophenethyl)-2-methylmalonate, compound **29** (2.244 g, 47 %) as a colorless oil. R_f = 0.80 (SiO_2, 25 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.51 (d, *J* = 7.9 Hz, 1H, C_6H_4), 7.23 (d, *J* = 4.2 Hz, 2H, C_6H_4), 7.09-7.01 (m, 1H, C_6H_4), 4.24-4.10 (m, 4H, CH_2), 2.73-2.67 (m, 2H, CH_2), 2.15-2.09 (m, 2H, CH_2), 1.53 (s, 3H, CH_3), 1.27 (t, *J* = 7.1 Hz, 6H, CH_3). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 172.1, 140.8, 132.8, 130.4, 127.8, 127.6, 124.3, 61.3, 53.5, 35.9, 31.2, 19.9, 14.1.



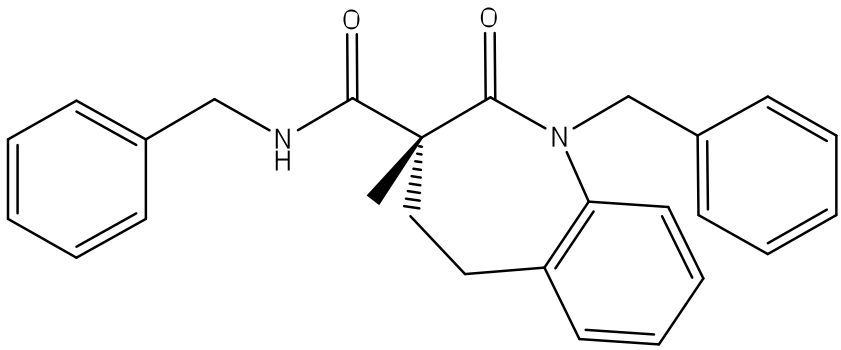
2-(2-bromophenethyl)-2-methylmalonic acid (30): Diethyl 2-(2-bromophenethyl)-2-methylmalonate, compound **29**, (1.006 g, 2.82 mmol) was dissolved in methanol (8.5 mL) followed by the addition of 4 M NaOH (2.8 mL). The reaction was refluxed overnight. The reaction mixture was cooled to room temperature, diluted with water (20 mL) and extracted with ether (20 mL). The aqueous phase was acidified via slow dropwise addition of 6 M HCl and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phases were dried over $MgSO_4$,

filtered and evaporated under reduced pressure to afford 2-(2-bromophenethyl)-2-methylmalonic acid, compound **30** (574.6 mg, 68 %) which was used without further purification. Melting point: 161-166 ^{o}C; ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.52 (d, J = 7.9 Hz, 1H, C_6H_4), 7.28 (d, J = 4.2 Hz, 2H, C_6H_4), 7.12-7.06 (m, 1H, C_6H_4), 4.92 (s, 2H, OH), 2.76-2.70 (m, 2H, CH_2), 2.09-2.03 (m, 2H, CH_2), 1.50 (s, 3H, CH_2). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 174.3, 141.0, 132.5, 130.2, 127.6, 127.5, 123.6, 53.1, 36.0, 31.0, 19.1.



***N*^{1}, *N*^{3}-dibenzyl-2-(2-bromophenethyl)-2-methylmalonamide (31)**: 2-(2-bromophenethyl)-2-methylmalonic acid, compound **30**, (529.0 mg, 1.76 mmol) was dissolved in 2 mL of $SOCl_2$ and stirred at 60 ^{o}C for 4 hours. The excess $SOCl_2$ was removed by rotary evaporation under reduced pressure. The crude product was redissolved in $CHCl_3$ (5 mL) and subjected to rotary evaporation under reduced pressure. This process of redissolving the crude product in $CHCl_3$ followed by rotary evaporation was repeated a total of three times to ensure complete removal of any remaining $SOCl_2$. The crude product was redissolved in $CHCl_3$ (10 mL) and cooled to 0 ^{o}C followed by the addition of benzylamine (0.42 mL, 3.87 mmol) on ice. The reaction mixture was allowed to warm to room temperature and left stirring for one hour. The reaction mixture was cooled back down to 0 ^{o}C followed by the addition of triethyamine (0.54 mL, 3.87 mmol) on ice.

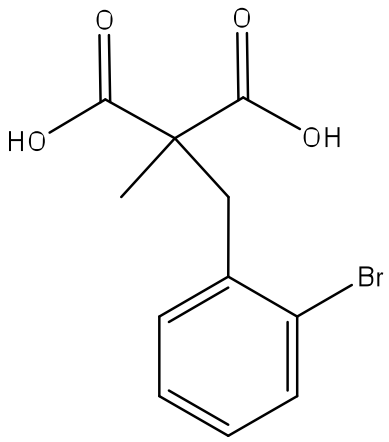
The reaction mixture was warmed to room temperature and refluxed overnight. The reaction was cooled to room temperature and extracted with 1 M HCl (4 x 10 mL). The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified via flash chromatography eluting at 40 % EtOAc:Hexanes to afford N^1, N^3-dibenzyl-2-(2-bromophenethyl)-2-methylmalonamide, compound **31** (365.5 mg, 43 %) as a white solid. Melting point: 113-115 ^oC; R_f = 0.35 (SiO_2, 40 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.48 (dd, J_1 = 8.0 Hz, J_2 = 0.9 Hz, 1H, C_6H_4), 7.36-7.17 (m, 12H, C_6H_4), 7.15-7.10 (m, 1H, C_6H_4), 7.07-7.02 (m, 1H, C_6H_4), 4.52-4.39 (m, 3H, CH_2), 2.71-2.65 (m, 2H, CH_2), 2.18-2.11 (m, 2H, CH_2), 1.58 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 172.6, 140.5, 137.9, 132.7, 130.6, 128.8, 127.9, 127.7, 127.6, 127.5, 124.2, 53.1, 44.0, 39.2, 31.8, 19.8.



***N*, 1-dibenzyl-3-methyl-2-oxo-2,3,4,5-tetrahydro-1H-benzo[b]azepine-3-carboxamide (32)** A 10 mL Schlenk flask was charged with N^1, N^3-dibenzyl-2-(2-bromophenethyl)-2-methylmalonamide (31.4 mg, 0.065 mmol), Cs_2CO_3 (29.6 mg, 0.091 mmol), 5 mol % $Pd(OAc)_2$ and 10 mol % Cy_2MOP. The flask was evacuated and backfilled with argon a total of three times. Toluene (1.1 mL) was added via syringe under a stream of argon, the reaction was sealed and left stirring at 100 ^oC for 48 hours. The reaction mixture was cooled to room temperature, diluted with CH_2Cl_2 (10 mL) and filtered through a short plug of celite. The crude product was

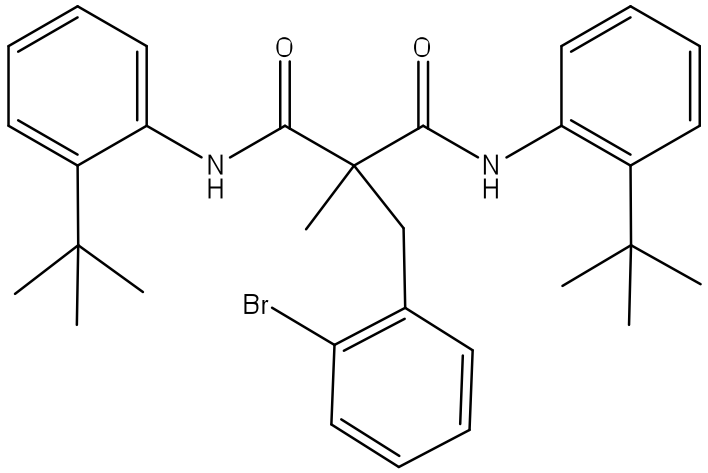
purified by preparative plate TLC eluting at 30 % EtOAc:Hexanes to afford compound **32** (13 mg, 50 %) as an off-white solid. R_f = 0.30 (SiO_2, 40 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.33-7.04 (m, 15H, Ar), 6.97 (d, *J* = 8.0 Hz, 1H, Ar), 5.34 (s, 1H, NH), 5.12 (d, *J* = 14.4 Hz, 1H, CH_2), 4.86 (d, *J* = 14.4 Hz, 1H, CH_2), 4.05 (dd, J_1 = 14.2 Hz, J_2 = 5.7 Hz, 1H, CH_2), 3.80 (dd, J_1 = 14.3 Hz, J_2 = 4.7 Hz, 1H, CH_2), 3.08-2.97 (m, 1H, CH_2), 2.59-2.51 (m, 1H, CH_2), 2.44-2.40 (m, 1H, CH_2), 1.99-1.91 (m, 1H, CH_2), 1.41 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 172.9, 171.8, 140.6, 137.7, 137.5, 136.9, 129.4, 129.0, 128.8, 128.7, 128.6, 128.5, 128.3, 128.1, 127.7, 127.5, 127.4, 127.2, 124.1, 29.7, 29.1, 25.9.

3.5 Towards the Synthesis of *t*-butyl substituted Quinolinone



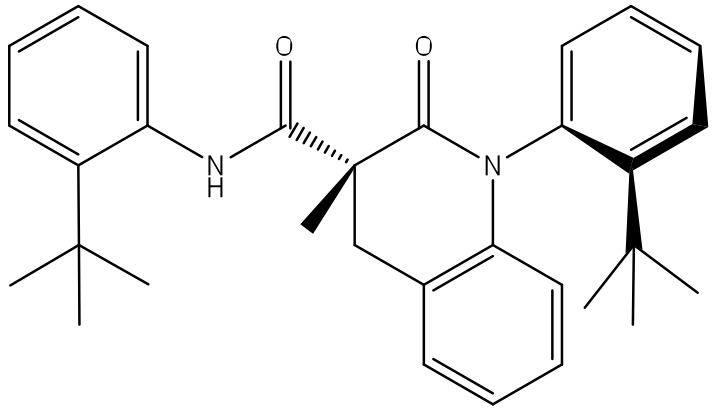
2-(2-bromobenzyl)-2-methylmalonic acid (34): Diethyl 2-(2-bromobenzyl)-2-methylmalonate,[47] (3.6 g, 10.5 mmol) was dissolved in methanol (10.8 mL) followed by the addition of 4 M NaOH (10.8 mL). The reaction was refluxed overnight. The reaction mixture was cooled to room temperature, diluted with water (20 mL) and extracted with ether (20 mL). The aqueous phase was cooled to 0^{o}C and acidified via slow dropwise addition of 6 M HCl. The

white suspension was extracted with CH_2Cl_2 (3 x 30 mL) and the combined organic phases were dried over $MgSO_4$, filtered and evaporated under reduced pressure to afford 2-(2-bromophenethyl)-2-methylmalonic acid, compound **34** (2.19 g, 73 %) which was used without further purification. Melting point: 172-175 ^oC; ^1H-NMR ($(CD_2)_3O$, 400 MHz): δ 7.60 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H, C_6H_4), 7.37, (dd, J_1 = 7.7 Hz, J_2 = 1.7 Hz, 1H, C_6H_4), 7.28 (td, J_1 = 7.4 Hz, J_2 = 1.3 Hz, 1H, C_6H_4), 7.16 (td, J_1 = 7.9 Hz, J_2 = 1.8 Hz, 1H, C_6H_4), 3.53 (s, 2H, CH_2), 1.34 (s, 3H, CH_3). ^{13}C-NMR ($(CD_2)_3O$, 400 MHz): 205.6, 172.4, 136.7, 133.0, 131.4, 128.7, 127.6, 125.9, 54.4, 39.0, 18.6.



2-(2-bromobenzyl)-*N*^{1},*N*^{3}-bis(2-(*tert*-butyl)phenyl)-2-methylmalonamide (35): 2-(2-bromobenzyl)-2-methylmalonic acid (529.0 mg, 1.76 mmol) was dissolved in 2 mL of $SOCl_2$ and stirred at 60 ^oC for 4 hours. The excess $SOCl_2$ was removed by rotary evaporation under reduced pressure. The crude product was redissolved in $CHCl_3$ (5 mL) and subjected to rotary evaporation under reduced pressure. This process of redissolving the crude product in $CHCl_3$ followed by rotary evaporation was repeated a total of three times to ensure complete removal of any remaining $SOCl_2$. The crude product was redissolved in $CHCl_3$ (10 mL) and cooled to 0 ^oC followed by the addition of *t*-butylaniline (0.42 mL, 3.87 mmol) on ice. The reaction mixture

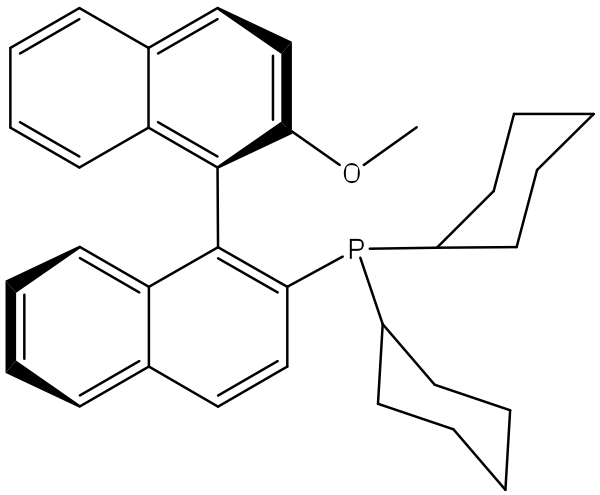
was allowed to warm to room temperature and left stirring for one hour. The reaction mixture was cooled back down to 0 ^{o}C followed by the addition of triethyamine (0.54 mL, 3.87 mmol) on ice. The reaction mixture was warmed to room temperature and refluxed overnight. The reaction was cooled to room temperature and extracted with 1 M HCl (4 x 10 mL). The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified via flash chromatography eluting at 40 % EtOAc:Hexanes to afford N^1, N^3-dibenzyl-2-(2-bromophenethyl)-2-methylmalonamide, compound **35** (365.5 mg, 43 %) as a white solid. Melting point: 125-130 ^{o}C; R_f = 0.45 (SiO_2, 15 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 8.67 (s, 2H, NH), 7.64-7.09 (m, 13H, C_6H_4), 3.80 (s, 2H, CH_2), 1.73 (s, 3H, CH_3), 1.39 (s, 18H, $(CH_3)_3$). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 170.7, 142.8, 136.2, 134.8, 133.3, 131.6, 128.8, 128.0, 127.8, 127.0, 126.4, 126.1, 56.3, 42.9, 34.4, 30.5, 29.7, 18.4.



(*R*,*S*)-*N*,1-bis(2-(*tert*-butyl)phenyl)-3-methyl-2-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide (36): A 10 mL Schlenk flask was charged with 2-(2-bromobenzyl)-N^1,N^3-bis(2-(*tert*-butyl)phenyl)-2-methylmalonamide, compound **35** (50 mg, 0.091 mmol), Cs_2CO_3 (17.6 mg, 0.127 mmol), $Pd(OAc)_2$ (5 mol %) and Cy_2MOP (10 mol %). The flask was evacuated and backfilled with argon a total of three times. Toluene (1.5 mL) was added via syringe under a

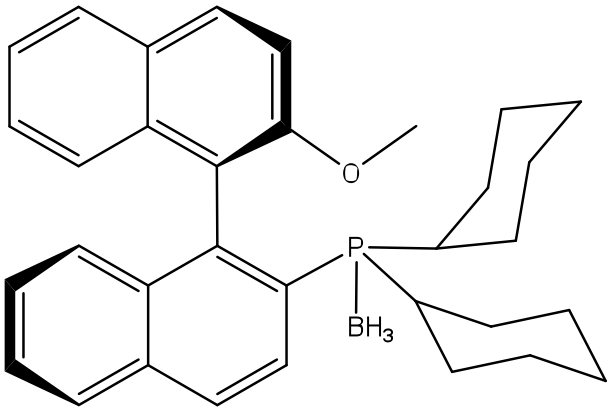
stream of argon, the reaction was sealed and left stirring at 100 ^{o}C for 48 hours. The reaction mixture was cooled to room temperature, diluted with CH_2Cl_2 (10 mL) and filtered through a short plug of celite. The crude product was purified via column chromatography eluting at 30 % EtOAc:Hexanes to afford compound **36** (42.3 mg, 99 %) as a white solid. Melting point: 175-180 ^{o}C; R_f = 0.40 (SiO_2, 15 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 8.37 (s, 1H, NH), 7.65-7.61 (m, 1H, C_6H_4), 7.47-7.26 (m, 5H, C_6H_4), 7.15-7.09 (m, 2H, C_6H_4), 7.05-7.01 (m, 2H, C_6H_4), 6.95 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1H, C_6H_4), 6.22-6.18 (m, 1H, C_6H_4), 3.78 (d, J = 15.6 Hz, 1H, CH_2), 3.08 (d, J = 15.6 Hz, 1H, CH_2), 1.77 (s, 3H, CH_3), 1.35 (s, 9H, $(CH_3)_3$), 1.24 (s, 9H, $(CH_3)_3$) (When the ^{1}H-NMR spectrum was ran in C_6D_6 there appeared to be a 13 % impurity which is most likely due to debromination of the starting material). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 173.3, 168.3, 147.4, 142.3, 140.7, 135.9, 135.2, 132.2, 129.4, 129.0, 128.9, 127.5, 127.2, 127.0, 126.6, 126.5, 125.9, 124.0, 123.9, 116.6, 50.7, 35.7, 35.2, 34.7, 34.5, 31.60, 31.55, 31.4, 30.54, 30.50, 25.3, 24.1, 20.7 (There are extra signals in the aliphatic region of the ^{13}C-NMR spectrum which might correspond to the debrominated starting material, however there is not enough evidence at this time to distinguish between the peaks corresponding to compound **36** and the peaks corresponding to compound **37**). HPLC (Chiaralcel OD-H column, eluting with 0.65 mL/min 2 % *i*-PrOH:Hexanes), t_R minor = 10.9 min (peak area = 1088767.27), t_R major = 12.9 min (peak area = 16418111.55), *ee* = 88 %

3.6 Synthesis of Cy_2MOP and $Cy_2MOP{\cdot}BH_3$



(*R)*-2(Dicyclohexylphosphino)-2'-methoxy-1,1'-binaphthyl) (41): A 10 mL Schlenk flask was charged with (*R*)-2'-methoxy-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate[46] (150 mg, 0.347 mmol), dicyclohexylphosphonium tetrafluoroborate[46] (99.2 mg, 0.347 mmol), $Pd(OAc)_2$ (5 mol %) and 1,1'-(bisdiisopropyl) phosphino ferrocene (6 mol %). The flask was evacuated and backfilled with argon a total of three times. DMSO (2.0 mL) and *N,N'*-diisopropylethylamine (0.6 mL) were added via syringe under a stream of argon. The reaction was sealed and left stirring at 120 ^{o}C for 48 hours. The reaction mixture was cooled to room temperature, diluted with EtOAc (40 mL) and washed with water (5 x 20 mL). The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified via flash chromatography eluting at 3 % EtOAc:Hexanes to afford (*R)*-2(Dicyclohexylphosphino)-2'-methoxy-1,1'-binaphthyl) (133 mg, 80 %) as a white solid. Melting point: 180-182 ^{o}C; $R_f = 0.50$ (SiO_2, 5 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 8.0 (d, J = 9.0 Hz, 1H, $C_{10}H_6$), 7.92-7.87 (m, 1H, $C_{10}H_6$), 7.84 (d, J = 8.1 Hz, 1H, $C_{10}H_6$), 7.78 (dd, J_1 = 8.5 Hz, J_2 = 1.3 Hz, 1H,

$C_{10}H_6$), 7.46-7.40 (m, 1H, $C_{10}H_6$), 7.39 (d, J = 9.0 Hz, 1H, $C_{10}H_6$), 7.29-7.23 (m, 1H, $C_{10}H_6$), 7.23-7.11 (m, 3H, $C_{10}H_6$), 6.91 (d, J = 8.6 Hz, 1H, $C_{10}H_6$), 3.75 (s, 3H, CH_3), 1.87-1.46 (m, 12H, C_6H_{11}), 1.29-0.86 (m, 11H, C_6H_{11}). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 154.37, 154.36, 143.56, 143.25, 135.20, 135.02, 134.30, 134.28, 133.56, 133.33, 133.26, 129.61, 129.22, 129.19, 128.52, 127.88, 127.82, 126.97, 126.95, 126.72, 126.26, 126.18, 125.99, 125.80, 123.19, 122.56, 122.48, 112.27, 60.43, 55.51, 35.44, 35.29, 34.54, 34.40, 30.68, 30.59, 30.50, 30.43, 30.01, 29.97, 29.90, 29.87, 27.67, 27.65, 27.59, 27.53, 27.39, 27.31, 27.20, 26.58, 26.40 (observed complexity results from C-P coupling). ^{31}P-NMR ($CDCl_3$, 400 MHz): δ -8.90. HPLC (Chiaralcel OD-H column, eluting with 0.65 mL/min 2 % *i*-PrOH:Hexanes), t_R major = 5.6 min (peak area = 7053734.00), t_R minor = 7.5 min (peak area = 401749.73), t_R minor = 10.9 min (peak area = 916931.01).

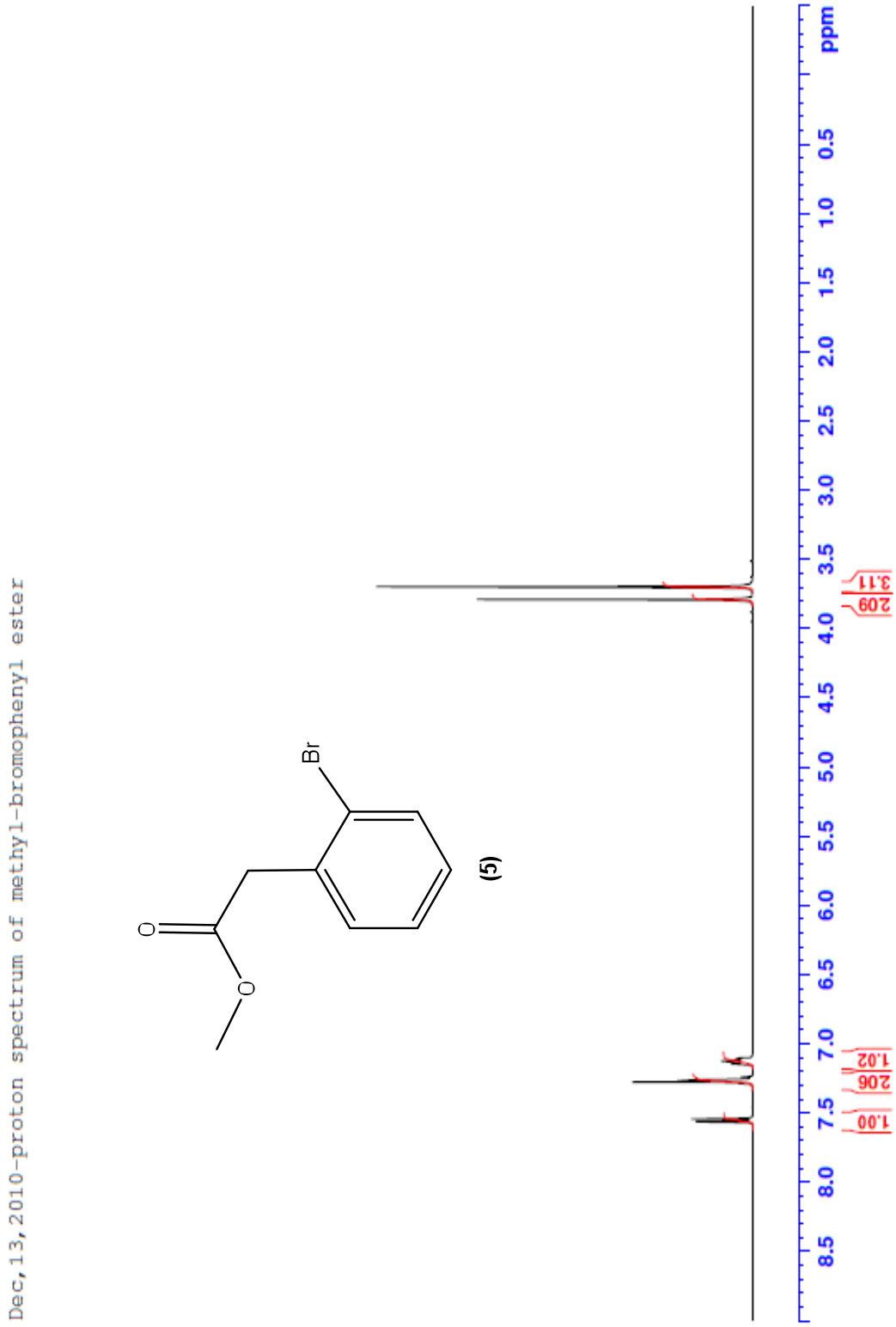


(*R)*-2(Dicyclohexylphosphino)-2'-methoxy-1,1'-binaphthyl) borane complex (42): A 10 mL Schlenk flask was charged with (*R)*-2(Dicyclohexylphosphino)-2'-methoxy-1,1'-binaphthyl), compound **41** (304.6 mg, 0.634 mmol) followed by addition of THF (0.6 mL) and cooled to 0 ^{o}C. A 1 M solution of borane THF complex (0.76 mL, 0.76 mmol) was added to the rapidly stirring mixture at 0 ^{o}C. The reaction mixture was stirred on ice for 30 minutes, diluted with EtOAc (10 mL) and extracted with water (50 mL). The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified via flash chromatography eluting with 3 % EtOAc:Hexanes to afford (*R)*-2(Dicyclohexylphosphino)-2'-methoxy-1,1'-binaphthyl) borane complex (228.5 mg, 73 %) as a white crystalline material. Melting point: 255-260 ^{o}C; R_f = 0.40 (SiO_2, 5 % EtOAc:Hexanes); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 8.10-7.80 (m, 5H, C_6H_{10}), 7.54-7.49 (m, 1H, C_6H_{10}), 7.42 (d, *J* = 9.1 Hz, 1H, $C_{10}H_6$), 7.33-7.28 (m, 1H, $C_{10}H_6$), 7.26-7.21 (m, 1H, $C_{10}H_6$), 7.17-7.12 (m, 2H, $C_{10}H_6$), 6.82 (d, *J* = 8.5 Hz, 1H, $C_{10}H_6$), 3.77 (s, 3H, CH_3), 2.1-0.4 (m, 26H, C_6H_{11}). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 155.13, 142.37, 134.98, 134.18, 134.17, 133.67, 130.45, 129.89, 129.81, 128.84, 127.94, 127.80, 127.48, 127.31, 127.22, 127.10, 126.84, 126.63, 126.13, 125.87, 125.63, 125.43, 123.40, 120.35, 120.32, 55.78, 34.61, 34.29, 34.09, 33.77, 28.22, 27.65, 27.48, 27.21, 27.10, 27.01, 26.89, 26.87, 26.48, 26.37, 25.93, 25.92, 25.80, 25.79, 21.05, 14.20 (observed complexity results from C-P coupling).

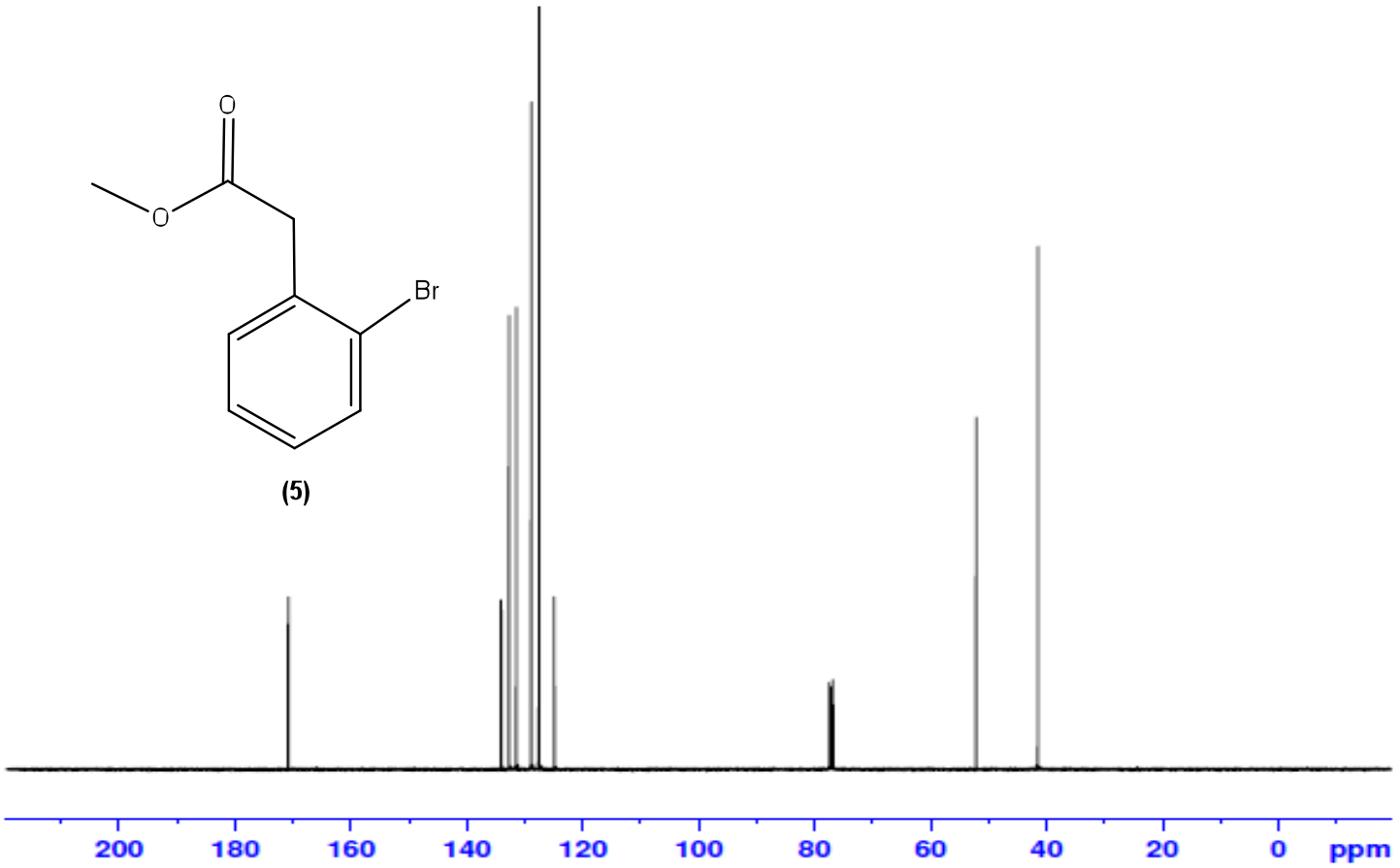
4 Conclusion

A non commercially available ligand, (*R)*-2(Dicyclohexylphosphino)-2'-methoxy-1,1'-binaphthyl), (*R*)-Cy_2MOP, has been synthesized in good yield, 80 %, and proved to be very effective in the palladium catalyzed intramolecular desymmetrization of di-nitrogen malonamides. The efficiency of this ligand can be attributed to the increased steric bulk provided by the dicyclohexylphosphino group, which speeds up the rate of reductive elimination thus increasing the rate at which the active catalyst is regenerated. Additionally an enantio- and diastereoselective Buchwald-Hartwig reaction has been developed through the desymmetrization of 2-(2-bromobenzyl)-N^1,N^3-bis(2-(*tert*-butyl)phenyl)-2-methylmalonamide using palladium/Cy_2MOP as the catalyst system to produce (3*R*,S_a)-*N*,1-bis(2-(*tert*-butyl)phenyl)-3-methyl-2-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide in excellent yield, with high enantio- and diastereoselectivity (99 %, 88 % *ee*). The absolute configuration of the formed diastereomer was determined by x-ray crystallography. This is the first example in which an enantio- and diastereoselective Buchwald-Hartwig reaction takes place in a single step from the preferential N-arylation of prochiral di-nitrogen malonamides. Application of the palladium/Cy_2MOP catalyst system in the intramolecular desymmetrization reaction also resulted in the formation of six membered ring benzomorpholinone heterocycles in excellent yield (88-99 %) however the *ee*`s of the products were quite low (3-20 % *ee*). A seven membered ring benzodiazepineone heterocycle was also synthesized using palladium/Cy_2MOP and the product was isolated in 50 % yield. Furthermore several synthetic routes towards the synthesis of five membered ring oxindoles were explored but none of them were successful. Lastly the synthesis of a precatalyst was attempted using Cy_2MOP and Pd(II)Me_2TMEDA however the isolated product does not appear to be the desired precatalyst.

