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FACULTÉ DES ÉTUDES SUPÉRIEURES ET POSTDOCTORALES

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The Use of Magnesium Mediated Carbometallation in Tandem Reactions and Multi-component Couplings

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The Use of Magnesium Mediated Carbometallation in Tandem Reactions and Multi-Component Couplings

By

Pierre E. Tessier

B.Sc. (Honours, Co-Op), University of Ottawa, 2001

A Thesis Submitted to the School of Graduate Studies and Research in Partial Fullfillment of the Requirements for the Degree of Master of Science

Ottawa-Carleton Chemistry Institute
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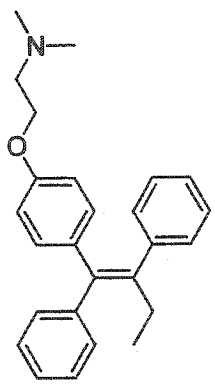
LIST OF ABBREVIATIONS

Δ	heat
acac	acetoxyacetyl
Bu	butyl
C	carbon
Cp	cyclopentadienyl
dba	dibenzilidine acetone
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEA	diethylamine
DMAP	4-dimethylaminopyridine
DMF	*N,N*-dimethylformamide
DMP	Dess-Martin Periodinane
DMSO	dimethyl sulfoxide
E	electrophile
ee	enantiomeric excess
EI	electron impact
Et	ethyl
Ether	diethyl ether
eq	equivalents
GC	gas chromatography
h	hour
IBX	*o*-Iodoxybenzoic Acid
IR	infrared
^{i}Pr	isopropyl
LDA	lithium diisopropylamine
m-CPBA	*m*-chloroperoxybenzoic acid
Me	methyl
min	minutes
ms	molecular sieves
NBS	*N*-bromosuccinimide

NMP	*N*-methyl pyrolidone
NMR	nuclear magnetic resonance
Ph	phenyl
ppm	parts per million
p-TsOH	*p*-toluene sulfonic acid
RT	room temperature
SET	single electron transfer
TBAF	tetrabutylammonium fluoride
TBAI	tetrabutylammonium iodide
TBS	*t*-butyldimethylsilyl
Tf	triflate
TFA	trifluroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl

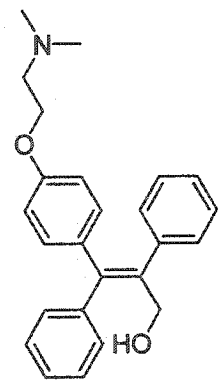
ABSTRACT

Magnesium-mediated carbometallation has been applied towards the synthesis of a variety of diverse synthetic targets. A novel carbometallation-palladium cross coupling reaction has been developed allowing for quick access to a wide variety of tetra-substituted alkenes. This methodology has been applied towards the synthesis of the anti-cancer agent (*Z*)-tamoxifen (**66**) and various analogues (**82**). Additional work has been done on the development of a new carbometallation-annulation reaction for the synthesis of unique bicyclic dienes based on natural chiral compounds such as camphor (**124**). This protocol has been employed towards the development of new chiral reagents including a chiral IBX derivative (**119**).



(*Z*)-Tamoxifen

66



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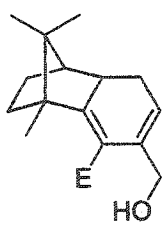

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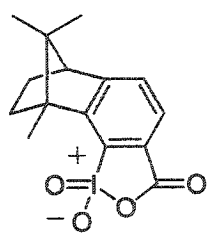

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I have to thank the rest of my family, my brother Darryl who has provided countless hours of conversation and advice, and who was never afraid to set me straight when I had "numpty" notions. My sister Sarah, and brother Ryan, who were always there for me and of course my parents whose love and support through the years can never be repaid.

I. Magnesium Mediated Carbometallation

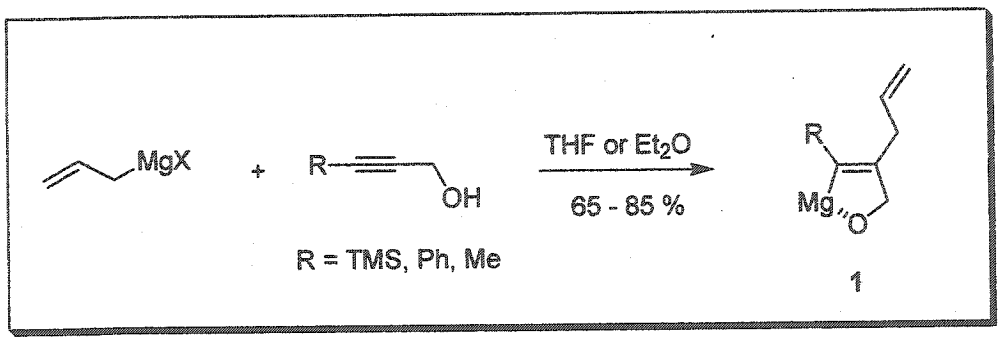
I-I. Carbometallation Introduction

The carbometallation reaction has been known for over 70 years, with the first reported example being attributed to Bähr and Ziegler in 1927.[1] The modern term carbometallation was introduced by Negishi, who suggested this process was a carbon metal addition across an unsaturated C-C bond, where the resulting metal carbon bond that is formed is available for subsequent transformations.[2]

The carbometallation reaction has been explored extensively, especially during the last decade. A wide variety of different metals have been employed including zinc, copper, lithium and tin, among others. Unsaturated acceptors have also been studied. Application towards substitution of alkynes, alkenes and allenes are possible. Most reported acceptors contain an allylic or homoallylic oxygen, with either a free hydroxyl or alkoxy being the most common substituent. These results are summarized in several review articles.[3]

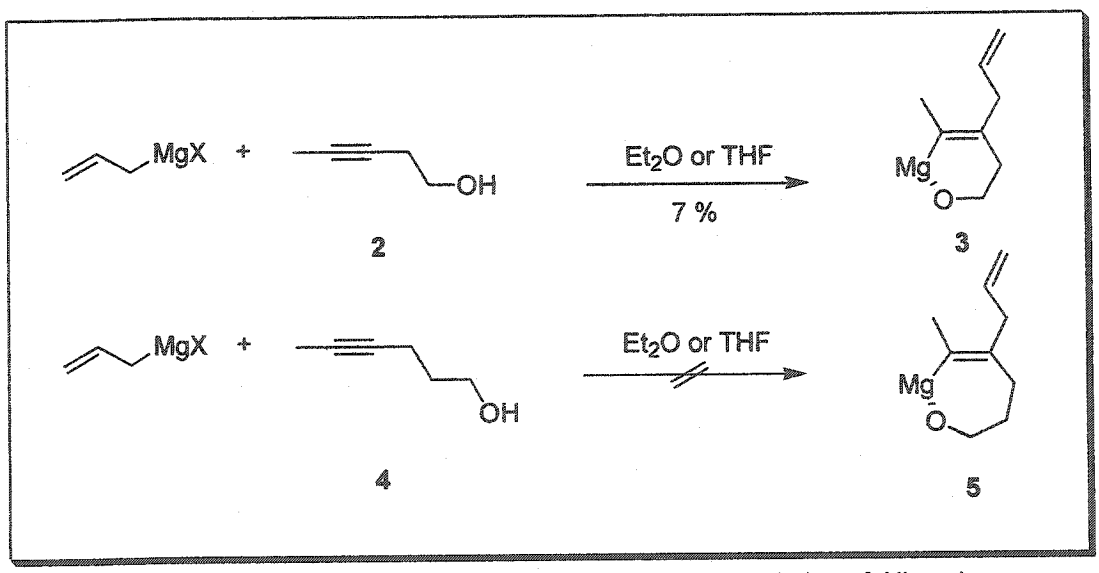
I-II. Magnesium Mediated Carbometallation

Grignard reagents have been used for many years as a facile method for the formation of C-C bonds, and although organo-magnesium reagents display poor reactivity towards non–functionalized triple bonds, allyl magnesium halides have been shown to react well with propargyl alcohols (Scheme 1).[4]



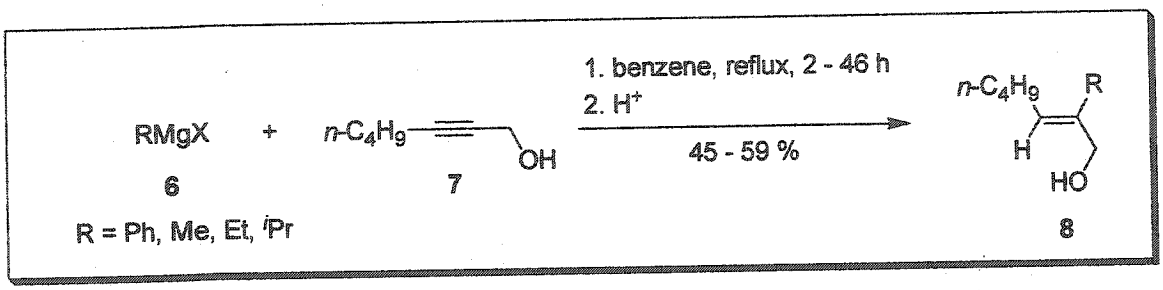
Scheme 1: *Magnesium Mediated Carbometallation of Propargyl Alcohols*

The reaction proceeds via intermediate chelate **1**, and upon quenching with an appropriate electrophile, allows for very well defined regio and stereochemistry in the synthesis of tetra-substituted alkenes. The role of the oxygen is quite important, as can be seen in analogous examples involving 3-pentyn-1-ol (**2**) and 4-hexyn-1-ol (**4**). In these cases, the yields drop to 7 % and 0 % respectively, as the formation of the chelate becomes more difficult (Scheme 2).



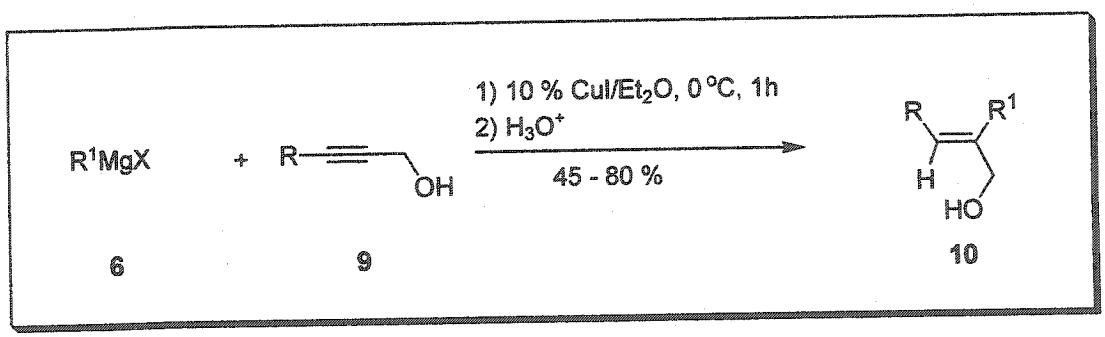
Scheme 2: *Effect of Chain Length on Carbomagnesiation of Alkynols*

Initial attempts to expand the carbometallation of propargyl alcohols to include Grignard reagents other than allyl magnesium halides met with mixed results. The reaction could be conducted with other Grignard reagents, but the yields were generally lower and required much harsher conditions (Scheme 3).[5]



***Scheme 3:** Magnesium Mediated Carbometallation of 5 - Heptynol*

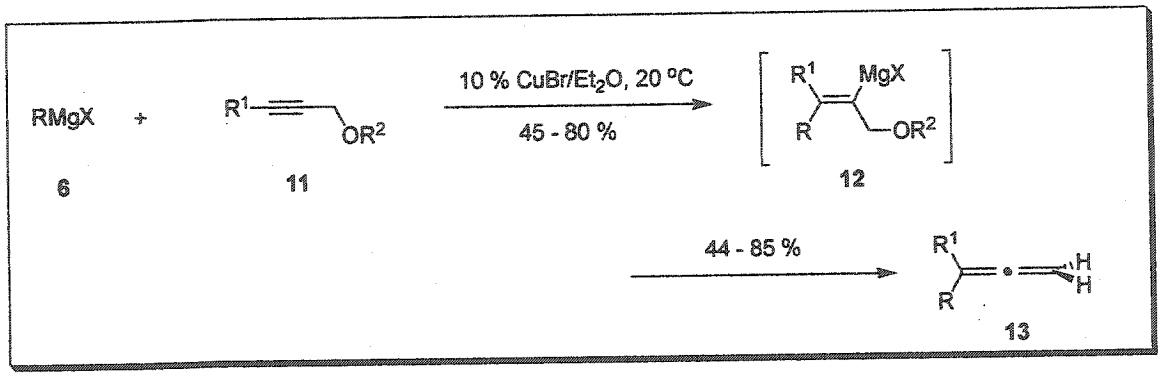
Use of catalytic copper (I) iodide as an additive circumvents these problems, presumably due to transmetallation with the magnesium to form a much softer nucleophile. These conditions allow for improved yields with most Grignard reagents (except vinyl), under much milder reaction conditions while still maintaining well defined regio and stereochemistry (Scheme 4).[6]



***Scheme 4:** Carbomagnesiation with Copper (I) Iodide*

Investigations to try and extend this heteroatom assistance to other functionalities besides propargyl alcohols, have met with limited success, with propargyl amines

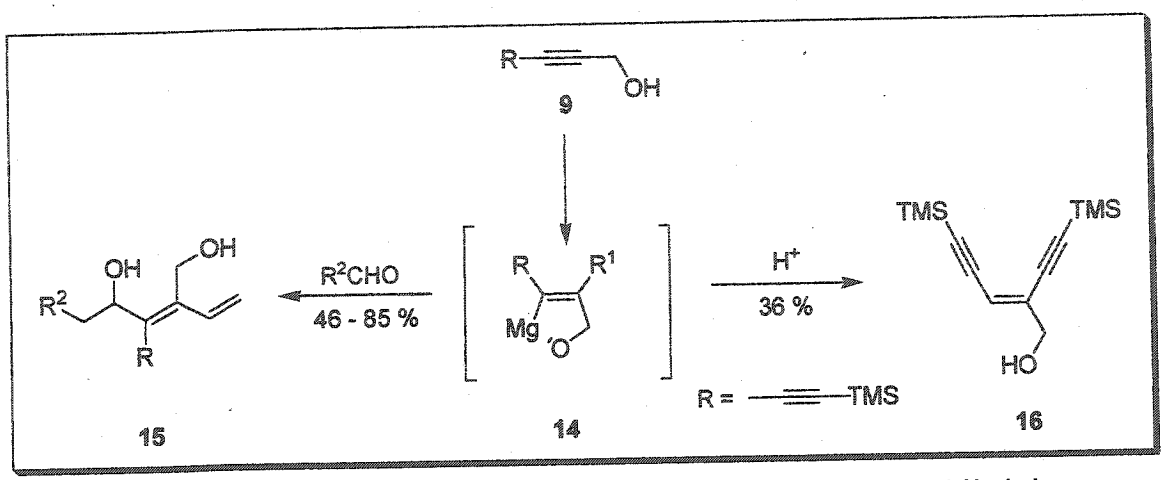
reacting under carefully controlled conditions.[7] Propargylic ethers, on the other hand, have been shown to react with Grignard reagents to form allenes exclusively (**13**). In these cases, a copper catalyst has no effect other than to allow the reaction to occur under milder conditions (Scheme 5).[8]



Scheme 5: *Allenes via Carbomagnesiation of Propargylic Ethers*

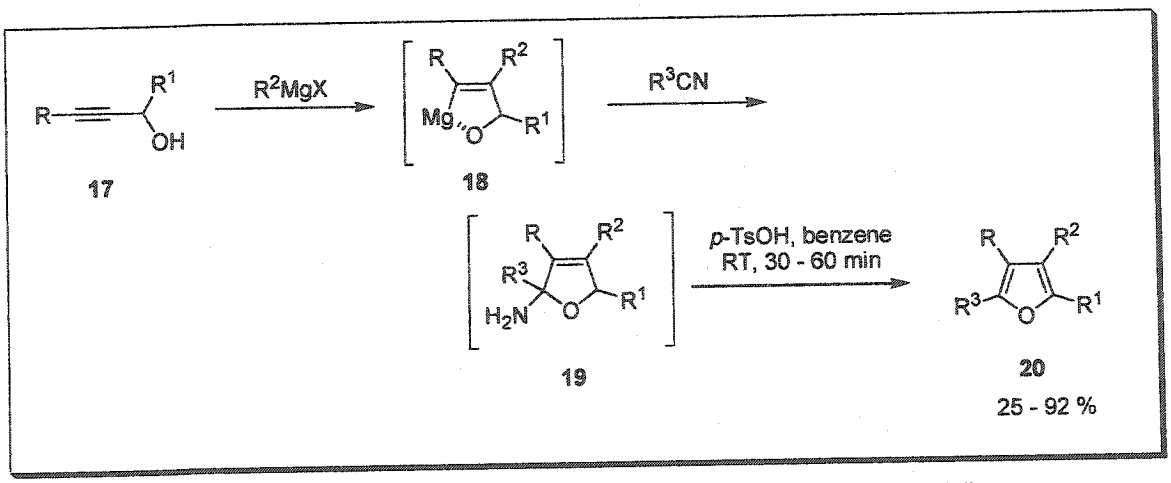
I-III. Magnesium Mediated Carbometallation for Synthesis.