5 Appendix:

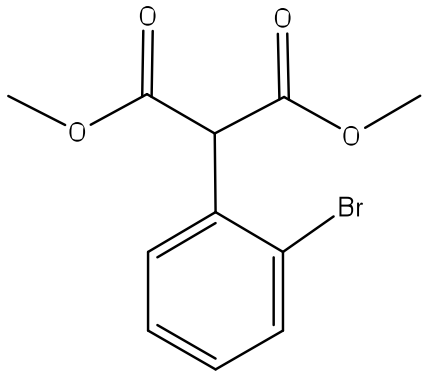

Dec,13,2010-proton spectrum of methyl-bromophenyl ester
Br
O
O
(5)
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.00
2.06
1.02
2.09
3.11

Dec,13,2010-Carbon spectrum of methyl-bromophenyl ester



(5)

May21,2011-dimethyl-bromophenyl malonate



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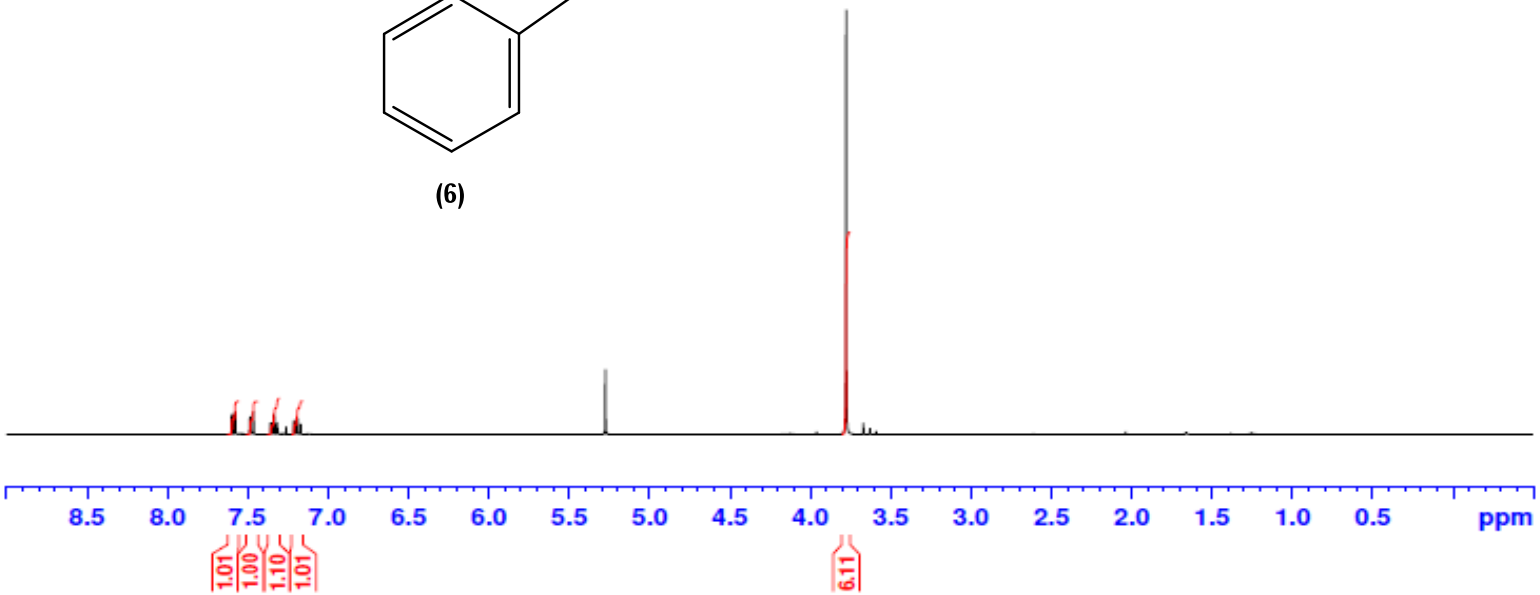
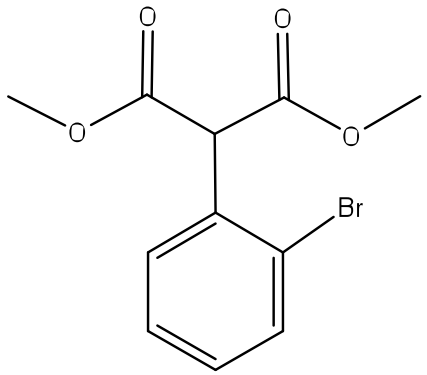


May21,2011-dimethyl-bromophenyl malonate, carbon spectrum



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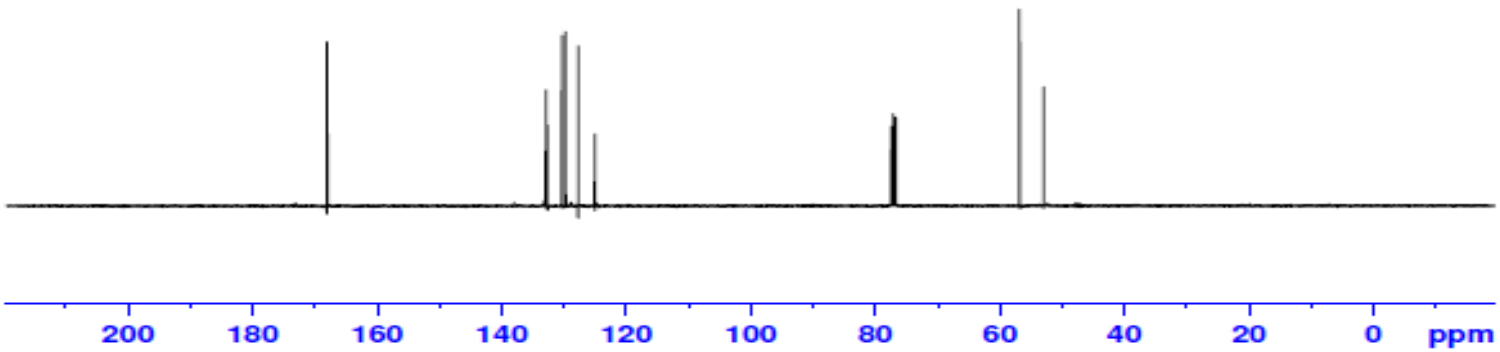
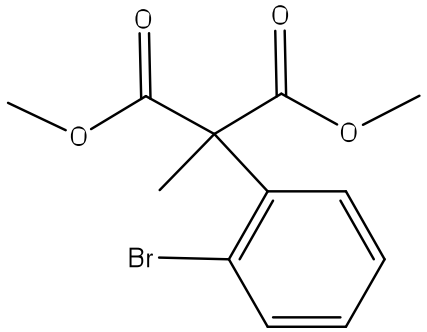
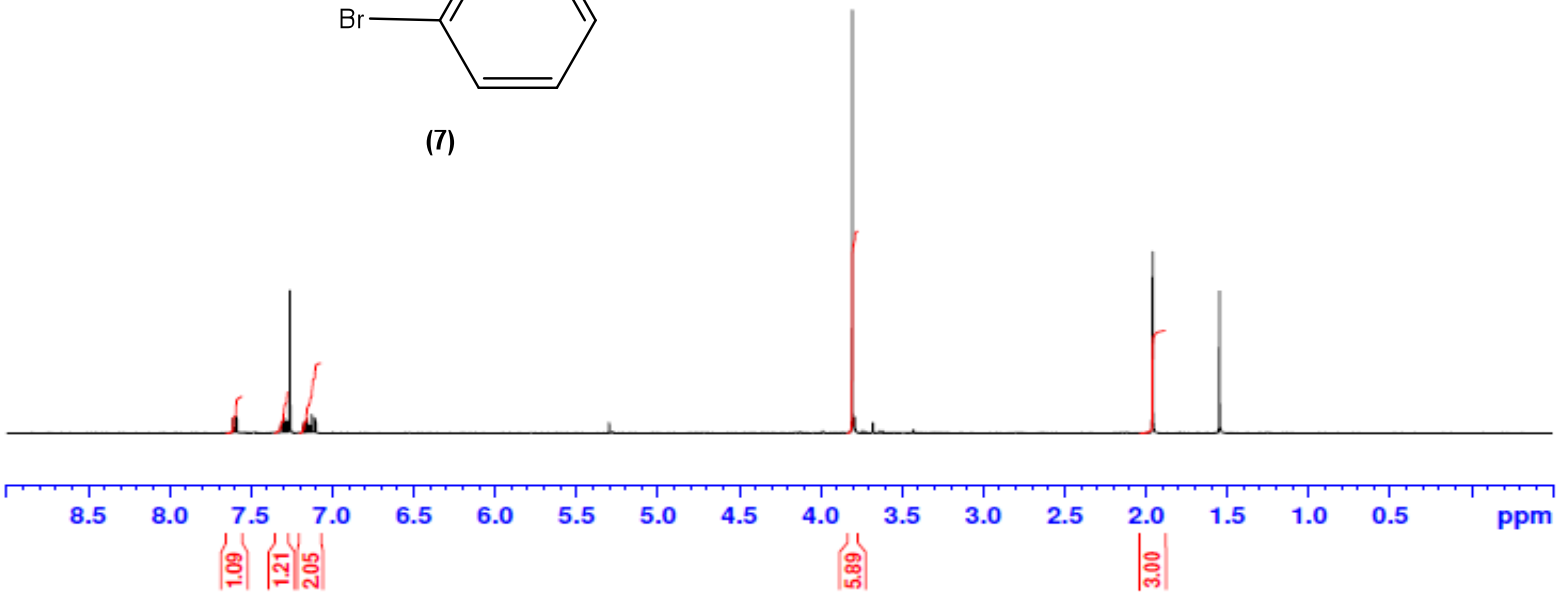


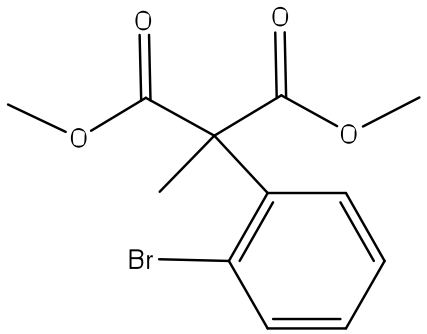
July16,2011-proton spectrum of dimethyl-methyl-bromophenylmalonate



(7)

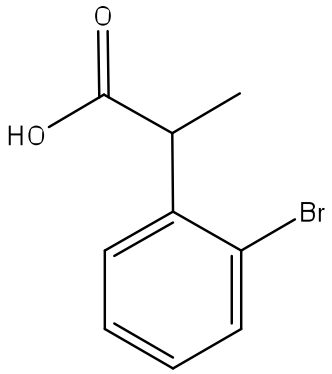


jan24,2011-di-methyl-methyl-bromophenyl ester 5-mem ring precursor carbon spec



(7)

August5,2011-5-mem ring precursor decarboxylated compound



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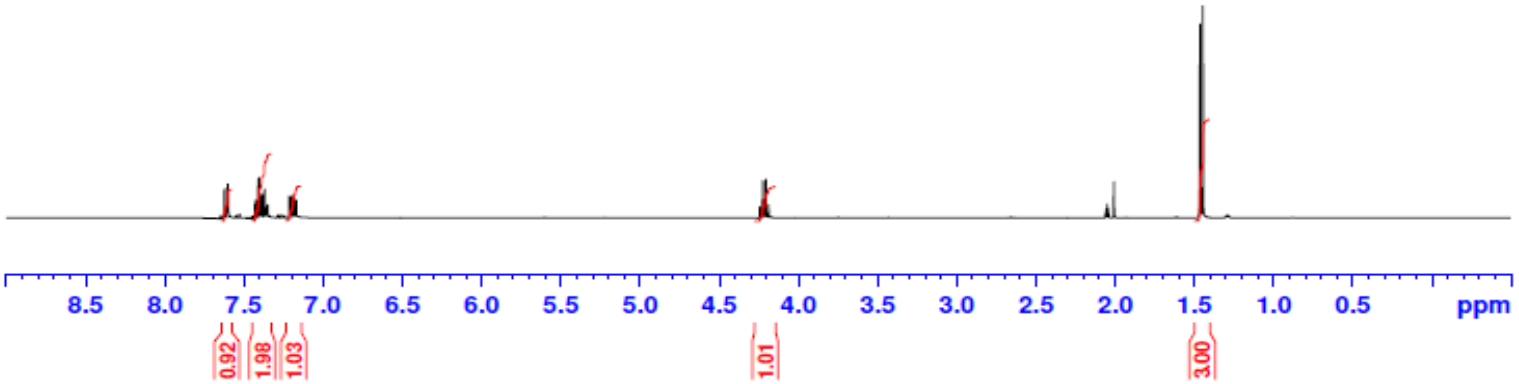
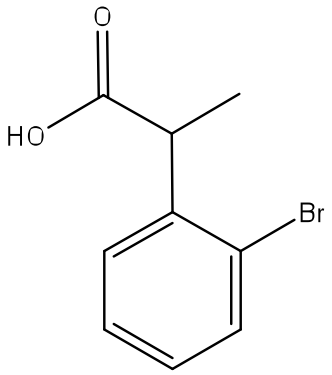


August5,2011-5-mem ring precursor decarboxylated compound(carbon spectrum)



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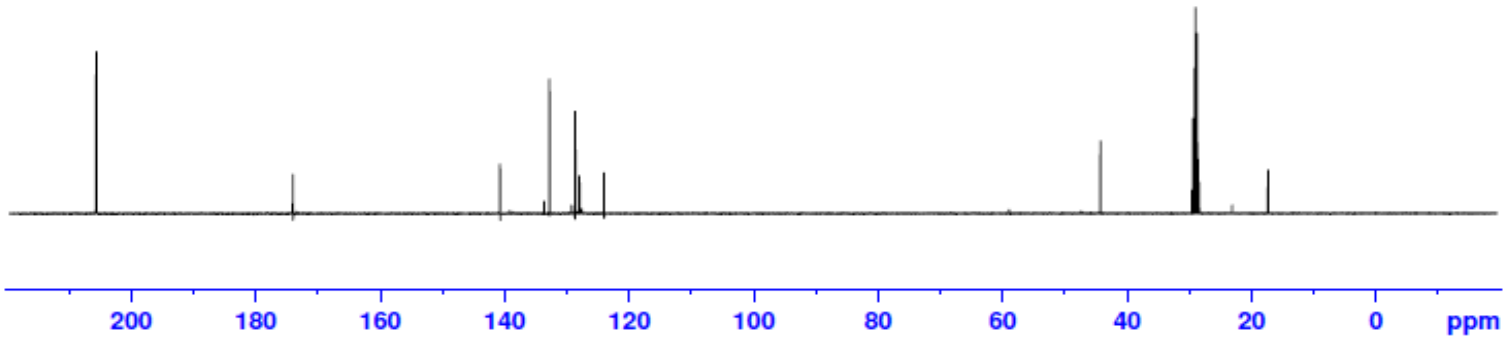
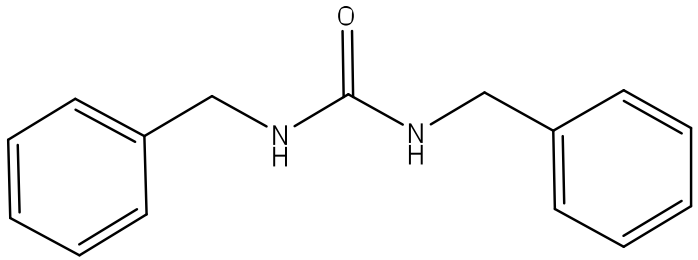


August29,2011-dibenzylurea



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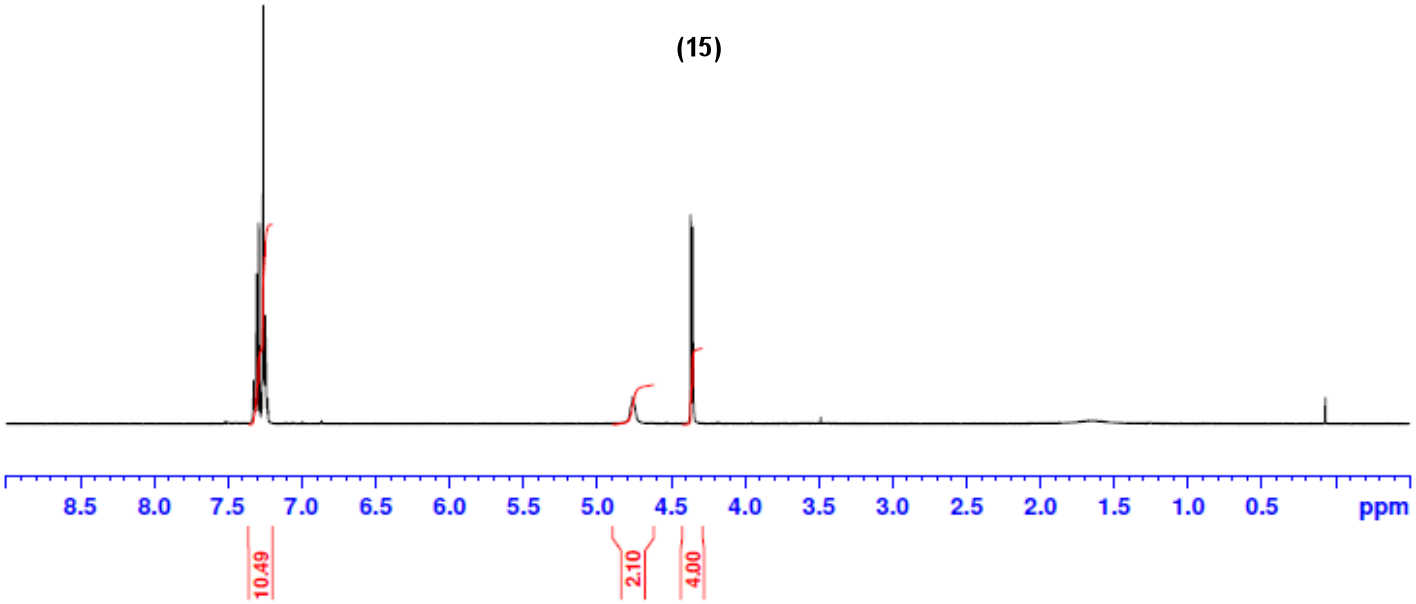

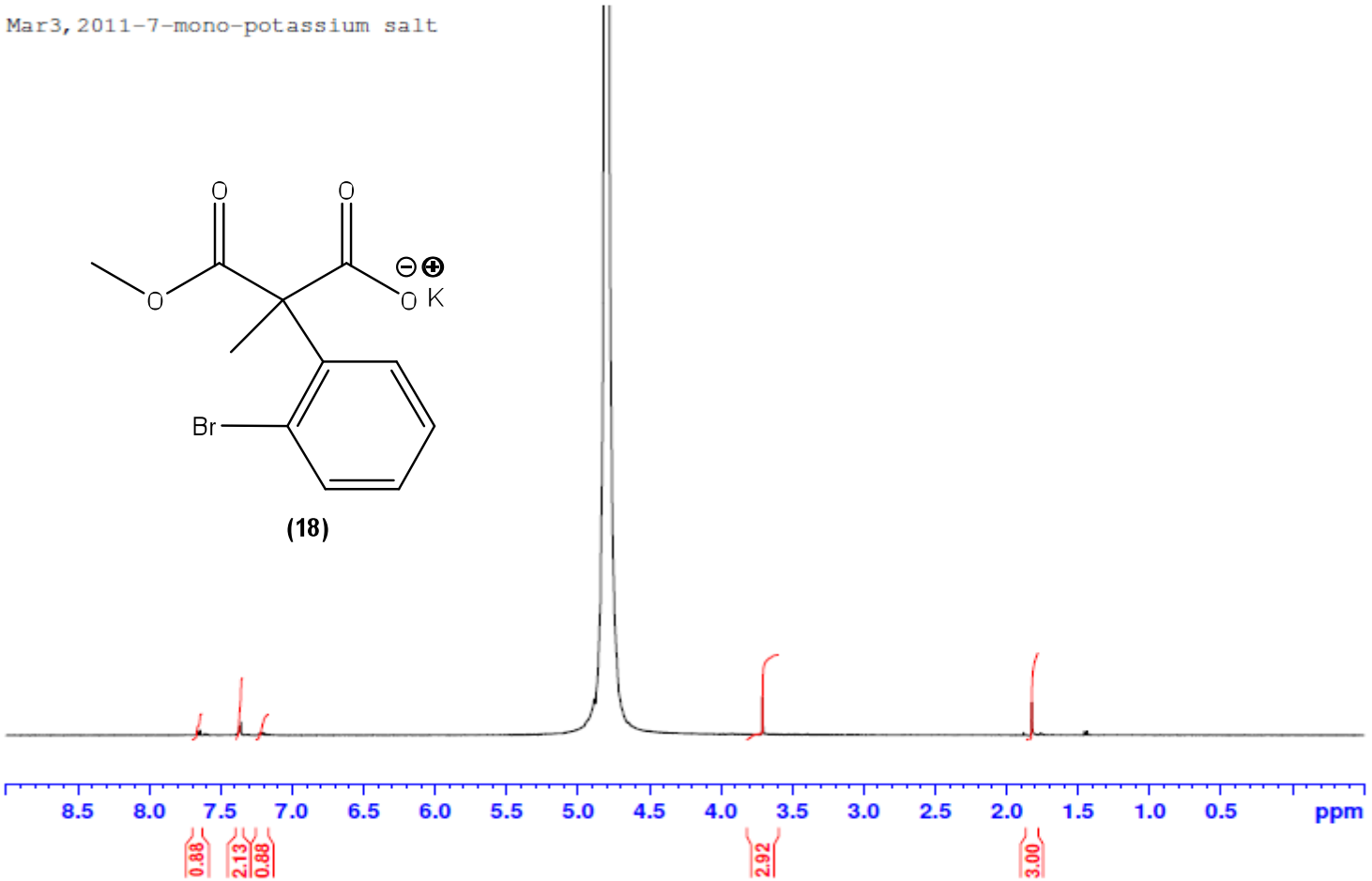
Mar3,2011-7-mono-potassium salt
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O
O K
Br
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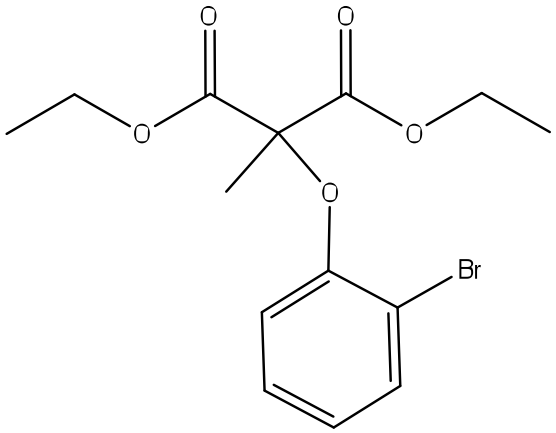
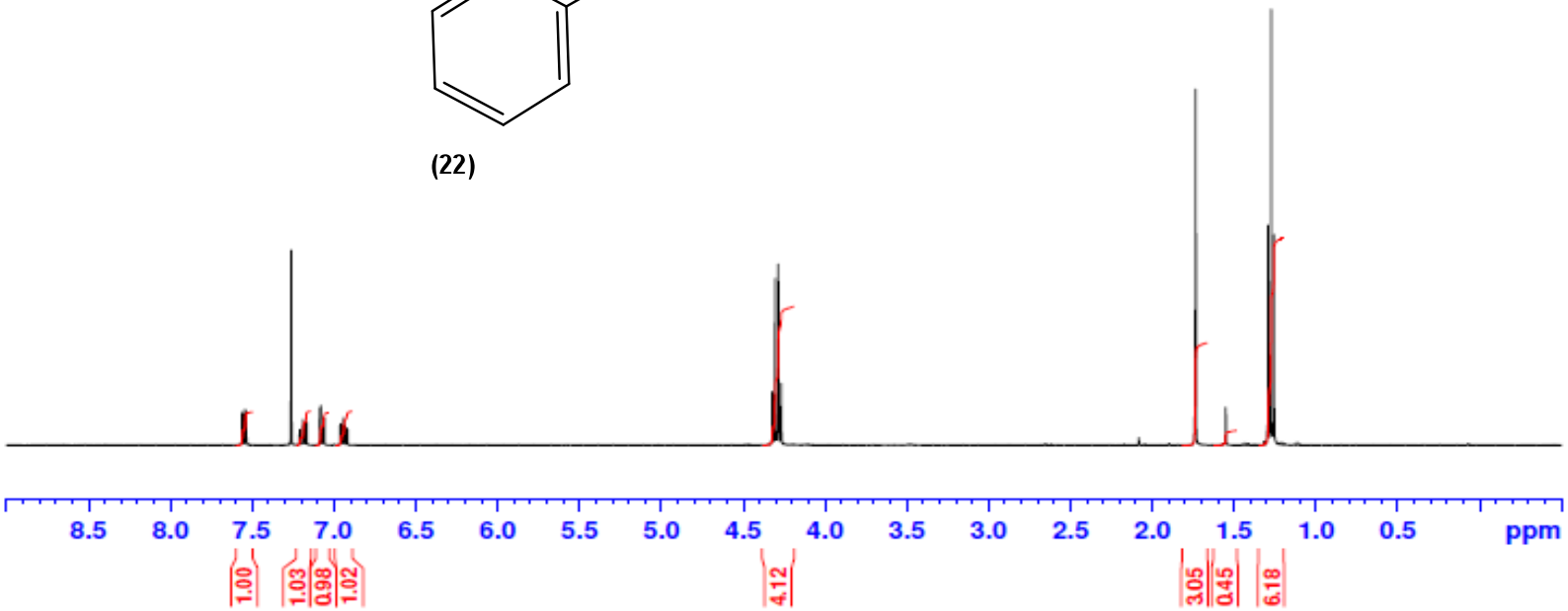
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.88
2.13
0.88
2.92
3.00

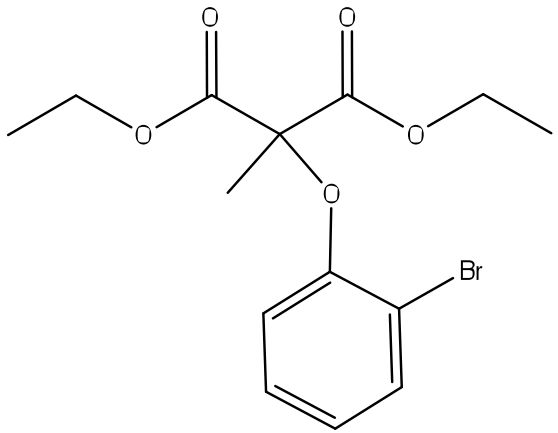
Mar.7,2011-proton spectrum of benzomorpholinone precursor diethyl ester



(22)

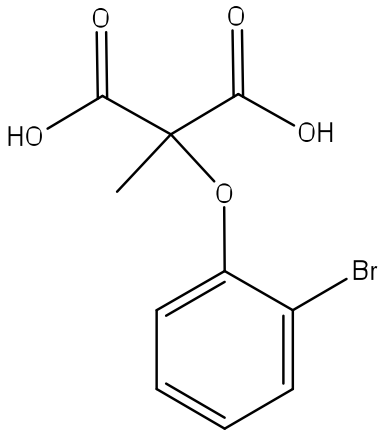


Mar.7,2011-carbon spectrum of benzomorpholinone precursor diethyl ester

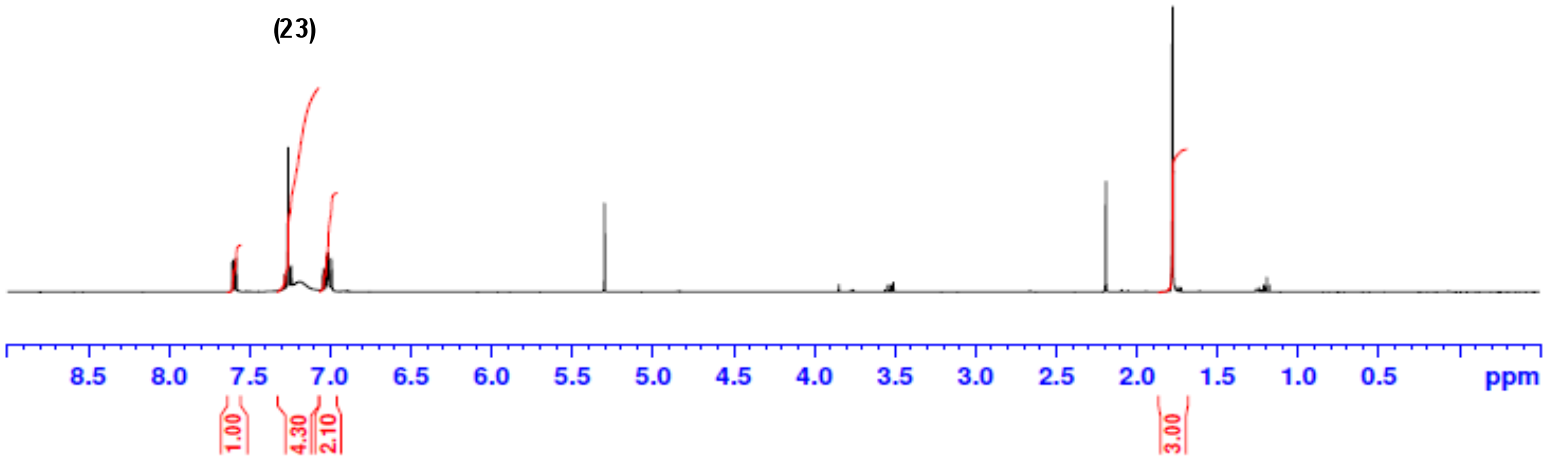


(22)

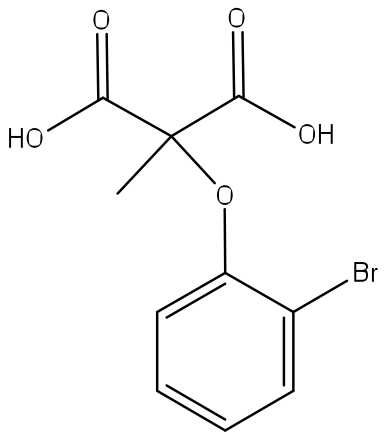
May18,2011-6mem ring with oxygen di acid



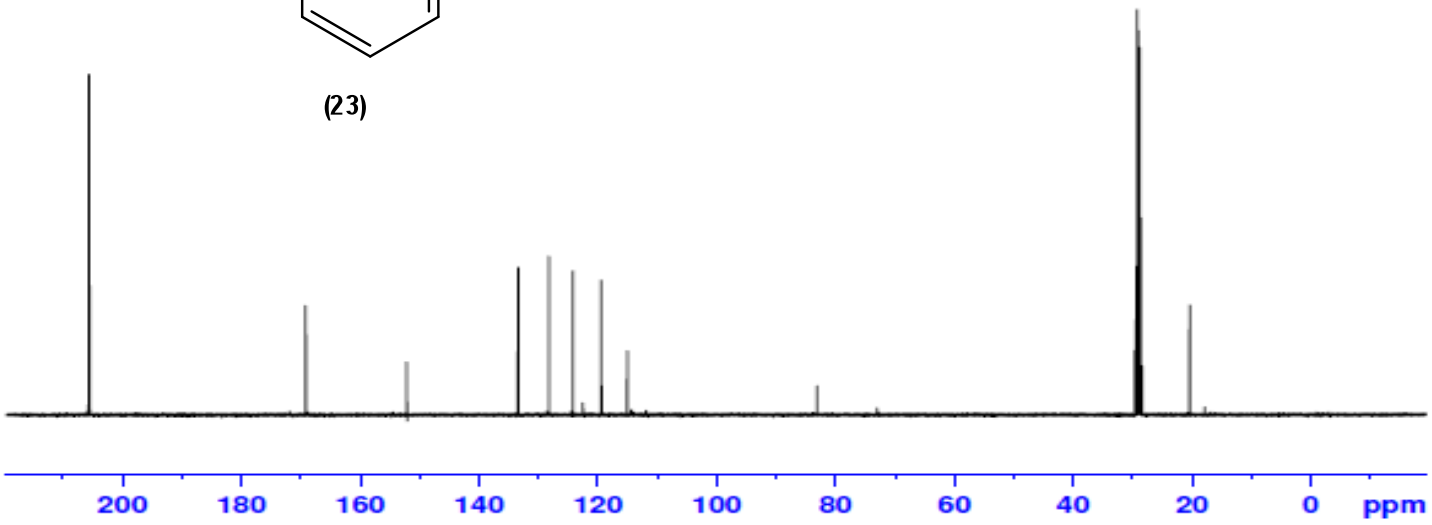
(23)



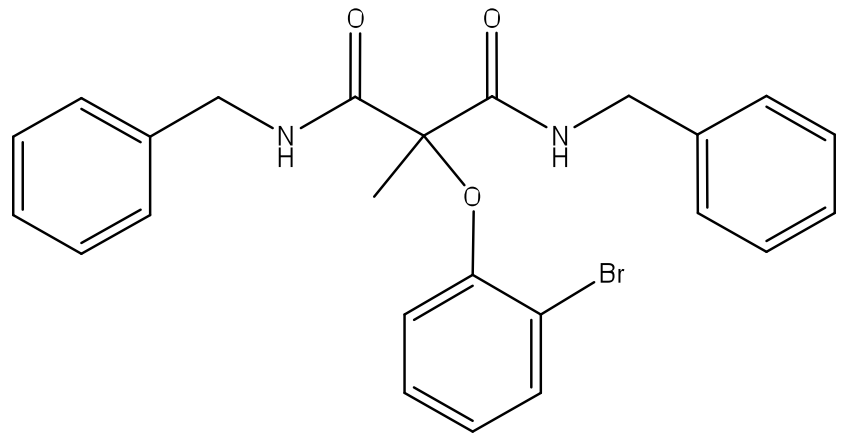
june26,2011-Benzomorpholinone precursor di-carboxylic acid 13C-NMR