Fallis and co-workers have revealed that the nature of the solvent system used is critical for the success of carbomagnesiation of propargylic alcohols with vinyl Grignard reagents. In general, use of a non polar co-solvent such as cyclohexane gives yields that are both higher and much more reproducible. This protocol is also quite effective for the use of acetylenic Grignard reagents and provides a facile route into a variety of synthetic products including enediynes and dienediols (Scheme 6).[9]



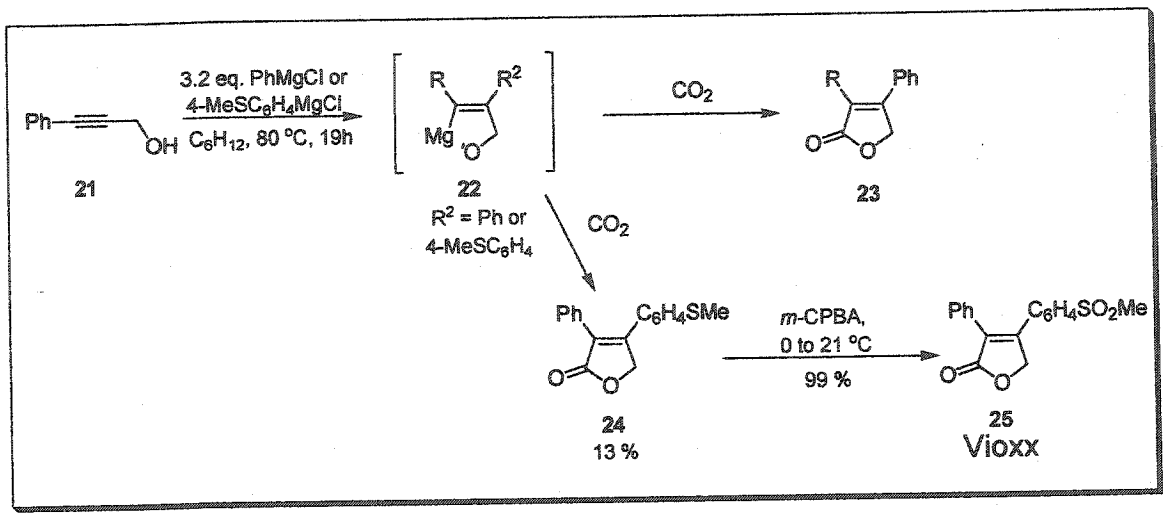
Scheme 6: *Enediynes and Dienediols via Carbomagnesiation of Propargyl Alcohols*

One of the most attractive aspects of the carbometallation reaction is that it is a three component coupling. Each of the three components, namely the organometallic, the unsaturated acceptor, and the electrophile can be varied to give a remarkable diversity of products with ease. Fallis and co-workers have exploited magnesium-mediated carbometallation to quickly generate complex synthetic targets. Carbometallation of propargyl alcohols have been shown to quench readily with various nitriles to give the hemiaminal **19**. Subsequent treatment with acid results in dehydration to substituted furans (**20**), with yields associated with primary propargylic alcohols superior to those with secondary alcohols (Scheme 7).[10]



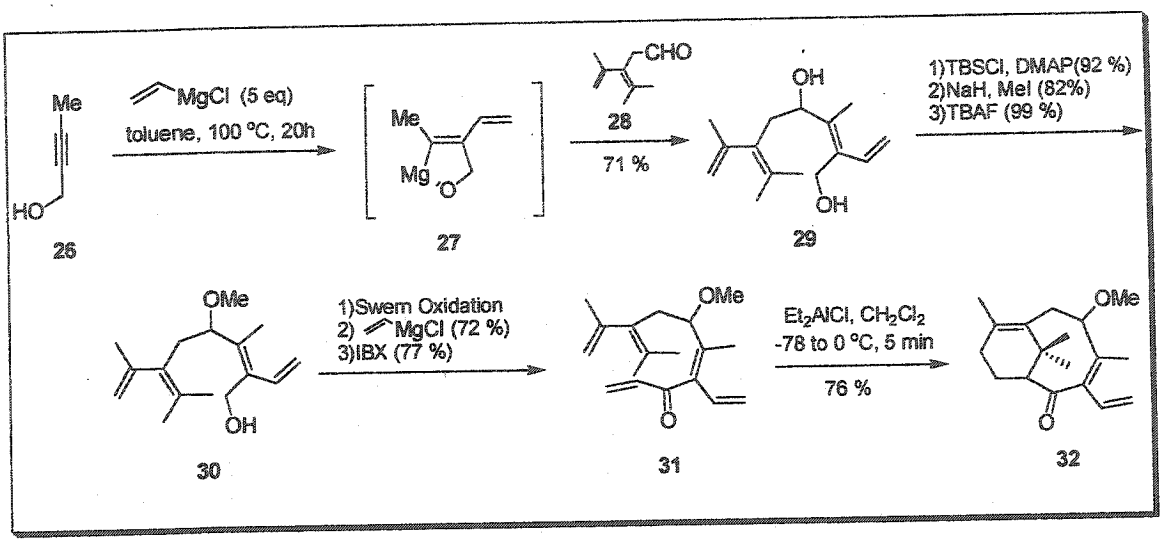
Scheme 7: *Substituted Furans via Magnesium Mediated Carbometallation*

Changing the electrophile to carbon dioxide also provides a simple route into substituted furanones. Variation of the propargyl alcohol and Grignard reagent leads to a number of furanones with different substitution patterns, of which some are of great practical interest. Use of 4-thioanisyl magnesium chloride leads to furanone **24**, which upon oxidation with *m*-CPBA gives the Merck anti-inflammatory drug Vioxx® (**25**) in two steps (Scheme 8).[11]



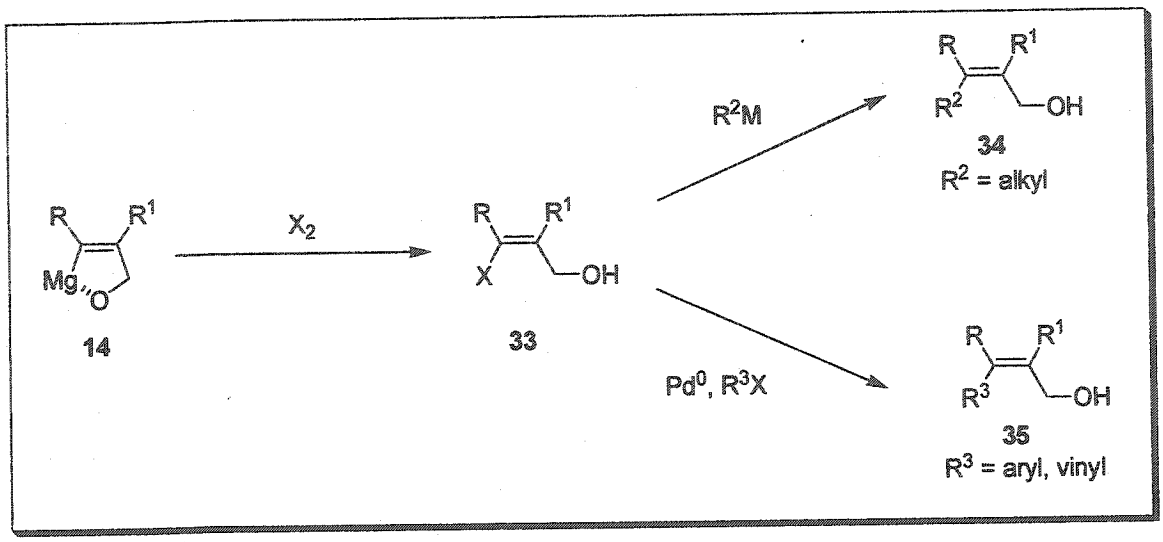
Scheme 8: Furanones and Vioxx® via Carbomagnesiation of Propargyl Alcohols

Magnesium mediated carbometallation has also been employed as the key step in a quick route to taxane AB ring analogs. Carbometallation can proceed with 2-butynol and vinyl magnesium chloride, and can then quenched with aldehyde **28**. Subsequent transformations lead to the penta-ene **31** which is subjected to a Lewis acid catalyzed Diels Alder reaction to give the functionalized AB taxane **32** in only eight steps and 22 % overall yield (Scheme 9).[12]



Scheme 9: A Functionalized AB Taxane via Carbomagnesiation

The number of electrophiles available for quenching the carbometallation product does have limitations, namely that the electrophile must undergo nucleophilic attack, and must have sufficient steric accessibility to allow this attack to take place. The nature of the magnesium intermediate as a cyclic chelate provides limitations as well, because of its somewhat lowered reactivity. For example, it has been found that alkyl halides other than allyl halides do not add readily. This can be circumvented by quenching with a halogen source to give the corresponding vinyl halide, which can then be reacted with further organometallics to give the alkylation products, or with aryl or vinyl halides and a palladium species to give aryl and vinyl substitution patterns (Scheme 10).[13]

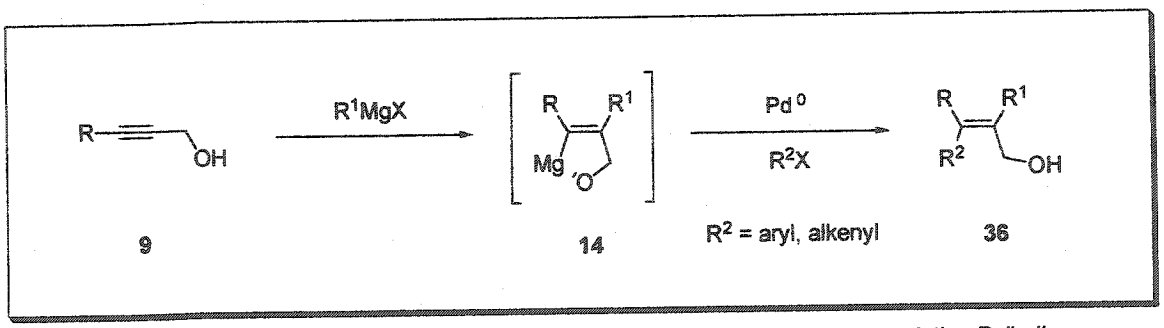


Scheme 10: *Tetrasubstituted Alkenes via Magnesium Mediated Carbometallation*

II. Magnesium Mediated Carbometallation Results

II-I. Tandem Carbomagnesiation-Palladium Cross Coupling

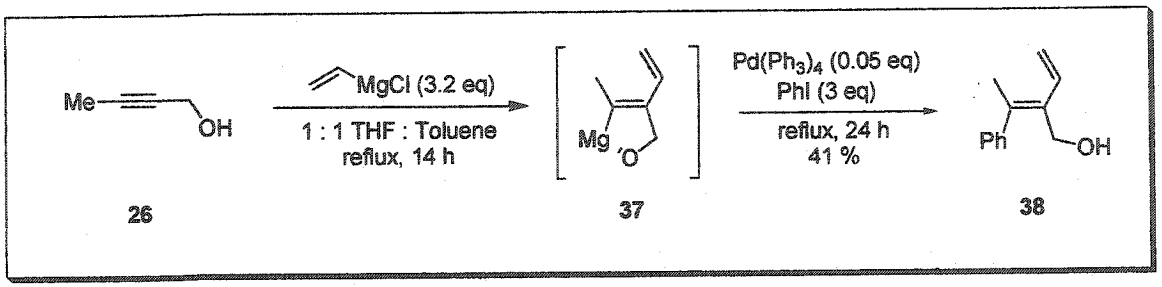
As mentioned previously, magnesium mediated carbometallation of propargylic alcohols has been employed extensively for the preparation of vinyl halides through use of an electrophilic halogen source such as iodine or *N*-bromosuccinimide. These vinyl halides can then be cross coupled through a variety of reactions employing palladium catalysts to give alkenyl and aryl alkenes, a process that has been used extensively in the Fallis laboratory. Although powerful, this process has the disadvantage of requiring two steps to complete the desired transformation. The initial product arising from carbomagnesiation of propargyl alcohols with Grignard reagents is the magnesium chelate **14**, and it was anticipated that the carbon-magnesium bond from this chelate could undergo a palladium catalyzed cross coupling reaction with either an aryl or vinyl halide (Scheme 11). This protocol would allow for quick access to a wider range of tetra-substituted alkenes without the need to proceed through an intermediate vinyl halide.



***Scheme 11:** A General Route to Tetrasubstituted Alkenes via a Carbomagnesiation-Palladium Cross Coupling Strategy*

Our initial attempt at this strategy involved use of 2-butynol as a substrate, with vinyl magnesium chloride. After 16 hours of refluxing, $Pd(PPh_3)_4$ in 5 mol % was added as a catalyst. In this case, three equivalents of phenyl iodide were added as the cross coupling partner, and the reaction refluxed for an additional 24 hours. An excess of the

Grignard reagent was used for the carbometallation reaction, so we assumed there would be competition in the cross coupling between the aryl halide with the magnesium chelate **14**, and excess vinyl magnesium chloride, a problem that was circumvented with an excess of aryl halide. Rather than using cyclohexane as a non-polar co-solvent, toluene was chosen because of its higher boiling point to aid in the cross coupling. Under these conditions the reaction was successful and alcohol **38** was obtained in 41% yield (Scheme 12).



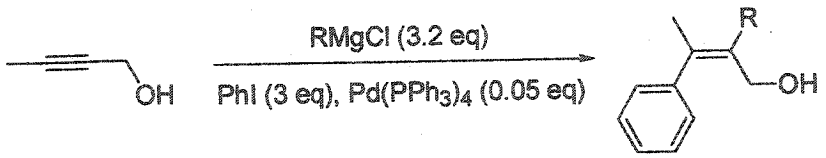
Scheme 12 : *Carbomagnesiation of 2-Butynol with Vinyl Magnesium Chloride Followed by Palladium Cross Coupling with Phenyl Iodide*

II-I-i. Grignard Studies.

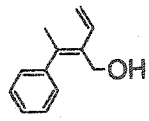
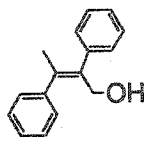
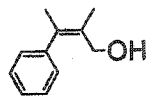
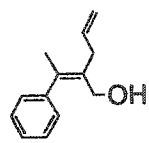
Our next studies centered on determining the effect of the Grignard reagent on the yield of the reaction. For these studies a standard set of reaction conditions was chosen employing 2-butynol as the substrate, with 5 mol % of $Pd(PPh_3)_4$ and 3 equivalents of phenyl iodide (Table 1).

The best Grignard reagents for this reaction were phenyl and allyl magnesium chloride giving yields of 73 and 60% for their respective alcohols (**39b, 39d**) (Entries b, d).

Table 1: Carbometallation of 2-Butynol Followed by Palladium Cross Coupling with PhI



26 **39**

Entry	Grignard	Alcohol	Yield
a		 **39a**	41
b	PhMgCl	 **39b**	73[14]
c	MeMgCl	 **39c**	10
d		 **39d**	60[14]

Use of vinyl magnesium chloride provides a lower yield (Entry a), while use of methyl magnesium chloride leads to a dramatic drop in yield all the way down to 10 % (Entry c). This is perhaps not surprising when one takes into account the fact that magnesium mediated carbometallation does not work well with alkyl Grignard reagents in the absence of a copper catalyst.[6] Addition of copper (I) iodide could possibly have increased the yield for this particular example, but, in order to generate a standard set of conditions, it was not included.

Interestingly enough, it seems that the yield of the reaction is highly influenced by the nature of the organo-magnesium reagent used. In these examples the yield of the

reaction seems to follow the trend of Grignard reagent reactivity in carbometallation reactions, with allyl and phenyl being best, followed by vinyl, and finally by alkyl.

II-I-ii. Cross Coupling Partner Studies.

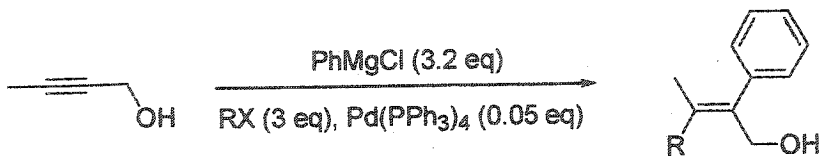
With the reactivity of the Grignard reagent established, the next step was to determine the effect of the cross coupling partner on the yield. Once again the same reaction conditions were employed. Phenyl magnesium chloride was added to 2-butynol, while varying the cross coupling partner (Table 2).

In these cases, the nature of the cross coupling partner did not seem to affect results to a large extent. Both aryl iodides and aryl bromides gave yields that were similar to those found previously with phenyl magnesium chloride (Entries a, b). Even when an electron donating substituent was added onto the ring system as in the case of the methoxy group on *p*-bromo anisole, the yield did not decrease significantly (Entry d). Alkenyl halides also seemed to cross couple just as efficiently giving alcohol **40c** in 71% when 2-bromo-3-methyl-but-2-ene was used in the cross coupling (Entry c). The procedure also seems to be tolerant of silicon functionality, as 3-trimethylsilanyl-prop-2-yn-1-ol was carbometallated with vinyl magnesium chloride and cross coupled with phenyl iodide to give alcohol **40e** in 61% yield (Entry e).

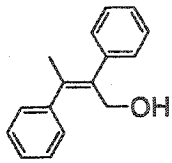
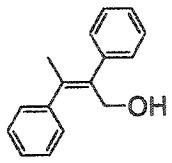
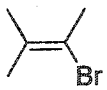
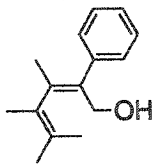
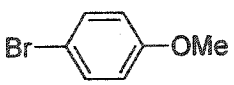
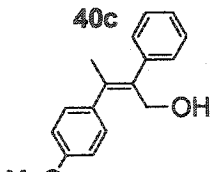
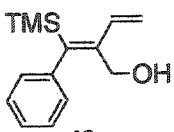
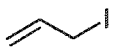
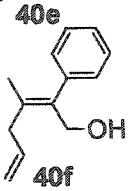
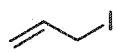
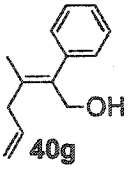
The documented lowered reactivity of cyclic chelate **14** towards alkyl halides[13] is often a source of frustration in the preparation of certain carbometallation targets. For example, quenching with allyl iodide for 3 hours at room temperature gives only material quenched with a proton from work up, and none of the desired product **40g**. Refluxing the allyl iodide for 24 hours is necessary to override the stability of the magnesium chelate to give allyl alcohol **40g** in 64% yield (Entry g).

Given the high yields obtained with aryl and vinyl halides, an experiment was performed to determine if palladium could be employed to increase the yield of quenching with allyl halides as well. Unfortunately, it was found that no increase in yield resulted from the use of these conditions, and alcohol **40f** was isolated in only 46% yield (Entry f).

Table 2: Carbometallation of 2-Butynol Followed by Palladium Cross Coupling with RX



26 **40**

Entry	Halide	Alcohol	Yield
a	PhI	 **40a**	73[14]
b	PhBr	 **40b**	72
c		 **40c**	71[14]
d		 **40d**	71[14]
e	PhI 	 **40e**	61[15]
f		 **40f**	46[14]
g		 **40g**	64*

* No palladium added

The results of the cross-couplings with various halides confirmed our previous conclusions that the nature of the cross coupling partner has very little effect on the overall yield of the reaction, and that the overriding factor in the reaction is the efficacy of the initial carbometallation. Grignard reagents that have higher reactivity lead to tetrasubstituted alkenes in higher yields regardless of the cross coupling partner used, while the reverse is true for Grignard reagents with poor reactivity such as vinyl or alkyl Grignard reagents.

II-I-iii. Iron Catalyzed Cross Coupling

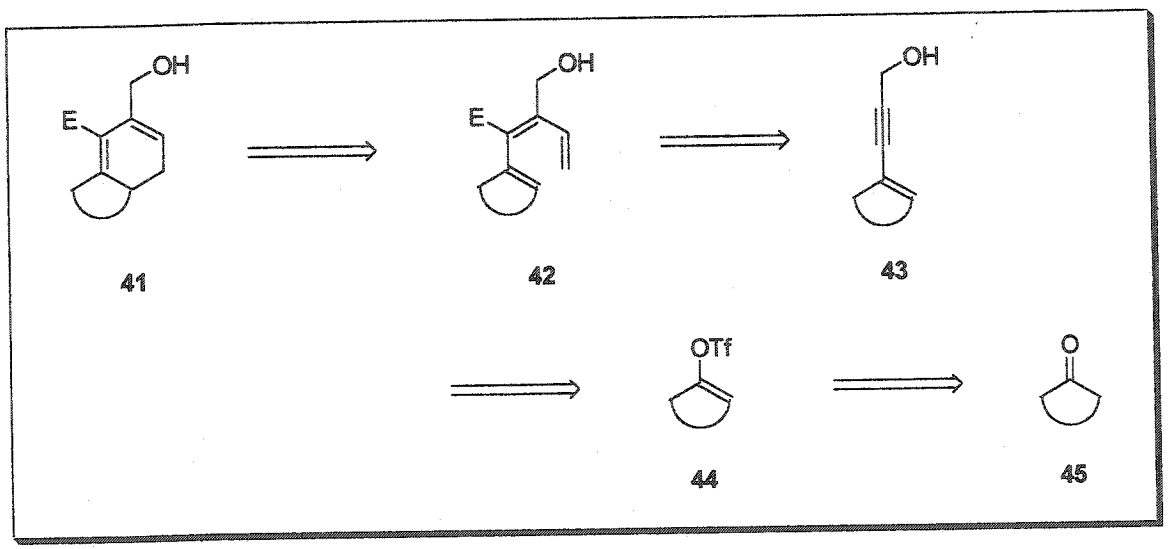
Fürstner and co-workers have recently shown that Grignard reagents can be coupled with aryl halides through use of a variety of different iron catalysts.[16] Not only does the use of iron allow for catalysts that are much cheaper and more environmentally benign than traditional catalysts, but the reaction also proceeds readily with aryl chlorides, which are quite challenging for many palladium catalysts.

In light of these positive results, we hoped to incorporate iron catalysts into our carbometallation-cross coupling strategy, in order to make the process even more synthetically interesting. In a manner analogous to previous examples, 2-butynol was carbometallated with phenyl magnesium chloride, and the cross-coupling attempted with 5 mol % of an iron catalyst and phenyl iodide following the Fürstner procedure. Unfortunately, when the reaction was performed with either $FeCl_3$ or $Fe(acac)_3$ as a catalyst absolutely no cross coupling was observed, and only material quenched with a proton was recovered.

II-II. Tandem Carbomagnesiation-Annulation.

With the development of an efficient protocol for the addition of vinyl magnesium chloride to propargyl alcohols available from previous work in the Fallis laboratory,[9] we devised a new tandem carbometallation-annulation strategy.

Starting with cyclic ketone **45**, treatment with a base to deprotonate, followed by trapping of the enolate as a triflate would yield vinyl triflates (**42**) that could be coupled to propargyl alcohol to give substituted vinyl propargyl alcohols (**43**) (Scheme 13).



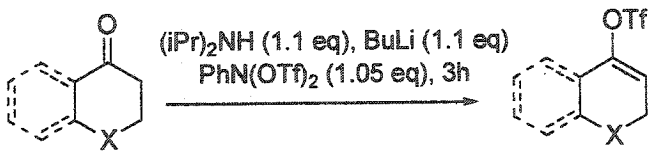
***Scheme 13:** A Magnesium Mediated Carbometallation-Annulation Strategy*

Vinyl propargylic alcohols (**43**) could then be carbometallated with vinyl magnesium chloride and quenched with various electrophiles to give substituted trienes (**42**) that could then be heated to induce an electrocyclic ring closure to give cyclohexadienes (**41**). These dienes could then either be aromatized or left as dienes for possible use in Diels-Alder reactions. It was hoped that this sequence could be performed on chiral cyclic compounds so that a variety of chiral annulated systems could be synthesized, for use as chiral building blocks.

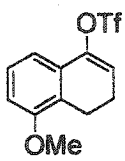
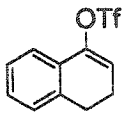
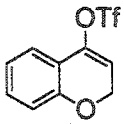
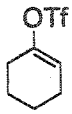
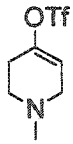
II-II-i. Carbometallation-Annulation of Achiral Cyclic Ketones.

In order to investigate this strategy under conditions that were as simple as possible, a variety of achiral cyclic ketones were chosen as model substrates. These experiments involved treatment of the substrates with LDA, followed by subsequent trapping of the resulting enolate with *N*-phenyltrifluromethanesulfonimde to yield the corresponding cyclic vinyl triflates in good yields (Table 3).

Table 3: Conversion of Cyclic Ketones to Vinyl Triflates

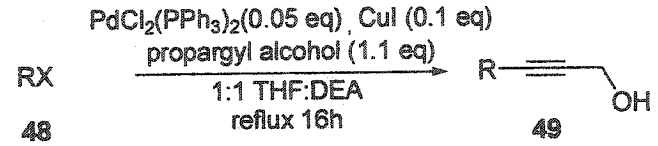


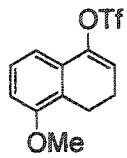
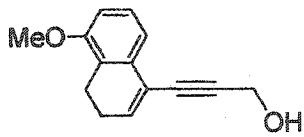
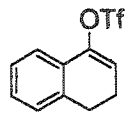
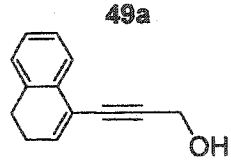
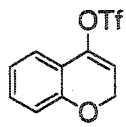
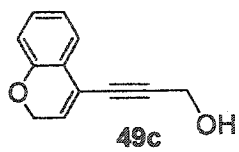
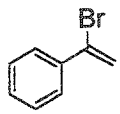
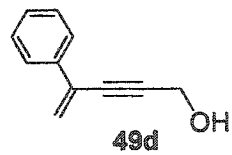
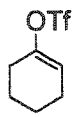
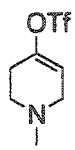
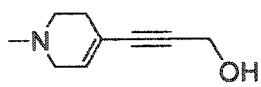
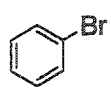
46 **47**

Entry	Vinyl Triflate	Yield (%)
a	 **47a**	82
b	 **47b**	82
c	 **47c**	66
d	 **47d**	55
e	 **47e**	54

Although initially triflic anhydride was used as a triflating reagent it was quickly found that in some cases this reagent promoted decomposition of the substrate or simply did not react. In order to get a general procedure that could be used for all compounds, the milder reagent *N*-phenyltrifluromethanesulfonimide was used in all examples.

Table 4: Sonogashira Coupling of Vinyl and Aryl Triflates and Bromides to Propargyl Alcohol

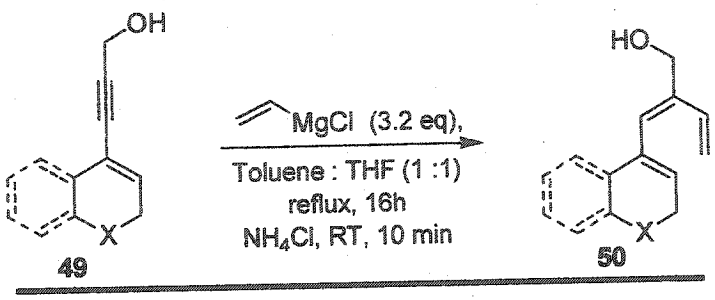


Entry	Substrate	Propargyl Alcohol	Yield (%)
a		 **49a**	53
b		 **49b**	53
c		 **49c**	15
d		 **49d**	0
e		 **49e**	64
f		 **49f**	93
g		 **49g**	85

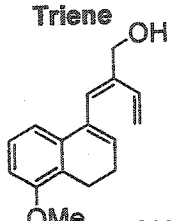
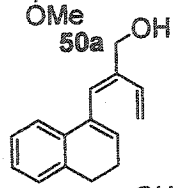
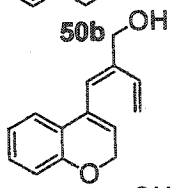
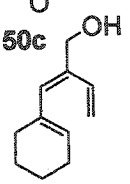
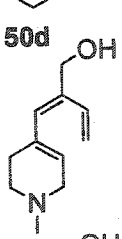
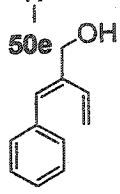
The next step in the sequence involved the coupling of vinyl triflates (**47**) to propargyl alcohol using the Sonogashira cross-coupling reaction (Table 4). In most cases the yields for this reaction were acceptable, but the reaction did seem to be very substrate dependent. In the case of triflate **47c** the yield was very low, which is not surprising since according to literature this compound is a very poor substrate for use in palladium coupling reactions (Entry c).[17] When 2-bromo styrene was used as a substrate this reaction could not be made to proceed at all with multiple attempts to couple this compound to propargyl alcohol leading only to decomposition products (Entry d).

With the vinyl propargyl alcohols in hand the next reaction performed was carbometallation with vinyl magnesium chloride followed by quenching with ammonium chloride (Table 5). Toluene was used as the non-polar co-solvent except in cases where solubility problems arose, in which case only THF was used (Entries c and e). In general, when cyclic hydrocarbons were used as substrates the yields for these reactions were quite high ranging from 77% to 90% (Entries a, b and d). When a heteroatom was introduced into the substrate the yields dropped off dramatically. In the case of **49f** which has a tetra-hydro pyridine moiety, the yield was only 15% (Entry e). Whereas when the substrate was an oxygen heterocycle the reaction failed to proceed at all (Entry c). When **49g** was used as a substrate the major product recovered was 3-phenyl-prop-2-en-1-ol in which the triple bond was reduced to the corresponding double bond. This was the case not only when vinyl magnesium chloride was used, but also when phenyl magnesium chloride was used as well. Compound **50f** proved to be very difficult to separate from the undesired major product and hence was carried forward as a mixture for subsequent studies.

Table 5: Carbometallation of Vinyl Propargyl Alcohols with Vinyl Magnesium Chloride

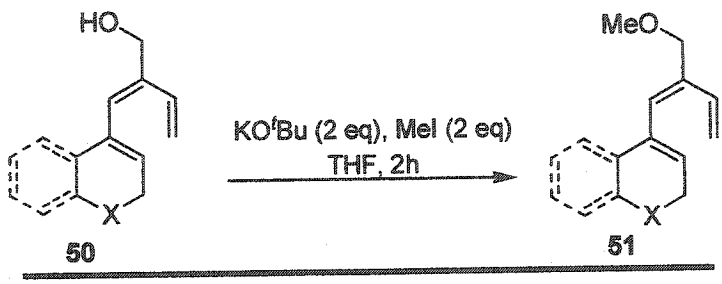


49 **50**

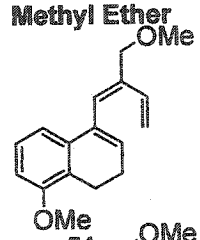
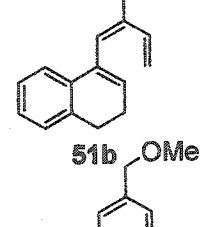
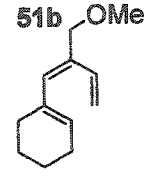
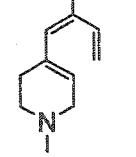
Entry	Triene	Yield (%)
a	 **50a**	78
b	 **50b**	77
c	 **50c**	0
d	 **50d**	90
e	 **50e**	15
f	 **50f**	31

The next step in the sequence was to induce the trienes to undergo electrocyclic cyclization under thermal conditions. Initial studies involved refluxing these compounds in toluene, which led only to an inseperable mixture of products. It was also found that the allylic oxygen in these compounds is extremely prone to oxidation to the corresponding aldehyde, which is formed simply upon standing at room temperature in $CDCl_3$ over night. To circumvent this problem the allylic alcohols were protected as the corresponding methyl ethers using sodium hydride or potassium *tert*-butoxide and methyl iodide (Table 6).

Table 6: Protection of Allylic Alcohols as Methyl Ethers

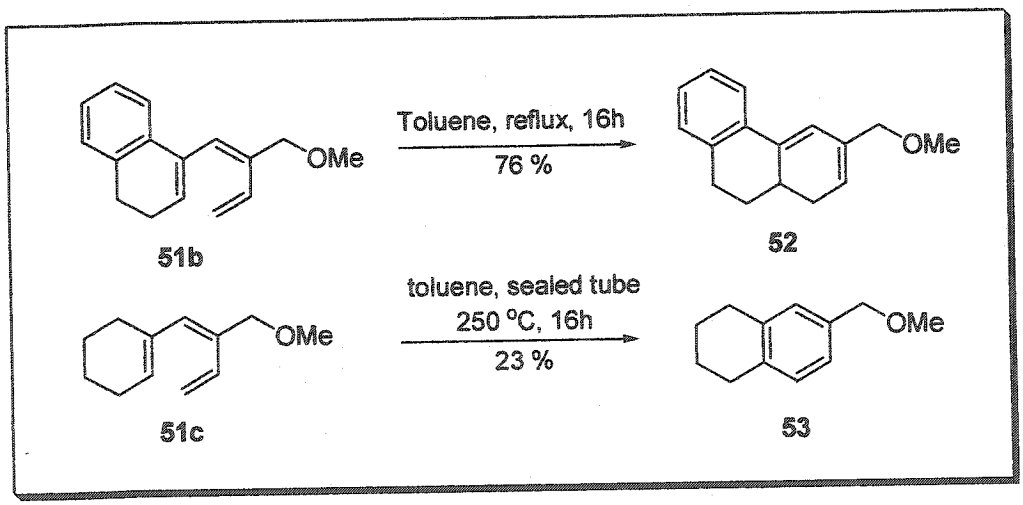


50 **51**

Entry	Methyl Ether	Yield (%)
a	 **51a**	99
b	 **51b**	87
c	 **51c**	99
d	 **51d**	0

Yields, as expected, were excellent for this step. The exception was substrate **50e** which did not react well and also showed considerable water solubility that hindered its isolation.

Cyclization of these preliminary compounds proved to be challenging. Initial attempts using substrate **51c** showed that refluxing in toluene was insufficient to induce cyclization, as was heating at 150 °C in a sealed tube. In this case, extremely forcing conditions were required, and upon heating to 250 °C in a sealed tube **51c** did cyclize, although aromatization of the resulting ring system occurred as well (Scheme 14). Substrate **51b** underwent cyclization under much milder conditions. Refluxing in toluene proved to be sufficient to promote cyclization to the desired diene. Presumably the extra aromatic ring donates electron density to the triene system, allowing cyclization at much lower temperatures.



Scheme 14: *Cylization of Achiral Trienes*

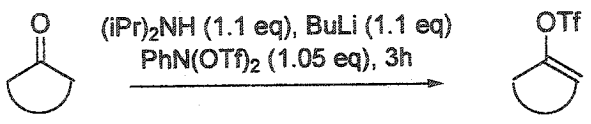
Based on previous results, it was thought that compound **51a**, with a structure similar to **51b**, as well as a methoxy group able to donate extra electron density would be able to cyclize very readily. Unfortunately this compound could not be induced to cyclize in refluxing toluene, and simply decomposed under sealed tube conditions. Compound **50f** was also studied to determine if cyclization directly onto aromatic rings could be

achieved. In this case, high temperatures all the way up to 250 °C in a sealed tube failed to yield any product, with only starting material being recovered.

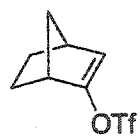
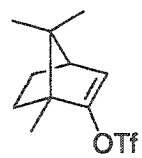
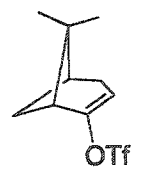
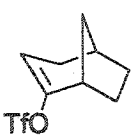
II-II-ii. Carbometallation-Annulation of Bicyclic Ketones.

With the experimental route now validated, attempts were made to extend this methodology to include chiral bicyclic systems. For this purpose, camphor, racemic norcamphor, nopinone and racemic bicyclo[3.2.1]octan-2-one were chosen as substrates. These ketones were treated with LDA and trapped as vinyl triflates (Table 7).

Table 7: Vinyl Triflates from Bicylic Ketones



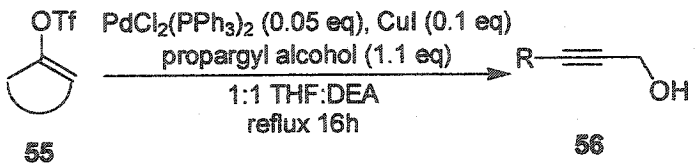
54 **55**

Entry	Vinyl Triflate	Yield (%)
a	 **55a**	59
b	 **55b**	77
c	 **55c**	54
d	 **55d**	87

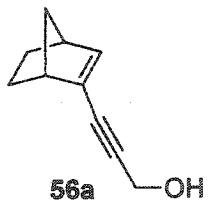
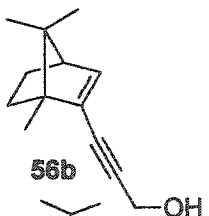
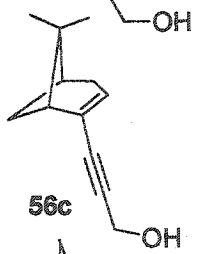
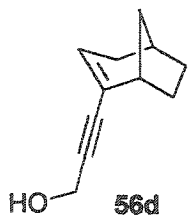
Once again the mild triflating reagent *N*-phenyltrifluromethanesulfonimide was used, as it was found that triflic anhydride caused camphor to rearrange.

The vinyl triflates were coupled to propargyl alcohol utililizing a Sonogashira reaction with $Pd(PPh_3)_2Cl_2$ and copper (I) iodide (Table 8). Yields in all cases were quite good, ranging from 60 – 89%.

Table 8: Vinyl Propargyl Alcohols from Vinyl Triflates

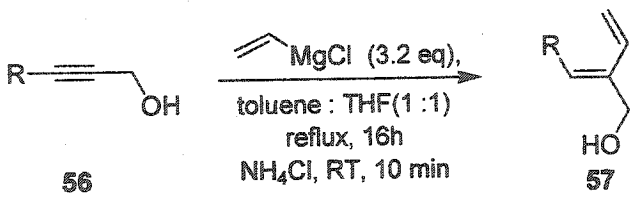


55 **56**

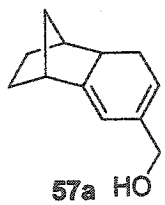
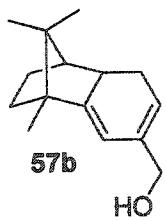
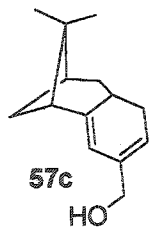
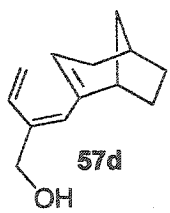
Entry	Vinyl Triflate	Yield (%)
a	 **56a**	60
b	 **56b**	81
c	 **56c**	89
d	 **56d**	65

The vinyl propargyl alcohols were then subjected to carbometallation with vinyl magnesium chloride, followed by quenching with ammonium chloride solution. Surprisingly, in these cases the temperature of the carbometallation reaction was often sufficient for the cyclization to occur at the same time (Table 9).

Table 9: Carbometallation of Bicyclic Vinyl Propargyl Alcohols



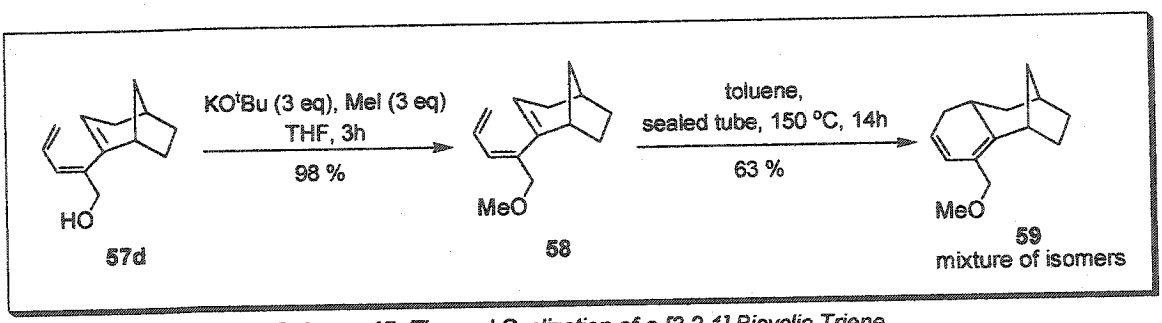
56 **57**

Entry	Product	Yield (%)
a	 **57a**	43
b	 **57b**	81
c	 **57c**	73*
d	 **57d**	64

* (5 : 1) toluene : THF employed as solvent

In the examples employing a camphor (**56b**) or norcamphor (**56a**) moeity a 1:1 toluene : THF solvent system provided sufficient temperature to promote the cyclization to the desired diene in 81 and 43% respectively (Entries a and b). In the case of the nopinone based substrate (**56c**), however, the reaction was incomplete and a mixture of cyclized and uncyclized product was recovered. This was rectified by changing the solvent system to a 5:1 toluene : THF mixture, with the higher temperatures yielding only cyclized material (Entry c). Compound **56d** with a [3.2.1] bicyclic moiety proved much most resistant to cyclization. In this case even when the solvent system was changed to allow for higher reflux temperatures only triene **57d** was recovered (Entry d).

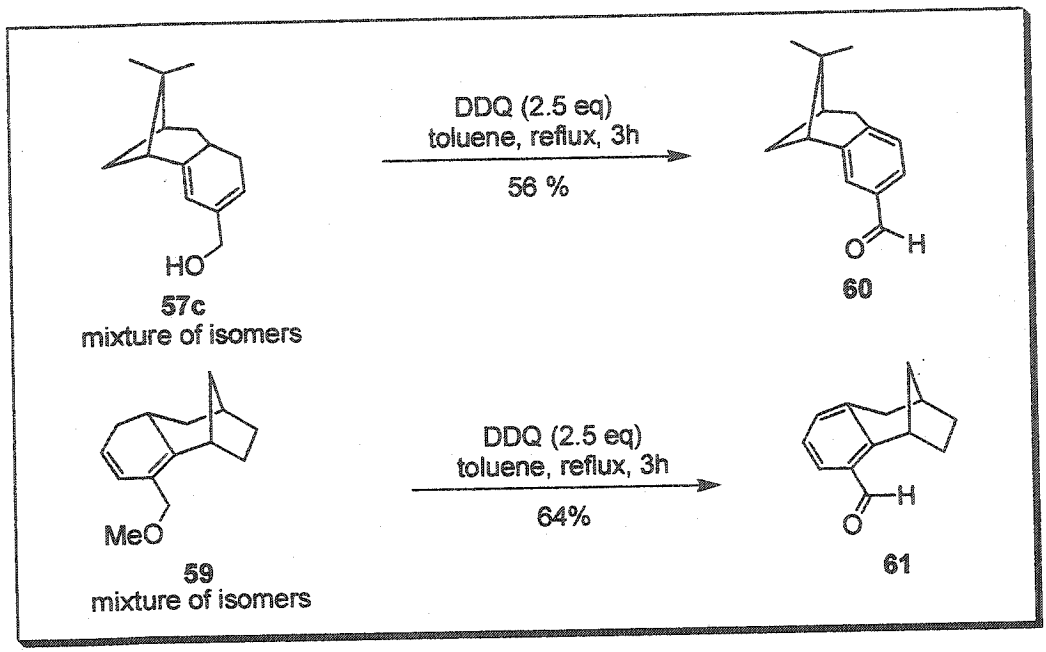
In order to cyclize **57d**, it was first necessary to once again protect the allylic alcohol as a methyl ether, employing potassium *tert*-butoxide and methyl iodide (Scheme 15). Cyclization was then induced by heating triene **58** in a sealed tube at 150 °C for 14 hours to afford the corresponding product (**59**) in 63% yield.