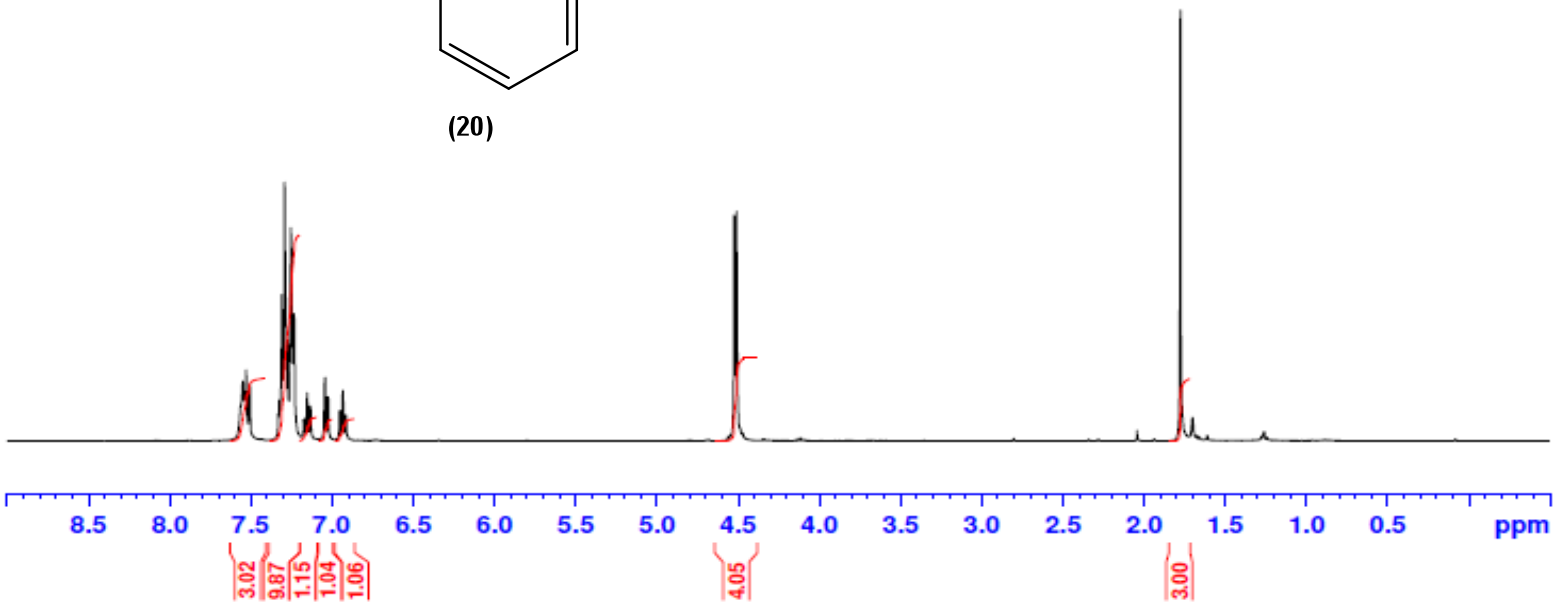
(23)



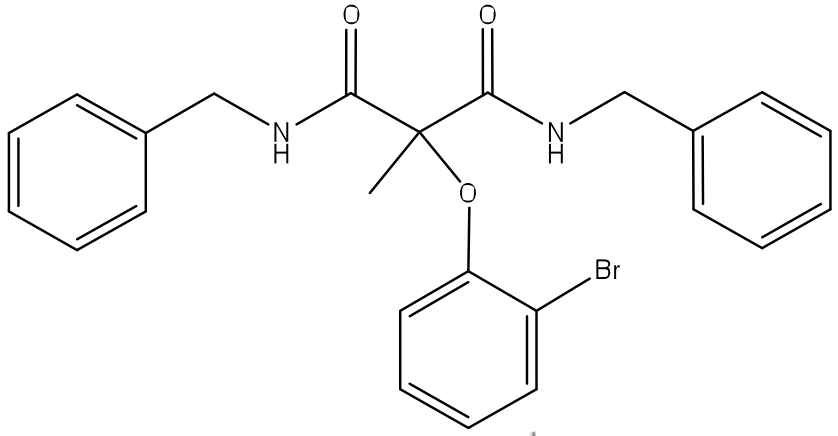
May31,2011-benzomorpholinone precursor dibenzylamide



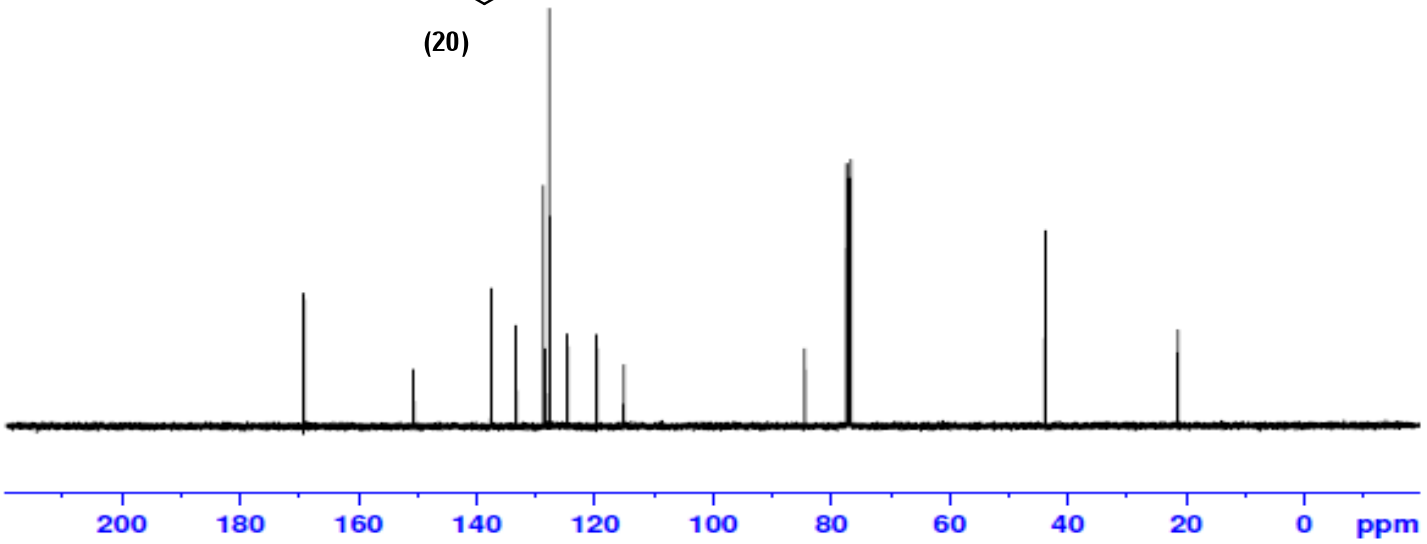
(20)



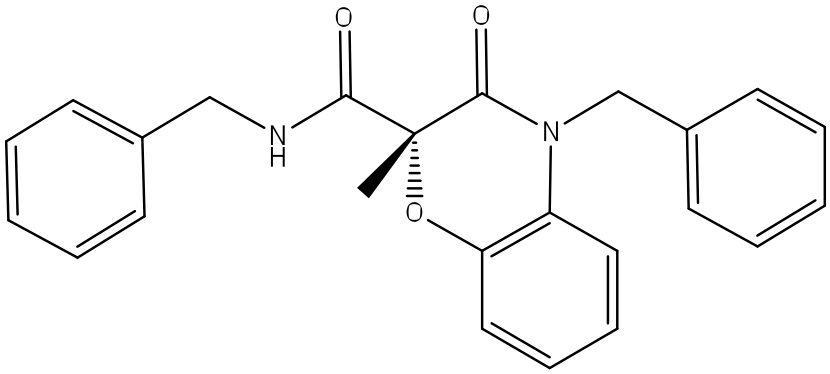
May31,2011-benzomorpholinone precursor dibenzylamide carbon spectrum



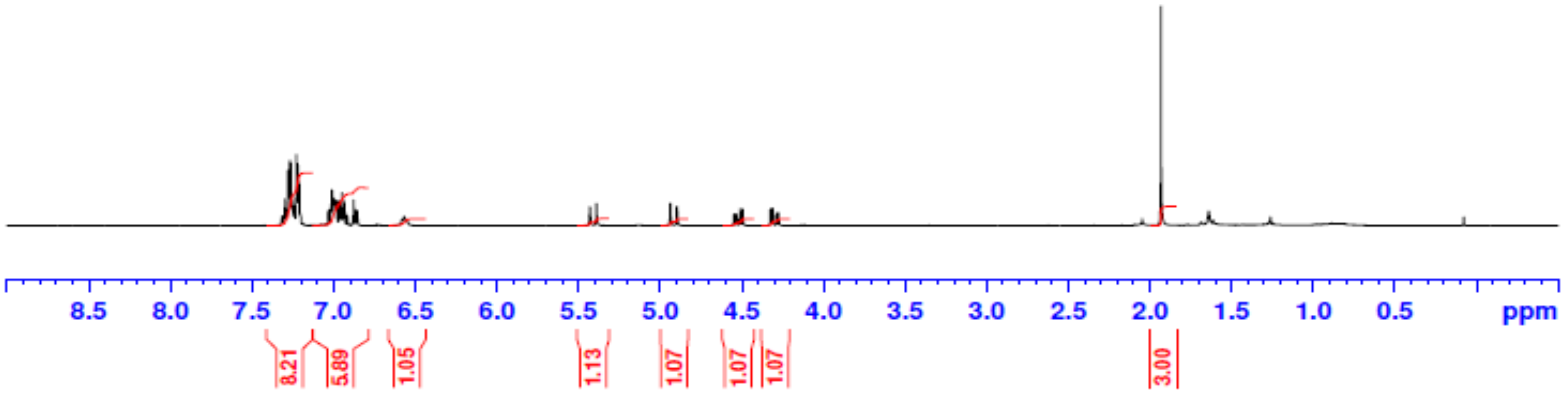
(20)



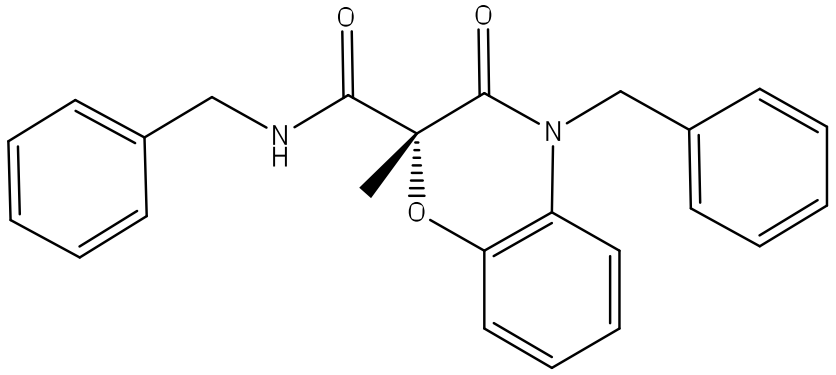
July13,2011-BnBenzomorpholinone proton spectrum



(21)



July13,2011-BnBenzomorpholinone Carbon spectrum



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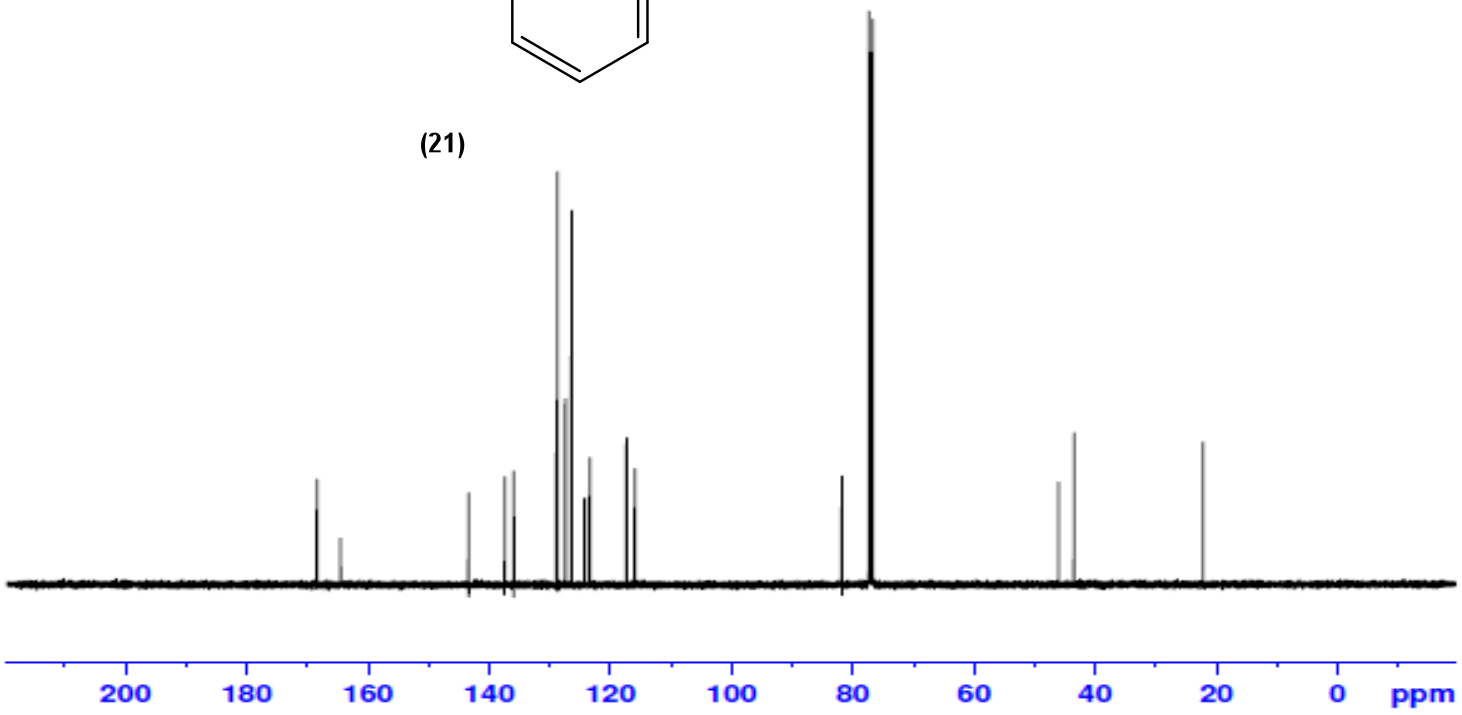
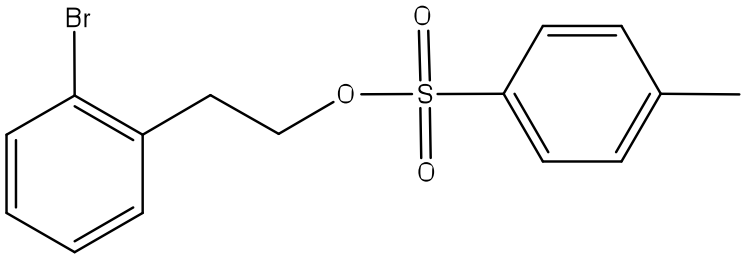
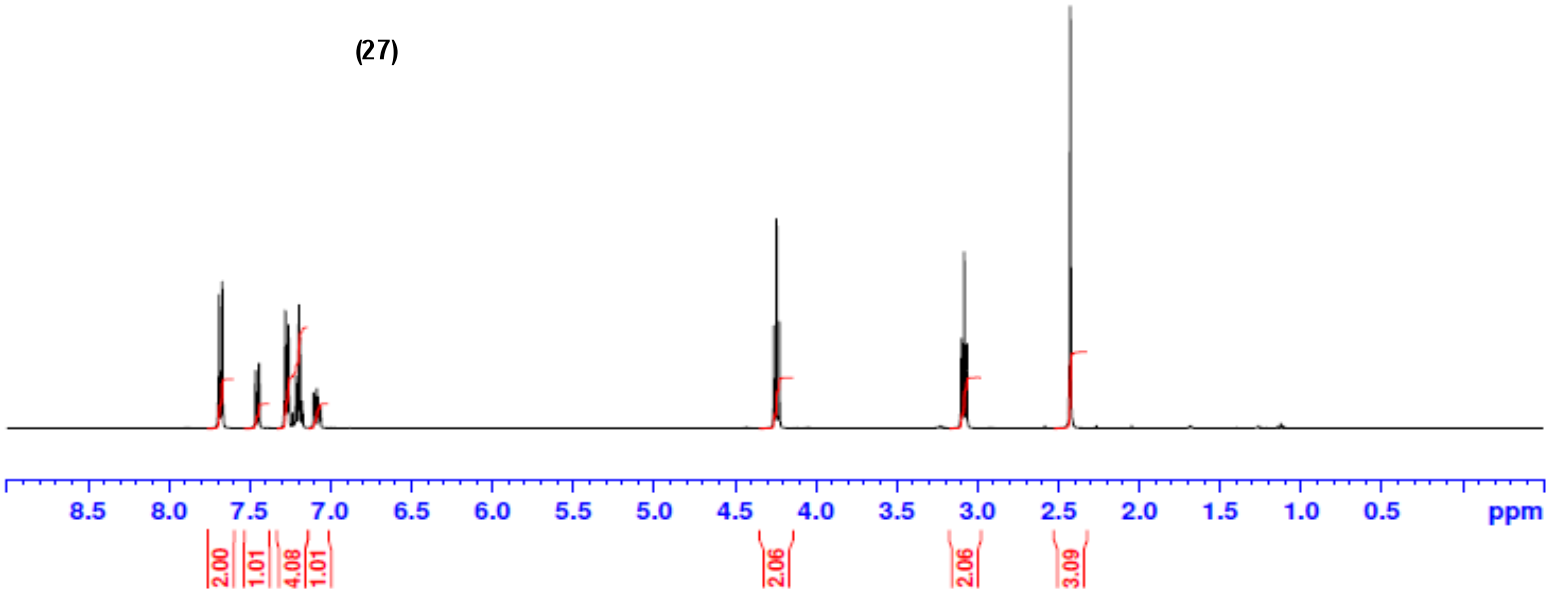


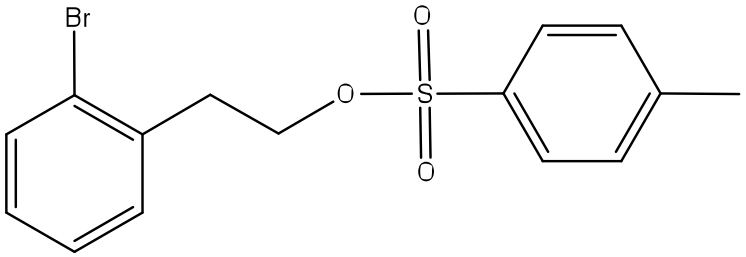
Dec,13,2010-H-NMR of tosylate ester



(27)



Dec,13,2010-C13-NMR of tosylate ester



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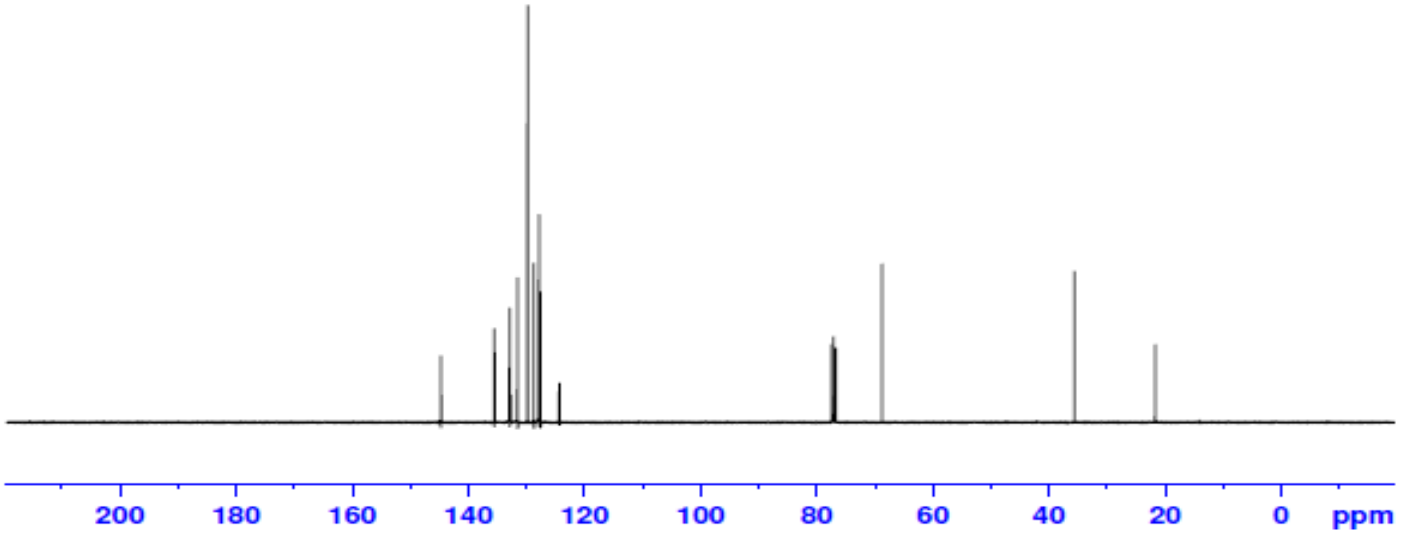
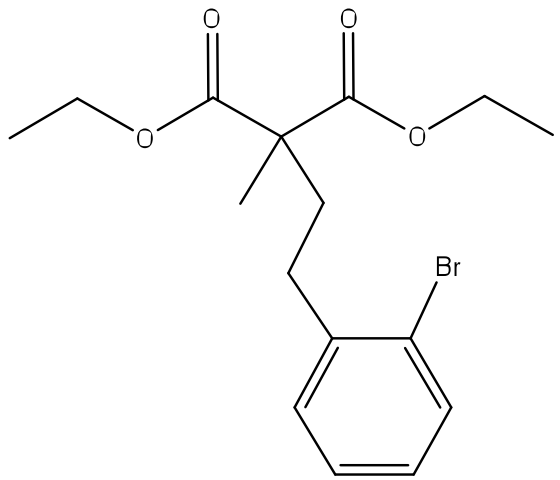
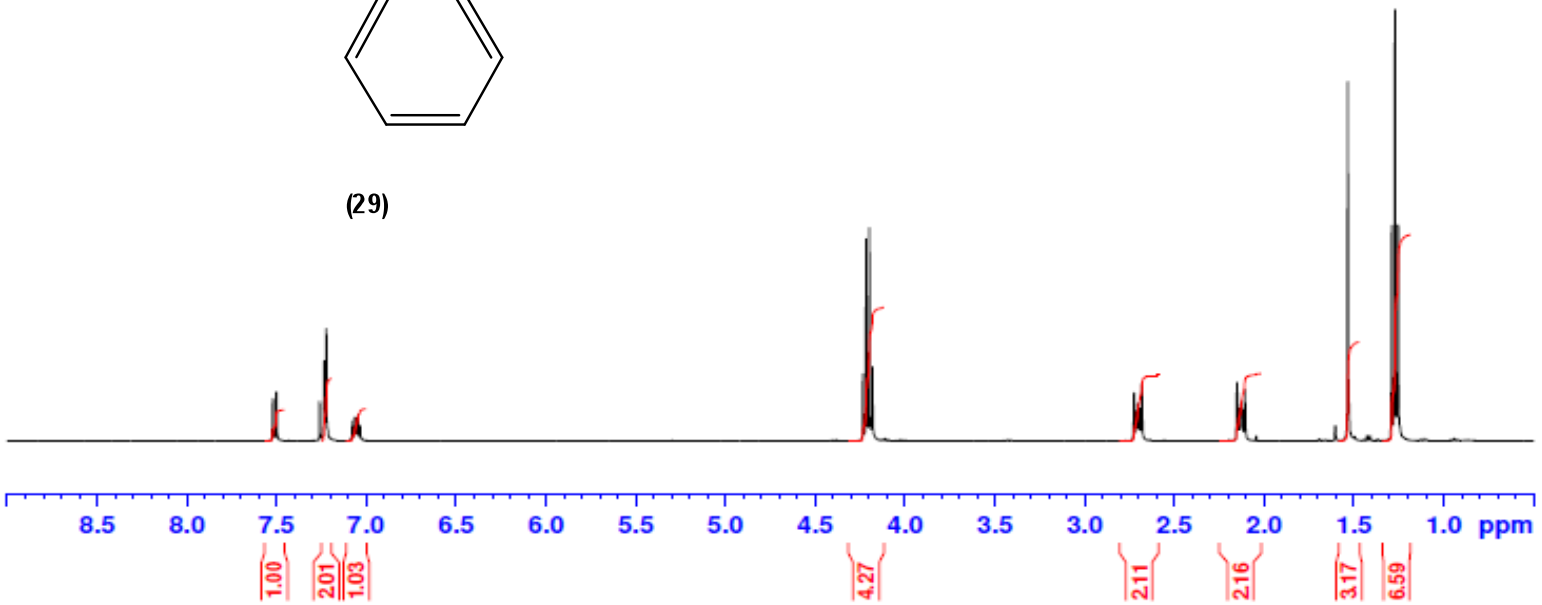


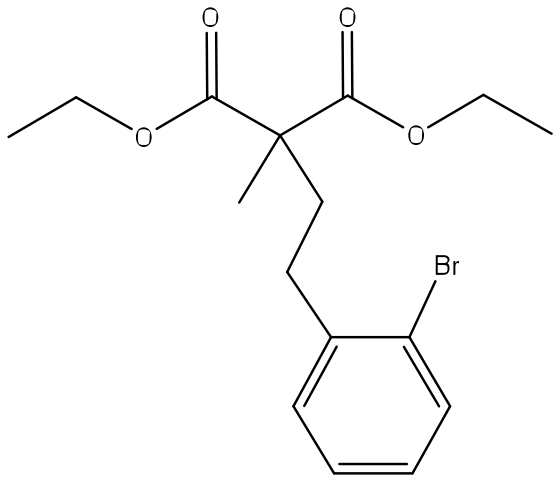
jan19,2011-7-membered ring diester precursor



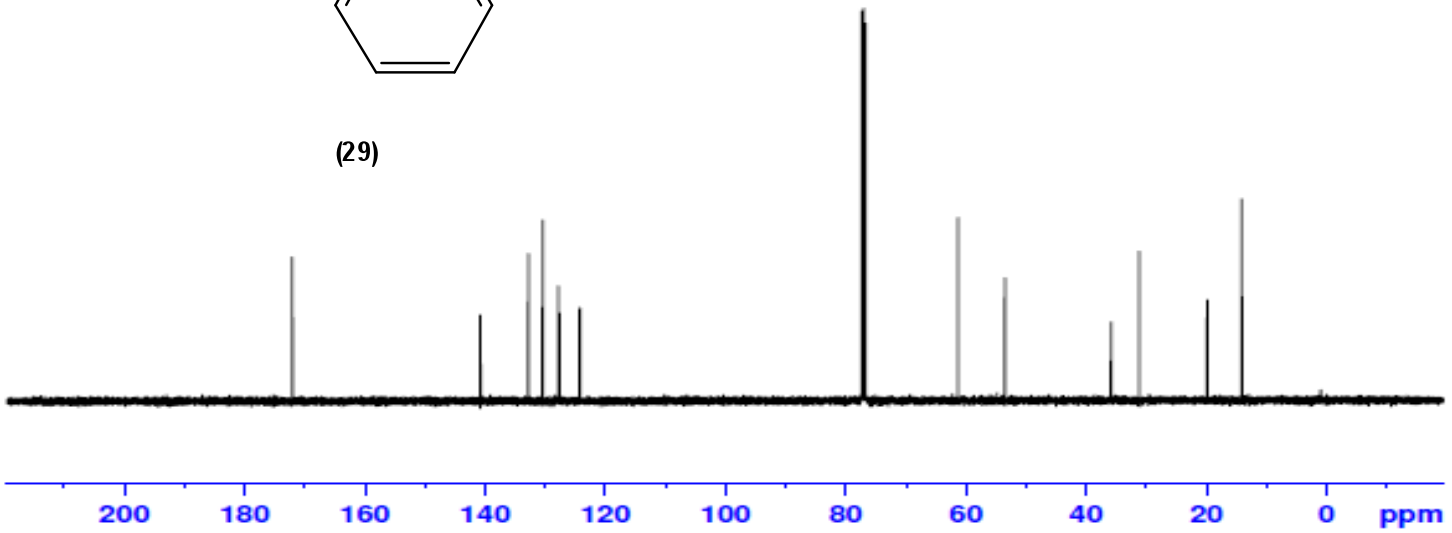
(29)



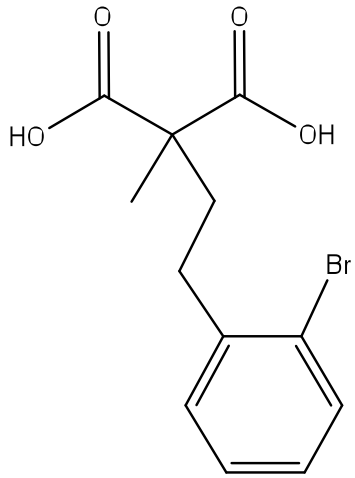
jan19,2011-7-membered ring diester precursor carbon spectrum



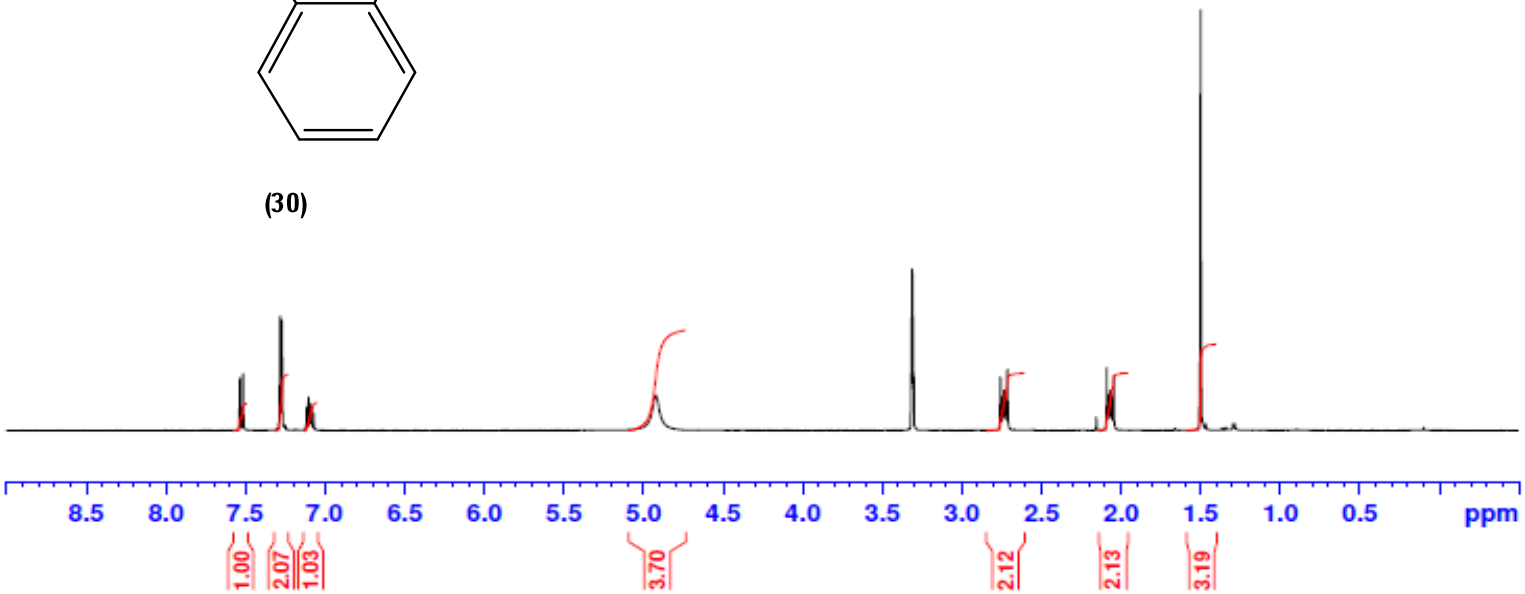
(29)



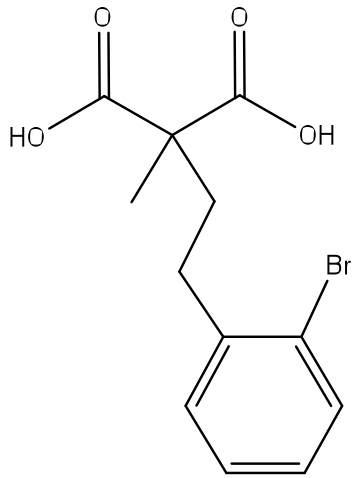
jan21,2011-7-mem-ring di acid precursor



(30)