Scheme 15: *Thermal Cyclization of a [3.2.1] Bicyclic Triene*

The higher temperatures necessary to facilitate cyclization of the compounds with the nopinone (**56c**) and [3.2.1] bicylic moiety (**58**), provided sufficient energy to allow isomerization of the double bonds to the thermodynamically more stable products. As a result a mixture of isomers was isolated in each case, but upon subsequent treatment with DDQ in refluxing toluene, only the aromatized products were isolated in both cases (Scheme 16). In both cases, the compounds isolated had been oxidized to the corresponding aldehyde. Although not surprising for mixture **57c**, it was unexpected that

DDQ would allow for the conversion of a methyl ether to an aldehyde as was observed for **59**.



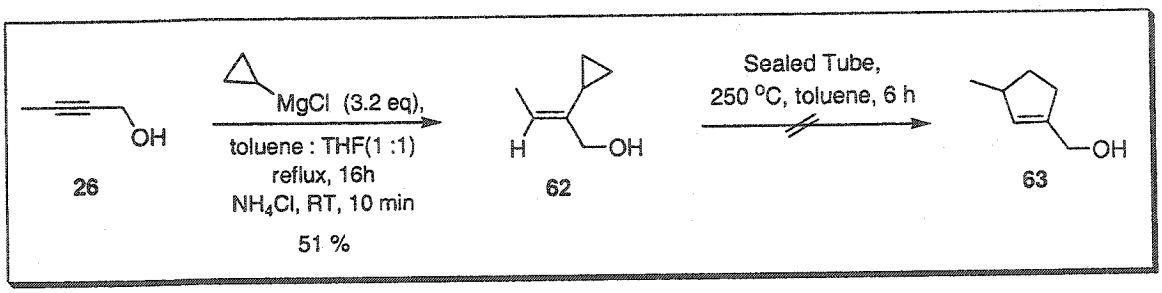
Scheme 16: *Aromatization of Bicyclic Diene Mixtures with DDQ*

It can be seen from the various bicyclic examples, that the nature of the ring system has a large effect upon the temperature required for cyclization. It appears that ring strain plays a role in this effect, with the most strained [2.2.1] bicyclic systems requiring the lowest temperatures, while the least strained [3.2.1] system requiring the highest. Presumably these systems with a high degree of ring strain lead to a transition state that is lower in energy, thereby lowering the temperature required for cyclization, although a more comprehensive explanation has not yet been postulated.

II-III. Carbomagnesiation with Cyclopropyl Magnesium Bromide.

It has been known for quite some time that vinyl cyclopropanes can be induced under thermal conditions to undergo rearrangement to substituted cyclopentene rings.[18] Carbometallation of propargyl alcohols with cyclopropyl Grignard reagents could provide an easy route to highly substituted vinyl cyclopropanes, which could then be induced to thermally rearrange, providing an efficient route to substituted cyclopentenes.

Initially 2-butynol was carbometallated with cyclopropyl magnesium bromide and quenched with ammonium chloride. This readily provided compound **62** in 51% yield (Scheme 17).



***Scheme 17:** Attempted Synthesis of a Substituted Cyclopentene via Carbometallation*

Thermal rearrangement of **62** proved to be quite challenging. Refluxing in toluene provided no reaction, as did temperature increases up to 250 °C in a sealed tube which resulted in the formation of multiple decomposition products, none of which were identified as compound **63**.

III. Tamoxifen.

III-1. Introduction.

It has been well established that estrogens such as estrone (**64**) and 17β-estradiol (**65**) (Figure 1) are the primary hormones responsible for the development and regulation of female sex organs and mammary glands.[19] Estrogens have more recently been found to play a role in the growth and maintenance of a number of other tissues in both men and women including the central nervous system, the skeleton, and the cardiovascular system.[20]

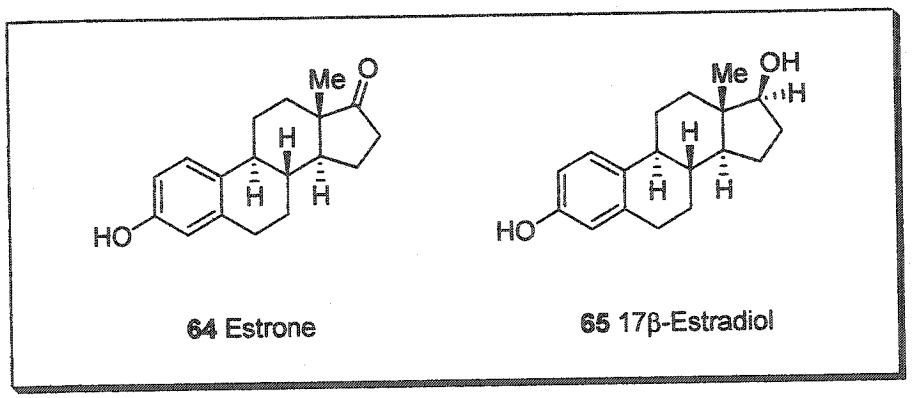


***Figure 1:** Structures of Estrone and 17β-Estradiol*

The decreased production of ovarian estrogens after menopause has been linked to several postmenopausal conditions including coronary artery disease and osteoporosis.[20b,21] Estrogen replacement therapy has emerged as an effective method for reduction of these pathologies, but side effects of this treatment include increased risk of endometrial and breast cancer.[22]

Recently, several estrogen mimics have emerged that antagonize the estrogen receptors on breast and uterine tissue, while at the same time mimicking the effect of estrogen on bone and the cardiovascular system.[23] Estrogen mimics with such

simultaneous agonistic and antagonistic behaviour have been termed "selective estrogen receptor modulators" (SERM).[23b]

One SERM that has found widespread use in the treatment of estrogen sensitive breast cancer is tamoxifen (Nolvadex®, **66**, Figure 2). Tamoxifen was first described by Harper and Walpole in 1966,[24] and has been used for more than 20 years as a breast cancer treatment, while also being recently approved for chemoprevention of the disease.[25] Interestingly, it is only the (*Z*) isomer of tamoxifen that has any useful biological activity. The (*E*) isomer of tamoxifen (**67**) not only has no clinical use, but has been found to be a full estrogen receptor agonist in rat models.[26]

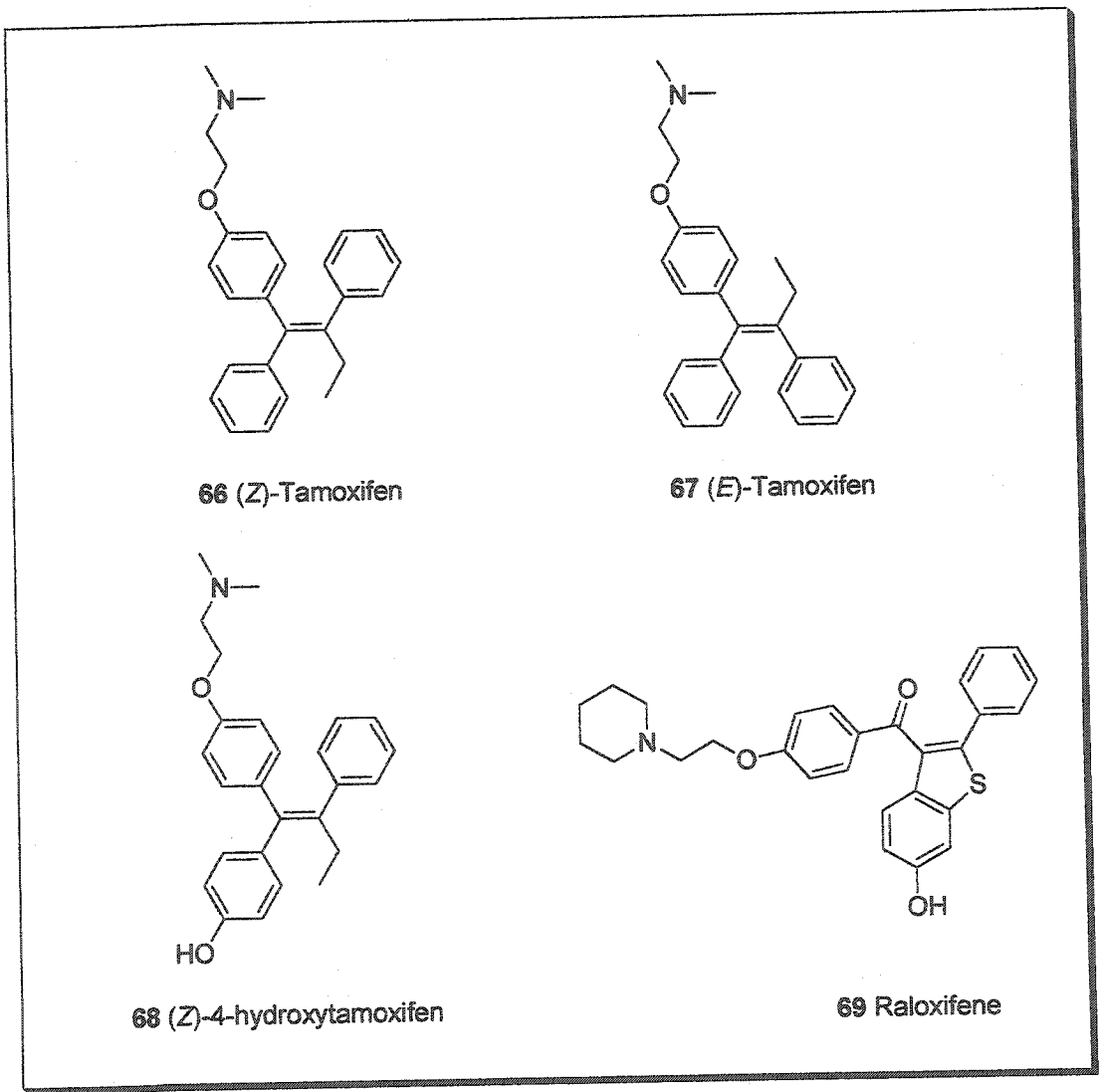


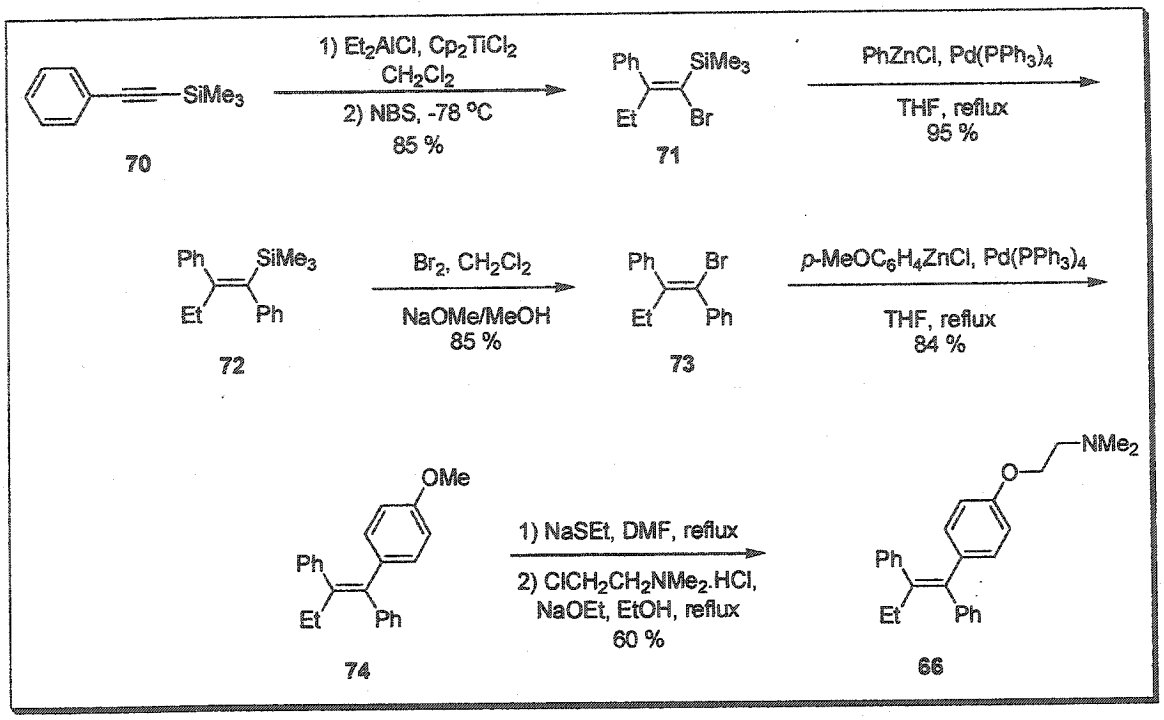
Figure 2: *Structures of (Z)-Tamoxifen, (E)-Tamoxifen, (Z)-4-Hydroxytamoxifen, and Raloxifene*

Tamoxifen itself has served as a basis for the discovery of new and more potent SERMs. The active metabolite of tamoxifen in the body is the hydroxylated compound (*Z*)-4-hydroxytamoxifen (**68**), a compound having a much higher affinity for the estrogen receptor than tamoxifen itself.[27] Structural modifications of tamoxifen have also led to the discovery of several other SERMs, including the compound Raloxifene (**69**), which contains a central benzothiophene moiety and is now in advanced clinical trials for the treatment of osteoporosis.[28]

Many of the SERM's that have been discovered thus far have a number of common structural features. One of the key requirements is two aryl groups separated by two atoms, usually in the form of a stilbene-like core, although others have been employed. In addition, higher activity tends to result from the presence of a third aryl ring with a *p*-(4-aminoethoxy) substituent. SERM activity is believed to occur through binding of the stilbene cores to the receptor, with projection of the substituted third aryl ring into a region of space that corresponds to the 11 position of an estratriene nucleus (*i.e.* estradiol or estrone).[29]

To date, there have been several different syntheses of tamoxifen and 4-hydroxytamoxifen. Most of these however, have not been done stereoselectively, leading to a mixture of (*Z*) and (*E*) isomers that can only be separated by HPLC or fractional crystallization.[30]

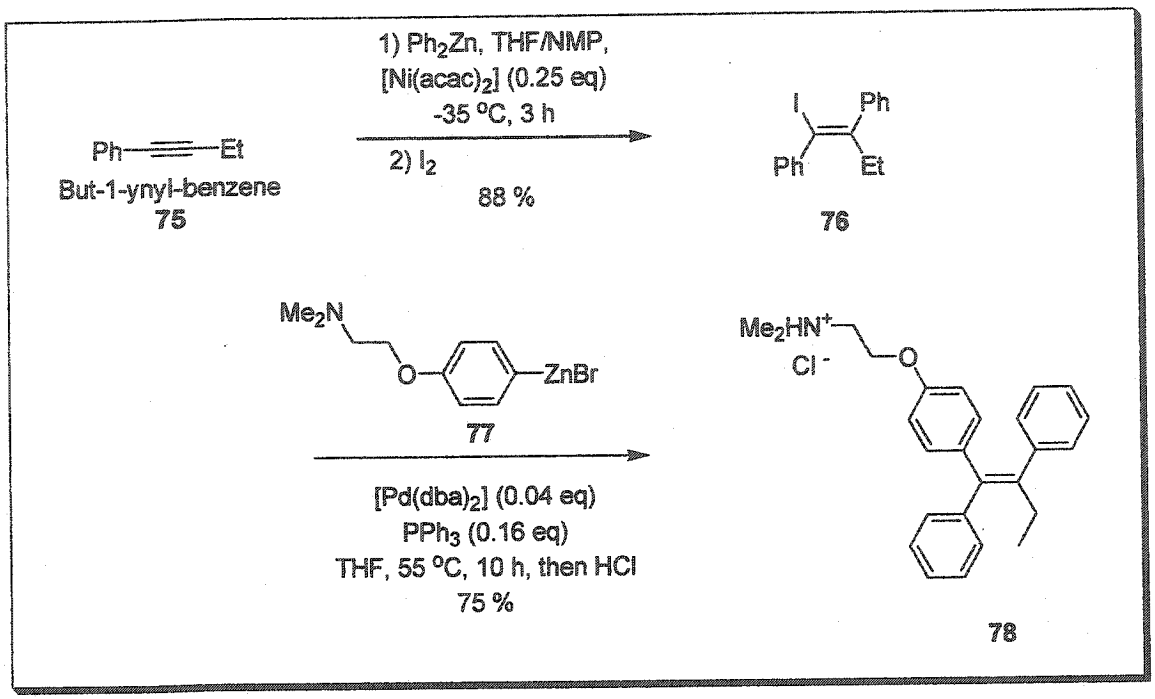
Currently, there are two efficient stereoselective syntheses of (*Z*)-tamoxifen, both of which employ a carbometallation strategy. In the first synthesis, Miller and co-workers carbometallated phenyl(trimethylsilyl)acetylene with diethylaluminum chloride-titanocene dichloride to give a organo-titanium species, which was quenched with NBS to give tetrasubstituted alkene **71** in 85% yield (Scheme 18).[31]



***Scheme 18:** Synthesis of (Z)-Tamoxifen via Carbometallation of Alkynylsilanes*

Alkene **71** was then subjected to a palladium catalyzed Negishi cross coupling employing phenylzinc chloride to give **72** in 95% yield. The trimethylsilyl group was converted to a bromide, that was subsequently coupled with (*p*-methoxyphenyl)zinc chloride in another Negishi coupling to give the tetrasubstituted alkene **74**. Finally, the methoxy aryl compound was converted to (*Z*)-tamoxifen through initial exposure to sodium ethanethiolate, and subsequent treatment with (3-chloro-propyl)-dimethyl-amine hydrochloride and sodium ethoxide in ethanol. This gave (*Z*)-tamoxifen in 30% yield over six steps.

In the second case, Knochel and co-workers performed a very efficient synthesis by initial *syn* carbozincation of but-1-ynyl-benzene with diphenylzinc and a nickel catalyst (Scheme 19).[32] The organo-zinc compound formed from this reaction was quenched with iodine to give vinyl iodide **76** in 88% yield. A subsequent palladium catalyzed Negishi coupling with arylzinc bromide **77** afforded the hydrochloride salt of (*Z*)- tamoxifen (**78**) in 75% yield (66% over two steps).



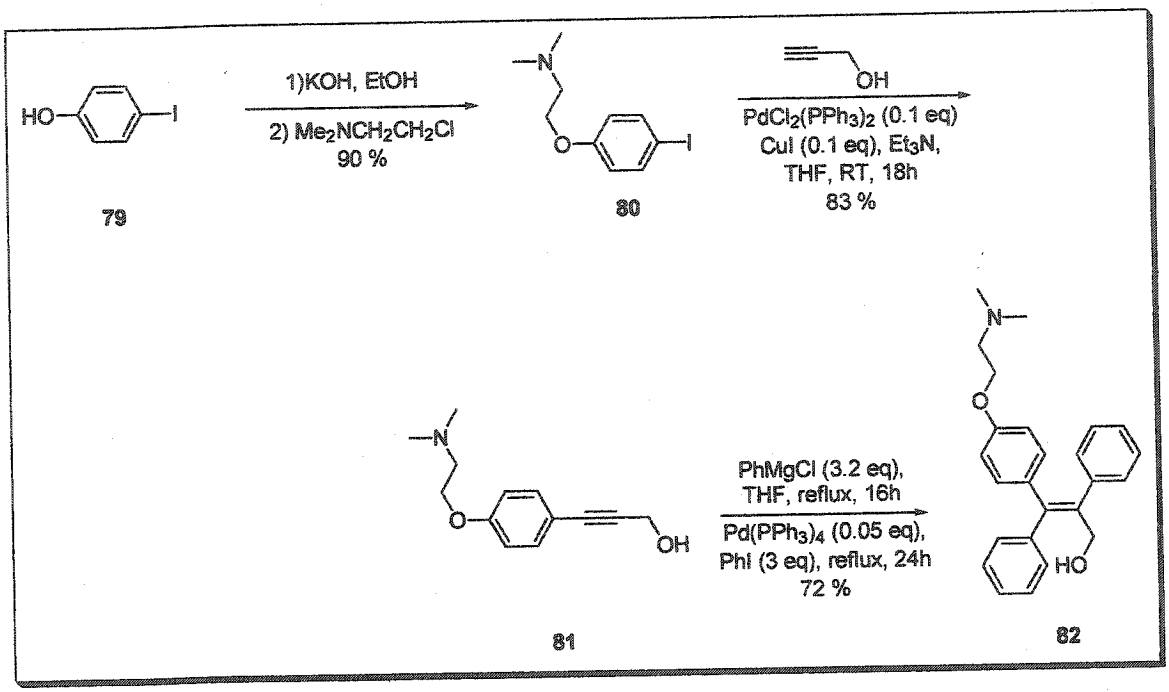
Scheme 19: *Synthesis of (Z)-Tamoxifen Hydrochloride via Nickel-Catalyzed Carbozincation of Alkynes*

III-II. Synthesis of (*Z*)-Tamoxifen and Assorted Analogues.

With a continual need for the development of new SERMs, along with our own lab's interest in the synthesis of cancer therapeutic agents, a strategy towards (*Z*)-tamoxifen analogues was developed. Not only would the carbometallation-palladium cross coupling procedure allow for a new stereoselective synthesis of (*Z*)-tamoxifen, but some new derivatives could also be prepared with new functionality in an area of the molecule that has not been thoroughly investigated thus far.

In the first step of the synthesis, 4-iodophenol (**79**) was deprotonated with potassium hydroxide to form the phenoxide salt, and was subsequently alkylated with 2-(dimethylamino)ethyl chloride following a literature procedure (Scheme 20).[33] Aryl iodide **80** was then coupled to propargyl alcohol to give compound **81** in 83% yield.[34] The next step was to subject this substituted propargyl alcohol to the carbometallation-

cross coupling process, using phenyl magnesium chloride. Unfortunately, compound **81** was not soluble in non-polar solvents, so in this case, the reaction was done in straight THF. Following carbometallation, phenyl iodide and $Pd(PPh_3)_4$ were added, and after 24 hours at reflux **82** was isolated in 72% yield.

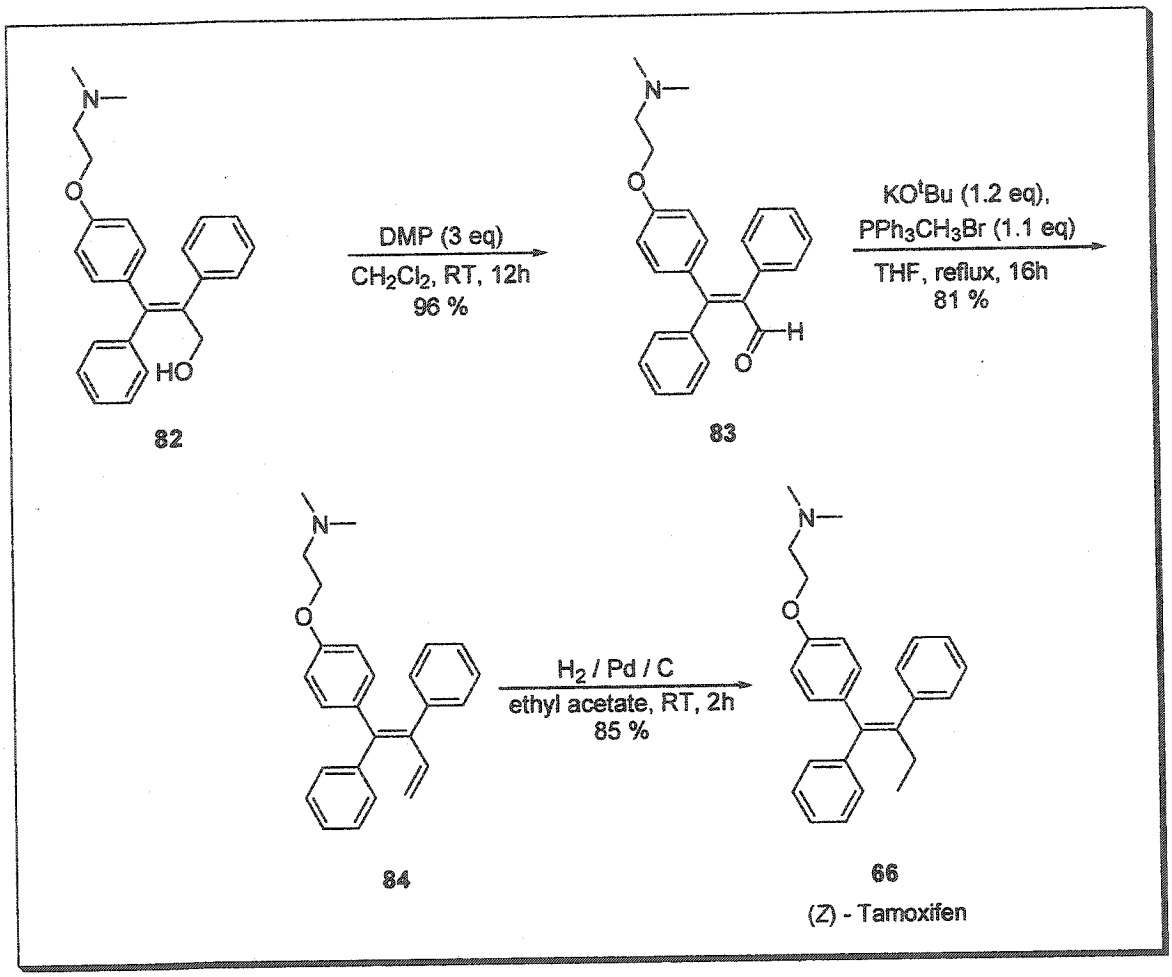


Scheme 20: *Synthesis of a (Z)-Tamoxifen Analogue via a Carbometallation Strategy*

Initially it was thought that the most efficient strategy would be to convert alcohol **82** to the corresponding mesylate, upon which treatment with an organometallic such as methyl lithium or methyl magnesium chloride would allow for displacement of the mesyl group to yield (*Z*)-tamoxifen. This strategy turned out to be ineffective, as treatment of **82** with mesyl chloride and a base led only to a mixture of different products, with the desired mesylate being only a minor product.

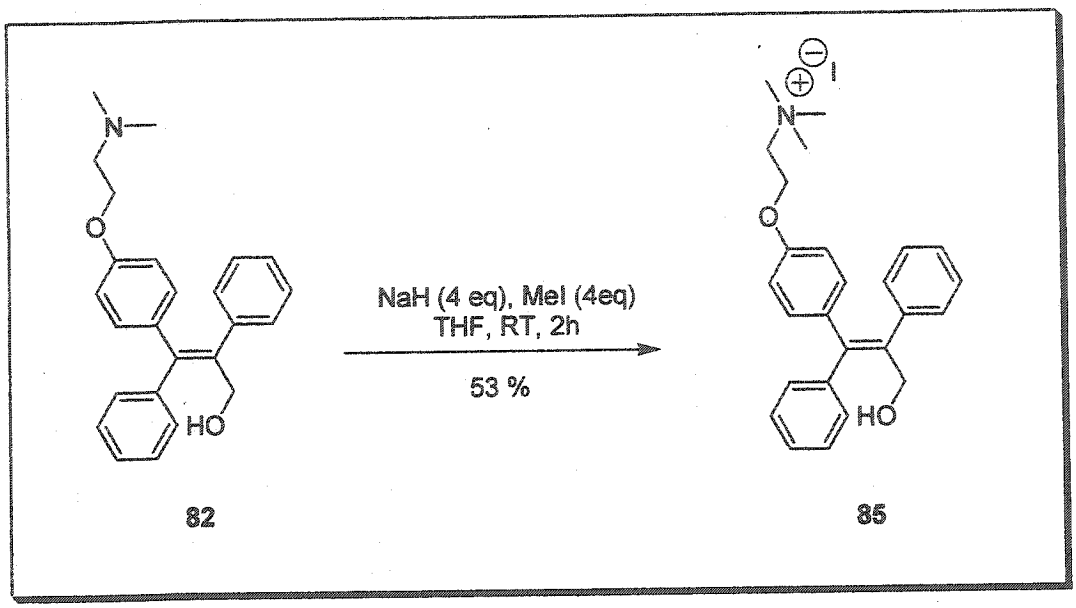
Alternatively, a new route was devised in which **82** was initially oxidized with Dess-Martin Periodinane to give the corresponding aldehyde (**60**) in 96% yield (Scheme 21). A Wittig reaction with methyl triphenylphosphonium bromide and potassium *tert*-

butoxide afforded diene **61** in 81% yield, before selective hydrogenation of the mono-substituted double bond gave (*Z*)-tamoxifen (**66**) in 85% yield.



***Scheme 21:** (Z)-Tamoxifen via a New Magnesium Mediated Carbometallation Strategy*

In the hopes of further mimicking the (*Z*)-tamoxifen structure an attempt was made to convert alcohol **82** to the corresponding methyl ether. Upon treatment of **82** with sodium hydride and excess methyl iodide, the only product recovered was derivative **85** with alkylation occurring selectively on the nitrogen without any methylation of the oxygen (Scheme 22).



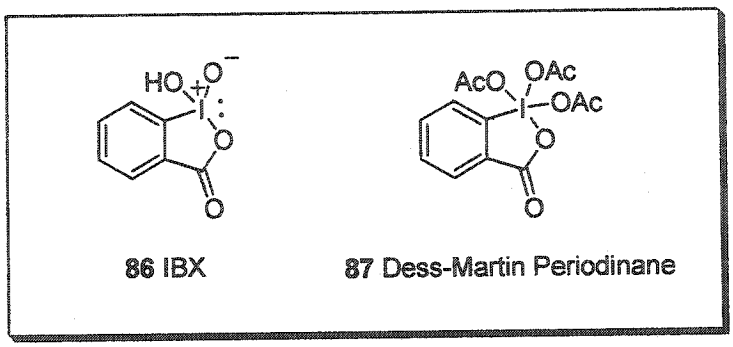
Scheme 22: *Synthesis of a New Water Soluble (Z)-Tamoxifen Derivative*

Although not the desired compound, **85** is a water soluble iodide salt and hence should be much more bioavailable than other derivatives. Compounds **82**, **83**, **84**, and **85** are all novel (*Z*)-tamoxifen derivatives, and are currently undergoing biological evaluation of their binding ability to estrogen receptors.

IV. IBX.

IV-1. Introduction.

o-Iodoxybenzoic Acid (IBX, **86**, Figure 3), is a powerful oxidant known for over 100 years. Until recently, widespread use of IBX has remained limited due to its virtual insolubility in organic solvents other than DMSO, and its apparent shock sensitive nature.[35]



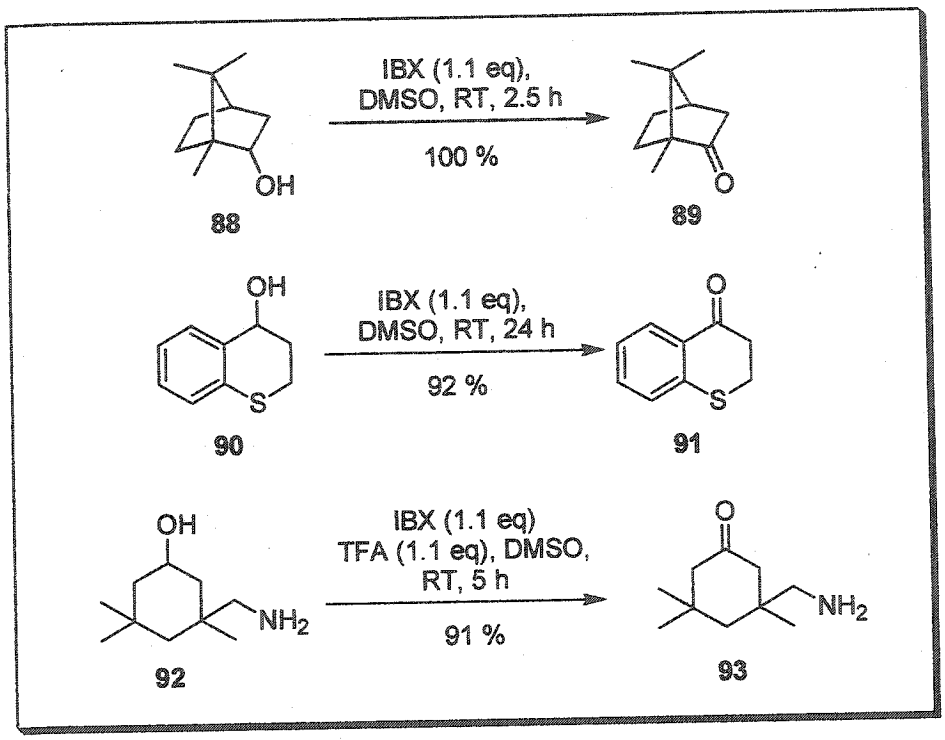
86 IBX **87** Dess-Martin Periodinane

Figure 3: *IBX and the Dess-Martin Periodinane*

Historically, IBX has received more recognition as a starting material for another useful oxidant, the Dess-Martin Periodinane (**87**). Formed through treatment of IBX with acetic anhydride and acetic acid,[36] the Dess-Martin Periodinane has proven remarkably successful in the selective oxidation of alcohols into carbonyl compounds.[37] Also, this reagent has shown an indefinite shelf life, and greater solubility in most organic solvents.[36]

Although all hypervalent iodine compounds are powerful oxidizing agents, IBX has markedly different properties than many of these oxidants, including the closely related analogues iodoxybenzene and *m*-iodoxybenzioc acid.[35] IBX in DMSO can be employed for the oxidation of primary alcohols to aldehydes at room temperature without risk of over-oxidation to acids.

IBX has also proven to be effective in the oxidation of secondary alcohols to ketones under analogous conditions. Even sterically hindered alcohols are readily oxidized, as in the case of camphol (**88**), which undergoes oxidation to camphor (**89**) when treated with IBX in DMSO at room temperature (Scheme 23).[38]



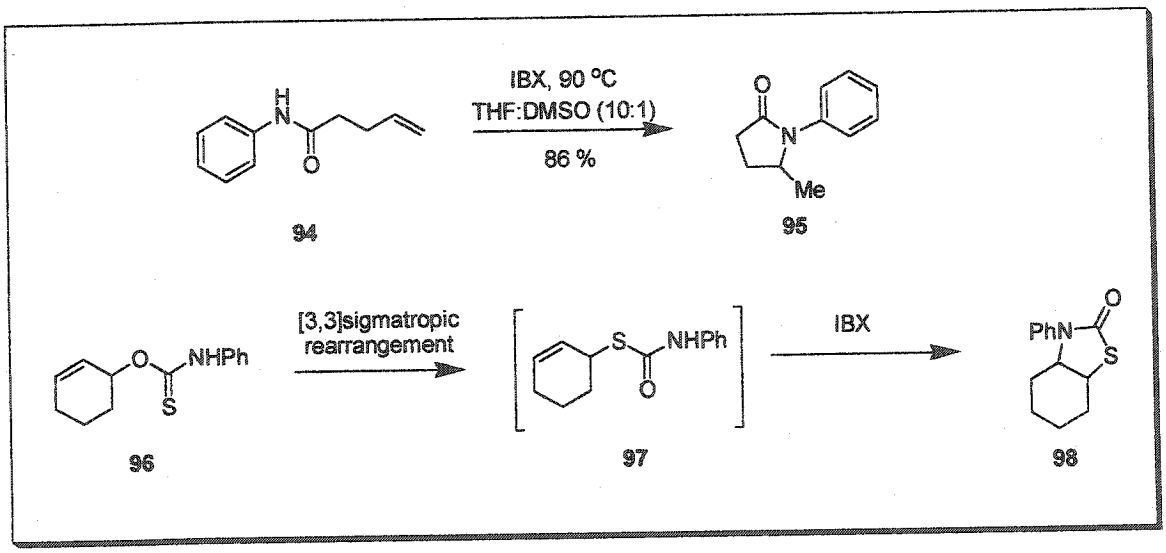
***Scheme 23:** Selected Oxidations with IBX*

The mild oxidizing properties of IBX make it of great use when oxidizing compounds with sensitive functional groups. Oxidation with IBX occurs cleanly in the presence of thioethers or the 1,3-dithiolane protecting group. For example, oxidation of thiochroman-4-ol (**90**), even using 10 equivalents of IBX, is achieved cleanly to yield thiochroman-4-one (**91**) with no detection of the corresponding sulfoxide or sulfone byproducts.[39] IBX is also tolerant of amine functionality and can therefore be used for the successful oxidation of amino alcohols to amino carbonyls. This synthetic problem most often requires the protection of the amino group prior to oxidation.[40] IBX provides an alternate method as it oxidizes alcohols selectively even with primary, secondary, or

tertiary amines are present. Oxidation of alcohol **92** occurs selectively, without degradation of the amine functionality, to give compound **93** in 91% yield.[39]

IBX has also shown tolerance to other functionalities as well, including both isolated and conjugated double bonds,[38] carboxylic acids,[38] carboxylic esters and carboxamides,[39] as well as oxidizable heteroaromatic rings such as furan, pyridine, and indole.[38]

Nicolaou and co-workers have recently shown that IBX is capable of a number of powerful transformations for the construction of heterocyclic systems.[41,42] When anilides such as **94** with an unsaturated moiety are exposed to IBX they undergo cyclization to the corresponding heterocycles (Scheme 24).[42]

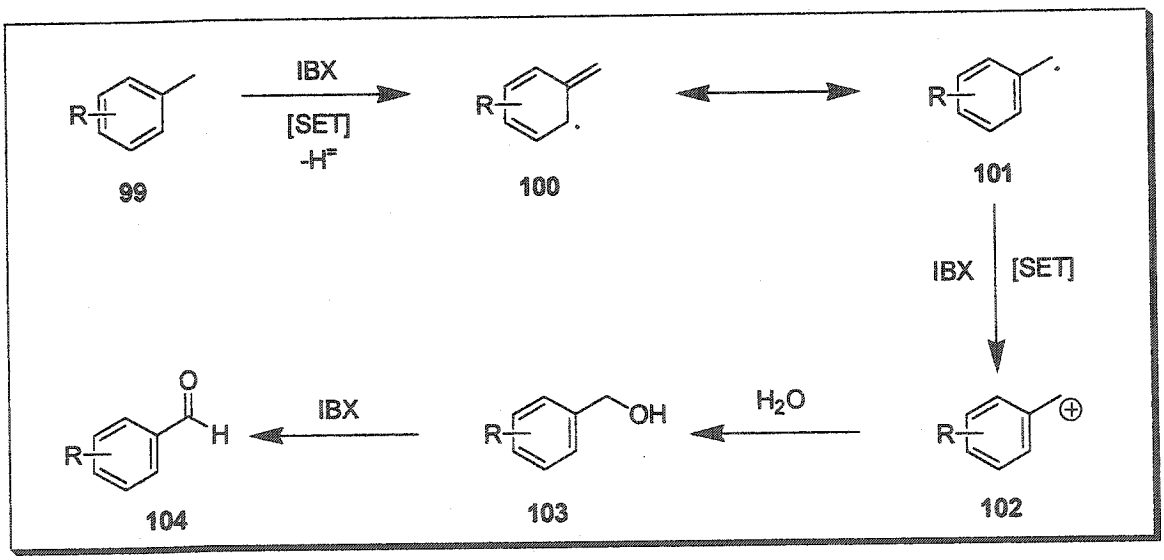


Scheme 24:Heterocyclic Ring Systems via IBX

Carbamates, and open chain ureas can also be used as substrate for transformation to the respective oxazolidinone, or cyclic urea compounds. The reaction is tolerant to a variety of groups on the aryl ring, and allows for the formation of both quaternary centers and spirocyclic compounds, although primary allylic amines are necessary for cyclic ureas, as secondary allylic amines decompose upon heating.[42,43] Aryl thionocarbamates (**96**) in contrast to other examples do not undergo direct cyclization. Instead a [3,3]-

sigmatropic rearrangement initially occurs to the corresponding allylic thionocarbamate (**97**) which then is cyclized by IBX to give a thiozolidinone (**98**).[43]