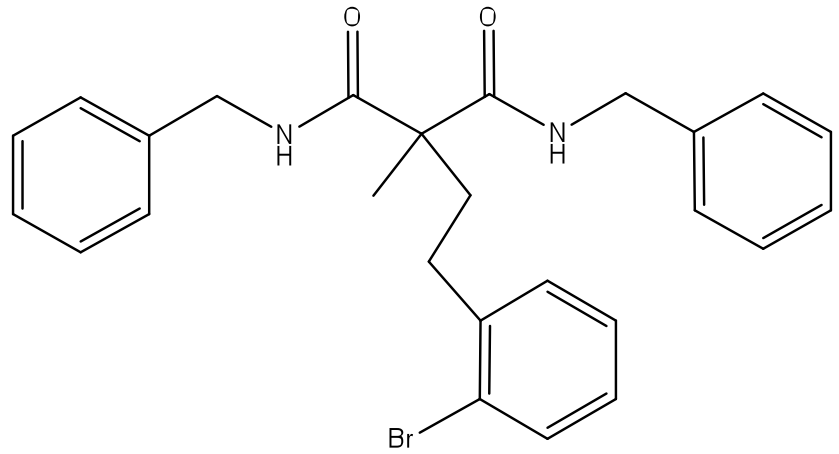


jan21,2011-7-mem-ring di acid precursor carbon spectrum

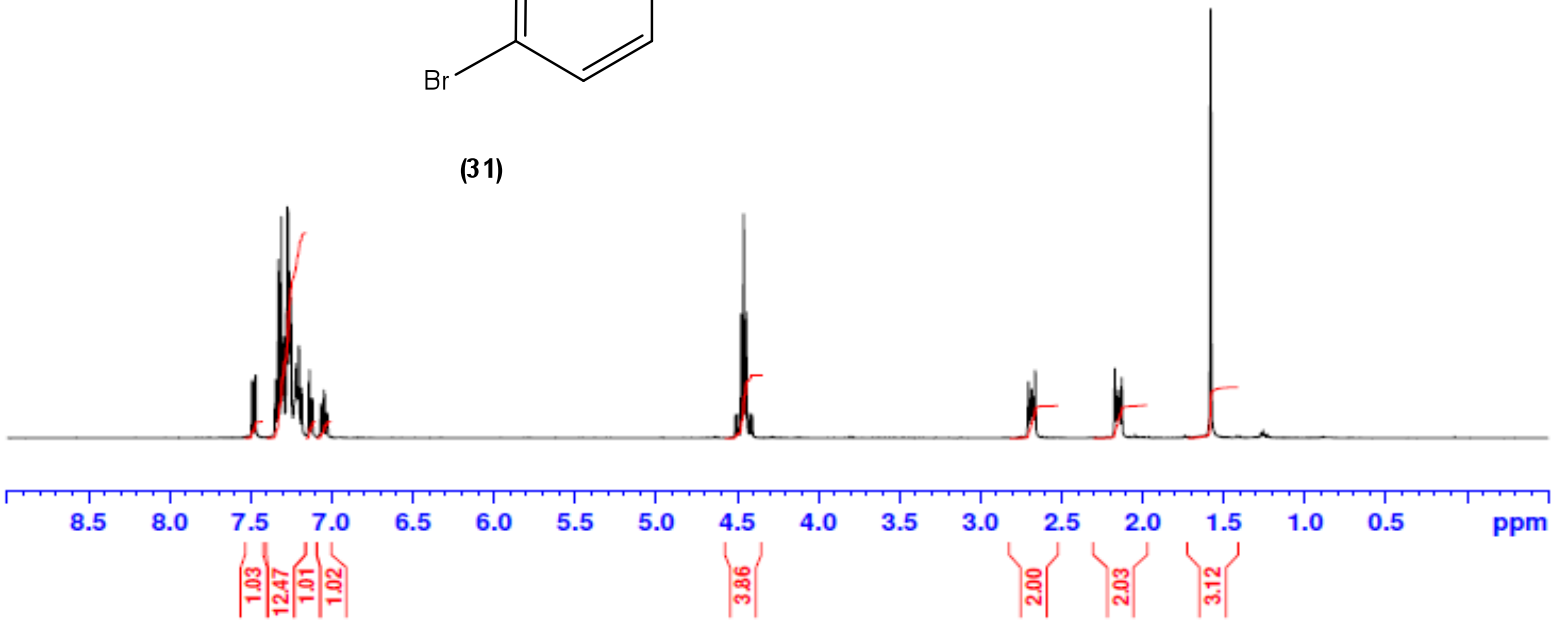


(30)

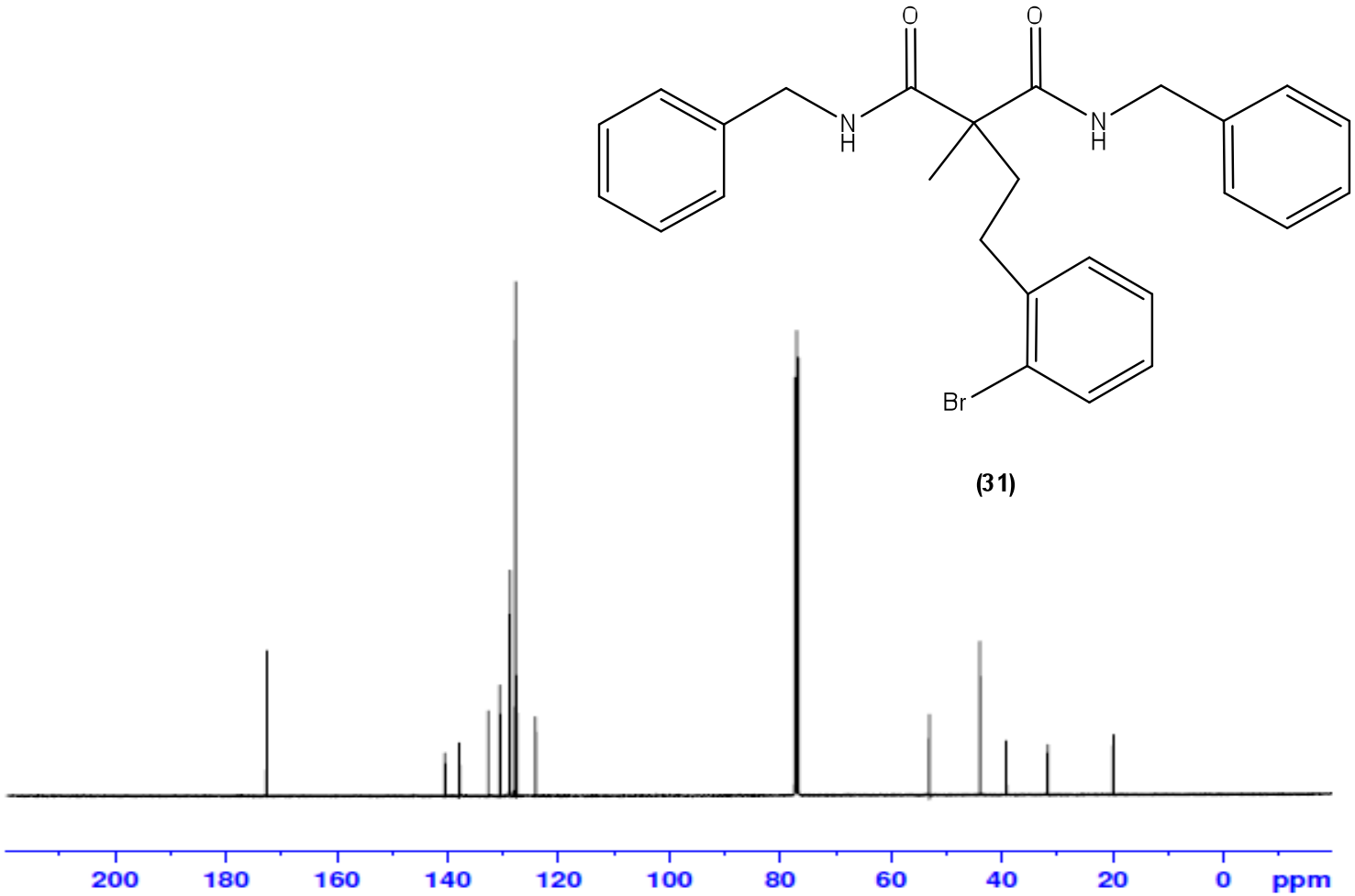
Feb6, 2011- 7-membered ring heterocycle precursor-di benzylamide



(31)

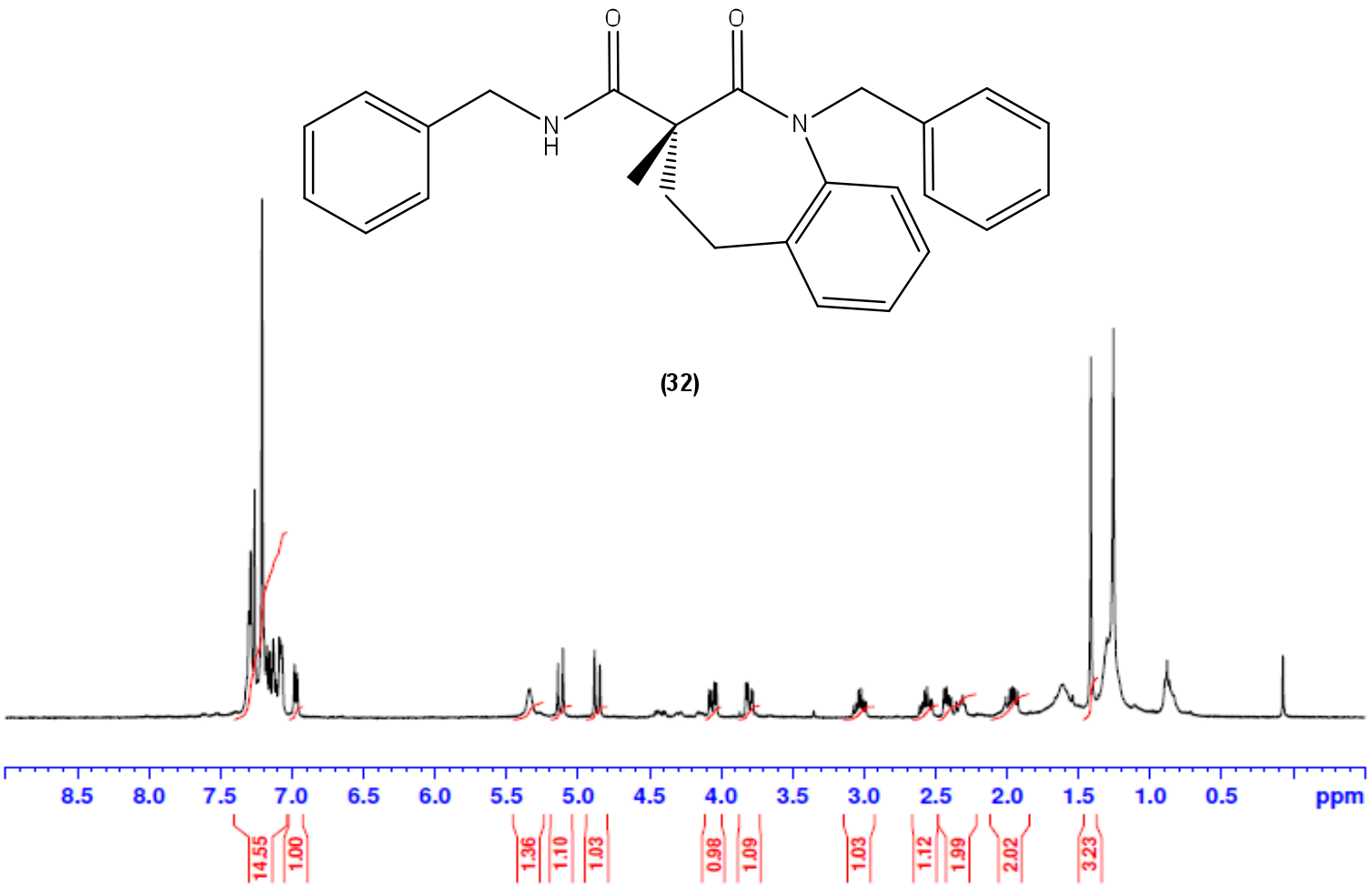


Feb6,2011- 7-membered ring heterocycle precursor-di benzylamide carbon spectru



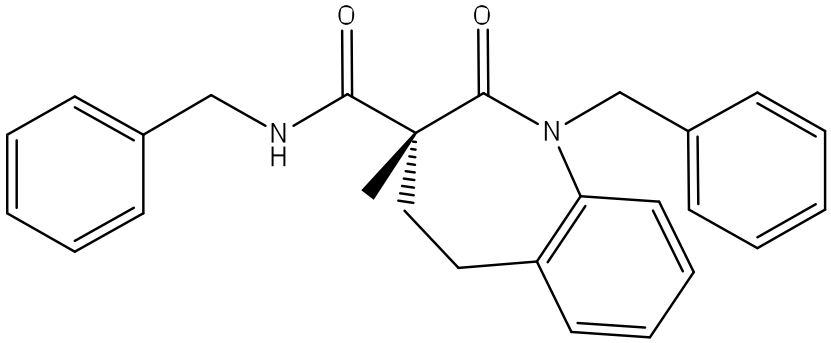
(31)

July9,2011-seven membered ring heterocycle proton spectrum



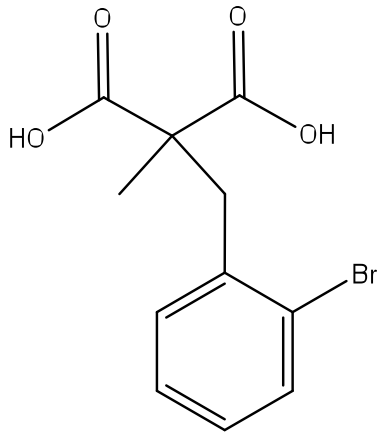
(32)

July9,2011-seven membered ring heterocycle carbon spectrum

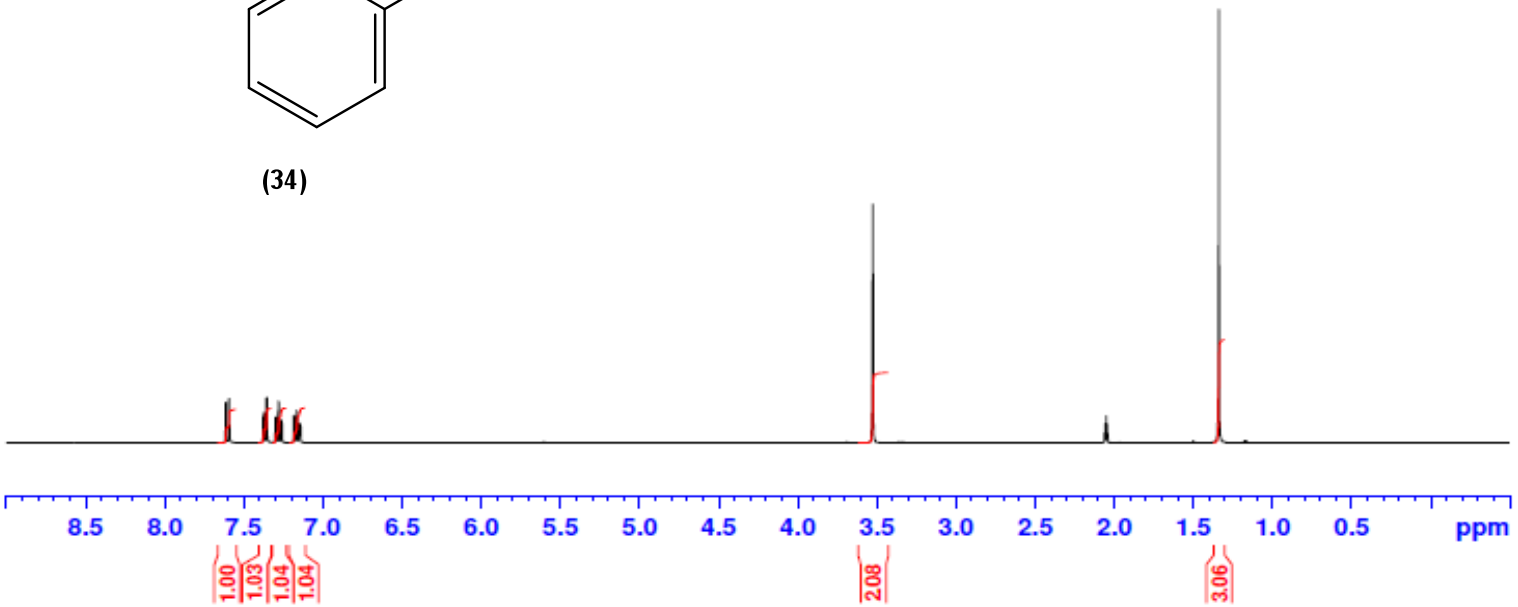


(32)

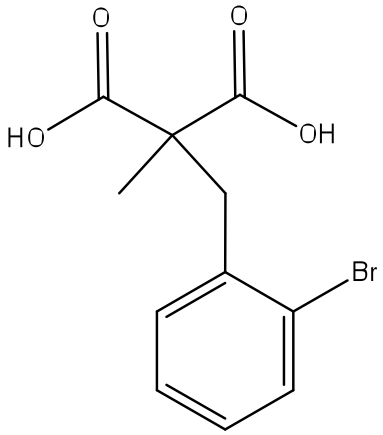
July16,2011-6membered ring quinolinone precursor di-acid



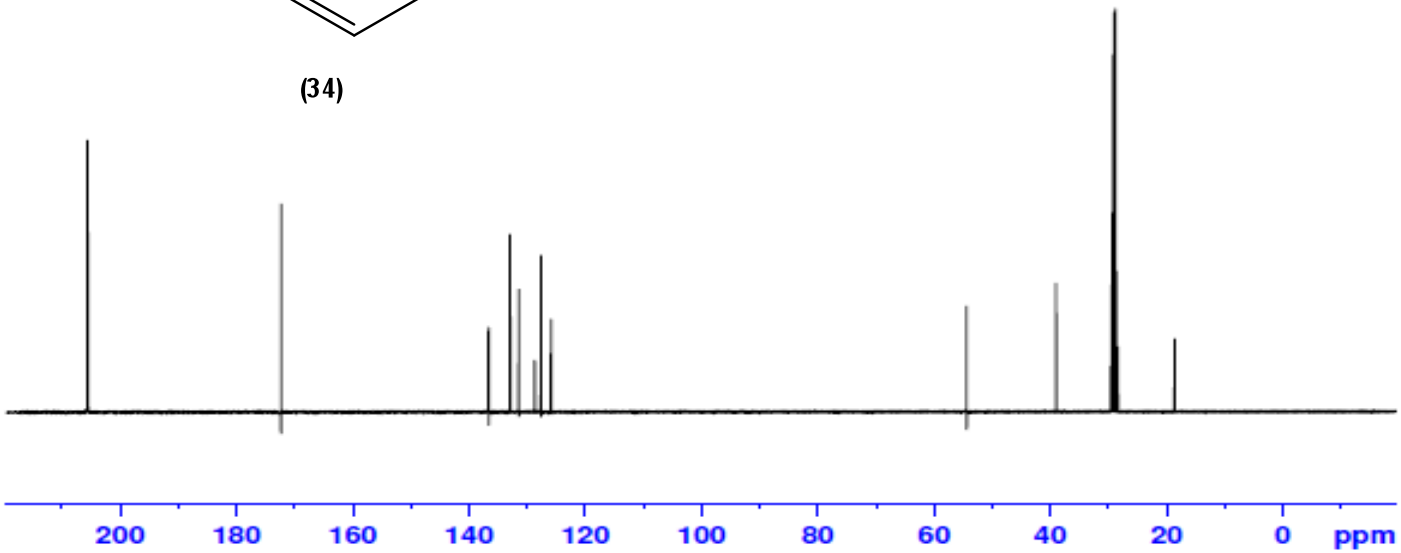
(34)



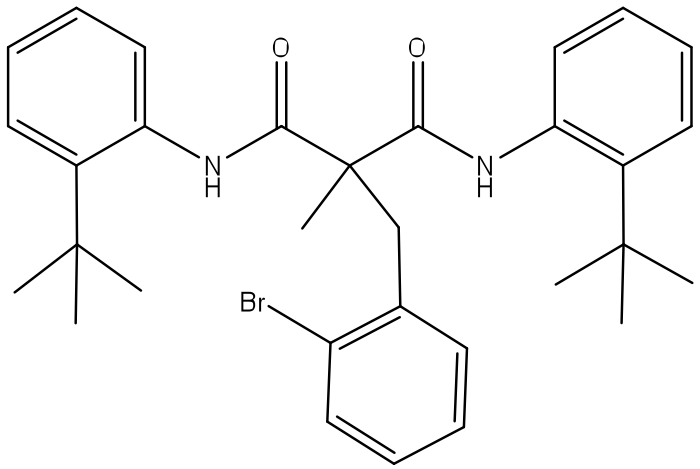
July16,2011-6membered ring quinolinone precursor di-acid-carbon spectrum



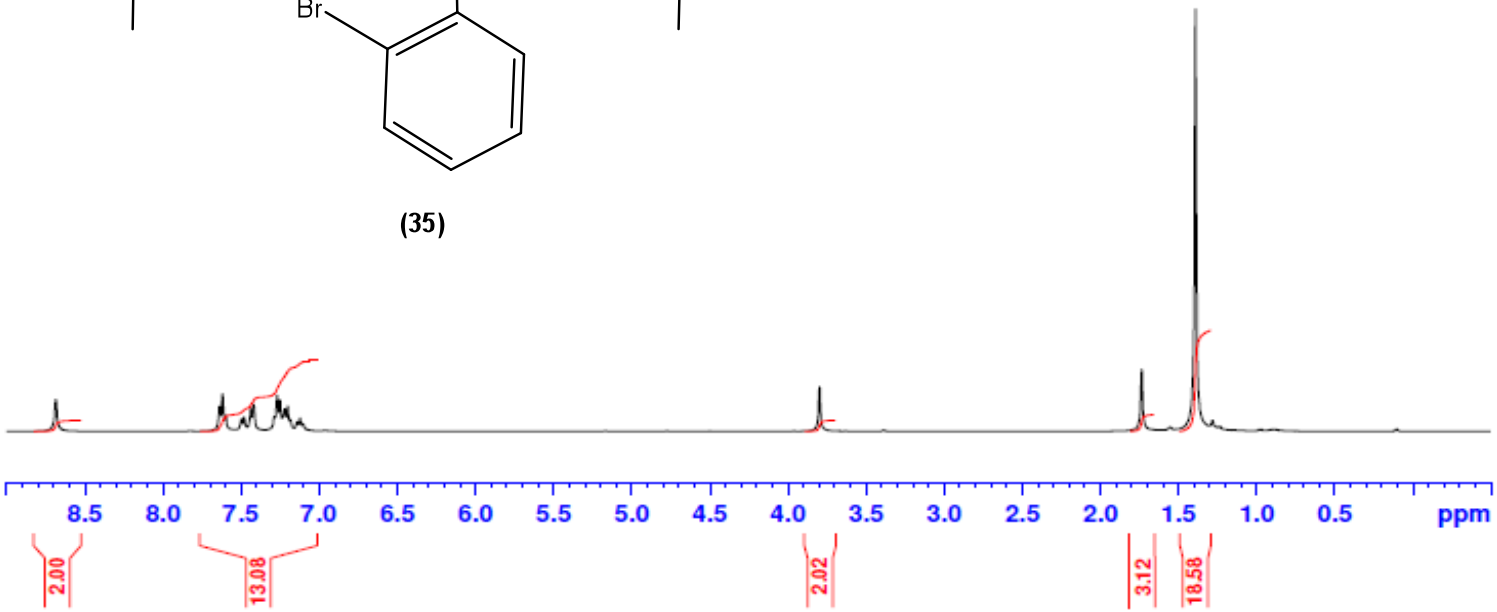
(34)



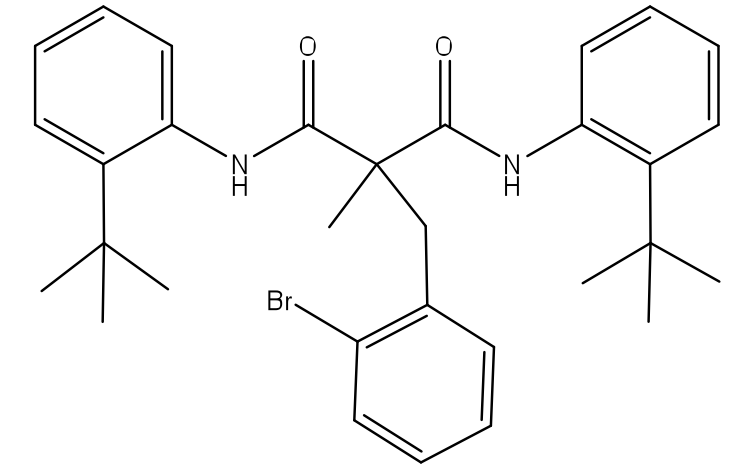
jan9,2011-di-t-butylamide



(35)

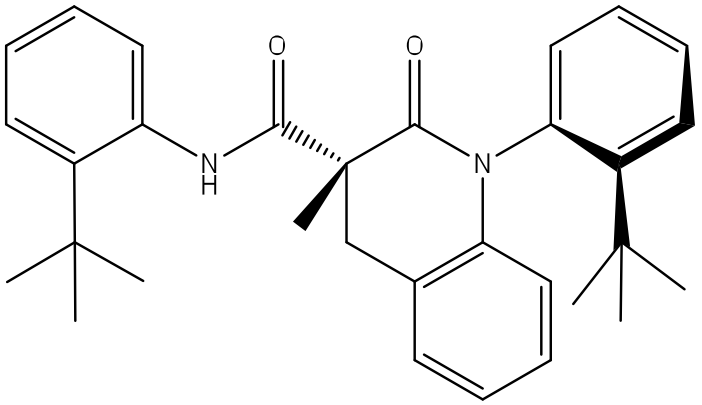


jan9,2011-di-t-butylamide-carbon spectrum

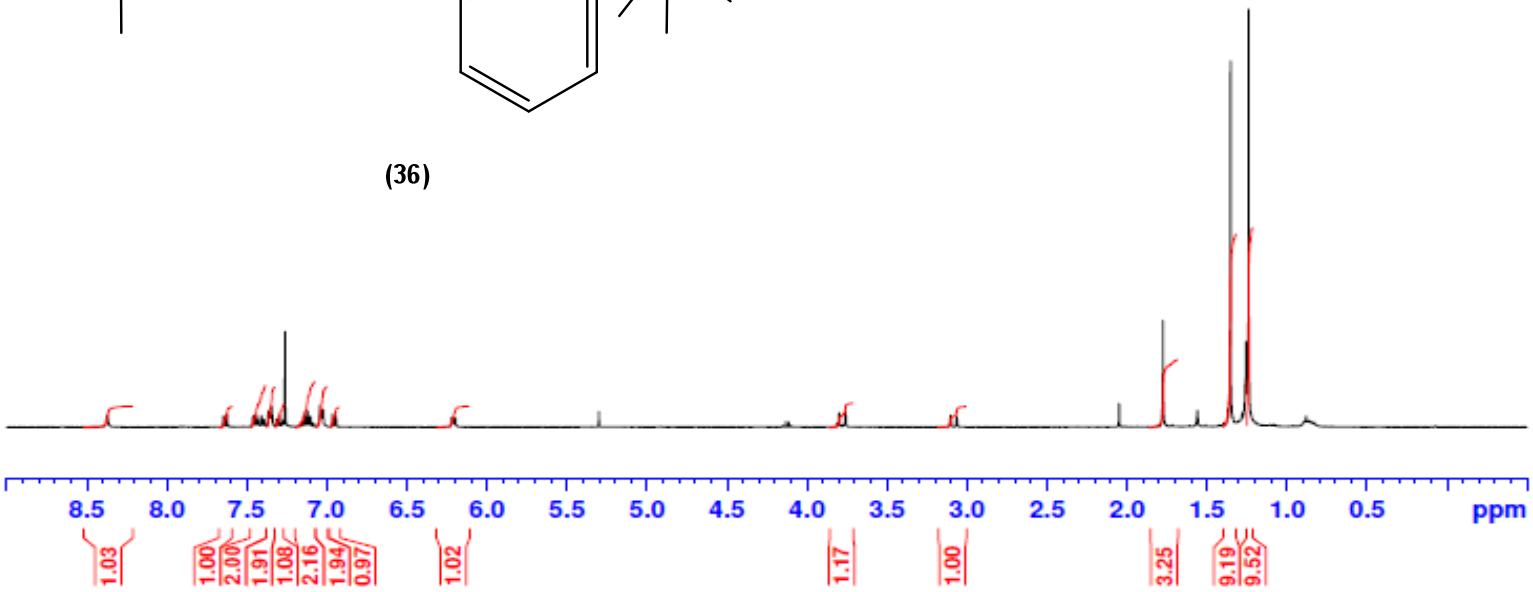


(35)

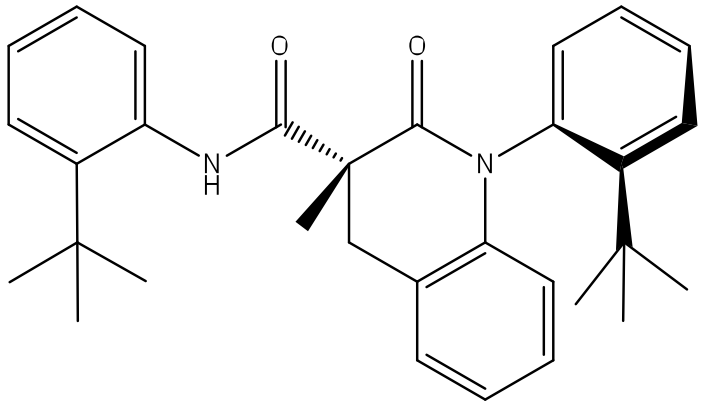
Feb8,10-t-butylquinolinone



(36)

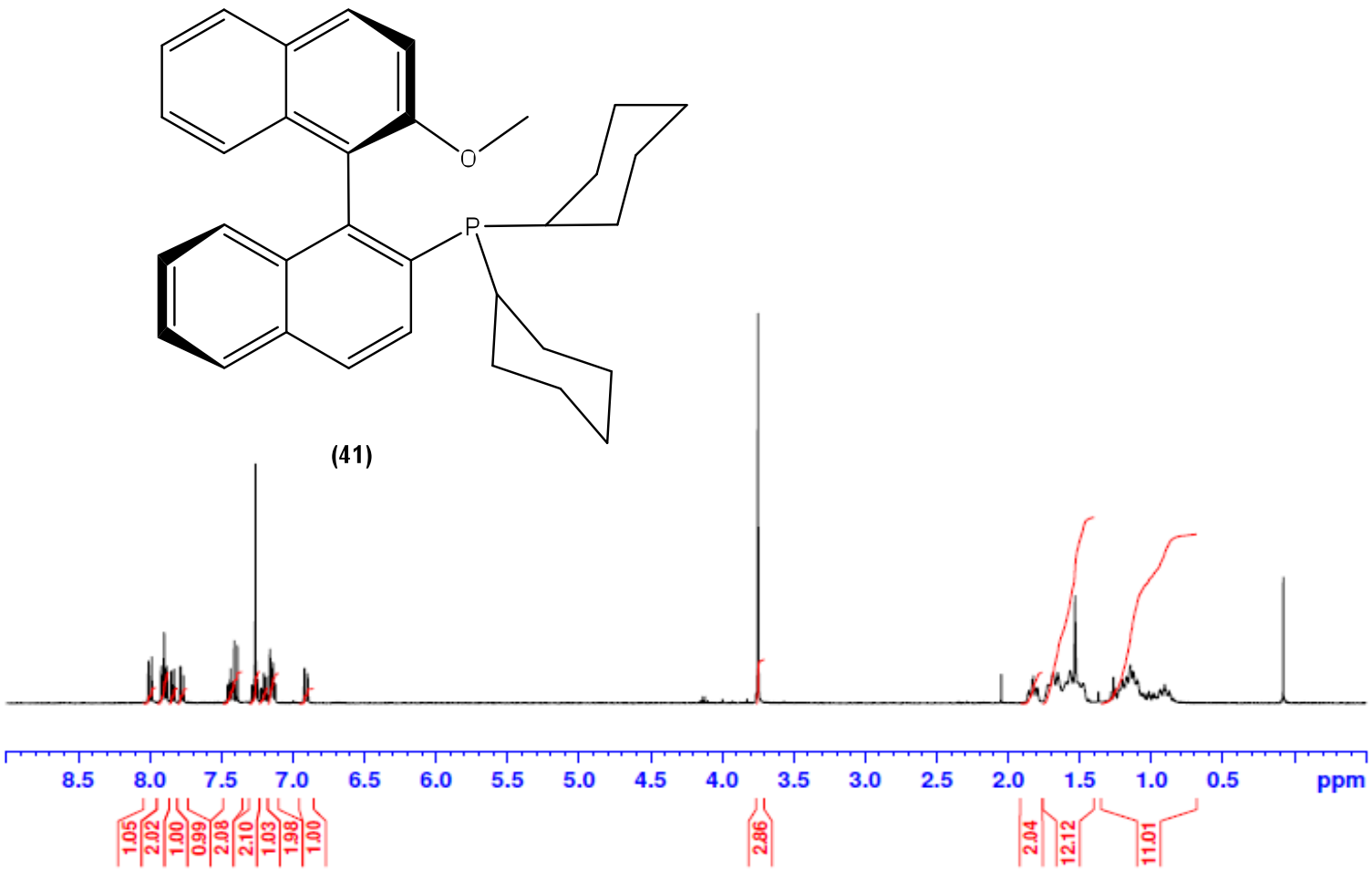


July27,2011-t-butylquinolinone-carbon spectrum



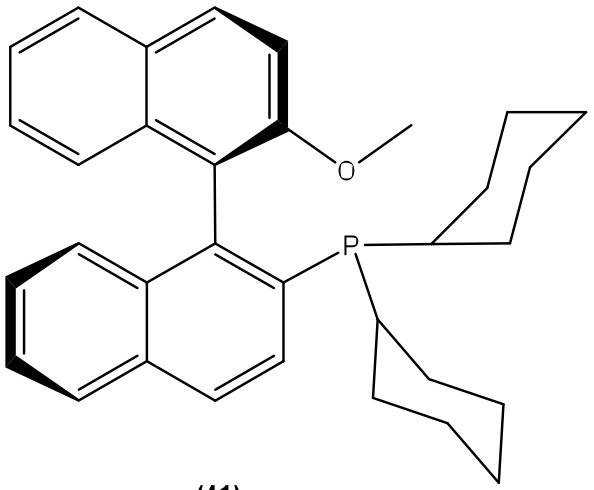
(36)