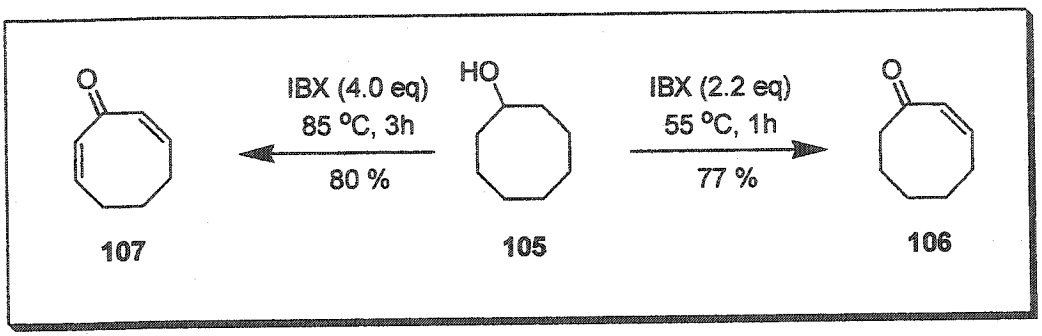
The use of IBX is not limited to the oxidation of compounds containing existing oxygen. Postulated to proceed via a single electron transfer mechanism, IBX has proven effective in the oxidation of carbon atoms adjacent to aromatic systems. Treatment of a compound containing a benzylic carbon (**99**) with 3 equivalents of IBX in DMSO or DMSO/flurobenzene mixtures at 80 – 90 °C, leads to the oxidation of the benzylic carbon to the corresponding aldehyde (**104**). The first two equivalents of IBX perform single electron transfer reactions to form a benzylic cation (**102**) that reacts with water to give an alcohol, which in turn is oxidized to the corresponding aldehyde by the third equivalent of IBX (Scheme 25).[44]



Scheme 25: *Oxidation of Benzylic Carbons via Single Electron Transfer*

The synthesis of α,β-unsaturated carbonyl compounds from saturated alcohol and carbonyl compounds has also been proven possible through use of IBX as an oxidant. Treatment of a saturated carbonyl compound with IBX gives the desired α,β-unsaturated carbonyl compound. The reaction is quite general, and tolerant of a variety of functional groups, and provides a non-toxic route to the oxidized products. Saturated alcohols can

be treated with an extra equivalent of IBX to affect the oxidation of the alcohol to corresponding aldehyde or ketone followed by transformation to the desired α,β-unsaturated carbonyl, allowing for an elegant one-pot synthesis. The level of unsaturation in the final product can be further manipulated simply by adjusting the amount of IBX used in the reaction. For example when cyclooctanol (**105**) is treated with 2.2 equivalents of IBX the oxidation proceeds cleanly to give the mono-unsaturated cyclooctanone (**106**) in 77% yield. When the amount of oxidant is adjusted to 4 equivalents however, the reaction proceeds exclusively to the corresponding di-unsaturated cyclooctanone (**107**) product in 80% yield (Scheme 26).[45]



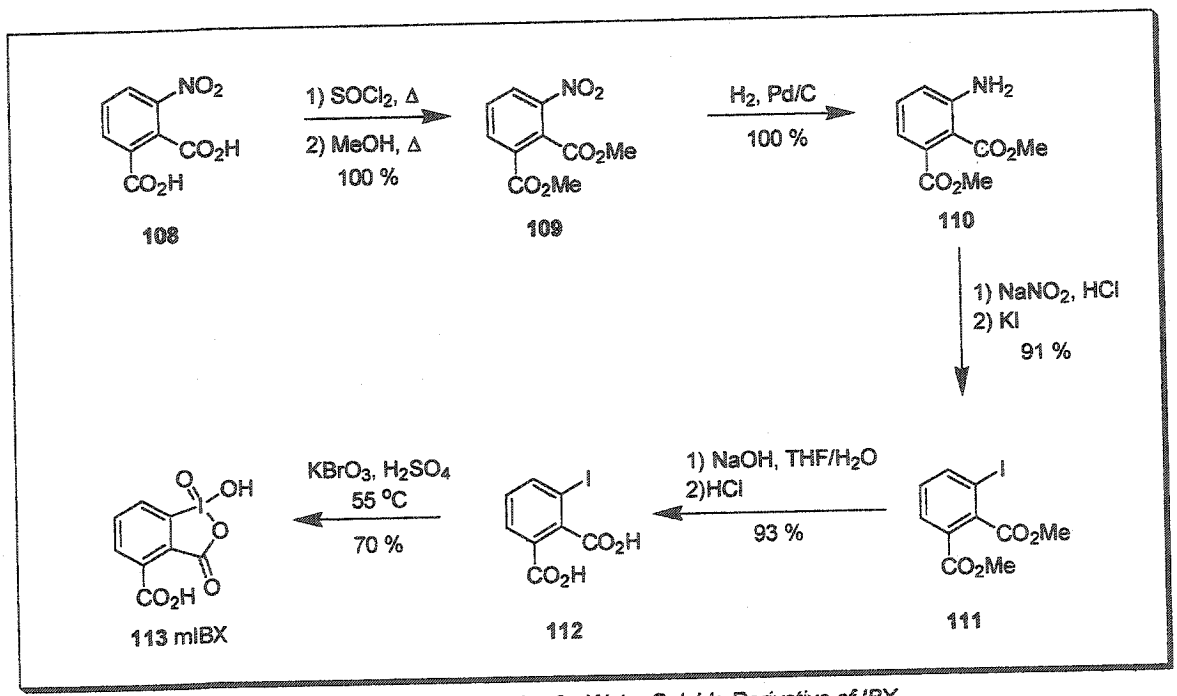
Scheme 26: *α-β-Unsaturated Carbonyl Compounds from Alcohols via IBX*

The desirable properties of IBX have led to the development of new derivatives based on the core structure. These derivatives have been shown to display different, and often advantageous properties that have made them synthetically useful in their own right.

The desire for an oxidizing agent that could act as a more environmentally benign alternative to traditional reagents has prompted the synthesis of a derivative of IBX that is soluble in water. So-called mIBX (**113**) has been synthesized with the addition of a carboxylic acid moiety on the aryl ring to facilitate solubility in water. In this way mIBX has been shown to oxidize a variety of alcohols to the corresponding aldehydes in both water and THF : water mixtures in fair to excellent yields.[46]

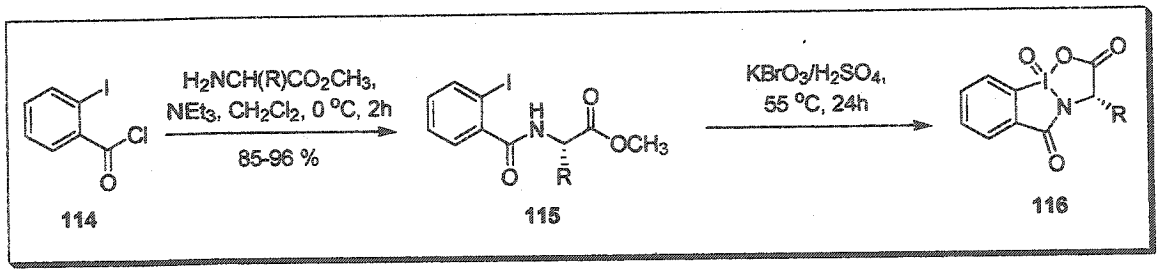
The synthesis of mIBX begins with the commercially available 2-nitrophtalic acid (**108**). Esterfication of **108** is accomplished through conversion to the acid chloride,

followed by treatment with methanol to give nitrodiester **109** (Scheme 27). Catalytic hydrogenation then gives the corresponding aminodiester **110**, before diazotization followed by iodination with KI provides dimethyl iodophtalate (**111**). Saponification of the diester with NaOH, followed by acidic workup gives mIBX diacid precursor **112**. Final treatment of the diacid with $KBrO_3$ in dilute acid, in a manner analogous to the synthesis of IBX, gives the final product mIBX.



***Scheme 27:** Synthesis of a Water Soluble Derivative of IBX*

Recently, Zhdankin and co-workers reported the synthesis of several new chiral derivatives of IBX. 2-Iodobenzoyl chloride (**114**) was coupled with the methyl esters of several amino acids and subsequently oxidized with potassium bromate in acid to give the corresponding chiral IBX analogues **116** (Scheme 28).[47]



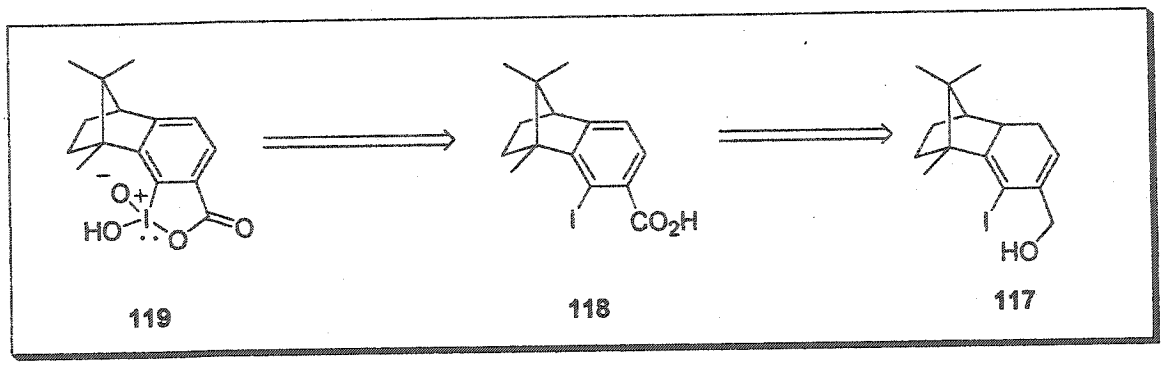
Scheme 28: Synthesis of Chiral Amino Acid Based IBX Derivatives

Derivatives **116** proved to be much more soluble in organics, much less shock sensitive, and quite effective for the oxidation of primary alcohols to aldehydes. Oxidation of sulfides to sulfoxides using these derivatives did proceed with enantioselectivity, however, the enantiomeric excess from this oxidation was quite modest with 16 % ee being the best result obtained.

IV-II. Studies Towards a Chiral IBX Derivative.

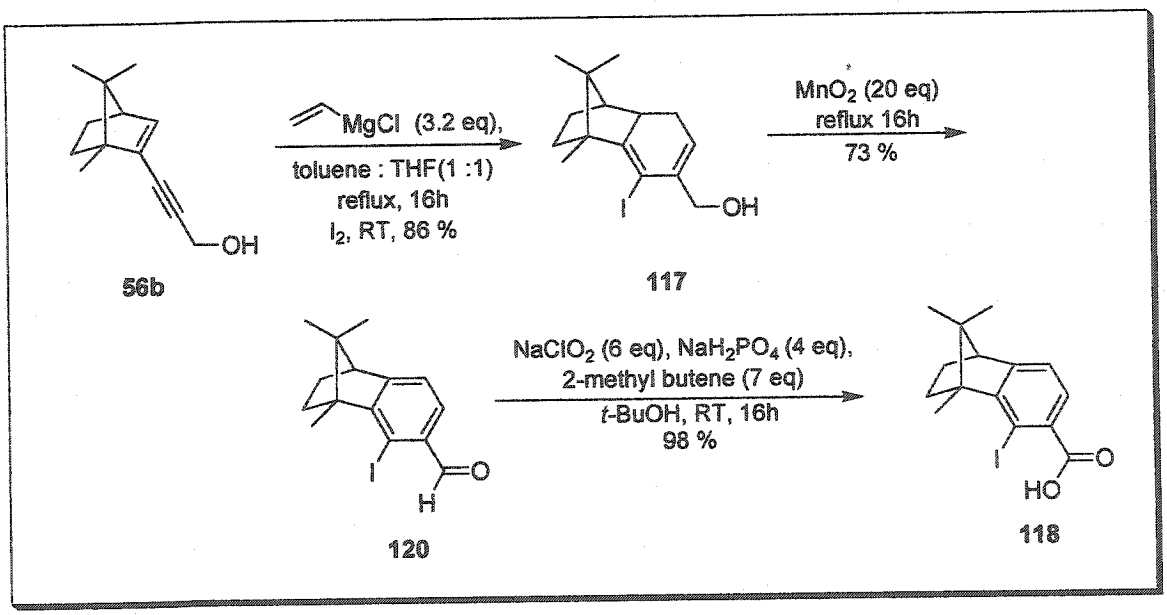
To date there are very few effective reagents that are capable of performing oxidations in an enantioselective manner. A chiral oxidizing agent would have a number of useful applications including the oxidation of sulfides to chiral sulfoxides, and the possible resolution of racemic alcohols through selective oxidation of one enantiomer.

The work of Zhdankin and co-workers has shown that chiral derivatives of IBX can be synthesized through use of amino acids and the exploitation of their natural chirality. Use of our carbometallation-annulation strategy on a camphor propargyl alcohol, as previously described, would provide an easy route to a chiral IBX derivative with camphor incorporated into the structure (Scheme 29).



Scheme 29: *Proposed Route to a Chiral Camphor Based IBX Derivative*

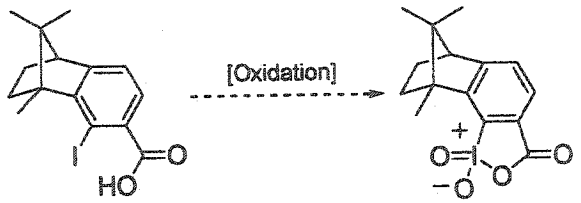
To begin the synthesis, **56b** was carbometallated with vinyl magnesium chloride and quenched with a solution of I_2 in THF to give iodo alcohol **117** in 86% yield (Scheme 30). Manganese dioxide was then used to affect two transformations at once, aromatization of the newly formed ring, and oxidation of the primary alcohol to give aldehyde **120**. This aldehyde was then oxidized to the corresponding carboxylic acid through treatment with $NaOCl_2$ and NaH_2PO_4 in *tert*-butanol to give **118** in 98% yield.



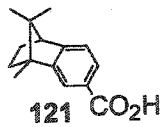
Scheme 30: *Towards a Chiral IBX Derivative*

The final step was then to oxidize **118** to a chiral IBX derivative. IBX itself is formed through oxidation of 2-iodobenzoic acid using potassium bromate in dilute sulfuric acid. We started our investigations by using these standard reaction conditions, but unfortunately no reaction took place (Table 10, Entry 1).

Table 10: Attempts at Oxidation of **118** to a Chiral IBX Derivative



118 **119**

Entry	Conditions	Result
1	$KBrO_3$ (1.3 eq), 0.75 M H_2SO_4, 55 °C, 3h	No Reaction
2	$KBrO_3$ (1.3 eq), 2 : 1 1.12 M H_2SO_4 : MeCN, 55 °C, 3h	No Reaction
3	$KBrO_3$ (1.3 eq), 1 : 2 2.25 M H_2SO_4 MeCN, 55 °C, 3h	Decomposition Products
4	Oxone (3 eq), $NaHCO_3$, H_2O, 55 °C, 3h	 **121** CO_2H
5	$KBrO_3$ (1.3 eq), TBAI (0.1 eq), 1 : 1 toluene : 1.5 M H_2SO_4, 55 °C, 3h	No Reaction
6	$KBrO_3$ (1.3 eq), 1 : 1 1.5 M H_2SO_4 : MeCN 55 °C, 3h	Possible Product

The problem at this point appeared to be solubility. The introduction of the hydrophobic camphor piece made the substrate much less soluble in water and hence oxidation could not occur. To circumvent this problem oxidation was attempted with mixed solvent systems. When the reaction was attempted under similar conditions, but with a 2:1 water : acetonitrile solvent mixture, once again no reaction was observed (Entry 2). When a 1:2 water : acetonitrile ratio was used, the reaction did occur, but only a mixture of decomposition products was recovered (Entry 3). Changing the oxidant was

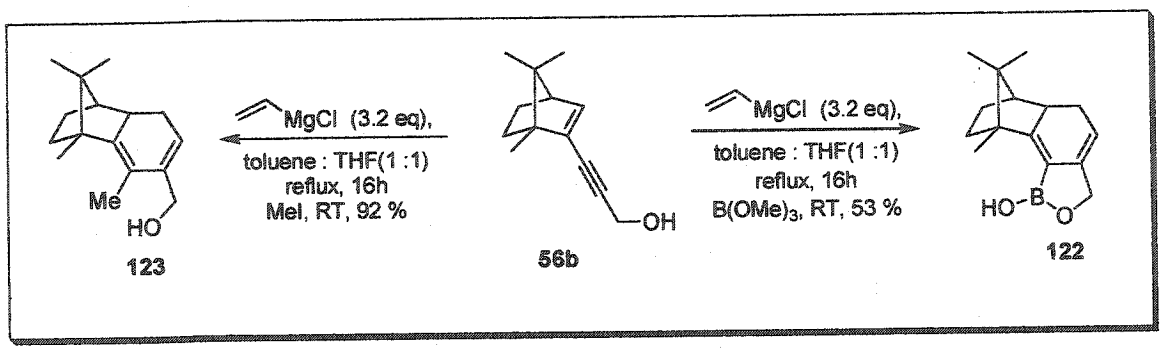
not productive, as a reaction performed with OXONE led only to dehalogenated product **121** (Entry 4). The oxidation was also attempted under phase transfer conditions, employing TBAI as a phase transfer catalyst in a toluene:water solvent mixture. Unfortunately once again no reaction took place (Entry 5). Once it was established that alternative oxidation procedures were not viable, we proceeded to reexamine the effect of the solvent, with another reaction being performed employing a 1:1 water:acetonitrile solvent system. Under these conditions the oxidation does appear to proceed as desired. In several cases a product precipitates out, which is pure and distinct from the starting material according to ^{1}H NMR. Unfortunately this compound is very difficult to characterize and the reaction is still irreproducible. Repeated attempts using identical reaction conditions gave either our suspected product or no reaction at all.

There is now a definite need to fine tune the reaction conditions in order to make this reaction reproducible. After this is done the reaction should be scaled up, eliminating some of our encountered difficulties attributable to small scale reactions such as coating of the stir bar with our substrate.

Despite the encountered difficulties in this oxidation, our successes thus far lead us to believe that a reproducible procedure for the preparation of **119** can be achieved.

IV-III. Towards a Chiral Camphor Based Lewis Acid.

Carbometallation of our camphor propargyl alcohol followed by quench with other electrophiles has also been investigated. Compound **56b** has been carbometallated with vinyl magnesium chloride and quenched with both methyl iodide and trimethyl borate to give the corresponding cyclized products **123** and **122** in 92 and 53% respectively (Scheme 31).



123 **56b** **122**

Scheme 31: *Carbometallation of* ***56b*** *followed by Quench with Various Electrophiles*

Compound **122** is very interesting as there are almost no examples in the literature of borinic dienes of this type. Also, this compound can be aromatized and serve as a chiral Lewis acid catalyst for subsequent Diels-Alder reactions. Work is currently proceeding in our lab to investigate this possibility.

V. Experimental

General : Proton magnetic resonance spectra (^{1}H NMR) and proton decoupled carbon magnetic resonance spectra (^{13}C NMR) were measured at 500 MHz (Bruker AMX500 spectrometer), 300 MHz (Bruker Advance300 spectrometer) or 200 MHz (Varian Gemini 200 spectrometer) in deuterated chloroform unless otherwise noted. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane (δ scale). The multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad), number of protons and coupling constants (reported in Hz) are indicated in parentheses. Mass spectra (MS) were determined on a Kratos Concept 2H instrument, employing an ionization energy of 70 eV. Melting points were determined in capillary tubes with a Thomas-Hoover Unit-Melt apparatus. Infrared (IR) spectra were obtained either as neat films on sodium chloride discs or as a deuterated chloroform solution in a solution cell.

All non-aqueous reactions were performed under a dry nitrogen atmosphere in flame or oven dried glassware with a magnetic stir bar and rubber septum. Standard inert atmosphere techniques were employed for the handling of all air and moisture sensitive reagents. Room temperature is taken as 23 °C. Reactions were monitored by analytical thin layer chromatography (TLC) using commercial pre-coated aluminum sheets (0.2 mm layer thickness) with silica gel 60 F_{254} (E. Merck). Organic layers were dried using anhydrous magnesium sulfate and stripped of solvents at reduced pressures obtained by rotary evaporator connected to either a water or air aspirator. High boiling and trace solvents were removed on a vacuum pump.