june11,2011-proton spectrum of Cy2MOP

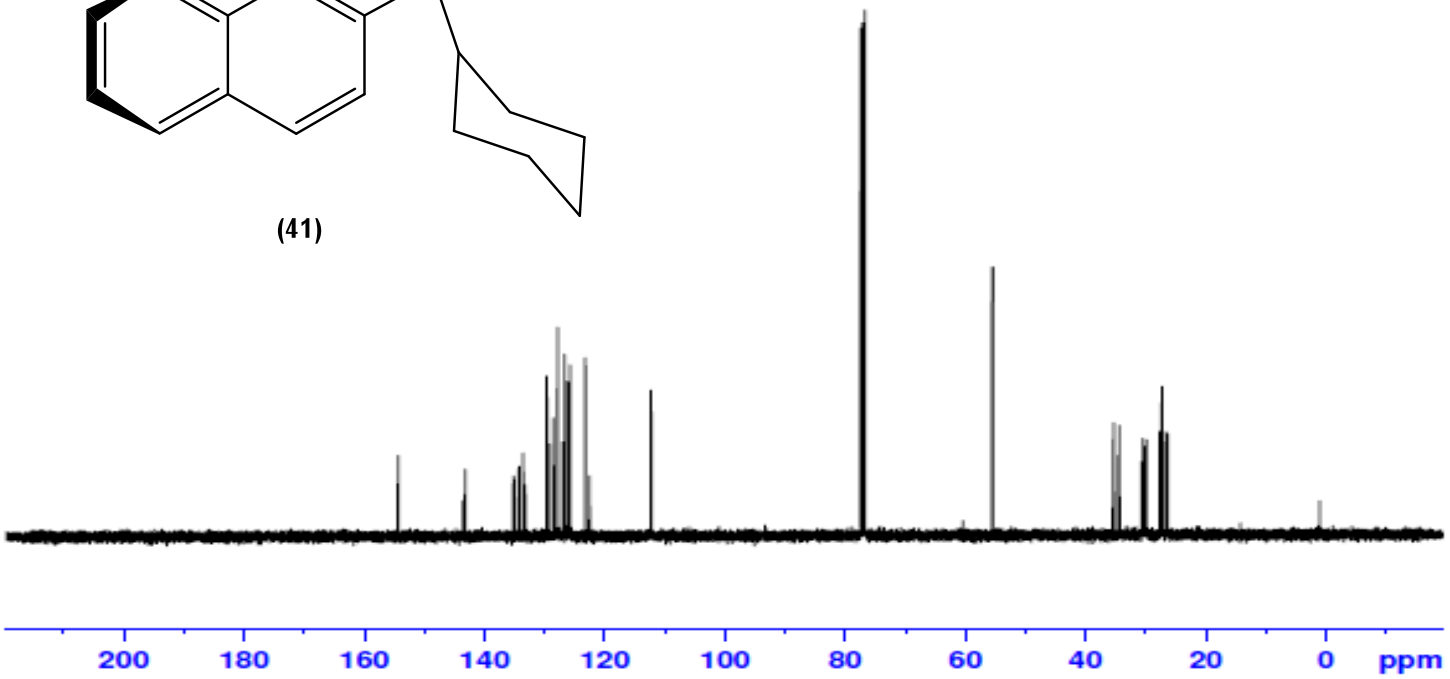


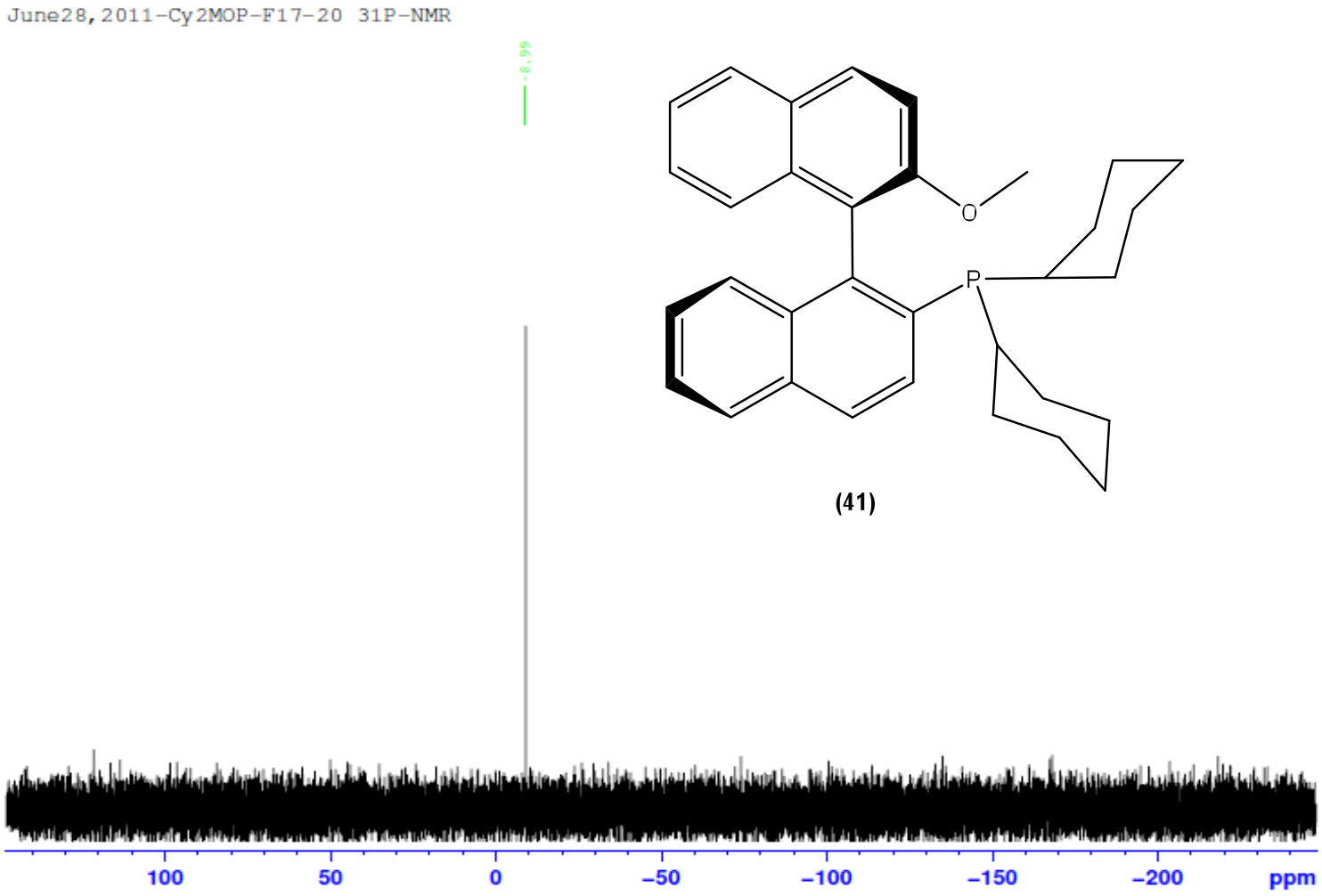
(41)

june11,2011-Cy2MOP-carbon spectrum



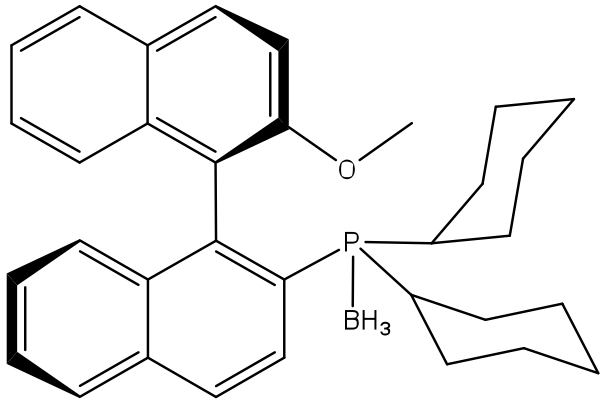
(41)



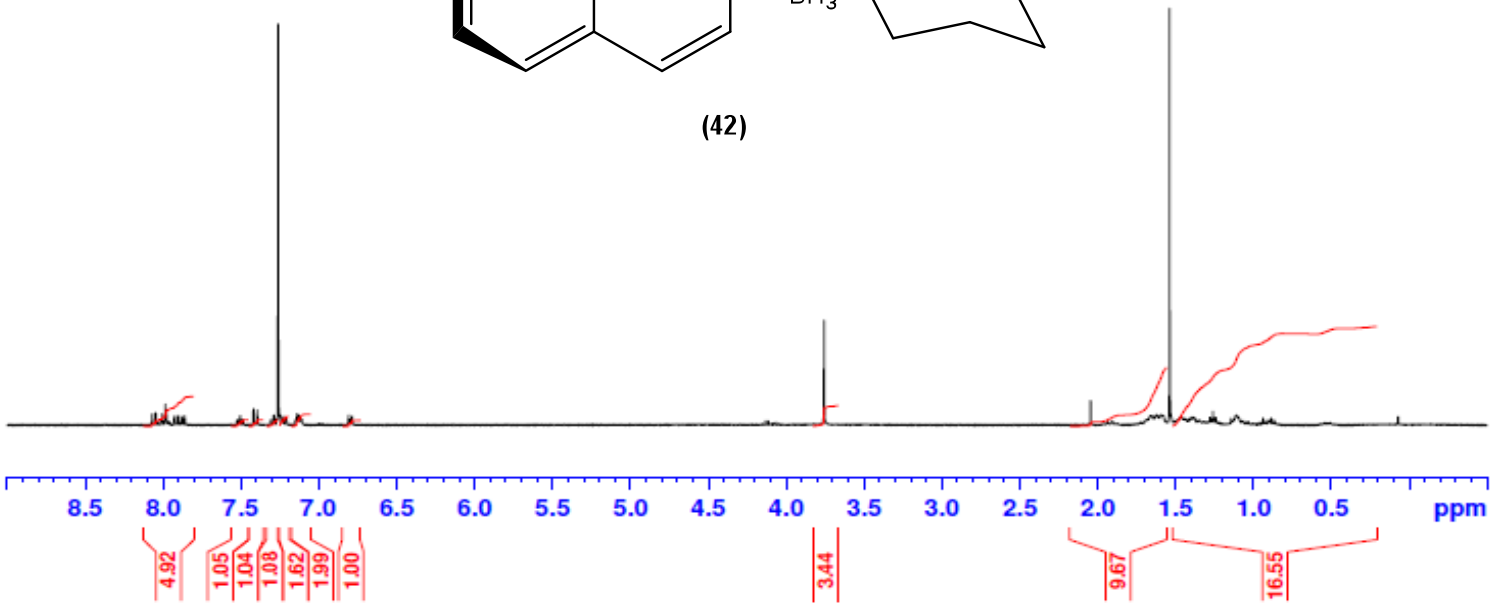

June28,2011-Cy2MOP-F17-20 31P-NMR
8.59
O
P
100
50
0
-50
-100
-150
-200
ppm

(41)

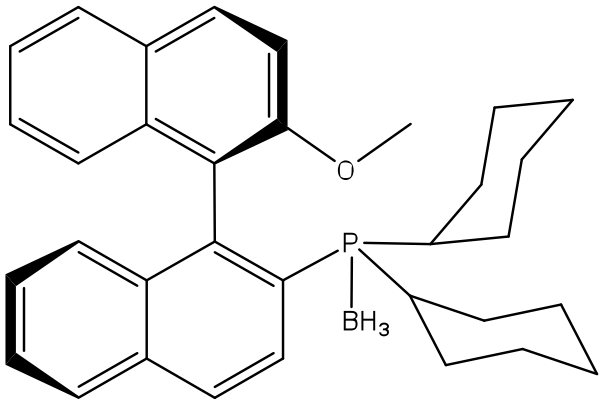
May6, 2011-Cy2MOP(BH3)



(42)

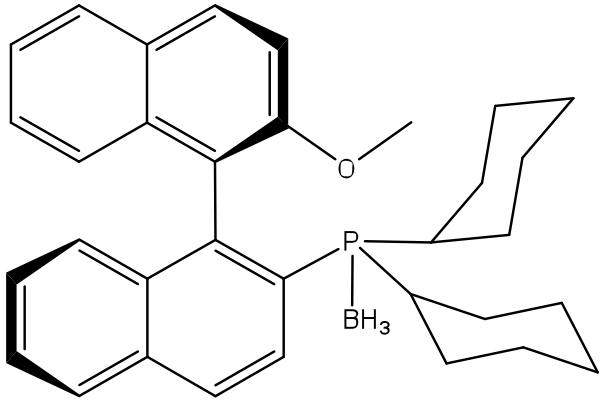


July9,2011-Cy2MOP(BH3) carbon spectrum

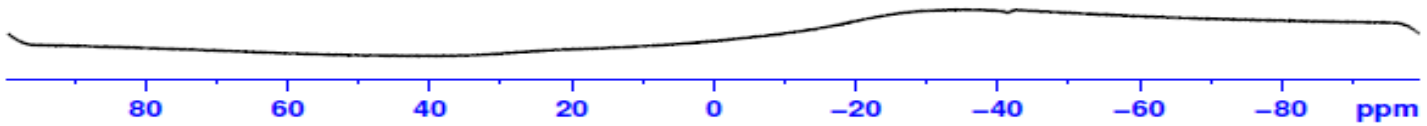


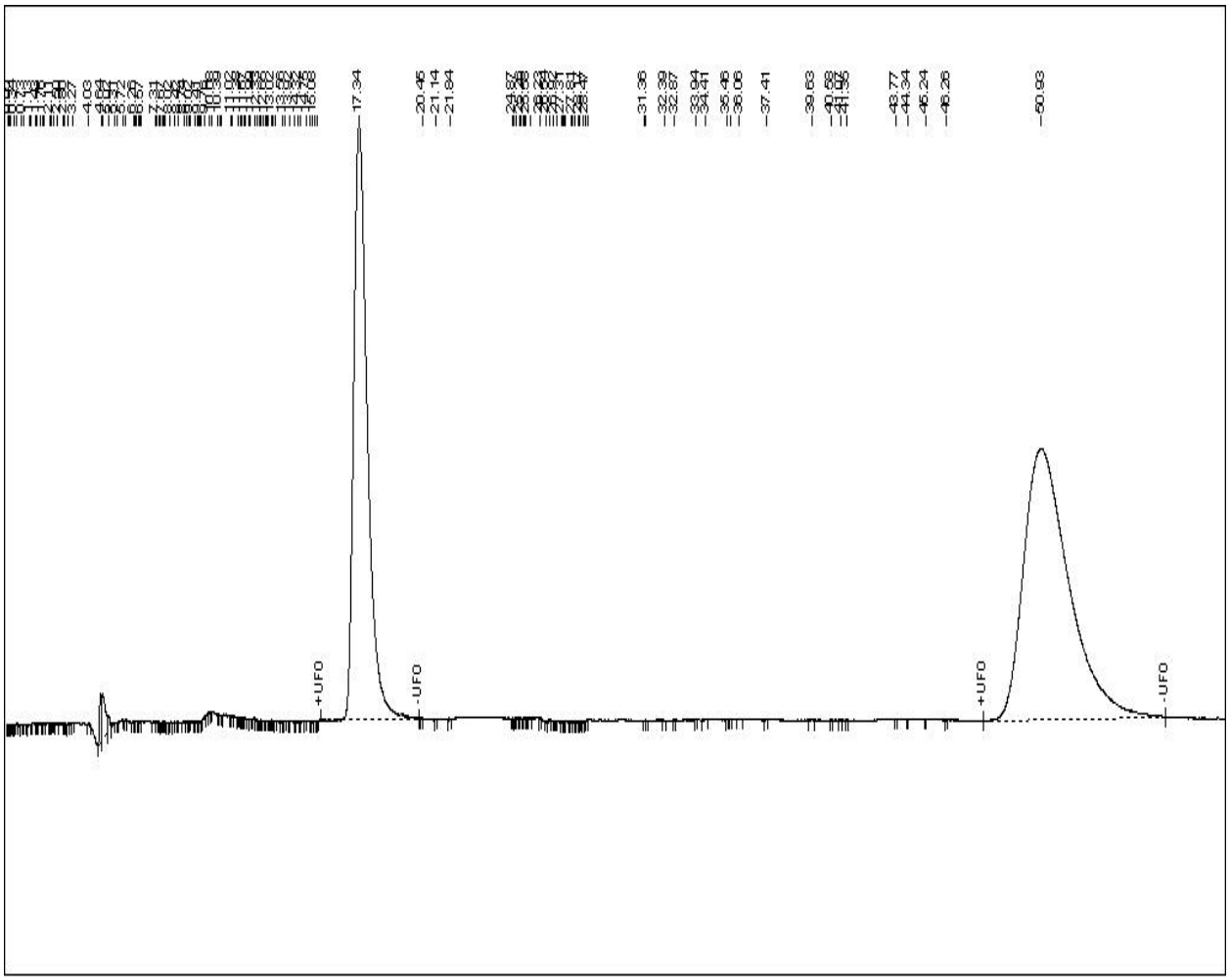
(42)

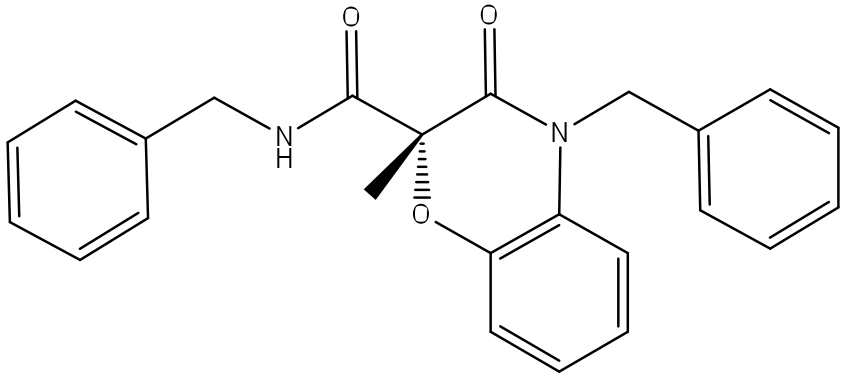
Boron-11 with proton decoupling



(42)







(21)

Isolated from Ligand = (*R*)-BINAP, Base = K_2CO_3
i.e. Table 1, entry 5

Software Version	: 6.3.1.0504	Date	: 7/27/2011 6:34:45 PM
Operator	: manager	Sample Name	: benzomorpholinone (R-BINAP, K2CO3)
Sample Number	: 001	Study	:
AutoSampler	: SER200	Rack/Vial	: 1/1
Instrument Name	: HPLC	Channel	: B
Instrument Serial #	: None	A/D mV Range	: 1000
Delay Time	: 0.00 min	End Time	: 59.99 min
Sampling Rate	: 2.5000 pts/s		
Sample Volume	: 1.000000 ul		
Sample Amount	: 1.0000	Area Reject	: 0.000000
Data Acquisition Time	: 7/27/2011 1:51:46 PM	Dilution Factor	: 1.00
		Cycle	: 1

Raw Data File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb001-20110727-135154.raw
Inst Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011 from
C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb001-20110727-135154.raw
Proc Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011.mth from
Calib Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011.mth from
Report Format File: C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011.rpt
Sequence File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011sequence.seq

DEFAULT REPORT

Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	0.049	222.00	67.03	0.01	0.01	BB	3.3118
2	0.152	100.12	69.85	0.00	0.00	BV	1.4333
3	0.204	201.88	69.05	0.01	0.01	VB	2.9235
4	0.338	259.00	67.86	0.01	0.01	BB	3.8166
5	0.507	199.00	43.72	0.01	0.01	BB	4.5515
6	0.727	228.00	30.17	0.01	0.01	BB	7.5569
7	0.858	145.20	37.59	0.01	0.01	BB	3.8623
8	1.131	413.60	59.78	0.02	0.02	BB	6.9181
9	1.195	62.80	39.43	0.00	0.00	BB	1.5926
10	1.430	144.80	60.22	0.01	0.01	BB	2.4046
11	1.497	190.60	74.28	0.01	0.01	BV	2.5660
12	1.650	767.95	78.38	0.03	0.03	VV	9.7973
13	1.762	150.65	71.48	0.01	0.01	VB	2.1075
14	1.850	192.60	58.20	0.01	0.01	BB	3.3092
15	2.109	73.00	37.48	0.00	0.00	BB	1.9477
16	2.202	54.00	42.38	0.00	0.00	BB	1.2741
17	2.280	94.00	33.55	0.00	0.00	BB	2.8014
18	2.503	290.80	64.96	0.01	0.01	BB	4.4769
19	2.804	128.40	56.32	0.00	0.00	BB	2.2796
20	2.865	92.00	46.14	0.00	0.00	BB	1.9939
21	3.020	196.00	55.68	0.01	0.01	BB	3.5201
22	3.269	112.80	24.25	0.00	0.00	BB	4.6512
23	4.033	349.60	67.23	0.01	0.01	BB	5.2003
24	4.641	12495.91	1805.36	0.48	0.48	BV	6.9216
25	4.734	21362.67	1705.21	0.81	0.81	VV	12.5279
26	5.017	4221.87	592.35	0.16	0.16	VV	7.1273
27	5.309	1047.95	56.90	0.04	0.04	VB	18.4184
28	5.451	47.77	29.18	0.00	0.00	BV	1.6370
29	5.719	515.83	38.52	0.02	0.02	VB	13.3911
30	5.875	209.20	42.70	0.01	0.01	BB	4.8991
31	6.259	458.01	79.12	0.02	0.02	BV	5.7891
32	6.306	194.29	87.73	0.01	0.01	VV	2.2146
33	6.365	491.46	101.91	0.02	0.02	VV	4.8227
34	6.477	334.31	87.50	0.01	0.01	VV	3.8209
35	6.566	271.53	80.12	0.01	0.01	VB	3.3892
36	6.627	39.60	32.61	0.00	0.00	BB	1.2142
37	7.309	685.60	86.14	0.03	0.03	BB	7.9594
38	7.395	245.00	64.36	0.01	0.01	BB	3.8066
39	7.496	116.00	69.70	0.00	0.00	BB	1.6643
40	7.575	66.20	44.19	0.00	0.00	BB	1.4980
41	7.668	115.98	67.11	0.00	0.00	BV	1.7281
42	7.726	171.22	57.47	0.01	0.01	VB	2.9791
43	7.798	178.60	65.23	0.01	0.01	BB	2.7381
44	8.019	113.20	44.79	0.00	0.00	BB	2.5272
45	8.273	253.60	40.50	0.01	0.01	BB	6.2612

7/27/2011 6:34:45 PM Result:

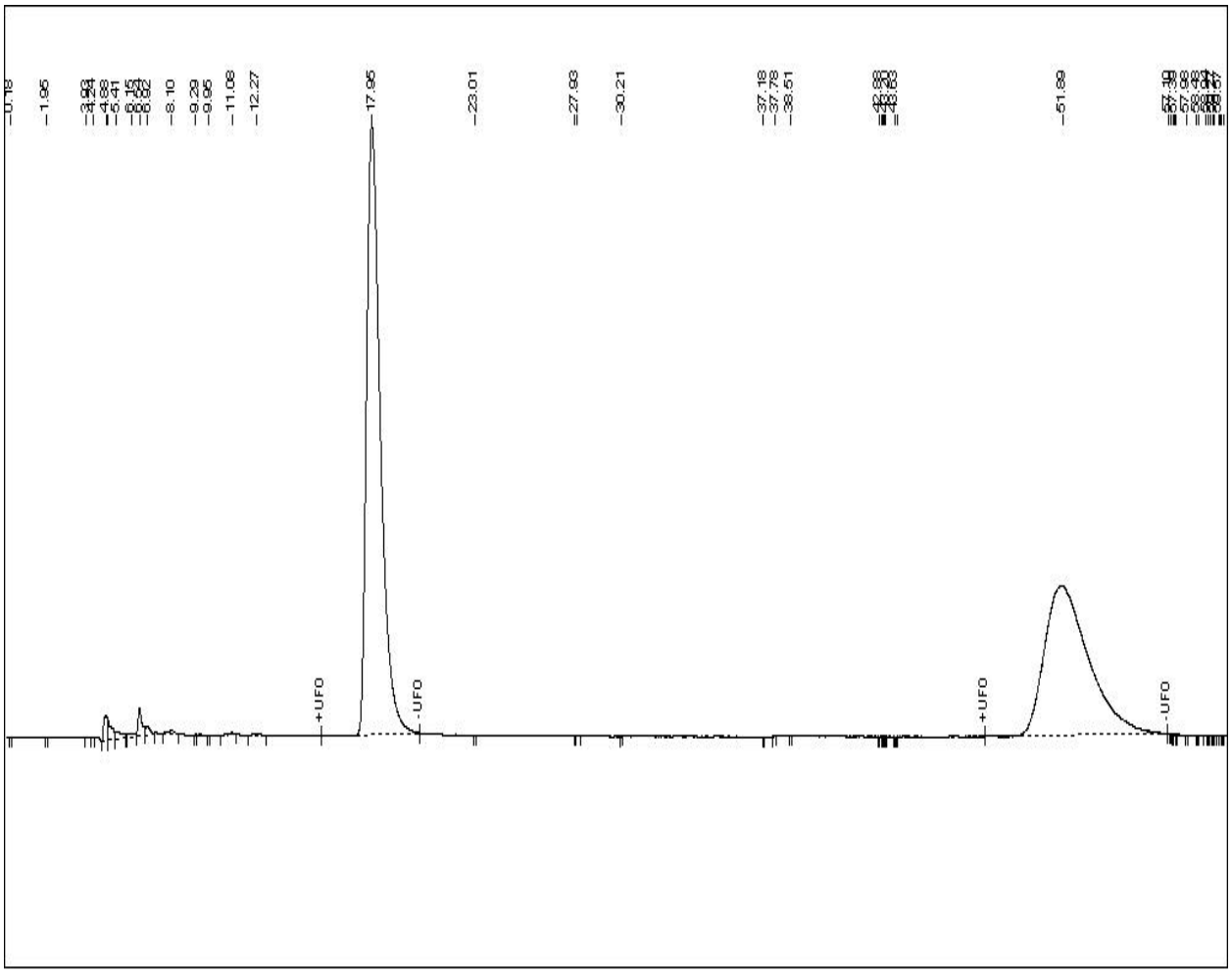
Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
46	8.416	140.80	37.22	0.01	0.01	BB	3.7831
47	8.737	391.00	54.81	0.01	0.01	BB	7.1344
48	8.865	285.40	50.65	0.01	0.01	BB	5.6351
49	8.961	114.80	46.17	0.00	0.00	BB	2.4862
50	9.023	130.80	42.04	0.00	0.00	BB	3.1111
51	9.241	92.80	45.84	0.00	0.00	BB	2.0246
52	9.408	103.92	52.52	0.00	0.00	BV	1.9787
53	9.458	91.17	52.40	0.00	0.00	VV	1.7400
54	9.533	102.91	41.92	0.00	0.00	VB	2.4549
55	9.582	66.80	37.26	0.00	0.00	BB	1.7929
56	9.763	403.00	61.22	0.02	0.02	BB	6.5826
57	9.998	392.12	61.14	0.01	0.01	BV	6.4130
58	10.084	136.68	48.90	0.01	0.01	VB	2.7952
59	10.395	44.00	24.10	0.00	0.00	BB	1.8258
60	10.523	200.04	57.86	0.01	0.01	BV	3.4575
61	10.592	165.96	58.54	0.01	0.01	VB	2.8349
62	11.016	158.63	52.46	0.01	0.01	BV	3.0239
63	11.087	233.97	66.06	0.01	0.01	VB	3.5417
64	11.378	124.20	47.10	0.00	0.00	BB	2.6371
65	11.507	182.40	63.06	0.01	0.01	BB	2.8923
66	11.556	143.40	62.36	0.01	0.01	BB	2.2995
67	11.669	124.20	66.23	0.00	0.00	BB	1.8753
68	11.754	201.20	60.07	0.01	0.01	BB	3.3495
69	11.897	210.00	63.23	0.01	0.01	BB	3.3210
70	11.988	154.00	41.47	0.01	0.01	BB	3.7134
71	12.205	539.20	136.12	0.02	0.02	BB	3.9613
72	12.332	254.80	44.24	0.01	0.01	BB	5.7601
73	12.438	63.20	49.87	0.00	0.00	BB	1.2673
74	12.531	179.60	60.31	0.01	0.01	BB	2.9778
75	12.651	127.00	43.51	0.00	0.00	BB	2.9188
76	12.751	62.00	51.02	0.00	0.00	BB	1.2152
77	12.832	124.31	37.56	0.00	0.00	BV	3.3091
78	12.890	146.09	45.61	0.01	0.01	VB	3.2030
79	13.019	134.40	61.13	0.01	0.01	BB	2.1986
80	13.077	109.20	46.13	0.00	0.00	BB	2.3670
81	13.205	146.00	52.26	0.01	0.01	BB	2.7935
82	13.556	216.40	57.09	0.01	0.01	BB	3.7903
83	13.675	133.60	36.92	0.01	0.01	BB	3.6188
84	13.922	117.60	47.55	0.00	0.00	BB	2.4730
85	14.175	117.20	37.29	0.00	0.00	BB	3.1432
86	14.318	180.00	31.57	0.01	0.01	BB	5.7008
87	14.436	97.60	62.95	0.00	0.00	BB	1.5505
88	14.751	210.40	20.97	0.01	0.01	BB	10.0351
89	14.951	267.41	72.36	0.01	0.01	BV	3.6957
90	15.079	368.79	76.66	0.01	0.01	VV	4.8107
91	15.166	237.60	73.34	0.01	0.01	VB	3.2397
92	15.309	141.60	57.88	0.01	0.01	BB	2.4463
93	17.340	1018747.76	21870.50	38.83	38.83	MM	46.5809
94	20.451	140.80	39.12	0.01	0.01	BB	3.5990
95	21.136	60.00	25.28	0.00	0.00	BB	2.3736
96	21.842	429.80	53.45	0.02	0.02	BB	8.0409
97	24.874	151.61	54.06	0.01	0.01	BV	2.8046
98	24.925	139.39	68.60	0.01	0.01	VB	2.0318
99	24.973	108.54	56.94	0.00	0.00	BV	1.9061
100	25.051	164.46	49.44	0.01	0.01	VB	3.3261
101	25.256	164.44	52.76	0.01	0.01	BV	3.1169
102	25.340	321.87	74.82	0.01	0.01	VV	4.3020
103	25.417	106.29	59.49	0.00	0.00	VB	1.7865
104	25.501	281.83	67.73	0.01	0.01	BV	4.1611
105	25.576	57.37	46.07	0.00	0.00	VB	1.2453
106	25.765	244.40	56.02	0.01	0.01	BB	4.3627
107	26.231	289.20	69.52	0.01	0.01	BB	4.1602
108	26.542	312.80	61.86	0.01	0.01	BB	5.0564
109	26.741	348.80	46.00	0.01	0.01	BB	7.5828
110	26.922	59.60	39.36	0.00	0.00	BB	1.5142
111	27.066	71.20	35.62	0.00	0.00	BB	1.9989
112	27.315	242.40	51.39	0.01	0.01	BB	4.7172
113	27.394	107.50	67.88	0.00	0.00	BV	1.5836
114	27.436	202.14	72.29	0.01	0.01	VV	2.7964

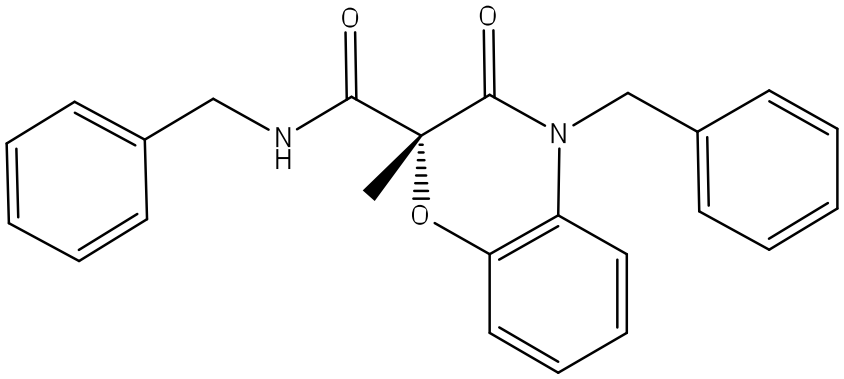
7/27/2011 6:34:45 PM Result:

Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
115	27.500	513.97	60.82	0.02	0.02	VB	8.4505
116	27.805	147.60	58.10	0.01	0.01	BB	2.5405
117	27.847	50.00	43.79	0.00	0.00	BB	1.1418
118	27.991	130.40	42.18	0.00	0.00	BB	3.0915
119	28.170	148.40	66.43	0.01	0.01	BB	2.2339
120	28.223	74.60	46.29	0.00	0.00	BB	1.6116
121	28.409	262.40	70.72	0.01	0.01	BB	3.7106
122	28.475	139.97	64.21	0.01	0.01	BV	2.1797
123	28.593	215.23	32.07	0.01	0.01	VB	6.7118
124	31.363	124.45	30.13	0.00	0.00	BV	4.1304
125	31.467	192.35	40.03	0.01	0.01	VB	4.8049
126	32.391	255.60	38.49	0.01	0.01	BB	6.6399
127	32.874	124.20	28.06	0.00	0.00	BB	4.4262
128	33.941	81.20	19.79	0.00	0.00	BB	4.1025
129	34.411	351.60	30.30	0.01	0.01	BB	11.6056
130	35.458	107.60	22.83	0.00	0.00	BB	4.7132
131	35.651	77.20	29.61	0.00	0.00	BB	2.6072
132	36.057	281.40	31.77	0.01	0.01	BB	8.8563
133	37.413	219.60	28.15	0.01	0.01	BB	7.7997
134	39.628	389.60	35.16	0.01	0.01	BB	11.0818
135	40.583	116.40	29.23	0.00	0.00	BB	3.9815
136	41.067	172.80	26.57	0.01	0.01	BB	6.5025
137	41.349	71.00	25.60	0.00	0.00	BB	2.7735
138	43.766	88.00	27.84	0.00	0.00	BB	3.1607
139	44.338	84.00	38.41	0.00	0.00	BB	2.1871
140	45.243	47.00	24.24	0.00	0.00	BB	1.9393
141	46.255	70.00	27.80	0.00	0.00	BB	2.5182
142	50.927	1539462.16	9973.42	58.68	58.68	MM	154.3565
		2623423.72	43040.98	100.00	100.00		

Missing Component Report

Component	Expected Retention (Calibration File)
July27,2011BnBenzomorpholinone	0.001





(21)

Isolated from Ligand = (*R*)-BINAP, Base = Cs_2CO_3
i.e. Table 1, entry 7

Software Version	: 6.3.1.0504	Date	: 7/27/2011 6:47:52 PM
Operator	: manager	Sample Name	: benzomorpholinone (R-BINAP, CS2CO3)
Sample Number	: 003	Study	:
AutoSampler	: SER200	Rack/Vial	: 1/3
Instrument Name	: HPLC	Channel	: B
Instrument Serial #	: None	A/D mV Range	: 1000
Delay Time	: 0.00 min	End Time	: 59.99 min
Sampling Rate	: 2.5000 pts/s		
Sample Volume	: 1.000000 ul		
Sample Amount	: 1.0000	Area Reject	: 0.000000
Data Acquisition Time	: 7/27/2011 3:53:39 PM	Dilution Factor	: 1.00
		Cycle	: 1

Raw Data File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb003-20110727-155455.raw
Inst Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011 from
C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb003-20110727-155455.raw
Proc Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011.mth from
Calib Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011.mth from
Report Format File: C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011.rpt
Sequence File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011sequence.seq

DEFAULT REPORT

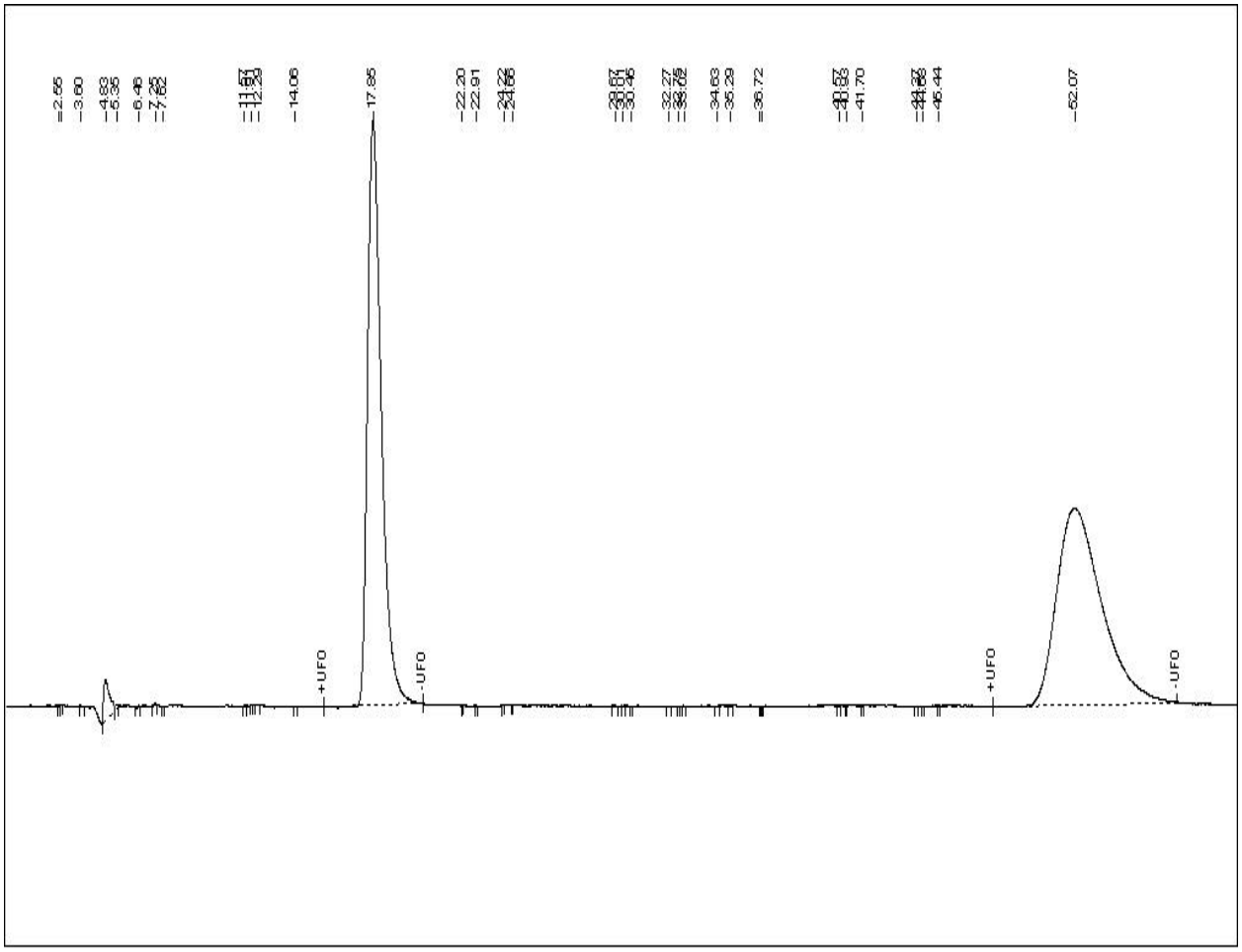
Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	0.176	63.60	19.60	0.00	0.00	BB	3.2455
2	1.947	67.20	23.37	0.00	0.00	BB	2.8752
3	3.926	342.40	39.79	0.01	0.01	BB	8.6060
4	4.244	166.80	26.24	0.00	0.00	BB	6.3565
5	4.877	25329.68	2461.43	0.49	0.49	BV	10.2906
6	4.965	30691.44	2242.80	0.60	0.60	VV	13.6844
7	5.406	16688.53	764.12	0.32	0.32	VV	21.8401
8	6.146	8024.44	328.39	0.16	0.16	VV	24.4357
9	6.535	34517.16	2609.76	0.67	0.67	VV	13.2262
10	6.917	11482.24	811.22	0.22	0.22	VB	14.1542
11	8.103	6595.60	318.80	0.13	0.13	BB	20.6887
12	9.294	135.60	29.03	0.00	0.00	BB	4.6703
13	9.945	93.80	27.07	0.00	0.00	BB	3.4655
14	11.078	3608.80	173.35	0.07	0.07	BB	20.8180
15	12.270	6557.20	264.06	0.13	0.13	BB	24.8319
16	17.947	2801143.53	59207.34	54.44	54.44	MM	47.3107
17	23.006	99.00	28.36	0.00	0.00	BB	3.4910
18	27.935	103.60	44.40	0.00	0.00	BB	2.3332
19	28.046	269.80	35.93	0.01	0.01	BB	7.5100
20	30.214	103.60	25.35	0.00	0.00	BB	4.0861
21	37.185	102.80	29.22	0.00	0.00	BB	3.5175
22	37.777	396.60	45.89	0.01	0.01	BB	8.6426
23	38.513	120.40	28.93	0.00	0.00	BB	4.1611
24	42.877	117.20	48.10	0.00	0.00	BB	2.4364
25	43.001	194.80	48.82	0.00	0.00	BB	3.9904
26	43.044	54.80	35.75	0.00	0.00	BB	1.5330
27	43.137	105.46	47.93	0.00	0.00	BV	2.2004
28	43.202	71.14	42.78	0.00	0.00	VB	1.6630
29	43.627	101.20	51.33	0.00	0.00	BB	1.9717
30	43.766	40.40	29.38	0.00	0.00	BB	1.3751
31	51.887	2193959.25	14573.34	42.64	42.64	MM	150.5461
32	57.101	240.00	51.02	0.00	0.00	BB	4.7042
33	57.201	95.20	64.76	0.00	0.00	BB	1.4700
34	57.250	97.26	63.27	0.00	0.00	BV	1.5372
35	57.314	299.74	84.17	0.01	0.01	VB	3.5613
36	57.393	242.29	77.55	0.00	0.00	BV	3.1243
37	57.469	166.91	45.42	0.00	0.00	VB	3.6744
38	57.984	169.60	59.48	0.00	0.00	BB	2.8515
39	58.478	155.60	65.02	0.00	0.00	BB	2.3932
40	58.585	177.60	37.15	0.00	0.00	BB	4.7810
41	58.938	367.20	85.06	0.01	0.01	BB	4.3170
42	59.028	184.85	83.70	0.00	0.00	BV	2.2086
43	59.074	133.55	74.31	0.00	0.00	VB	1.7972
44	59.166	391.22	80.07	0.01	0.01	BV	4.8859
45	59.272	254.02	78.86	0.00	0.00	VV	3.2211

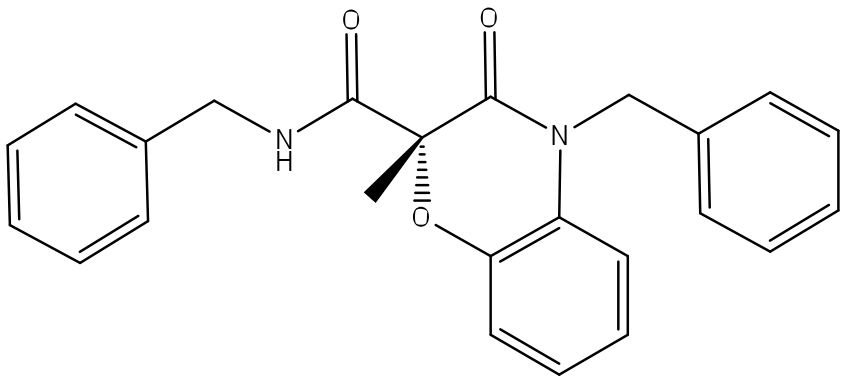
7/27/2011 6:47:52 PM Result:

Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
46	59.331	79.16	52.09	0.00	0.00	VB	1.5195
47	59.572	258.40	45.40	0.01	0.01	BB	5.6916
48	59.624	165.20	45.62	0.00	0.00	BB	3.6213
49	59.722	71.40	38.06	0.00	0.00	BB	1.8761
50	59.799	42.00	33.43	0.00	0.00	BB	1.2565
		5144939.27	85626.31	100.00	100.00		

Missing Component Report

Component	Expected Retention (Calibration File)
July27,2011BnBenzomorpholinone	0.001





(21)

Isolated from Ligand = (*R*)-MOP, Base = Cs_2CO_3
i.e. Table 1, entry 8

Software Version	: 6.3.1.0504	Date	: 7/27/2011 6:41:30 PM
Operator	: manager	Sample Name	: benzomorpholinone (R-MOP, CS2CO3)
Sample Number	: 002	Study	:
AutoSampler	: SER200	Rack/Vial	: 1/2
Instrument Name	: HPLC	Channel	: B
Instrument Serial #	: None	A/D mV Range	: 1000
Delay Time	: 0.00 min	End Time	: 59.99 min
Sampling Rate	: 2.5000 pts/s		
Sample Volume	: 1.000000 ul		
Sample Amount	: 1.0000	Area Reject	: 0.000000
Data Acquisition Time	: 7/27/2011 2:52:42 PM	Dilution Factor	: 1.00
		Cycle	: 1

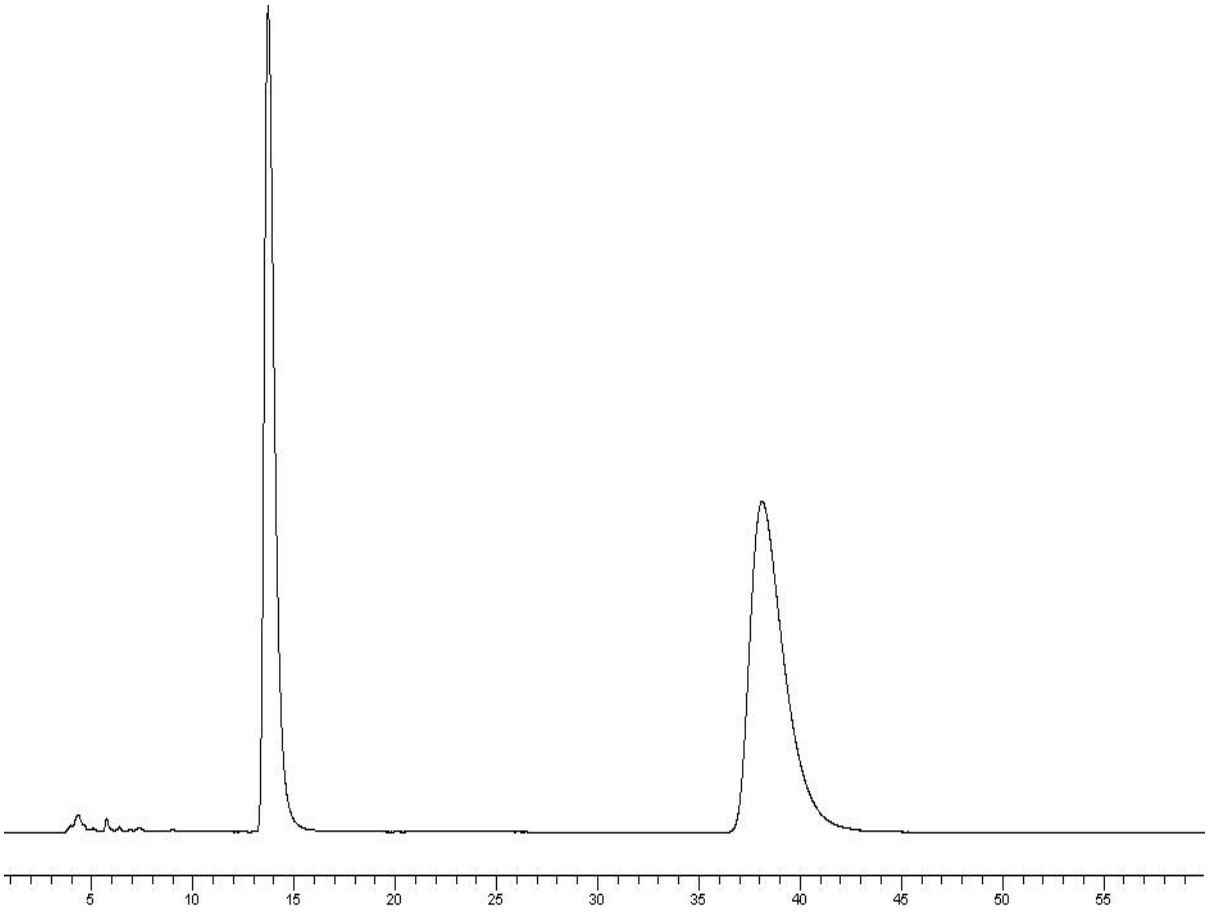
Raw Data File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb002-20110727-145656.raw
Inst Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011 from
C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb002-20110727-145656.raw
Proc Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011.mth from
Calib Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011.mth from
Report Format File: C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011.rpt
Sequence File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\July27,2011sequence.seq

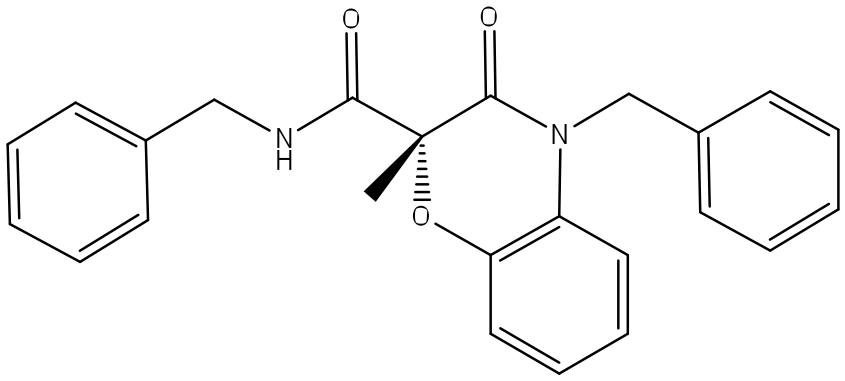
DEFAULT REPORT

Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	2.548	167.50	51.45	0.01	0.01	BV	3.2556
2	2.650	214.30	44.53	0.01	0.01	VB	4.8130
3	3.600	366.80	44.37	0.01	0.01	BB	8.2672
4	4.829	37210.89	1893.23	1.39	1.39	BV	19.6547
5	5.350	1391.91	140.08	0.05	0.05	VB	9.9368
6	6.464	275.20	38.16	0.01	0.01	BB	7.2117
7	7.248	600.40	70.90	0.02	0.02	BB	8.4688
8	7.621	92.40	24.28	0.00	0.00	BB	3.8052
9	11.573	249.60	57.18	0.01	0.01	BB	4.3648
10	11.914	59.60	23.33	0.00	0.00	BB	2.5547
11	12.294	317.80	37.45	0.01	0.01	BB	8.4865
12	14.064	149.20	24.07	0.01	0.01	BB	6.1998
13	17.853	1265584.01	26910.32	47.23	47.23	MM	47.0297
14	22.197	49.60	23.77	0.00	0.00	BB	2.0865
15	22.909	70.00	20.04	0.00	0.00	BB	3.4922
16	24.221	129.60	24.96	0.00	0.00	BB	5.1916
17	24.656	41.60	19.64	0.00	0.00	BB	2.1179
18	29.674	352.40	37.99	0.01	0.01	BB	9.2769
19	30.009	171.40	30.22	0.01	0.01	BB	5.6717
20	30.453	95.00	18.95	0.00	0.00	BB	5.0127
21	32.272	149.20	22.72	0.01	0.01	BB	6.5678
22	32.752	66.80	18.06	0.00	0.00	BB	3.6990
23	33.022	156.00	33.76	0.01	0.01	BB	4.6208
24	34.628	198.40	22.01	0.01	0.01	BB	9.0133
25	35.293	151.20	26.88	0.01	0.01	BB	5.6248
26	36.722	84.00	25.48	0.00	0.00	BB	3.2967
27	36.845	150.60	45.02	0.01	0.01	BB	3.3449
28	40.571	155.80	26.59	0.01	0.01	BB	5.8596
29	40.931	86.80	22.69	0.00	0.00	BB	3.8252
30	41.703	186.00	32.81	0.01	0.01	BB	5.6688
31	44.369	95.20	26.49	0.00	0.00	BB	3.5935
32	44.683	72.60	22.87	0.00	0.00	BB	3.1739
33	45.435	83.20	21.19	0.00	0.00	BB	3.9258
34	52.073	1370314.47	9069.05	51.14	51.14	MM	151.0979
		2679539.47	38950.55	100.00	100.00		

Missing Component Report

Component	Expected Retention (Calibration File)
July27,2011BnBenzomorpholinone	0.001





(21)

Isolated from Ligand = (*R*)-Cy_2MOP, Base = Cs_2CO_3
i.e. Table 1, entry 6

Software Version	: 6.3.1.0504	Date	: 7/13/2011 10:18:02 AM
Operator	: manager	Sample Name	: Benzomorpholine cyclized with Cy2MOP
Sample Number	: 001	Study	:
AutoSampler	: SER200	Rack/Vial	: 1/1
Instrument Name	: HPLC	Channel	: B
Instrument Serial #	: None	A/D mV Range	: 1000
Delay Time	: 0.00 min	End Time	: 59.99 min
Sampling Rate	: 2.5000 pts/s		
Sample Volume	: 1.000000 ul		
Sample Amount	: 1.0000	Area Reject	: 0.000000
Data Acquisition Time	: 7/12/2011 7:53:48 PM	Dilution Factor	: 1.00
		Cycle	: 1

Raw Data File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb001-20110712-195355.raw
Inst Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\AugustoJuly12,2011method2 from C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb001-20110712-195355.raw
Proc Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\AugustoJuly12,2011method2.mth from
Calib Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\AugustoJuly12,2011method2.mth from
Report Format File: C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\AugustoJuly12,2011method2.rpt
Sequence File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\AugustoJuly12,2011sequence2.seq

DEFAULT REPORT

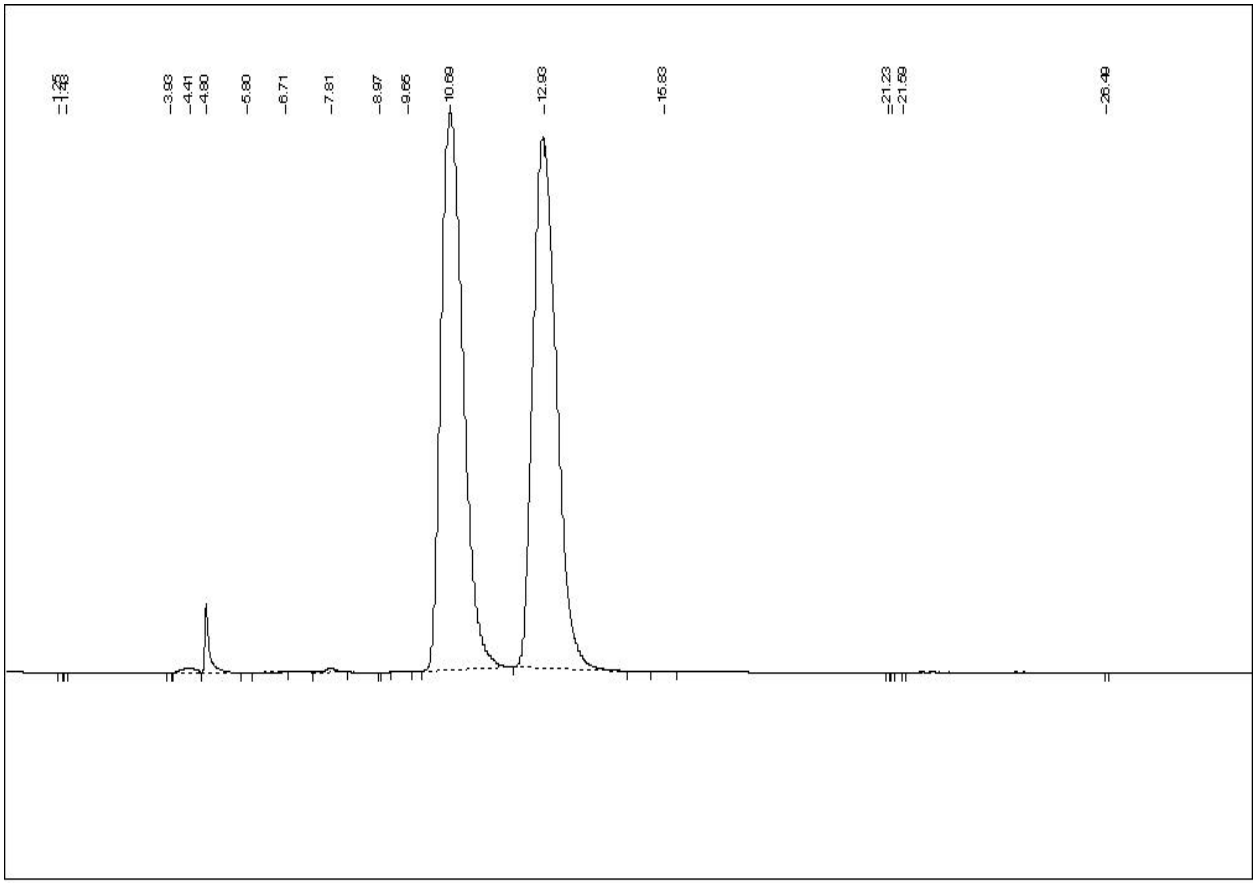
Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	0.804	197.20	42.13	0.00	0.00	BB	4.6812
2	2.354	447.20	27.85	0.00	0.00	BB	16.0551
3	3.967	18539.91	1363.57	0.13	0.13	BV	13.5966
4	4.348	90556.09	3530.02	0.62	0.62	VE	25.6531
5	5.045	6774.40	483.23	0.05	0.05	EB	14.0191
6	5.480	586.95	79.51	0.00	0.00	BV	7.3825
7	5.728	30779.28	2667.53	0.21	0.21	VV	11.5385
8	6.361	9588.17	834.44	0.07	0.07	VB	11.4905
9	6.882	3799.73	312.34	0.03	0.03	BV	12.1654
10	7.327	12267.87	704.51	0.08	0.08	VB	17.4133
11	8.069	203.40	40.69	0.00	0.00	BB	4.9991
12	8.386	715.49	54.32	0.00	0.00	BV	13.1729
13	9.011	5246.51	259.88	0.04	0.04	VB	20.1879
14	9.547	254.80	32.08	0.00	0.00	BB	7.9426
15	10.239	155.20	31.99	0.00	0.00	BB	4.8516
16	11.402	168.20	28.35	0.00	0.00	BB	5.9329
17	13.712	6320578.20	174285.10	43.31	43.31	BB	36.2657
18	19.357	291.20	29.00	0.00	0.00	BB	10.0402
19	20.436	135.20	37.42	0.00	0.00	BB	3.6126
20	21.234	106.00	23.18	0.00	0.00	BB	4.5719
21	24.227	262.40	34.20	0.00	0.00	BB	7.6725
22	26.002	90.80	33.40	0.00	0.00	BB	2.7188
23	26.423	96.40	31.19	0.00	0.00	BB	3.0907
24	26.674	132.40	29.99	0.00	0.00	BB	4.4144
25	27.255	212.40	44.26	0.00	0.00	BB	4.7987
26	28.896	130.00	26.77	0.00	0.00	BB	4.8555
27	30.947	40.00	28.04	0.00	0.00	BB	1.4264
28	31.461	101.20	32.88	0.00	0.00	BB	3.0778
29	32.804	75.60	28.61	0.00	0.00	BB	2.6426
30	33.098	68.40	42.94	0.00	0.00	BB	1.5930
31	33.363	66.40	24.61	0.00	0.00	BB	2.6983
32	33.840	88.00	29.11	0.00	0.00	BB	3.0225
33	35.183	441.60	51.86	0.00	0.00	BB	8.5151
34	35.390	122.80	60.79	0.00	0.00	BB	2.0202
35	36.226	73.20	47.99	0.00	0.00	BB	1.5253
36	38.123	8088409.20	69567.81	55.42	55.42	BB	116.2665
37	44.101	69.40	42.64	0.00	0.00	BB	1.6277
38	47.298	66.40	28.74	0.00	0.00	BB	2.3102
39	47.357	92.80	35.23	0.00	0.00	BB	2.6340
40	48.469	52.40	28.48	0.00	0.00	BB	1.8400
41	49.027	240.60	23.48	0.00	0.00	BB	10.2459
42	49.883	59.00	33.90	0.00	0.00	BB	1.7404
43	50.975	193.60	52.90	0.00	0.00	BB	3.6601
44	51.441	92.80	35.68	0.00	0.00	BB	2.6007
45	51.585	119.20	34.03	0.00	0.00	BB	3.5033

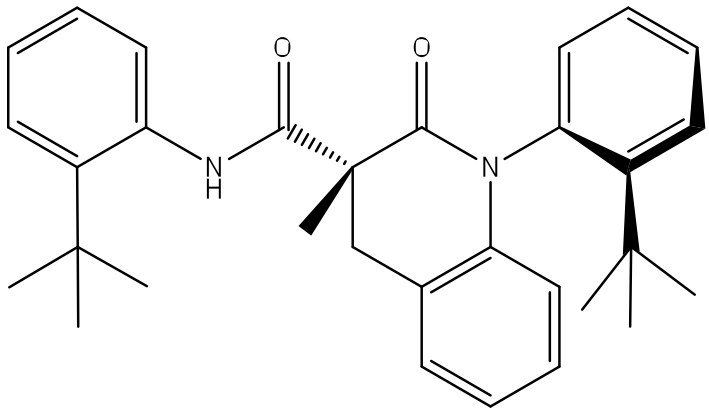
7/13/2011 10:18:02 AM Result:

Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
46	52.348	76.00	54.28	0.00	0.00	BB	1.4000
47	53.384	97.40	20.38	0.00	0.00	BB	4.7794
48	53.735	126.80	32.06	0.00	0.00	BB	3.9552
49	54.143	351.40	36.95	0.00	0.00	BB	9.5105
50	54.606	89.60	13.48	0.00	0.00	BB	6.6464
51	54.840	104.80	29.33	0.00	0.00	BB	3.5729
52	55.043	148.20	49.13	0.00	0.00	BB	3.0163
53	56.336	176.80	38.57	0.00	0.00	BB	4.5840
54	57.221	77.60	26.99	0.00	0.00	BB	2.8747
55	58.622	160.60	33.67	0.00	0.00	BB	4.7693
56	59.235	143.80	40.14	0.00	0.00	BB	3.5824
57	59.488	72.40	33.92	0.00	0.00	BB	2.1346
		14594413.40	255705.58	100.00	100.00		

Missing Component Report

Component	Expected Retention (Calibration File)
Benzomorpholine cyclized with Cy2MOP	0.001





(36)

Isolated from Ligand = S-Phos precatalyst, Base = Cs_2CO_3
i.e. Table 3, entry 7

Software Version	: 6.3.1.0504	Date	: 8/13/2011 5:16:39 PM
Operator	: manager	Sample Name	: t-butylquin(racemic)
Sample Number	: 002	Study	:
AutoSampler	: SER200	Rack/Vial	: 1/2
Instrument Name	: HPLC	Channel	: B
Instrument Serial #	: None	A/D mV Range	: 1000
Delay Time	: 0.00 min	End Time	: 29.99 min
Sampling Rate	: 2.5000 pts/s		
Sample Volume	: 1.000000 ul		
Sample Amount	: 1.0000	Area Reject	: 0.000000
Data Acquisition Time	: 8/12/2011 8:18:31 PM	Dilution Factor	: 1.00
		Cycle	: 1

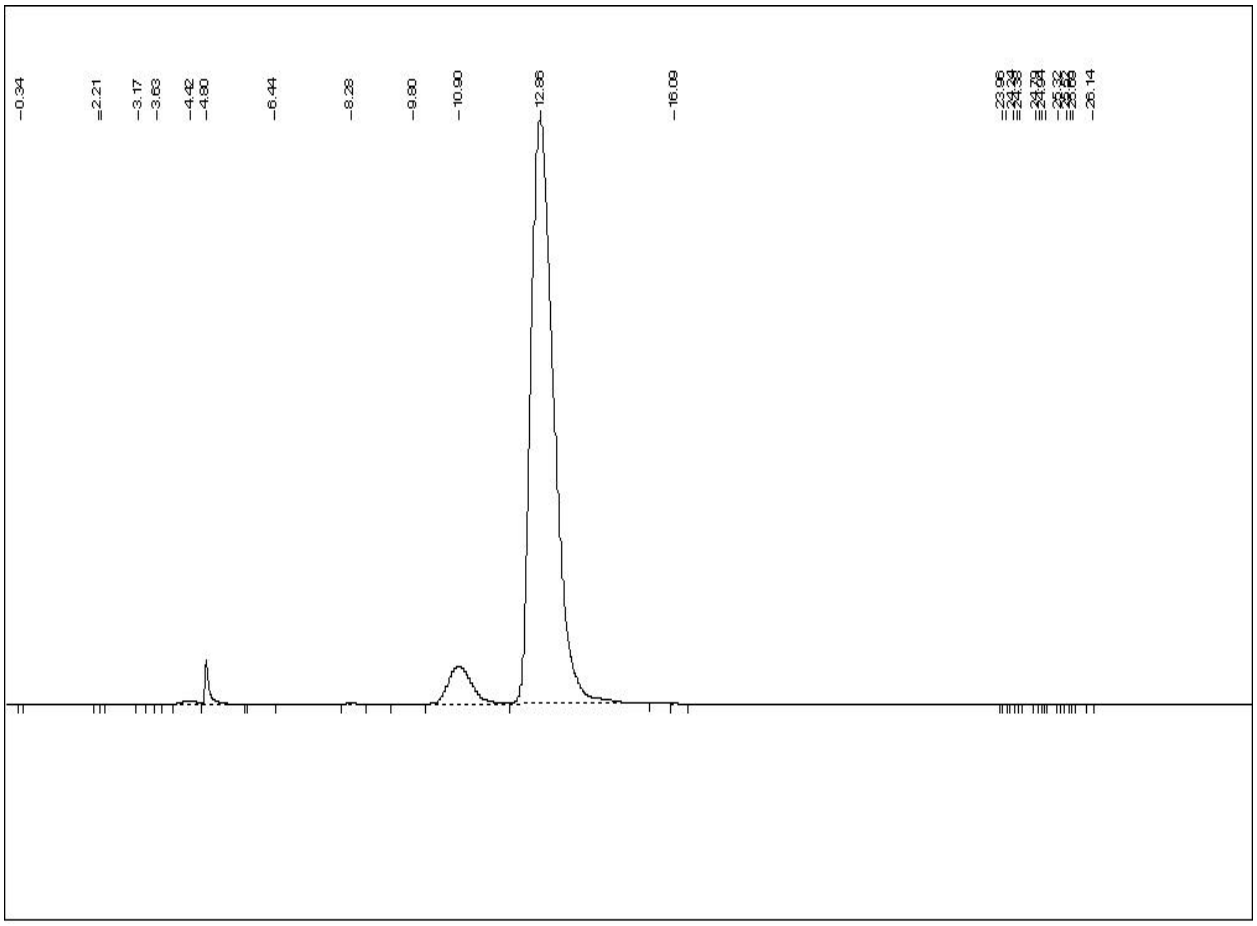
Raw Data File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb002-20110812-202246.raw
Inst Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011 from
C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb002-20110812-202246.raw
Proc Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011.mth from
Calib Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011.mth from
Report Format File: C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011.rpt
Sequence File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011sequence.seq