Petroleum ether refers to a mixture of hydrocarbons with a boiling range of 30 – 60 °C. Anhydrous tetrahydrofuran and diethyl ether were freshly distilled from sodium / benzophenone ketal. Anhydrous toluene, dichloromethane, and triethylamine were distilled from NaH or CaH. Acetonitrile, methanol and cyclohexane were used as an anhydrous solvent from Aldrich Chemical Company without further drying. *N*-BuLi was used as commercially available solution in hexanes from Aldrich Chemical Company. Grignard reagents were purchased from Fluka Chemika-BioChemika and were used as solutions in tetrahydrofuran and titrated against diphenyl ditelluride. All commercial

starting materials were purchased from Alrich Chemical .Company unless otherwise stated.

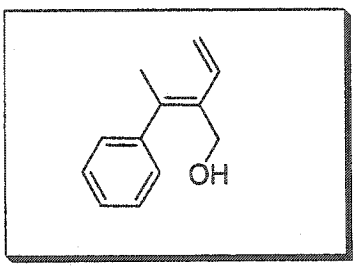
General Conditions A for a Carbometallation / Palladium Cross Coupling Reaction : The appropriate propargyl alcohol was dissolved in dry toluene (volume equal to the amount of Grignard to be used). The appropriate Grignard reagent (in THF) was then added to the reaction mixture dropwise at room temperature. The mixture was refluxed over night under a nitrogen atmosphere. $Pd(Ph_3)_4$ (0.05 eq) and the appropriate aryl or alkenyl halide (3 eq) were dissolved in THF (5 mL) and added via syringe to the reaction mixture, and allowed to continue refluxing for a further 24 hour period. The reaction was cooled to room temperature, and quenched with water (20 mL). 1M HCL (10 mL) was added and aqueous extraction was performed with diethyl ether (2 x 20 mL). Purification was achieved with neutral alumina gel chromatography employing a appropriate pet ether / ethyl acetate solvent system.

General Conditions B for Conversion of a Ketone to a Vinyl Triflate : Butyl lithium (1.1 eq) and diisopropyl amine (1.1 eq) were added to dry THF at – 78 ^{0}C to form LDA in solution. The appropriate ketone (1 eq) was added via syringe either as a neat liquid or as a solution in THF. The resulting solution was warmed to room temperature and allowed to stir for 30 minutes. The solution was cooled to –78 ^{0}C once again, and *N*-phenyltrifluromethanesulfonimide (1.05 eq) was dissolved in THF and added via syringe. The solution was warmed to room temperature and allowed to stir for 3 additional hours. The reaction was quenched with water (50 mL). Aqueous extraction was performed with diethyl ether (2 x 50 mL) and purification was achieved with silica gel chromatography employing an appropriate pet ether / ethyl acetate solvent system.

General Conditions C for Sonogashira Coupling of Propargyl Alcohol to a Vinyl Triflate : $Pd(PPh_3)_2Cl_2$ (0.05 eq) and copper (I) iodide (0.1 eq) were dissolved in a 1 : 1 solution of THF : DEA. The solution was degassed with N_2 gas for 10 minutes. The appropriate vinyl triflate (1 eq) was dissolved in THF and the solution degassed with N_2 for an additional 10 minutes. Propargyl alcohol (1.1 eq) was added via syringe and the

green solution changes colour to yellow, then orange then red. The solution was then allowed to reflux for 16 hours. The THF and DEA were removed under reduced pressure on a rotary evaporator. Purification was achieved with silica gel chromatography employing an appropriate pet ether / ethyl acetate solvent system.

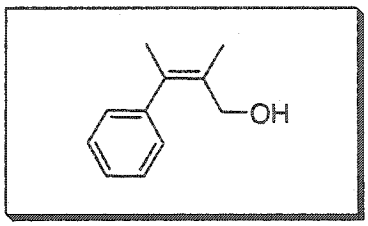
General Conditions D for the Carbometallation of a Vinyl Propargyl Alcohol : The appropriate vinyl propargyl alcohol was dissolved in either toluene or cyclohexane. Vinyl magnesium chloride in THF (3.2 eq) was added via syringe and the resulting solution refluxed for 16 hours. The reaction was cooled to 0 °C and was quenched with the appropriate electrophile, and allowed to stir for 30 minutes. The reaction was further quenched with water (50 mL). Aqueous extraction was performed with diethyl ether (2 x 50 mL) and purification was achieved with silica gel chromatography employing an appropriate pet ether / ethyl acetate solvent system.



3-Phenyl-2-vinyl-but-2-en-1-ol (39a): Prepared via **standard procedure A.** 2-butyn-4-ol (350 mg, 5 mmol), vinyl magnesium chloride (1.7 M, 9.4 mL), $Pd(Ph_3)_4$ (289 mg, 0.25 mmol), iodobenzene (1.94 mL ,18 mmol). Purification was achieved with neutral alumina gel chromatography employing a 4 : 1 pet ether / ethyl acetate solvent system. This afforded **39a** as a viscous yellow oil (360 mg, 41%).

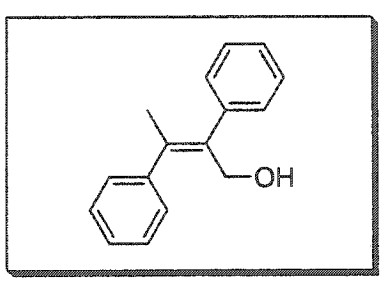
IR (neat): 3386 (s), 3020 (m), 2932 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.37 – 7.20 (m, 5H), 6.88 – 6.78 (dd, *J* = 11.1 Hz, 17.5 Hz, 1H), 5.52 (d, *J* = 16.9 Hz, 1H), 5.29 (d, *J* = 11.2 Hz, 1H), 4.17 (s, 2H), 2.14 (s, 3H), 1.70 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz):

δ 143.9, 140.6, 133.7, 133.0, 128.6, 128.1, 127.4, 115.3, 60.1, 21.3. MS (EI) m/z 174.1 (M^+ (1.0), 156.1 (4.8), 143.1 (100.0), 129.1 (23.7)). Exact mass cacld. For $C_{12}H_{14}O$: 174.1032. Observed: 174.1019.



2-Methyl-3-phenyl-but-2-en-1-ol (39c): Prepared via **standard procedure A.** 2-butyn-4-ol (350 mg, 5 mmol), methyl magnesium chloride (3 M, 5.4 mL), $Pd(Ph_3)_4$ (289 mg, 0.25 mmol), iodobenzene (1.94 mL ,18 mmol). Purification was achieved with neutral alumina gel chromatography employing a 8 : 1 pet ether / ethyl acetate solvent system. This afforded **39c** as a viscous yellow oil (80 mg, 10%).

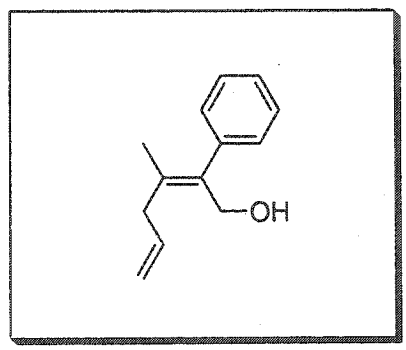
IR ($CDCl_3$) 3476 (m), 2929 (s), 2871 (s), cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.32 – 7.19 (m, 3H), 7.12 – 7.09 (m, 2H), 3.92 (s, 2H), 1.98 (s, 3H), 1.89, (s, 3H), 1.37 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 144.1, 135.2, 130.8, 128.5, 128.4, 126.8, 65.2, 21.6, 16.6. MS (EI) m/z 162.1 (M^+ (56.5), 147.1 (61.4), 129.1 (100.0), 105.1 (95,5)). Exact mass cacld. For $C_{11}H_{14}O$: 162.1041. Observed: 162.1037.



2,3-Diphenyl-but-2-en-1-ol (40a): Prepared via **standard procedure A.** 2-butyn-4-ol (350 mg, 5 mmol), phenyl magnesium chloride (2 M, 8 mL), $Pd(Ph_3)_4$ (289 mg, 0.25 mmol),), bromobenzene (1.90 mL ,18 mmol). Purification was achieved with neutral alumina gel chromatography employing a 7 : 1 pet ether / ethyl acetate solvent system. This afforded **40a** as a yellow solid (806 mg, 73%).

Mp=85 °C

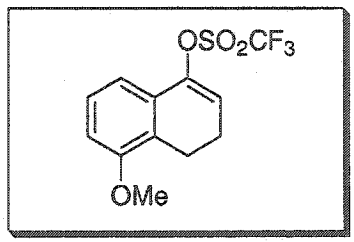
^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.45 – 7.29 (m, 10H), 4.21 (s, 2H), 1.95 (s, 3H), 1.61 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 143.3, 141.0, 137.8, 137.3, 129.6, 128.9, 128.8, 128.7, 128.4, 127.4, 64.7, 23.1.



3-Methyl-2-phenyl-hexa-2,5-dien-1-ol (40g): 2-Butyn-4-ol (350 mg, 5 mmol) was dissolved in toluene (8 mL). Phenyl magnesium chloride (2M in THF, 8 mL) was added dropwise at room temperature and the reaction heated at reflux for 16 hours. Allyl iodide (2 mL, 18 mmol) was added to the reaction mixture. The mixture was then allowed to continue refluxing for an additional 24 hours. Water (20 mL) was added to quench the reaction, along with 1M HCl (10 mL). Extraction was performed with diethyl ether (2 x 30 mL). Purification was achieved with neutral alumina gel chromatography employing a 8 : 1 pet ether / ethyl acetate solvent system to yield **40g** as a yellow oil (600mg, 64 %).

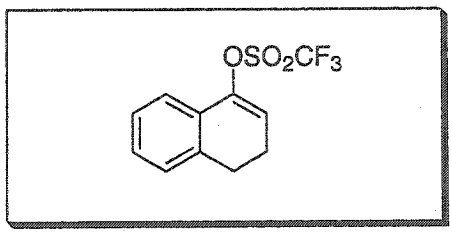
Mp = 85.0 °C. IR (neat) 3368 (s), 3056 (m), 2977 (m), 2915 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.36 – 7.17 (m, 5H), 5.94 – 5.81 (m, 1H), 5.15 – 5.05 (m, 2H), 4.31 (s, 2H),

3.01 (dt, J = 6.3 Hz, 1.5 Hz, 2H) 2.07 (br s, 1H), 1.61 (s,.3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 141.9, 136.6, 134.2, 129.1, 128.6, 127.0, 115.9, 63.3, 38.7, 20.8.



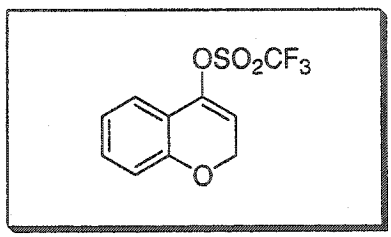
Trifluoro-methanesulfonic acid 5-methoxy-3,4-dihydro-naphthalen-1-yl ester (47a): Prepared via **standard procedure B**. Butyl lithium (6.0 mL, 2.5 M, 14.6 mmol), diisopropylamine (1.92 mL, 14.6 mmol), 6-methoxy tetralone (2.35 g, 13.3 mmol) in THF (5 mL), *N*-phenyltrifluromethanesulfonimide (5.05 g, 14.13 mmol) in THF (10 mL). Purification was achieved with silica gel chromatography employing a 19 :1 pet ether / ethyl acetate solvent system. This afforded **47a** as beige oil (3.30 g, 82%).

IR (neat); 2930 (s), 2724 (m), 1693 (s), 1608 (m), 1382 (m), 1230 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.27 (d, J = 8.4 Hz, 1H), 6.78 – 6.69 (m, 2H), 5.85 (t, J = 4.8 Hz, 1H), 3.79 (s, 3H), 2.82 (t, J = 8.0 Hz, 2H), 2.47 (dt, J = 4.6 Hz, 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.6, 146.7, 138.7, 131.3, 125.5, 123.1, 121.9, 121.1, 116.9, 115.1, 114.6, 112.6, 111.7, 55.6, 27.7, 22.6; MS (EI) m/z 308.0 (M^+ (70.6), 175.1 (41.1), 147.1 (100.0), 115.1 (37.9), 77.0 (28.8)); Exact mass calc'd. For $C_{12}H_{11}F_3O_4S$: 308.0328. Observed: 308.0326.



Trifluoro-methanesulfonic acid 3,4-dihydro-naphthalen-1-yl ester (47b): Prepared via **standard procedure B**. Butyl lithium (7.0 mL, 2.4 M, 16.7 mmol), diisopropylamine (2.18 mL, 16.7 mmol), tetralone (2.02 mL, 15.2 mmol) in THF (5 mL), *N*-phenyltrifluromethanesulfonimide (5.7 g, 16.0 mmol) in THF (10 mL). Purification was achieved with silica gel chromatography employing pure pet ether solvent system. This afforded **47b** as a colourless oil (6.11 g, 82 %). Characterization information was consistent with previously reported data for this compound.[47]

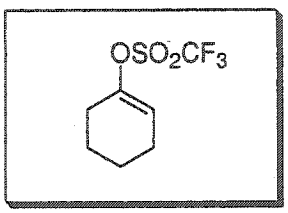
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37 – 7.35 (m, 1H), 7.27 – 7.25 (m, 2H), 7.18 – 7.17 (m, 1H), 6.02 (t, J = 4.8 Hz, 1H), 2.86 (t, J = 8.0 Hz, 2H), 2.52 – 2.48 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 146.4, 136.2, 129.1, 128.6, 127.7, 126.9, 122.4, 121.2, 119.9, 117.7, 117.4, 26.8, 22.3.



Trifluoro-methanesulfonic acid 2H-chromen-4-yl ester (47c) : Prepared via **standard procedure B**. Butyl lithium (11.9 mL, 2.5 M, 29.8 mmol), diisopropylamine (3.91 mL, 29.8 mmol), chromanone (4.0 g, 27.1 mmol) in THF (5 mL), *N*-phenyltrifluromethanesulfonimide (10.2 g, 28.5 mmol) in THF (10 mL). Purification was achieved with silica gel chromatography employing a 19 : 1 pet ether / ethyl acetate solvent system. This afforded **47c** as a colourless oil (5.0 g, 66 %). Characterization information was consistent with previously reported data for this compound.[17]

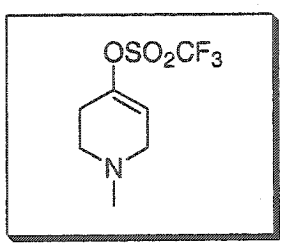
^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.41 – 7.39 (m, 1H), 7.25 – 7.20 (m, 1H), 6.97 – 6.93 (m, 1H), 6.85 – 6.81 (m, 1H), 5.74 (t, J = 4.6 Hz, 1H), 4.95 (d, J = 4.6 Hz, 2H); ^{13}C NMR

($CDCl_3$, 75 MHz): δ 155.1, 143.2, 131.6, 131.0, 130.0, 121.9, 121.7, 120.7, 119.5, 118.3, 117.1, 116.3, 65.1.



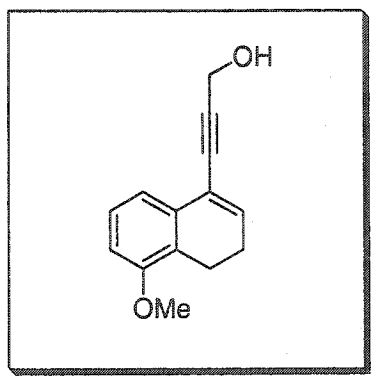
Trifluoro-methanesulfonic acid cyclohex-1-enyl ester (47d) : Prepared via **standard procedure B**. Butyl lithium (5.96 mL, 2.5 M, 14.9 mmol), diisopropylamine (1.95 mL, 14.9 mmol), cyclohexanone (1.4 mL, 13.5 mmol), *N*-phenyltrifluromethanesulfonimide (5.1 g, 14.2 mmol) in THF (10 mL). Purification was achieved with silica gel chromatography employing a pure pet ether solvent system. This afforded **47d** as a colourless oil (1.72 g, 55 %). Characterization information was consistent with previously reported data for this compound.[48]

^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.73 (t, J = 3.8 Hz, 1H), 2.29 – 2.20 (m, 2H), 2.17 – 2.13 (m, 2H), 1.82 – 1.70 (m, 2H), 1.63 – 1.54 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 149.3, 128.0, 121.7, 118.3, 115.3, 108.9, 27.3, 23.6, 22.4, 20.7.



Trifluoro-methanesulfonic acid 1-methyl-1,2,3,6-tetrahydro-pyridin-4-yl ester (47e) : Prepared via **standard procedure B**. Butyl lithium (3.52 mL, 2.5 M, 8.8 mmol), diisopropylamine (1.15 mL, 8.8 mmol), 1-methyl-4-piperidone (0.98 mL, 7.62 mmol), *N*-phenyltrifluromethanesulfonimide (3 g, 8.4 mmol) in THF (10 mL). Purification was achieved with silica gel chromatography employing a 5 : 1 pet ether / ethyl acetate solvent system. This afforded **47e** as a orange oil (1.05 g, 54%). Characterization information was consistent with previously reported data for this compound.[49]

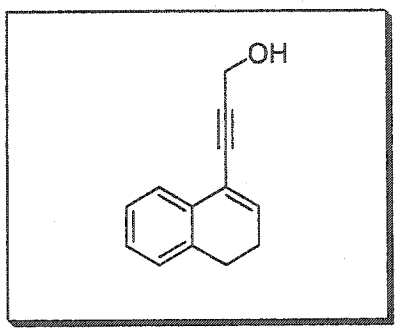
^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.72 (s, 1H), 3.28 (s, 2H), 2.88 (t, J = 5.6 Hz, 2H), 2.59 – 2.50 (m, 2H), 2.51 (s, 3H)



3-(5-Methoxy-3,4-dihydro-naphthalen-1-yl)-prop-2-yn-1-ol (49a) : Prepared via **standard procedure C.** $Pd(PPh_3)_2Cl_2$ (204 mg, 0.29 mmol), copper (I) iodide (110 mg, 0.58 mmol), THF : DEA (50 mL), (**47a**) (1.76 mg, 5.8 mmol) in THF (3 mL), propargyl alcohol (0.37 mL, 6.3 mmol). Purification was achieved with silica gel chromatography employing a 7 : 1 pet ether / ethyl acetate solvent system. This afforded **49a** as a viscous red oil (600 mg, 53%).

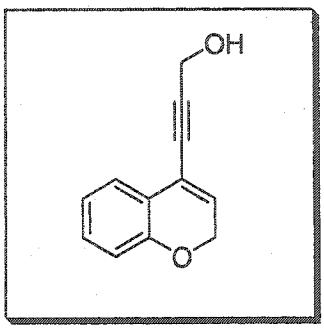
IR (neat); 3405 (s), 2944 (s), 2842 (s), 1690 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.45 (d, J = 8.4 Hz, 1H), 6.71 (dd, J = 8.4 Hz, 2.6 Hz, 1H), 6.65 (d, J = 2.6 Hz, 1H), 6.31 (t, J = 4.8 Hz, 1H), 4.48 (s, 2H), 3.78 (s, 3H), 2.73 (t, J = 8.0 Hz, 2H), 2.36 – 2.29

(m, 2H), 2.29 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ.159.5, 137.1, 133.9, 126.6, 126.0, 121.0, 113.9, 111.5, 88.3, 84.1, 55.7, 52.0, 28.0, 23.9; MS (EI) m/z 214.1 (M^+ (100.0), 171.1 (12.9), 152.1 (17.4), 115.1 (17.3), 63.0 (7.6)); Exact mass calc'd. For $C_{14}H_{14}O_2$: 214.0982. Observed: 214.0971.

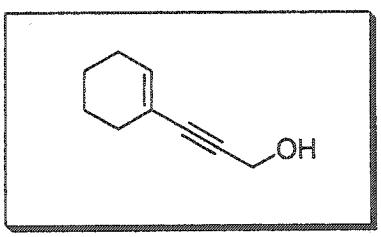


3-(3,4-Dihydro-naphthalen-1-yl)-prop-2-yn-1-ol (49b) : Prepared via **standard procedure C**. $Pd(PPh_3)_2Cl_2$ (428 mg, 0.61 mmol), copper (I) iodide (232 mg, 1.22 mmol), THF : DEA (50 mL), (**47b**) (3.4 g, 12.2 mmol) in THF (10 mL), propargyl alcohol (0.71 mL, 12.2 mmol). Purification was achieved with silica gel chromatography employing a 7 : 1 pet ether / ethyl acetate solvent system. This afforded **49b** as a viscous red oil (1.19 g, 53 %).