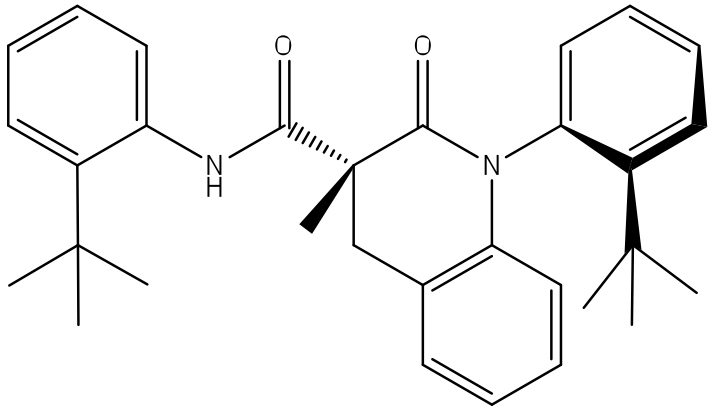
DEFAULT REPORT

Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	1.254	187.60	40.59	0.00	0.00	BB	4.6213
2	1.429	100.80	40.54	0.00	0.00	BB	2.4862
3	3.930	156.37	45.76	0.00	0.00	BV	3.4174
4	4.409	44638.43	1775.95	0.26	0.26	VB	25.1350
5	4.801	215075.00	28148.16	1.24	1.24	BB	7.6408
6	5.796	2587.34	260.06	0.01	0.01	BV	9.9490
7	6.705	2108.66	38.58	0.01	0.01	VB	54.6547
8	7.807	29351.20	1541.83	0.17	0.17	BB	19.0367
9	8.968	59.80	33.12	0.00	0.00	BB	1.8058
10	9.652	1963.80	86.45	0.01	0.01	BB	22.7168
11	10.689	8512436.20	228357.08	48.91	48.91	BB	37.2769
12	12.932	8591907.80	217996.93	49.37	49.37	BB	39.4130
13	15.832	3424.80	203.26	0.02	0.02	BB	16.8493
14	21.228	85.60	27.84	0.00	0.00	BB	3.0752
15	21.321	72.80	26.68	0.00	0.00	BB	2.7286
16	21.594	75.60	30.27	0.00	0.00	BB	2.4972
17	26.491	74.40	23.55	0.00	0.00	BB	3.1594
		17404306.20	478676.64	100.00	100.00		

Missing Component Report

Component	Expected Retention (Calibration File)
t-butylquin	0.001





(36)

Isolated from Ligand = (*R*)-Cy_2MOP, Base = Cs_2CO_3
i.e. Table 3, entry 5

Software Version	: 6.3.1.0504	Date	: 8/13/2011 5:31:48 PM
Operator	: manager	Sample Name	: t-butylquin(Cy2MOP,Cs2CO3)
Sample Number	: 001	Study	:
AutoSampler	: SER200	Rack/Vial	: 1/1
Instrument Name	: HPLC	Channel	: B
Instrument Serial #	: None	A/D mV Range	: 1000
Delay Time	: 0.00 min	End Time	: 29.99 min
Sampling Rate	: 2.5000 pts/s		
Sample Volume	: 1.000000 ul		
Sample Amount	: 1.0000	Area Reject	: 0.000000
Data Acquisition Time	: 8/12/2011 5:41:37 PM	Dilution Factor	: 1.00
		Cycle	: 1

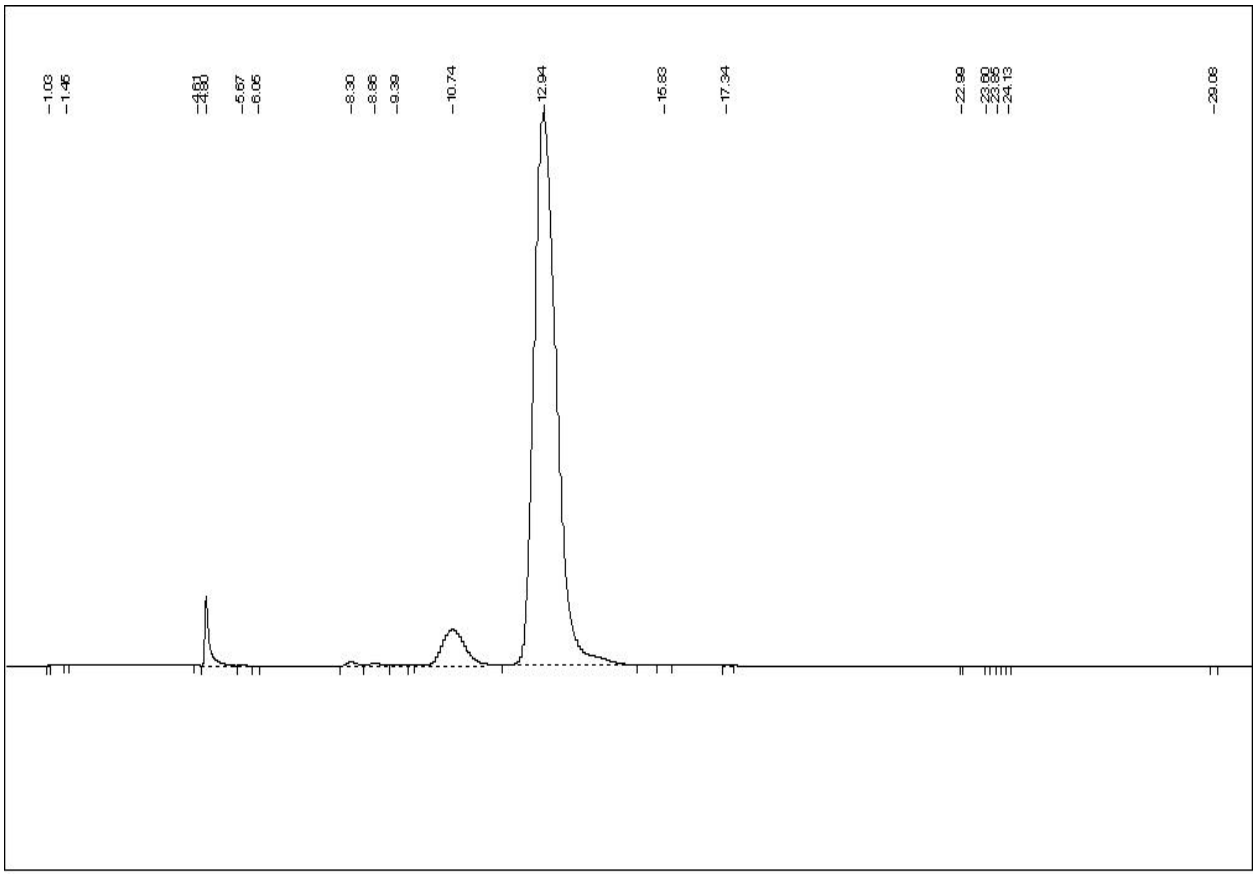
Raw Data File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb001-20110812-174145.raw
Inst Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011 from
C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb001-20110812-174145.raw
Proc Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011.mth from
Calib Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011.mth from
Report Format File: C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011.rpt
Sequence File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011sequence.seq

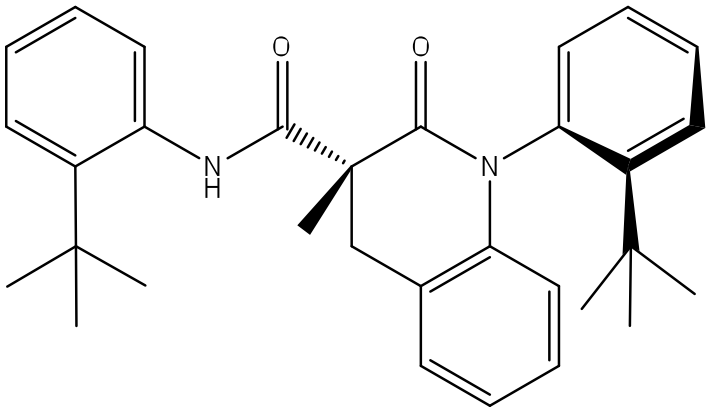
DEFAULT REPORT

Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	0.337	81.60	16.13	0.00	0.00	BB	5.0600
2	2.211	172.68	25.07	0.00	0.00	BV	6.8884
3	2.284	62.72	19.33	0.00	0.00	VB	3.2453
4	3.167	198.00	29.00	0.00	0.00	BB	6.8271
5	3.627	160.80	26.73	0.00	0.00	BB	6.0150
6	4.424	60440.70	2378.31	0.34	0.34	BV	25.4133
7	4.803	247431.10	32256.96	1.39	1.39	VB	7.6706
8	6.441	4898.20	48.52	0.03	0.03	BB	100.9591
9	8.281	10873.80	764.78	0.06	0.06	BB	14.2183
10	9.799	7097.98	207.30	0.04	0.04	BV	34.2394
11	10.895	1088767.27	27228.17	6.10	6.10	VV	39.9868
12	12.858	16418111.55	425850.93	92.02	92.02	VB	38.5537
13	16.085	1232.40	106.07	0.01	0.01	BB	11.6183
14	23.961	112.35	45.33	0.00	0.00	BV	2.4787
15	24.052	173.25	46.80	0.00	0.00	VB	3.7021
16	24.239	254.35	60.10	0.00	0.00	BV	4.2324
17	24.327	212.43	62.97	0.00	0.00	VV	3.3733
18	24.385	253.62	77.61	0.00	0.00	VB	3.2677
19	24.791	232.52	60.20	0.00	0.00	BV	3.8627
20	24.876	264.70	67.41	0.00	0.00	VV	3.9264
21	24.942	112.38	61.19	0.00	0.00	VB	1.8366
22	25.006	113.60	43.00	0.00	0.00	BB	2.6416
23	25.324	176.40	66.96	0.00	0.00	BB	2.6343
24	25.524	210.40	52.23	0.00	0.00	BB	4.0283
25	25.609	79.10	48.17	0.00	0.00	BV	1.6421
26	25.685	194.50	54.75	0.00	0.00	VB	3.5529
27	26.139	223.80	27.58	0.00	0.00	BB	8.1139
		17842142.20	489731.60	100.00	100.00		

Missing Component Report

Component	Expected Retention (Calibration File)
t-butylquin	0.001





(36)

Isolated from Ligand = (*R*)-Cy_2MOP, Base = K_2CO_3
i.e. Table 3, entry 4

Software Version	: 6.3.1.0504	Date	: 8/13/2011 5:22:59 PM
Operator	: manager	Sample Name	: t-butylquin(Cy2MOP, K2CO3)
Sample Number	: 003	Study	:
AutoSampler	: SER200	Rack/Vial	: 1/3
Instrument Name	: HPLC	Channel	: B
Instrument Serial #	: None	A/D mV Range	: 1000
Delay Time	: 0.00 min	End Time	: 29.99 min
Sampling Rate	: 2.5000 pts/s		
Sample Volume	: 1.000000 ul	Area Reject	: 0.000000
Sample Amount	: 1.0000	Dilution Factor	: 1.00
Data Acquisition Time	: 8/12/2011 8:49:27 PM	Cycle	: 1

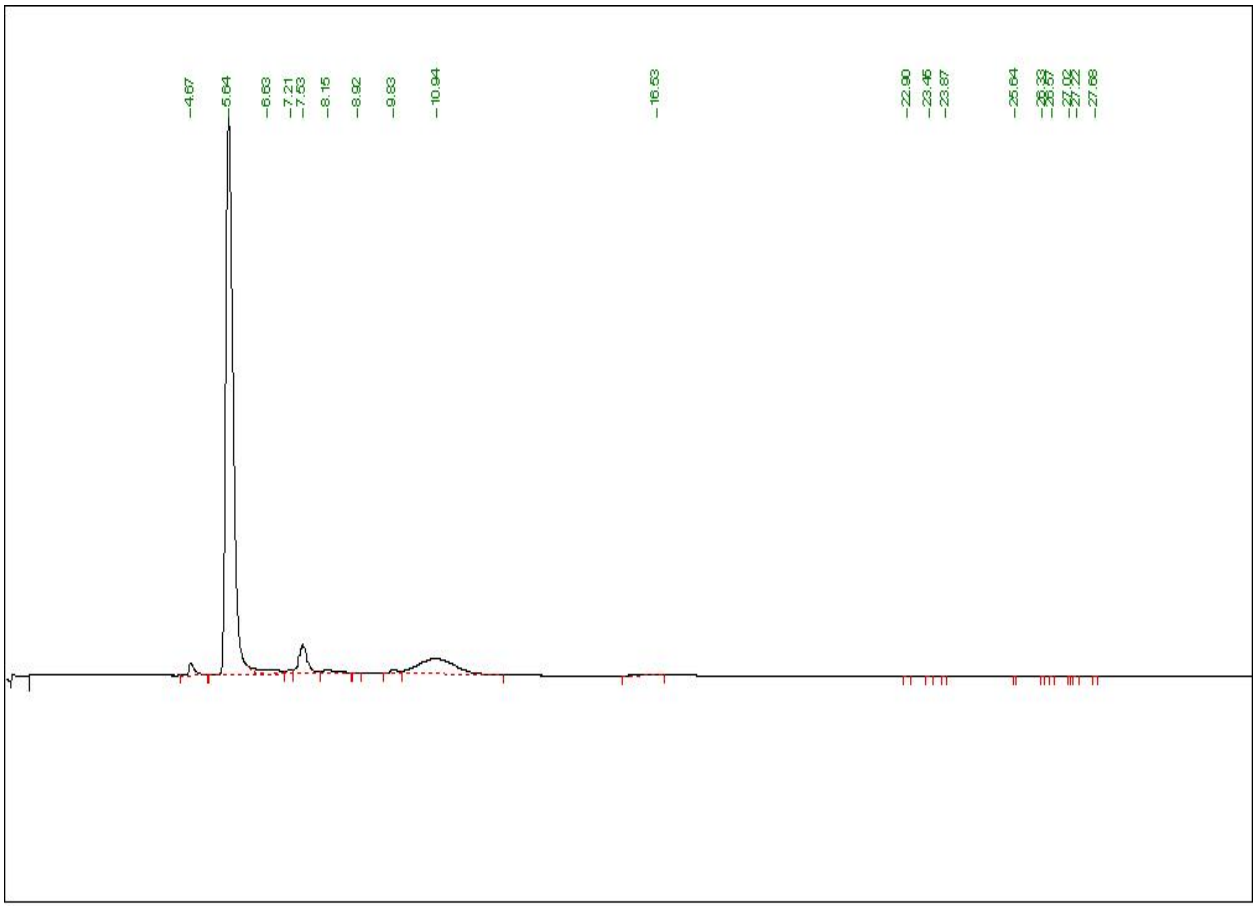
Raw Data File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb003-20110812-205341.raw
Inst Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011 from
C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb003-20110812-205341.raw
Proc Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011.mth from
Calib Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011.mth from
Report Format File: C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011.rpt
Sequence File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\August12,2011sequence.seq

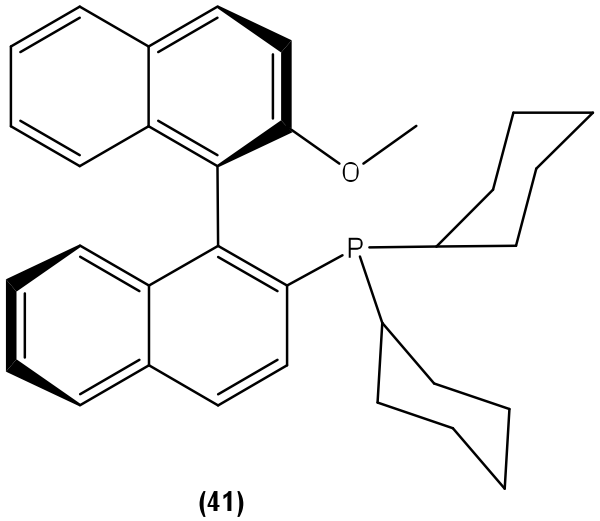
DEFAULT REPORT

Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	1.031	90.80	20.73	0.00	0.00	BB	4.3796
2	1.451	106.20	23.28	0.00	0.00	BB	4.5625
3	4.611	2858.80	464.81	0.03	0.03	BB	6.1504
4	4.801	224033.89	27910.44	2.47	2.47	BV	8.0269
5	5.667	10127.11	898.39	0.11	0.11	VB	11.2726
6	6.051	389.60	44.32	0.00	0.00	BB	8.7910
7	8.300	25095.55	1526.28	0.28	0.28	BV	16.4423
8	8.859	20069.76	873.27	0.22	0.22	VV	22.9824
9	9.385	5131.81	282.06	0.06	0.06	VV	18.1943
10	10.744	550555.19	14226.16	6.08	6.08	VV	38.7002
11	12.941	8221688.74	219752.36	90.73	90.73	VB	37.4134
12	15.826	1280.00	128.40	0.01	0.01	BB	9.9690
13	17.337	226.80	30.88	0.00	0.00	BB	7.3436
14	22.994	48.60	32.94	0.00	0.00	BB	1.4753
15	23.598	109.60	33.06	0.00	0.00	BB	3.3156
16	23.853	108.40	27.88	0.00	0.00	BB	3.8875
17	24.133	78.80	29.57	0.00	0.00	BB	2.6653
18	29.083	201.60	27.37	0.00	0.00	BB	7.3647
		9062201.26	266332.20	100.00	100.00		

Missing Component Report

Component	Expected Retention (Calibration File)
t-butylquin	0.001





(41)

Isolated from Ligand = dippf, Base = Hunig`s base

Software Version	: 6.3.1.0504	Date	: 8/13/2011 8:17:52 PM
Operator	: manager	Sample Name	: Cy2MOP
Sample Number	: 001	Study	:
AutoSampler	: SER200	Rack/Vial	: 0/0
Instrument Name	: HPLC	Channel	: B
Instrument Serial #	: None	A/D mV Range	: 1000
Delay Time	: 0.00 min	End Time	: 31.68 min
Sampling Rate	: 2.5000 pts/s		
Sample Volume	: 1.000000 ul		
Sample Amount	: 1.0000	Area Reject	: 0.000000
Data Acquisition Time	: 8/13/2011 5:41:52 PM	Dilution Factor	: 1.00
		Cycle	: 1

Raw Data File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb001-20110813-174152.raw <Incomplete>
Inst Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\Cy2MOPmethod.mth from
C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\datb001-20110813-174152.raw
Proc Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\Cy2MOPmethod.mth from
Calib Method : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\Cy2MOPmethod.mth from
Report Format File: C:\PenExe\TcWS\Ver6.3.1\Examples\\default.rpt
Sequence File : C:\PenExe\TcWS\Ver6.3.1\Examples\Augusto\Cy2MOPsequence.seq

DEFAULT REPORT

Peak #	Time [min]	Area [µV·s]	Height [µV]	Area [%]	Norm. Area [%]	BL	Area/Height [s]
-	0.001	0.00	0.00	0.00	0.00		----------
1	4.670	120076.60	12318.71	1.36	1.36	BB	9.7475
2	5.642	7053734.00	539025.99	79.99	79.99	BE	13.0861
3	6.632	180006.40	4300.40	2.04	2.04	EV	41.8581
4	7.210	40050.47	3146.11	0.45	0.45	VV	12.7301
5	7.530	401749.73	27520.99	4.56	4.56	VV	14.5979
6	8.155	56032.40	3237.41	0.64	0.64	VB	17.3078
7	8.923	304.80	41.28	0.00	0.00	BB	7.3845
8	9.829	37587.19	2531.69	0.43	0.43	BV	14.8467
9	10.936	916931.01	14247.36	10.40	10.40	VB	64.3579
10	16.533	11086.00	265.63	0.13	0.13	BB	41.7351
11	22.899	113.60	18.07	0.00	0.00	BB	6.2857
12	23.452	188.40	28.00	0.00	0.00	BB	6.7278
13	23.874	100.40	20.47	0.00	0.00	BB	4.9057
14	25.635	78.00	30.38	0.00	0.00	BB	2.5676
15	26.333	58.80	31.68	0.00	0.00	BB	1.8562
16	26.571	115.80	28.55	0.00	0.00	BB	4.0560
17	27.019	81.80	42.44	0.00	0.00	BB	1.9276
18	27.224	137.20	28.37	0.00	0.00	BB	4.8365
19	27.680	110.00	27.50	0.00	0.00	BB	4.0005
		8818542.60	606891.01	100.00	100.00		

Missing Component Report

Component	Expected Retention (Calibration File)
Cy2MOP	0.001

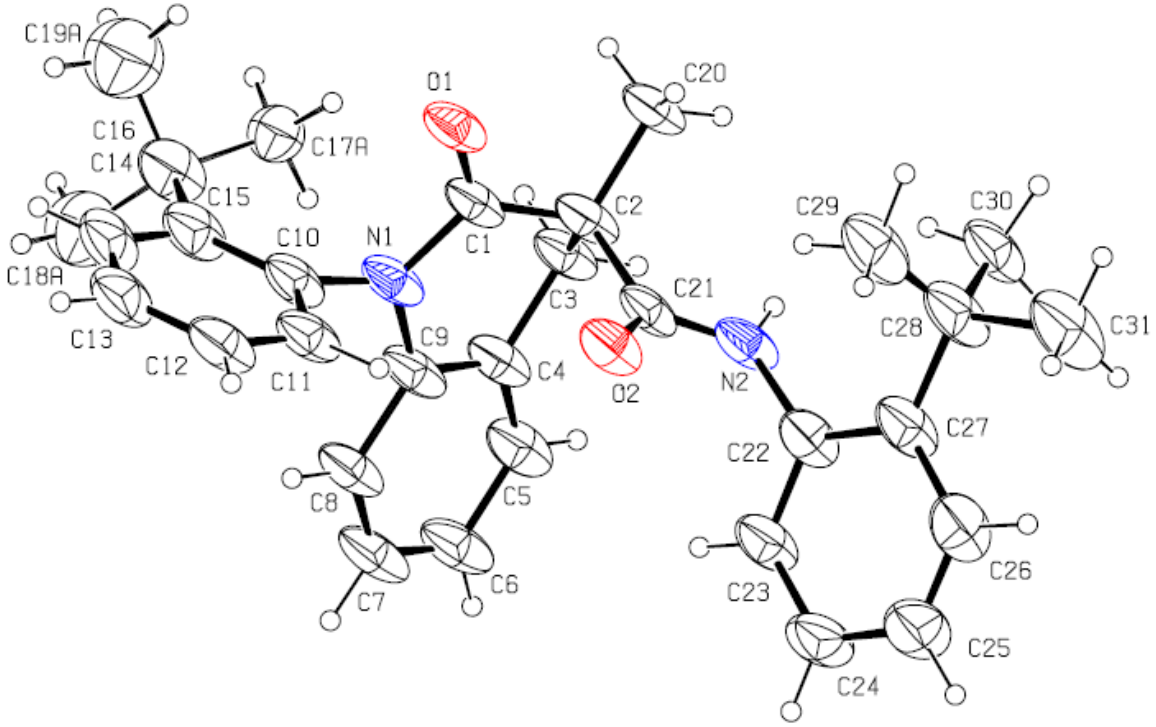

C19A
C16
C14
C17A
C15
C10
N1
C1
O1
C20
C2
C3
C21
O2
N2
C29
C30
C28
C31
C27
C22
C18A
C13
C12
C11
C9
C4
C8
C5
C7
C6
C23
C26
C25
C24

Table 1.Crystal data and structure refinement for k11200.

Identification code	loug16	
Empirical formula	C32 H37 Cl3 N2 O2	
Formula weight	587.99	
Temperature	150 K	
Wavelength	1.54178 Å	
Crystal system	Trigonal	
Space group	P31	
Unit cell dimensions	a = 12.8503(6) Å	α= 90°.
	b = 12.8503(6) Å	β= 90°.
	c = 16.9258(10) Å	γ = 120°.
Volume	2420.5(2) $Å^3$	
Z	3	
Density (calculated)	1.210 Mg/m^3	
Absorption coefficient	2.798 mm^{-1}	
F(000)	930	
Crystal size	0.16 x 0.11 x 0.11 mm^3	
Theta range for data collection	3.97 to 69.75°.	
Index ranges	-15<=h<=15, -15<=k<=15, -20<=l<=20	
Reflections collected	31931	
Independent reflections	5979 [R(int) = 0.057]	
Completeness to theta = 69.75°	99.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7351 and 0.5293	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5979 / 16 / 361	
Goodness-of-fit on F^2	1.040	
Final R indices [I>2sigma(I)]	R1 = 0.0706, wR2 = 0.2033	
R indices (all data)	R1 = 0.0799, wR2 = 0.2143	
Absolute structure parameter	0.04(2)	
Largest diff. peak and hole	0.476 and -0.248 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for k11200. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	4554(3)	7559(3)	131(4)	81(1)
C(2)	3928(3)	7123(3)	924(4)	85(1)
C(3)	4605(3)	8115(3)	1539(4)	85(1)
C(4)	5881(3)	8382(3)	1584(3)	82(1)
C(5)	6502(4)	8597(4)	2288(4)	90(2)
C(6)	7682(4)	8816(4)	2304(4)	100(2)
C(7)	8216(4)	8833(4)	1604(4)	98(2)
C(8)	7630(3)	8627(4)	893(4)	88(2)
C(9)	6440(3)	8379(3)	869(4)	84(1)
C(10)	6413(3)	8405(3)	-590(4)	84(1)
C(11)	6485(4)	7415(4)	-871(4)	87(2)
C(12)	7057(4)	7480(5)	-1570(4)	98(2)
C(13)	7544(4)	8525(5)	-1991(4)	104(2)
C(14)	7454(4)	9501(5)	-1712(5)	106(2)
C(15)	6894(4)	9476(4)	-1001(4)	101(2)
C(16)	6876(5)	10623(4)	-712(5)	122(2)
C(17A)	5952(9)	10436(9)	-62(6)	82(3)
C(18A)	8106(13)	11597(16)	-617(13)	142(6)
C(19A)	6390(20)	11030(20)	-1371(11)	159(7)
C(17B)	7574(16)	11613(14)	-1333(9)	126(5)
C(18B)	7890(10)	11294(11)	-84(7)	91(3)
C(19B)	5650(12)	10378(15)	-590(10)	121(5)
C(20)	2611(3)	6825(4)	847(4)	88(1)
C(21)	3964(3)	5965(3)	1114(3)	77(1)
C(22)	3647(4)	4521(4)	2167(4)	89(2)
C(23)	4784(4)	4826(4)	2443(4)	97(2)
C(24)	5002(5)	3982(5)	2793(4)	109(2)
C(25)	4039(5)	2817(5)	2854(5)	117(2)
C(26)	2921(5)	2508(4)	2590(5)	110(2)
C(27)	2682(4)	3358(4)	2229(4)	98(2)
C(28)	1408(4)	2954(4)	1916(6)	111(2)

C(29)	1424(5)	3182(6)	1052(5)	113(2)
C(30)	897(4)	3621(4)	2415(5)	105(2)
C(31)	527(6)	1608(5)	2093(7)	152(4)
C(32)	4818(4)	3448(4)	192(4)	87(1)
Cl(1)	3584(1)	2012(1)	179(1)	118(1)
Cl(2)	5331(2)	3917(2)	-766(1)	115(1)
Cl(3)	5971(2)	3506(2)	775(1)	133(1)
N(1)	5800(3)	8191(3)	154(3)	81(1)
N(2)	3542(3)	5497(3)	1836(3)	86(1)
O(1)	4029(2)	7388(2)	-490(3)	89(1)
O(2)	4335(2)	5525(2)	647(2)	87(1)

Table 3. Bond lengths [Å] and angles [°] for k11200.

C(1)-O(1)	1.209(7)
C(1)-N(1)	1.387(5)
C(1)-C(2)	1.520(8)
C(2)-C(3)	1.536(6)
C(2)-C(20)	1.543(5)
C(2)-C(21)	1.545(6)
C(3)-C(4)	1.500(5)
C(3)-H(3a)	0.9900
C(3)-H(3b)	0.9900
C(4)-C(5)	1.383(8)
C(4)-C(9)	1.409(8)
C(5)-C(6)	1.397(6)
C(5)-H(5)	0.9500
C(6)-C(7)	1.365(9)
C(6)-H(6)	0.9500
C(7)-C(8)	1.372(9)
C(7)-H(7)	0.9500
C(8)-C(9)	1.397(5)
C(8)-H(8)	0.9500
C(9)-N(1)	1.414(7)
C(10)-C(15)	1.382(7)
C(10)-C(11)	1.403(6)
C(10)-N(1)	1.437(7)
C(11)-C(12)	1.373(8)
C(11)-H(11)	0.9500
C(12)-C(13)	1.366(9)
C(12)-H(12)	0.9500
C(13)-C(14)	1.398(9)
C(13)-H(13)	0.9500
C(14)-C(15)	1.394(10)
C(14)-H(14)	0.9500
C(15)-C(16)	1.564(7)
C(16)-C(18a)	1.453(13)
C(16)-C(19b)	1.459(12)

C(16)-C(19a)	1.497(14)
C(16)-C(17b)	1.545(12)
C(16)-C(17a)	1.548(10)
C(16)-C(18b)	1.565(11)
C(17a)-H(17a)	0.9800
C(17a)-H(17b)	0.9800
C(17a)-H(17c)	0.9800
C(18a)-H(18a)	0.9800
C(18a)-H(18b)	0.9800
C(18a)-H(18c)	0.9800
C(19a)-H(19a)	0.9800
C(19a)-H(19b)	0.9800
C(19a)-H(19c)	0.9800
C(17b)-H(17d)	0.9800
C(17b)-H(17e)	0.9800
C(17b)-H(17f)	0.9800
C(18b)-H(18d)	0.9800
C(18b)-H(18e)	0.9800
C(18b)-H(18f)	0.9800
C(19b)-H(19d)	0.9800
C(19b)-H(19e)	0.9800
C(19b)-H(19f)	0.9800
C(20)-H(20a)	0.9800
C(20)-H(20b)	0.9800
C(20)-H(20c)	0.9800
C(21)-O(2)	1.202(6)
C(21)-N(2)	1.350(7)
C(22)-C(27)	1.389(6)
C(22)-C(23)	1.390(7)
C(22)-N(2)	1.440(6)
C(23)-C(24)	1.382(8)
C(23)-H(23)	0.9500
C(24)-C(25)	1.389(8)
C(24)-H(24)	0.9500
C(25)-C(26)	1.360(9)
C(25)-H(25)	0.9500

C(26)-C(27)	1.414(8)
C(26)-H(26)	0.9500
C(27)-C(28)	1.543(8)
C(28)-C(29)	1.490(11)
C(28)-C(31)	1.551(7)
C(28)-C(30)	1.563(9)
C(29)-H(29a)	0.9800
C(29)-H(29b)	0.9800
C(29)-H(29c)	0.9800
C(30)-H(30a)	0.9800
C(30)-H(30b)	0.9800
C(30)-H(30c)	0.9800
C(31)-H(31a)	0.9800
C(31)-H(31b)	0.9800
C(31)-H(31c)	0.9800
C(32)-Cl(1)	1.730(5)
C(32)-Cl(2)	1.740(6)
C(32)-Cl(3)	1.751(6)
C(32)-H(32)	1.0000
N(2)-H(2)	0.8800

O(1)-C(1)-N(1)	120.5(5)
O(1)-C(1)-C(2)	123.8(3)
N(1)-C(1)-C(2)	115.8(5)
C(1)-C(2)-C(3)	108.5(4)
C(1)-C(2)-C(20)	109.3(5)
C(3)-C(2)-C(20)	111.1(4)
C(1)-C(2)-C(21)	105.9(3)
C(3)-C(2)-C(21)	112.3(4)
C(20)-C(2)-C(21)	109.6(3)
C(4)-C(3)-C(2)	109.0(3)
C(4)-C(3)-H(3A)	109.9
C(2)-C(3)-H(3A)	109.9
C(4)-C(3)-H(3B)	109.9
C(2)-C(3)-H(3B)	109.9
H(3A)-C(3)-H(3B)	108.3

C(5)-C(4)-C(9)	119.8(4)
C(5)-C(4)-C(3)	123.0(5)
C(9)-C(4)-C(3)	117.2(4)
C(4)-C(5)-C(6)	121.1(6)
C(4)-C(5)-H(5)	119.4
C(6)-C(5)-H(5)	119.4
C(7)-C(6)-C(5)	118.2(6)
C(7)-C(6)-H(6)	120.9
C(5)-C(6)-H(6)	120.9
C(6)-C(7)-C(8)	122.4(4)
C(6)-C(7)-H(7)	118.8
C(8)-C(7)-H(7)	118.8
C(7)-C(8)-C(9)	120.1(5)
C(7)-C(8)-H(8)	119.9
C(9)-C(8)-H(8)	119.9
C(8)-C(9)-C(4)	118.4(5)
C(8)-C(9)-N(1)	122.7(5)
C(4)-C(9)-N(1)	118.8(3)
C(15)-C(10)-C(11)	122.1(5)
C(15)-C(10)-N(1)	124.2(4)
C(11)-C(10)-N(1)	113.7(4)
C(12)-C(11)-C(10)	120.9(5)
C(12)-C(11)-H(11)	119.6
C(10)-C(11)-H(11)	119.6
C(13)-C(12)-C(11)	118.5(5)
C(13)-C(12)-H(12)	120.7
C(11)-C(12)-H(12)	120.7
C(12)-C(13)-C(14)	120.2(6)
C(12)-C(13)-H(13)	119.9
C(14)-C(13)-H(13)	119.9
C(15)-C(14)-C(13)	123.0(6)
C(15)-C(14)-H(14)	118.5
C(13)-C(14)-H(14)	118.5
C(10)-C(15)-C(14)	115.3(5)
C(10)-C(15)-C(16)	124.8(6)
C(14)-C(15)-C(16)	119.9(5)

C(18A)-C(16)-C(19A)	104.3(12)
C(19B)-C(16)-C(17B)	113.2(10)
C(18A)-C(16)-C(17A)	118.3(10)
C(19A)-C(16)-C(17A)	99.2(10)
C(18A)-C(16)-C(15)	108.9(9)
C(19B)-C(16)-C(15)	111.4(7)
C(19A)-C(16)-C(15)	107.6(10)
C(17B)-C(16)-C(15)	106.6(8)
C(17A)-C(16)-C(15)	116.7(6)
C(19B)-C(16)-C(18B)	122.3(9)
C(17B)-C(16)-C(18B)	91.6(8)
C(15)-C(16)-C(18B)	109.4(6)
C(16)-C(17A)-H(17A)	109.5
C(16)-C(17A)-H(17B)	109.5
C(16)-C(17A)-H(17C)	109.5
C(16)-C(18A)-H(18A)	109.5
C(16)-C(18A)-H(18B)	109.5
C(16)-C(18A)-H(18C)	109.5
C(16)-C(19A)-H(19A)	109.5
C(16)-C(19A)-H(19B)	109.5
C(16)-C(19A)-H(19C)	109.5
C(16)-C(17B)-H(17D)	109.5
C(16)-C(17B)-H(17E)	109.5
H(17D)-C(17B)-H(17E)	109.5
C(16)-C(17B)-H(17F)	109.5
H(17D)-C(17B)-H(17F)	109.5
H(17E)-C(17B)-H(17F)	109.5
C(16)-C(18B)-H(18D)	109.5
C(16)-C(18B)-H(18E)	109.5
H(18D)-C(18B)-H(18E)	109.5
C(16)-C(18B)-H(18F)	109.5
H(18D)-C(18B)-H(18F)	109.5
H(18E)-C(18B)-H(18F)	109.5
C(16)-C(19B)-H(19D)	109.5
C(16)-C(19B)-H(19E)	109.5
H(19D)-C(19B)-H(19E)	109.5

C(16)-C(19B)-H(19F)	109.5
H(19D)-C(19B)-H(19F)	109.5
H(19E)-C(19B)-H(19F)	109.5
C(2)-C(20)-H(20A)	109.5
C(2)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(2)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
O(2)-C(21)-N(2)	123.5(4)
O(2)-C(21)-C(2)	121.8(5)
N(2)-C(21)-C(2)	114.8(4)
C(27)-C(22)-C(23)	121.7(4)
C(27)-C(22)-N(2)	122.9(4)
C(23)-C(22)-N(2)	115.3(4)
C(24)-C(23)-C(22)	121.3(4)
C(24)-C(23)-H(23)	119.4
C(22)-C(23)-H(23)	119.4
C(23)-C(24)-C(25)	117.2(5)
C(23)-C(24)-H(24)	121.4
C(25)-C(24)-H(24)	121.4
C(26)-C(25)-C(24)	122.1(5)
C(26)-C(25)-H(25)	118.9
C(24)-C(25)-H(25)	118.9
C(25)-C(26)-C(27)	121.5(5)
C(25)-C(26)-H(26)	119.3
C(27)-C(26)-H(26)	119.3
C(22)-C(27)-C(26)	116.2(5)
C(22)-C(27)-C(28)	124.3(5)
C(26)-C(27)-C(28)	119.5(4)
C(29)-C(28)-C(27)	111.3(5)
C(29)-C(28)-C(31)	109.9(7)
C(27)-C(28)-C(31)	111.7(6)
C(29)-C(28)-C(30)	113.0(6)
C(27)-C(28)-C(30)	107.2(5)
C(31)-C(28)-C(30)	103.5(5)

C(28)-C(29)-H(29A)	109.5
C(28)-C(29)-H(29B)	109.5
H(29A)-C(29)-H(29B)	109.5
C(28)-C(29)-H(29C)	109.5
H(29A)-C(29)-H(29C)	109.5
H(29B)-C(29)-H(29C)	109.5
C(28)-C(30)-H(30A)	109.5
C(28)-C(30)-H(30B)	109.5
H(30A)-C(30)-H(30B)	109.5
C(28)-C(30)-H(30C)	109.5
H(30A)-C(30)-H(30C)	109.5
H(30B)-C(30)-H(30C)	109.5
C(28)-C(31)-H(31A)	109.5
C(28)-C(31)-H(31B)	109.5
H(31A)-C(31)-H(31B)	109.5
C(28)-C(31)-H(31C)	109.5
H(31A)-C(31)-H(31C)	109.5
H(31B)-C(31)-H(31C)	109.5
CL1-C(32)-CL2	110.2(3)
CL1-C(32)-CL3	111.0(3)
CL2-C(32)-CL3	110.1(3)
CL1-C(32)-H(32)	108.5
CL2-C(32)-H(32)	108.5
CL3-C(32)-H(32)	108.5
C(1)-N(1)-C(9)	121.8(5)
C(1)-N(1)-C(10)	116.7(4)
C(9)-N(1)-C(10)	120.0(3)
C(21)-N(2)-C(22)	123.3(4)
C(21)-N(2)-H(2)	118.4
C(22)-N(2)-H(2)	118.4

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for k11200. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	34(2)	30(2)	175(4)	-9(2)	-5(2)	15(1)
C(2)	37(2)	43(2)	175(5)	-20(2)	-9(2)	21(2)
C(3)	38(2)	37(2)	179(5)	-18(2)	-12(2)	17(1)
C(4)	39(2)	35(2)	171(4)	-20(2)	-9(2)	18(1)
C(5)	52(2)	47(2)	168(5)	-28(2)	-10(3)	21(2)
C(6)	46(2)	66(3)	183(5)	-38(3)	-27(3)	25(2)
C(7)	39(2)	62(2)	189(5)	-37(3)	-16(3)	23(2)
C(8)	38(2)	52(2)	173(5)	-24(2)	-8(2)	21(2)
C(9)	35(2)	36(2)	176(5)	-24(2)	-13(2)	13(1)
C(10)	38(2)	40(2)	167(4)	-13(2)	-4(2)	14(1)
C(11)	42(2)	47(2)	170(5)	-18(2)	-12(2)	20(2)
C(12)	48(2)	75(3)	169(5)	-20(3)	-9(3)	29(2)
C(13)	48(2)	88(4)	156(5)	-5(3)	-6(3)	19(2)
C(14)	49(2)	61(3)	184(6)	5(3)	5(3)	10(2)
C(15)	50(2)	46(2)	192(6)	-6(3)	-6(3)	13(2)
C(16)	69(3)	37(2)	250(8)	8(3)	-1(4)	20(2)
C(20)	36(2)	57(2)	172(5)	-13(2)	-6(2)	23(2)
C(21)	30(2)	40(2)	153(4)	-14(2)	-1(2)	11(1)
C(22)	56(2)	42(2)	171(5)	-5(2)	11(2)	26(2)
C(23)	50(2)	54(2)	187(5)	-5(3)	4(3)	27(2)
C(24)	68(3)	81(3)	194(6)	6(3)	3(3)	50(3)
C(25)	84(3)	69(3)	209(7)	16(4)	10(4)	47(3)
C(26)	84(3)	50(2)	195(6)	6(3)	27(4)	34(2)
C(27)	52(2)	45(2)	190(5)	-13(3)	7(3)	20(2)
C(28)	45(2)	42(2)	224(8)	-17(3)	-1(3)	7(2)
C(29)	58(3)	83(3)	167(6)	-32(4)	-8(3)	12(2)
C(30)	44(2)	59(2)	198(6)	-4(3)	11(3)	16(2)
C(31)	72(3)	44(2)	314(12)	-16(4)	12(5)	10(2)
C(32)	69(3)	57(2)	142(4)	-9(2)	9(3)	36(2)
Cl(1)	84(1)	57(1)	198(2)	9(1)	6(1)	25(1)
Cl(2)	106(1)	96(1)	145(1)	16(1)	17(1)	51(1)

Cl(3)	108(1)	168(2)	147(1)	-31(1)	-28(1)	86(1)
N(1)	37(2)	38(1)	165(3)	-18(2)	-10(2)	17(1)
N(2)	41(2)	42(2)	175(4)	-18(2)	-6(2)	22(1)
O(1)	40(1)	47(1)	175(3)	-9(2)	-13(2)	18(1)
O(2)	54(1)	42(1)	167(3)	-14(2)	1(2)	25(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for k11200.

	x	y	z	U(eq)
H(3A)	4586	8849	1387	102
H(3B)	4215	7848	2062	102
H(5)	6120	8595	2769	108
H(6)	8101	8950	2790	119
H(7)	9022	8993	1608	118
H(8)	8034	8653	417	106
H(11)	6133	6691	-574	105
H(12)	7112	6812	-1756	117
H(13)	7945	8589	-2476	125
H(14)	7791	10214	-2020	127
H(17A)	6254	10355	453	122
H(17B)	5187	9707	-175	122
H(17C)	5829	11130	-50	122
H(18A)	8112	12359	-562	213
H(18B)	8578	11633	-1081	213
H(18C)	8456	11455	-143	213
H(19A)	6377	11758	-1209	238
H(19B)	5568	10395	-1495	238
H(19C)	6897	11205	-1839	238
H(17D)	7621	12363	-1162	189
H(17E)	7156	11366	-1842	189
H(17F)	8387	11736	-1390	189
H(18D)	8647	11386	-285	137
H(18E)	7671	10828	407	137
H(18F)	7988	12089	19	137
H(19D)	5606	11100	-713	181
H(19E)	5418	10150	-38	181
H(19F)	5102	9720	-937	181
H(20A)	2588	7515	620	133
H(20B)	2234	6644	1370	133

H(20C)	2173	6125	501	133
H(23)	5424	5630	2389	116
H(24)	5777	4189	2984	131
H(25)	4166	2218	3088	140
H(26)	2287	1702	2650	132
H(29A)	2024	4020	939	169
H(29B)	629	3029	885	169
H(29C)	1627	2647	763	169
H(30A)	1325	4476	2279	157
H(30B)	1005	3526	2979	157
H(30C)	39	3277	2302	157
H(31A)	-293	1411	1958	228
H(31B)	566	1452	2656	228
H(31C)	751	1110	1778	228
H(32)	4568	4005	423	105
H(2)	3185	5803	2119	103

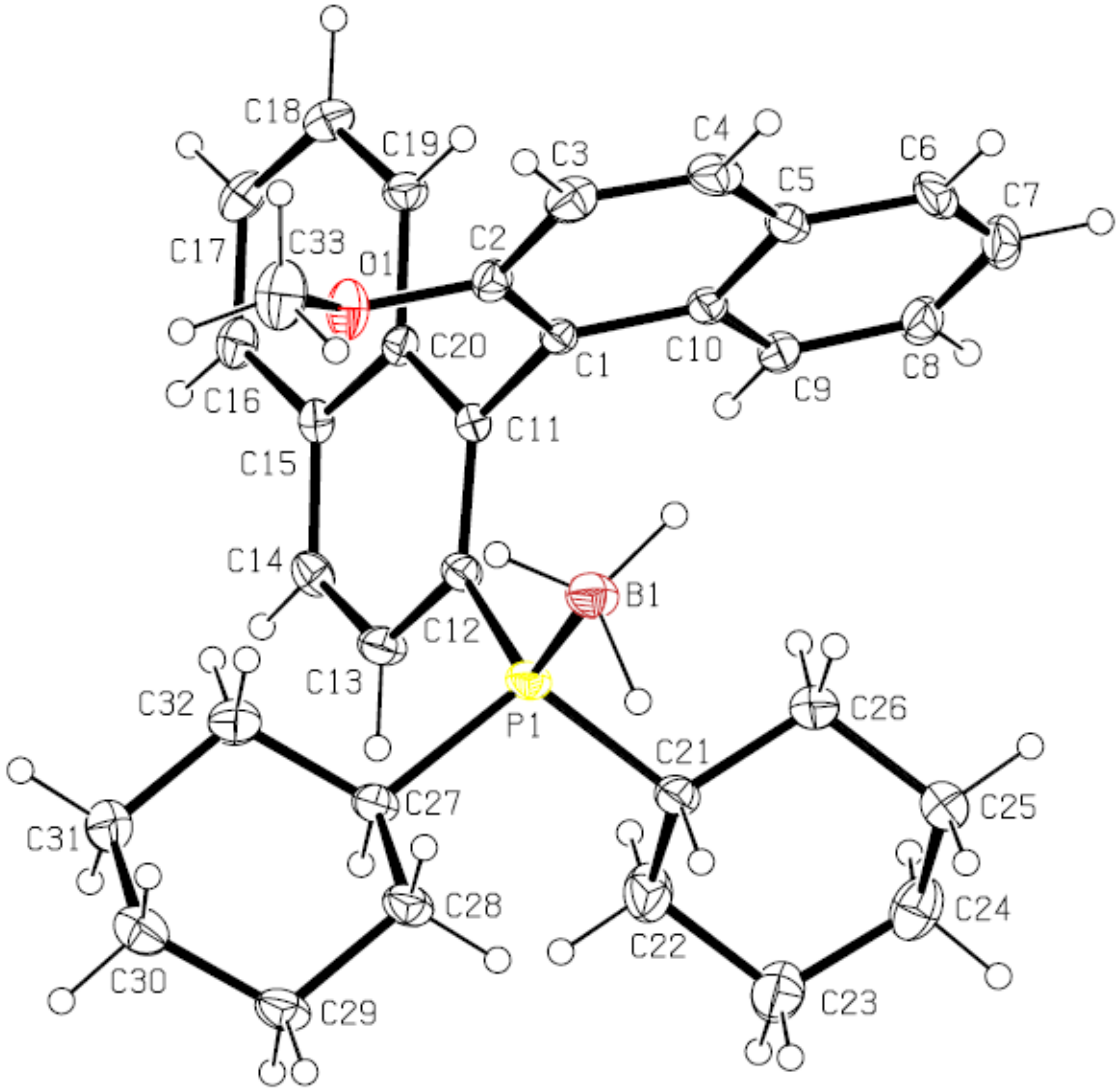

C18
C19
C3
C4
C6
C5
C7
C17
C33
O1
C2
C20
C1
C10
C8
C9
C16
C11
C15
C14
B1
C12
C13
C32
P1
C26
C21
C27
C25
C31
C28
C24
C22
C30
C29
C23

Table 1.Crystal data and structure refinement for k11125a.

Identification code	k11125a	
Empirical formula	C33 H40 B O P	
Formula weight	494.43	
Temperature	150(1) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 8.0421(4) Å	α= 90°.
	b = 17.1348(2) Å	β= 90°.
	c = 19.9983(6) Å	γ = 90°.
Volume	2755.76(16) $Å^3$	
Z	4	
Density (calculated)	1.192 Mg/m^3	
Absorption coefficient	0.124 mm^{-1}	
F(000)	1064	
Crystal size	0.30 x 0.28 x 0.06 mm^3	
Theta range for data collection	2.59 to 27.48°.	
Index ranges	-10<=h<=9, -22<=k<=19, -25<=l<=24	
Reflections collected	24491	
Independent reflections	6306 [R(int) = 0.0764]	
Completeness to theta = 27.48°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.005 and 0.742	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6306 / 0 / 338	
Goodness-of-fit on F^2	1.029	
Final R indices [I>2sigma(I)]	R1 = 0.0502, wR2 = 0.1076	
R indices (all data)	R1 = 0.0898, wR2 = 0.1245	
Absolute structure parameter	-0.14(10)	
Largest diff. peak and hole	0.233 and -0.450 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for k11125a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
P(1)	8027(1)	10158(1)	8301(1)	28(1)
O(1)	9747(2)	9304(1)	9969(1)	37(1)
C(1)	7419(3)	10095(1)	9907(1)	21(1)
C(2)	9014(3)	9993(1)	10143(1)	26(1)
C(3)	9773(3)	10571(1)	10538(1)	35(1)
C(4)	8919(4)	11234(2)	10695(1)	37(1)
C(5)	7267(3)	11356(1)	10494(1)	31(1)
C(6)	6338(4)	12030(1)	10666(1)	40(1)
C(7)	4718(4)	12116(2)	10470(1)	44(1)
C(8)	3951(3)	11535(1)	10086(1)	37(1)
C(9)	4814(3)	10881(1)	9900(1)	29(1)
C(10)	6492(3)	10770(1)	10091(1)	25(1)
C(11)	6642(3)	9478(1)	9485(1)	22(1)
C(12)	6729(3)	9480(1)	8790(1)	26(1)
C(13)	5877(3)	8881(1)	8428(1)	31(1)
C(14)	5048(3)	8293(1)	8745(1)	29(1)
C(15)	5009(3)	8250(1)	9454(1)	25(1)
C(16)	4259(3)	7618(1)	9795(1)	31(1)
C(17)	4236(3)	7597(1)	10478(1)	36(1)
C(18)	4951(3)	8205(1)	10850(1)	33(1)
C(19)	5707(3)	8821(1)	10540(1)	27(1)
C(20)	5778(3)	8860(1)	9826(1)	22(1)
C(21)	6645(3)	10798(1)	7812(1)	31(1)
C(22)	5358(4)	10415(2)	7357(2)	46(1)
C(23)	4463(4)	11035(2)	6934(2)	51(1)
C(24)	3644(4)	11652(2)	7362(2)	48(1)
C(25)	4879(4)	12017(2)	7839(1)	45(1)
C(26)	5788(4)	11399(2)	8259(1)	45(1)
C(27)	9031(3)	9503(1)	7688(1)	29(1)
C(28)	10207(3)	9956(1)	7223(1)	35(1)
C(29)	10976(3)	9413(1)	6701(1)	37(1)

C(30)	11900(3)	8740(2)	7029(1)	41(1)
C(31)	10758(4)	8293(2)	7506(1)	42(1)
C(32)	9973(4)	8836(2)	8024(1)	39(1)
C(33)	11503(3)	9250(2)	10013(2)	49(1)
B(1)	9696(4)	10818(2)	8709(2)	37(1)

Table 3. Bond lengths [Å] and angles [°] for k11125a.

P(1)-C(12)	1.842(2)
P(1)-C(21)	1.843(3)
P(1)-C(27)	1.848(2)
P(1)-B(1)	1.935(3)
O(1)-C(2)	1.364(3)
O(1)-C(33)	1.419(3)
C(1)-C(2)	1.377(3)
C(1)-C(10)	1.424(3)
C(1)-C(11)	1.491(3)
C(2)-C(3)	1.407(3)
C(3)-C(4)	1.363(4)
C(3)-H(3A)	0.9500
C(4)-C(5)	1.404(4)
C(4)-H(4A)	0.9500
C(5)-C(6)	1.417(3)
C(5)-C(10)	1.430(3)
C(6)-C(7)	1.368(4)
C(6)-H(6A)	0.9500
C(7)-C(8)	1.400(4)
C(7)-H(7A)	0.9500
C(8)-C(9)	1.370(3)
C(8)-H(8A)	0.9500
C(9)-C(10)	1.416(3)
C(9)-H(9A)	0.9500
C(11)-C(12)	1.392(3)
C(11)-C(20)	1.439(3)
C(12)-C(13)	1.431(3)
C(13)-C(14)	1.364(3)
C(13)-H(13A)	0.9500
C(14)-C(15)	1.420(3)
C(14)-H(14A)	0.9500
C(15)-C(16)	1.415(3)
C(15)-C(20)	1.424(3)
C(16)-C(17)	1.367(3)

C(16)-H(16A)	0.9500
C(17)-C(18)	1.405(3)
C(17)-H(17A)	0.9500
C(18)-C(19)	1.367(3)
C(18)-H(18A)	0.9500
C(19)-C(20)	1.430(3)
C(19)-H(19A)	0.9500
C(21)-C(22)	1.526(4)
C(21)-C(26)	1.528(3)
C(21)-H(21A)	1.0000
C(22)-C(23)	1.536(4)
C(22)-H(22A)	0.9900
C(22)-H(22B)	0.9900
C(23)-C(24)	1.510(4)
C(23)-H(23A)	0.9900
C(23)-H(23B)	0.9900
C(24)-C(25)	1.514(4)
C(24)-H(24A)	0.9900
C(24)-H(24B)	0.9900
C(25)-C(26)	1.536(4)
C(25)-H(25A)	0.9900
C(25)-H(25B)	0.9900
C(26)-H(26A)	0.9900
C(26)-H(26B)	0.9900
C(27)-C(32)	1.527(3)
C(27)-C(28)	1.537(3)
C(27)-H(27A)	1.0000
C(28)-C(29)	1.529(3)
C(28)-H(28A)	0.9900
C(28)-H(28B)	0.9900
C(29)-C(30)	1.520(4)
C(29)-H(29A)	0.9900
C(29)-H(29B)	0.9900
C(30)-C(31)	1.530(4)
C(30)-H(30A)	0.9900
C(30)-H(30B)	0.9900

C(31)-C(32)	1.529(3)
C(31)-H(31A)	0.9900
C(31)-H(31B)	0.9900
C(32)-H(32A)	0.9900
C(32)-H(32B)	0.9900
C(33)-H(33A)	0.9800
C(33)-H(33B)	0.9800
C(33)-H(33C)	0.9800
B(1)-H(1)	1.09(3)
B(1)-H(2)	1.09(3)
B(1)-H(3)	1.16(3)

C(12)-P(1)-C(21)	108.34(11)
C(12)-P(1)-C(27)	102.53(10)
C(21)-P(1)-C(27)	105.77(11)
C(12)-P(1)-B(1)	122.60(12)
C(21)-P(1)-B(1)	107.11(13)
C(27)-P(1)-B(1)	109.35(14)
C(2)-O(1)-C(33)	118.1(2)
C(2)-C(1)-C(10)	120.1(2)
C(2)-C(1)-C(11)	119.6(2)
C(10)-C(1)-C(11)	120.20(19)
O(1)-C(2)-C(1)	115.1(2)
O(1)-C(2)-C(3)	124.4(2)
C(1)-C(2)-C(3)	120.4(2)
C(4)-C(3)-C(2)	119.8(2)
C(4)-C(3)-H(3A)	120.1
C(2)-C(3)-H(3A)	120.1
C(3)-C(4)-C(5)	122.3(2)
C(3)-C(4)-H(4A)	118.8
C(5)-C(4)-H(4A)	118.8
C(4)-C(5)-C(6)	123.4(2)
C(4)-C(5)-C(10)	117.9(2)
C(6)-C(5)-C(10)	118.6(2)
C(7)-C(6)-C(5)	121.3(3)
C(7)-C(6)-H(6A)	119.3

C(5)-C(6)-H(6A)	119.3
C(6)-C(7)-C(8)	120.0(2)
C(6)-C(7)-H(7A)	120.0
C(8)-C(7)-H(7A)	120.0
C(9)-C(8)-C(7)	120.5(3)
C(9)-C(8)-H(8A)	119.8
C(7)-C(8)-H(8A)	119.8
C(8)-C(9)-C(10)	121.3(2)
C(8)-C(9)-H(9A)	119.4
C(10)-C(9)-H(9A)	119.4
C(9)-C(10)-C(1)	122.6(2)
C(9)-C(10)-C(5)	118.2(2)
C(1)-C(10)-C(5)	119.2(2)
C(12)-C(11)-C(20)	120.0(2)
C(12)-C(11)-C(1)	122.84(19)
C(20)-C(11)-C(1)	117.13(18)
C(11)-C(12)-C(13)	118.6(2)
C(11)-C(12)-P(1)	124.04(17)
C(13)-C(12)-P(1)	117.15(16)
C(14)-C(13)-C(12)	121.9(2)
C(14)-C(13)-H(13A)	119.0
C(12)-C(13)-H(13A)	119.0
C(13)-C(14)-C(15)	120.9(2)
C(13)-C(14)-H(14A)	119.6
C(15)-C(14)-H(14A)	119.6
C(16)-C(15)-C(14)	122.0(2)
C(16)-C(15)-C(20)	119.7(2)
C(14)-C(15)-C(20)	118.31(19)
C(17)-C(16)-C(15)	120.5(2)
C(17)-C(16)-H(16A)	119.8
C(15)-C(16)-H(16A)	119.8
C(16)-C(17)-C(18)	120.4(2)
C(16)-C(17)-H(17A)	119.8
C(18)-C(17)-H(17A)	119.8
C(19)-C(18)-C(17)	120.9(2)
C(19)-C(18)-H(18A)	119.5

C(17)-C(18)-H(18A)	119.5
C(18)-C(19)-C(20)	120.5(2)
C(18)-C(19)-H(19A)	119.8
C(20)-C(19)-H(19A)	119.8
C(15)-C(20)-C(19)	118.0(2)
C(15)-C(20)-C(11)	120.11(19)
C(19)-C(20)-C(11)	121.8(2)
C(22)-C(21)-C(26)	109.4(2)
C(22)-C(21)-P(1)	118.07(17)
C(26)-C(21)-P(1)	111.23(17)
C(22)-C(21)-H(21A)	105.7
C(26)-C(21)-H(21A)	105.7
P(1)-C(21)-H(21A)	105.7
C(21)-C(22)-C(23)	110.4(2)
C(21)-C(22)-H(22A)	109.6
C(23)-C(22)-H(22A)	109.6
C(21)-C(22)-H(22B)	109.6
C(23)-C(22)-H(22B)	109.6
H(22A)-C(22)-H(22B)	108.1
C(24)-C(23)-C(22)	112.1(2)
C(24)-C(23)-H(23A)	109.2
C(22)-C(23)-H(23A)	109.2
C(24)-C(23)-H(23B)	109.2
C(22)-C(23)-H(23B)	109.2
H(23A)-C(23)-H(23B)	107.9
C(23)-C(24)-C(25)	111.1(2)
C(23)-C(24)-H(24A)	109.4
C(25)-C(24)-H(24A)	109.4
C(23)-C(24)-H(24B)	109.4
C(25)-C(24)-H(24B)	109.4
H(24A)-C(24)-H(24B)	108.0
C(24)-C(25)-C(26)	111.9(2)
C(24)-C(25)-H(25A)	109.2
C(26)-C(25)-H(25A)	109.2
C(24)-C(25)-H(25B)	109.2
C(26)-C(25)-H(25B)	109.2

H(25A)-C(25)-H(25B)	107.9
C(21)-C(26)-C(25)	111.1(2)
C(21)-C(26)-H(26A)	109.4
C(25)-C(26)-H(26A)	109.4
C(21)-C(26)-H(26B)	109.4
C(25)-C(26)-H(26B)	109.4
H(26A)-C(26)-H(26B)	108.0
C(32)-C(27)-C(28)	109.8(2)
C(32)-C(27)-P(1)	112.22(16)
C(28)-C(27)-P(1)	111.36(16)
C(32)-C(27)-H(27A)	107.7
C(28)-C(27)-H(27A)	107.7
P(1)-C(27)-H(27A)	107.7
C(29)-C(28)-C(27)	110.71(19)
C(29)-C(28)-H(28A)	109.5
C(27)-C(28)-H(28A)	109.5
C(29)-C(28)-H(28B)	109.5
C(27)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	108.1
C(30)-C(29)-C(28)	111.5(2)
C(30)-C(29)-H(29A)	109.3
C(28)-C(29)-H(29A)	109.3
C(30)-C(29)-H(29B)	109.3
C(28)-C(29)-H(29B)	109.3
H(29A)-C(29)-H(29B)	108.0
C(29)-C(30)-C(31)	110.7(2)
C(29)-C(30)-H(30A)	109.5
C(31)-C(30)-H(30A)	109.5
C(29)-C(30)-H(30B)	109.5
C(31)-C(30)-H(30B)	109.5
H(30A)-C(30)-H(30B)	108.1
C(32)-C(31)-C(30)	111.5(2)
C(32)-C(31)-H(31A)	109.3
C(30)-C(31)-H(31A)	109.3
C(32)-C(31)-H(31B)	109.3
C(30)-C(31)-H(31B)	109.3

H(31A)-C(31)-H(31B)	108.0
C(27)-C(32)-C(31)	111.2(2)
C(27)-C(32)-H(32A)	109.4
C(31)-C(32)-H(32A)	109.4
C(27)-C(32)-H(32B)	109.4
C(31)-C(32)-H(32B)	109.4
H(32A)-C(32)-H(32B)	108.0
O(1)-C(33)-H(33A)	109.5
O(1)-C(33)-H(33B)	109.5
H(33A)-C(33)-H(33B)	109.5
O(1)-C(33)-H(33C)	109.5
H(33A)-C(33)-H(33C)	109.5
H(33B)-C(33)-H(33C)	109.5
P(1)-B(1)-H(1)	107.7(16)
P(1)-B(1)-H(2)	108.3(13)
H(1)-B(1)-H(2)	115(2)
P(1)-B(1)-H(3)	95.6(13)
H(1)-B(1)-H(3)	114.0(19)
H(2)-B(1)-H(3)	114(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for k11125a. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
P(1)	38(1)	25(1)	21(1)	-1(1)	3(1)	-6(1)
O(1)	26(1)	29(1)	56(1)	-1(1)	-1(1)	4(1)
C(1)	27(1)	18(1)	19(1)	2(1)	3(1)	-3(1)
C(2)	30(1)	22(1)	27(1)	2(1)	-1(1)	-1(1)
C(3)	37(2)	34(1)	34(1)	3(1)	-9(1)	-9(1)
C(4)	54(2)	32(1)	26(1)	-4(1)	-5(1)	-15(1)
C(5)	50(2)	21(1)	23(1)	-1(1)	7(1)	-8(1)
C(6)	67(2)	20(1)	32(2)	-7(1)	14(1)	-6(1)
C(7)	66(2)	23(1)	43(2)	6(1)	21(2)	9(1)
C(8)	45(2)	32(1)	35(2)	9(1)	12(1)	10(1)
C(9)	37(1)	26(1)	25(1)	5(1)	6(1)	1(1)
C(10)	35(1)	21(1)	20(1)	3(1)	6(1)	-2(1)
C(11)	26(1)	19(1)	22(1)	-1(1)	1(1)	2(1)
C(12)	32(1)	23(1)	22(1)	-2(1)	2(1)	-2(1)
C(13)	42(2)	30(1)	22(1)	-3(1)	1(1)	-6(1)
C(14)	31(1)	25(1)	31(1)	-7(1)	2(1)	-3(1)
C(15)	27(1)	19(1)	30(1)	-2(1)	1(1)	3(1)
C(16)	31(1)	23(1)	40(2)	2(1)	-2(1)	-2(1)
C(17)	36(2)	30(1)	40(2)	13(1)	0(1)	-3(1)
C(18)	36(1)	37(2)	27(1)	7(1)	0(1)	-1(1)
C(19)	30(1)	29(1)	23(1)	2(1)	2(1)	-1(1)
C(20)	21(1)	21(1)	25(1)	3(1)	1(1)	2(1)
C(21)	45(2)	24(1)	24(1)	0(1)	6(1)	-6(1)
C(22)	53(2)	32(2)	53(2)	-7(1)	-14(2)	1(1)
C(23)	58(2)	39(2)	56(2)	-4(1)	-23(2)	1(2)
C(24)	41(2)	39(2)	63(2)	15(1)	4(1)	-3(1)
C(25)	62(2)	37(2)	36(2)	-3(1)	4(1)	8(1)
C(26)	69(2)	37(2)	29(1)	2(1)	5(1)	8(1)
C(27)	37(1)	28(1)	22(1)	-2(1)	3(1)	-6(1)
C(28)	46(2)	32(1)	26(1)	-2(1)	9(1)	-8(1)
C(29)	45(2)	41(2)	26(1)	-3(1)	9(1)	-8(1)

C(30)	38(2)	49(2)	36(2)	-8(1)	3(1)	1(1)
C(31)	45(2)	39(2)	41(2)	0(1)	4(1)	10(1)
C(32)	45(2)	42(2)	32(1)	4(1)	7(1)	1(1)
C(33)	26(1)	47(2)	74(2)	2(2)	-3(1)	6(1)
B(1)	48(2)	32(2)	30(2)	-2(1)	0(1)	-11(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for k11125a.

	x	y	z	U(eq)
H(3A)	10877	10500	10696	42
H(4A)	9461	11626	10950	45
H(6A)	6849	12429	10923	48
H(7A)	4114	12569	10594	53
H(8A)	2824	11595	9953	45
H(9A)	4275	10494	9638	35
H(13A)	5890	8892	7953	38
H(14A)	4490	7907	8488	35
H(16A)	3767	7205	9547	37
H(17A)	3734	7169	10702	43
H(18A)	4908	8189	11325	40
H(19A)	6190	9226	10800	33
H(21A)	7391	11104	7509	37
H(22A)	4535	10129	7631	55
H(22B)	5914	10036	7058	55
H(23A)	5277	11287	6632	61
H(23B)	3609	10778	6654	61
H(24A)	2723	11414	7619	57
H(24B)	3167	12062	7070	57
H(25A)	4287	12381	8142	54
H(25B)	5705	12322	7582	54
H(26A)	6628	11657	8546	54
H(26B)	4981	11132	8554	54
H(27A)	8135	9269	7405	35
H(28A)	9582	10376	6994	42
H(28B)	11101	10201	7491	42
H(29A)	10086	9202	6410	45
H(29B)	11755	9712	6417	45
H(30A)	12869	8944	7279	49
H(30B)	12318	8380	6679	49

H(31A)	9869	8033	7247	50
H(31B)	11407	7884	7739	50
H(32A)	9198	8535	8309	47
H(32B)	10854	9054	8315	47
H(33A)	11872	8755	9817	73
H(33B)	11841	9271	10484	73
H(33C)	12011	9685	9770	73
H(1)	9090(40)	11152(16)	9105(15)	63(9)
H(2)	10730(30)	10449(14)	8870(12)	40(7)
H(3)	9980(30)	11178(14)	8229(14)	49(8)

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