IR (neat); 3359 (s), 2935 (s), 2830 (s), 1487 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.59 (d, J = 7.5 Hz, 1H), 7.23 (td, J = 7.4 Hz, 0.8 Hz, 1H), 7.18 (td, J = 7.4 Hz, 1.4 Hz, 1H), 7.10 (d, J = 7.3 Hz, 1H), 6.47 (t, J = 4.8 Hz, 1H), 4.52 (s, 2H), 2.78 (t, J = 7.9 Hz, 2H), 2.75 (br s, 1H), 2.38 – 2.34 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 135.8, 134.8, 132.3, 127.6, 127.2, 126.5, 124.8, 121.1, 88.1, 83.3, 51.3, 26.9, 23.4; MS (EI) m/z 184.1 (M^+ (100.0), 152.1 (62.8), 141.1 (51.8), 115.1 (41.4)); Exact mass calc'd. For $C_{13}H_{12}O$: 184.0860. Observed: 184.0832.

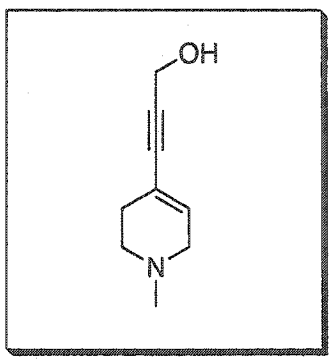


3-(2H-Chromen-4-yl)-prop-2-yn-1-ol (49c): Prepared via **standard procedure C.** $Pd(PPh_3)_2Cl_2$ (250 mg, 0.36 mmol), copper (I) iodide (136 mg, 0.71 mmol), THF : DEA (40 mL), (**47c**) (2.00 g, 7.14 mmol) in THF (10 mL), propargyl alcohol (0.46 mL, 7.85 mmol). Purification was achieved with silica gel chromatography employing a 4 : 1 pet ether / ethyl acetate solvent system. This afforded **49c** as a viscous red oil (195 mg, 15%). IR (neat); 3378 (s)2910 (m), 2838 (m), 1487 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.39 (d, J = 6.6 Hz, 1H), 7.13 (t, J = 7.7 Hz, 1H), 6.91 (t, J = 7.4 Hz, 1H), 6.77 (d, J = 8.0 Hz, 1H), 6.08 (m, 1H), 4.80 (d, J = 3.0 Hz, 2H), 4.48 (s, 2H), 1.23 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 153.9, 130.3, 128.0, 125.9, 121.9, 121.5, 119.1, 116.2, 90.5, 81.4, 65.6, 51.9; MS (EI) m/z 186.1 (M^+ (100.0), 171.0 (25.5), 155.1 (57.2), 128.1 (41.1) 77.0 (14.9), 63.0 (13.1)); Exact mass calc'd. For $C_{12}H_{10}O$: 186.0692. Observed: 186.0703.

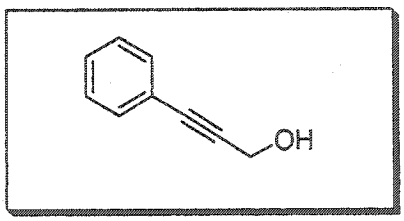


3-Cyclohex-1-enyl-prop-2-yn-1-ol (49e) : Prepared via **standard procedure C.** $Pd(PPh_3)_2Cl_2$ (175 mg, 0.25 mmol), copper (I) iodide (95 mg, 0.5 mmol), THF : DEA (30 mL), (**49d**) (1.15 g, 5.0 mmol) in THF (10 mL), propargyl alcohol (0.29 mL, 5.5 mmol).

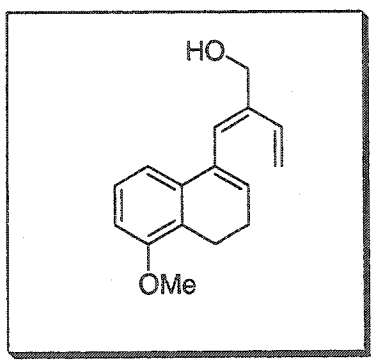
Purification was achieved with silica gel chromatography employing a 4 : 1 pet ether / ethyl acetate solvent system. This afforded **49e** as a viscous red oil (431 mg, 64%).
IR (neat); 3619 (s), 3438 (s), 2929 (s), 2871 (s), 1442 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 6.10 (quintet, J = 2.1 Hz, 1H), 4.35 (s, 2H), 2.10 – 2.05 (m, 4H), 1.63 – 1.54 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 135.5, 120.1, 87.6, 84.5, 51.6, 29.1, 25.6, 22.2, 21.4; MS (EI) m/z 136.1 (M^+ (100.0), 107.0 (51.7), 91.1 (58.1), 79.1 (78.1)); Exact mass calc'd. For $C_9H_{12}O$: 136.0887. Observed: 135.0886.



3-(1-Methyl-1,2,3,6-tetrahydro-pyridin-4-yl)-prop-2-yn-1-ol (49f) : Prepared via **standard procedure C.** $Pd(PPh_3)_2Cl_2$ (117 mg, 0.12 mmol), copper (I) iodide (63 mg, 0.33 mmol), THF : DEA (40 mL), (**47e**) (820 mg, 3.34 mmol) in THF (3 mL), propargyl alcohol (0.20 mL, 3.34 mmol). Purification was achieved with neutral alumina gel chromatography employing a 12 : 1 dichloromethane / methanol solvent system. This afforded **49f** as a viscous red oil (469 mg, 93%).
IR (neat); 3689 (s), 3348 (s), 2943 (m), 2782 (m), 1609 (m), 1454 (m), 1377 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.98 – 5.96 (m, 1H), 4.30 (s, 3H), 3.41 (br s, 1H), 3.02 (q, J = 3.3 Hz, 2H), 2.55 (t, J = 5.7 Hz, 2H), 2.34 (s, 3H), 2.34 – 2.30 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 131.2, 119.1, 87.4, 85.4, 54.6, 51.8, 51.3, 45.9, 30.0; MS (EI) m/z 151.1 (M^+ (54.2), 143.0 (16.0), 134.1 (15.6), 120.1 (14.9), 79.1 (13.5), 43.0 (100.0)); Exact mass calc'd. For $C_9H_{13}NO$: 151.0092. Observed: 151.0087.

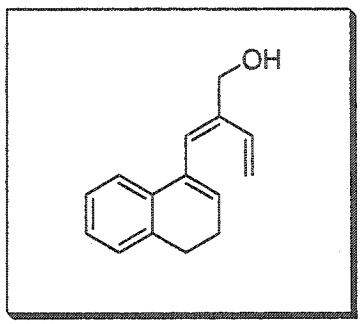


3-Phenyl-prop-2-yn-1-ol (49g) : Prepared according to literature procedure. Characterization data and experimental yield were in line with literature values. [50]
^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.45 – 7.40 (m, 2H), 7.31 – 7.25 (m, 3H), 4.49 (s, 2H), 2.88 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 132.1, 128.9, 128.7, 123.0, 87.7, 86.0, 51.8.



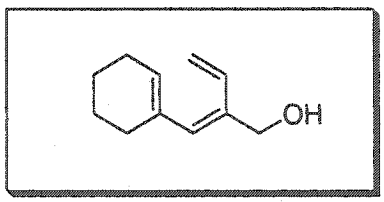
2-(5-Methoxy-3,4-dihydro-naphthalen-1-ylmethylene)-but-3-en-1-ol (50a) : Prepared via **standard procedure D.** Compound (**49a**) (510 mg, 2.52 mmol) in toluene (20 mL), vinyl magnesium chloride (4.9 mL, 1.7 M, 8.1 mmol) , saturated ammonium chloride (30 mL). Purification was achieved with silica gel chromatography employing a 3 : 1 pet ether / ethyl acetate solvent system. This afforded **50a** as a yellow oil (433 mg, 71%).
IR (neat); 3396 (s), 2934 (s), 2834 (s), 1567 (s), 1251 (s), 1042 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.06 (d, J = 8.4 Hz, 1H), 6.77 – 6.64 (m, 3H), 6.45 (s, 1H), 5.83 (t,

J = 4.0 Hz, 1H), 5.32 (t, J = 18.0 Hz, 1H), 5.10 (d, J = 11.3 Hz, 1H), 4.45 (s, 2H), 3.77 (s, 3H), 2.75 (t, J = 7.7 Hz, 2H), 2.56 (br s, 1H), 2.38 – 2.32 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.1, 139.0, 138.2, 133.5, 128.7, 128.3, 127.8, 125.9, 114.5, 114.2, 111.3, 64.3, 55.6, 28.8, 23.6; MS (EI) m/z 242.1 (M^+ (100.0), 211.1 (85.9), 196.1 (17.7), 165.1 (25.7), 115.1 (14.4)); Exact mass calc'd. For $C_{16}H_{18}O_2$: 242.1325. Observed: 242.1343.



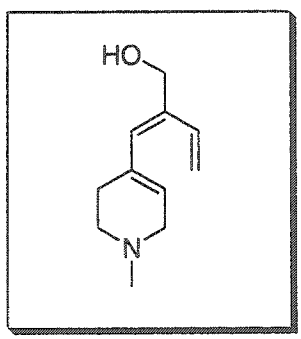
2-(3,4-Dihydro-naphthalen-2-ylmethylene)-but-3-en-1-ol (50b) : Prepared via **standard procedure D.** Compound (**49b**) (415 mg, 2.26 mmol) in cyclohexane (5 mL), vinyl magnesium chloride (4.0 mL, 1.7 M, 6.78 mmol) , NH_4Cl (20 mL). Purification was achieved with silica gel chromatography employing a 6 : 1 pet ether / ethyl acetate solvent system. This afforded **50b** as a yellow oil (370 mg, 77%).

IR (neat); 3606 (s), 3448 (m), 3054 (s), 2987 (s), 2306 (m), 1422 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.17 (s, 4H), 6.73 (ddd, J = 18.0 Hz, 11.3 Hz, 0.9 Hz, 1H), 6.49 (s, 1H), 5.98 (td, J = 4.7 Hz, 1.6 Hz, 1H), 5.39 (dt, J = 18.0 Hz, 0.9 Hz, 1H), 5.13 (dt, J = 11.3 Hz, 1.4 Hz, 1H), 4.48 (d, J = 1.1 Hz, 2H), 2.80 (t, J = 7.7 Hz, 2H), 2.42 – 2.37 (m, 2H), 2.20 (br s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 138.7, 135.9, 134.6, 133.4, 132.9, 129.8, 128.2, 127.4, 127.1, 126.4, 124.2, 114.2, 64.0, 27.8, 23.2; MS (EI) m/z 212.1 (M^+ (54.5), 181.1 (100.0), 165.1 (53.2), 141.1 (35.2), 128.1 (26.5)); Exact mass calc'd. For $C_{15}H_{16}O$: 212.1200. Observed: 212.1199.



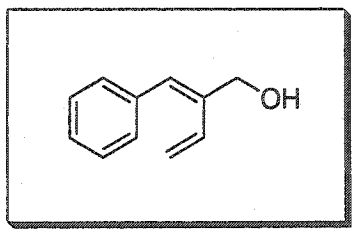
2-Cyclohex-1-enylmethylene-but-3-en-1-ol (50d) : Prepared via **standard procedure D.** Compound (**49e**) (400 mg, 2.94 mmol) in cyclohexane (5 mL), vinyl magnesium chloride (5.53 mL, 1.7 M, 8.64 mmol) , saturated ammonium chloride (20 mL). Purification was achieved with silica gel chromatography employing a 6 : 1 pet ether / ethyl acetate solvent system. This afforded **50d** as a yellow oil (433 mg, 90%).

IR (neat); 3338 (s), 2929 (s), 2858 (m), 1436 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 6.79 (ddd, J = 17.9 Hz, 11.3 Hz, 0.8 Hz, 1H), 5.98 (s, 1H), 5.65 (sextet, J = 2.0 Hz, 1H), 5.29 (d, J = 17.9 Hz, 1H), 5.07 (dt, J = 11.2 Hz, 1.4 Hz, 1H), 2.12 – 2.05 (m, 4H), 1.90 (br s, 1H), 1.64 – 1.54 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 134.7, 134.4, 133.2, 133.2, 129.7, 113.7, 64.8, 29.1, 25.7, 22.7, 22.0; MS (EI) m/z 164.1 (M^+ (17.0), 133.1 (32.9), 121.1 (25.2), 105.1 (28.1), 91.1 (100.0), 79.1 (37.8)); Exact mass calc'd. For $C_{11}H_{16}O$: 164.1189. Observed: 164.1177.

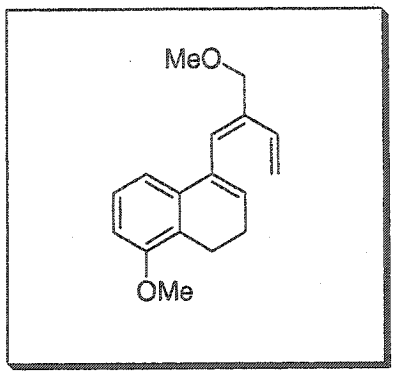


2-(1-Methyl-1,2,3,6-tetrahydro-pyridin-4-ylmethylene)-but-3-en-1-ol (50e) : Prepared via **standard procedure D.** Compound (**49f**) (600 mg, 3.97 mmol) in THF (10 mL), vinyl magnesium chloride (7.5 mL, 1.7 M, 12.7 mmol), saturated ammonium chloride (30 mL). Purification was achieved with silica gel chromatography employing a 12 : 1 dichloromethane / methanol solvent system. This afforded **50e** as an orange oil (102 mg, 15%).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.76 (dd, J = 17.9 Hz, 11.3 Hz, 1H), 5.95 (m, 1H), 5.54 (m, 1H), 5.25 (d, J = 17.8 Hz, 1H), 5.05 (d, J = 11.4 Hz, 1H), 4.24 (s, 2H), 3.03 (m, 2H), 2.54 (t, J = 5.7 Hz, 2H), 2.33 (s, 3H), 2.25 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 136.6, 133.3, 133.1, 130.4, 126.1, 114.7, 64.3, 54.9, 52.2, 45.8, 29.9; MS (EI) m/z 179.1 (M^+ (11.5), 161.1 (20.5), 105.1 (15.0), 43.0 (100.0); Exact mass calc'd. For $C_{11}H_{17}NO$: 179.1299. Observed: 179.1287.

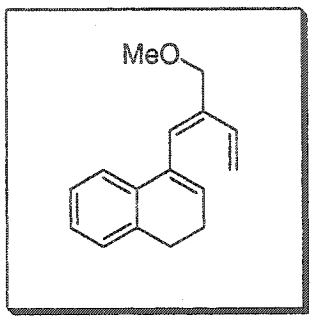


2-Benzylidene-but-3-en-1-ol (50f) : Prepared via **standard procedure D.** Compound (**49g**) (275 mg, 2.08 mmol) in Toluene (5 mL), vinyl magnesium chloride (4.2 mL, 1.6 M, 6.7 mmol) , saturated ammonium chloride (20 mL). Purification was attempted with silica gel chromatography employing a 6 : 1 pet ether / ethyl acetate solvent system. Compound could not be separated from other side products (101 mg, 31%).



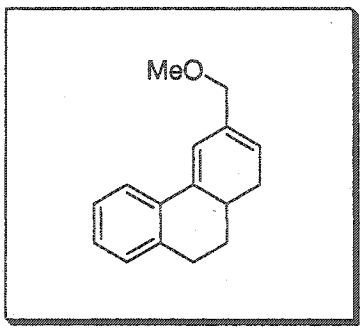
8-Methoxy-4-(2-methoxymethyl-buta-1,3-dienyl)-1,2-dihydro-naphthalene (51a) : **(50a)** (165 mg, 0.68 mmol) was dissolved in dry THF (20 mL). KO^{t}Bu in THF (3.4 mL, 1M, 3.4 mmol) was added via syringe and allowed to stir for 10 minutes. MeI (378 μL, 3.4 mmol) was added via syringe and the reaction allowed to stir at room temperature for 3h. The reaction was quenched with water (30 mL) and aqueous extraction was performed with diethyl ether (2 x 20 mL). This afforded **51a** as a yellow oil (168 mg, 99 %).

IR (neat); 2938 (s), 2836 (s), 1493 (s), 1248 (s), 1092 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.12 (d, J = 4.0 Hz, 1H), 6.74 – 6.65 (m, 3H), 6.37 (s, 1H), 5.84 (d, J = 4.5 Hz, 1H), 5.34 (t, J = 18.8 Hz, 1H), 5.08 (d, J = 11.2 Hz, 1H), 4.22 (s, 2H), 3.78 (s, 3H), 3.40 (s, 3H), 2.76 (t, J = 7.8 Hz, 2H), 2.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 158.8, 137.9, 135.9, 133.2, 130.0, 127.9, 127.4, 125.5, 114.4, 113.8, 111.0, 74.0, 57.9, 55.2, 28.5, 23.2; MS (EI) m/z 256.1 (M^+ (100.0), 225.1 (56.8), 211.1 (93.0), 171.1 (76.0), 115.1 (38.2), 45.0 (74.8)); Exact mass calc'd. For $C_{17}H_{20}O_2$: 256.1441. Observed: 256.1413.



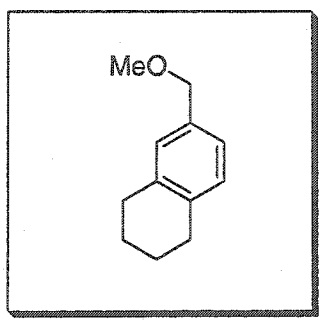
4-(2-Methoxymethyl-buta-1,3-dienyl)-1,2-dihydro-naphthalene (51b) : **(50b)** (160 mg, 0.79 mmol) was dissolved in THF (20 mL). Sodium hydride (60 mg, 1.58 mmol) and methyl iodide (0.24 mL, 3.95 mmol) were added and the solution allowed to stir at room temperature for 14 hours. Water (20 mL) was added and aqueous extraction with diethyl ether (3 x 20 mL) was performed. Purification was achieved through silica gel chromatography employing a 20 : 1 pet ether / ethyl acetate solvent system. This afforded **51b** as a colourless oil (155 mg, 87 %).

IR ($CDCl_3$); 3161 (m), 2936 (s), 2865 (s), 2814 (s), 1468 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.14 (s, 4H), 6.70 (ddd, J = 17.9 Hz, 11.4 Hz, 0.9 Hz, 1H), 6.41 (s, 1H), 5.98 (td, J = 5.7 Hz, 1.5 Hz, 1H), 5.39 (d, J = 17.8 Hz, 1H), 5.10 (dt, J = 11.2 Hz, 1.5 Hz, 1H), 2.79 (t, J = 6.7 Hz, 2H), 2.42 – 2.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 136.4, 135.1, 133.9, 133.4, 130.3, 130.2, 127.9, 127.5, 126.8, 124.7, 115.0, 74.4, 58.4, 28.3, 23.6; MS (EI) m/z 226.1 (M^+ (55.7), 196.1 (38.0), 181.1 (100.0), 165.1 (74.7), 141.1 (39.2), 115.1 (41.0); Exact mass calc'd. For $C_{16}H_{18}O$: 226.1376. Observed: 226.1394.



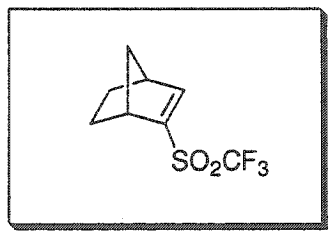
3-Methoxymethyl-1,9,10,10a-tetrahydro-phenanthrene (52) : Compound (**51b**) (110 mg, 0.49 mmol) was dissolved in toluene (20 mL) and refluxed over night. The toluene was removed under reduced pressure and purification was achieved through silica gel chromatography employing a 30 : 1 pet ether / ethyl acetate solvent system. This afforded **52** as a yellow oil (83 mg, 76 %).

IR (neat); 3155 (m), 2936 (m), 2253 (s), 1803 (m), 1461 (s), 1377 (s), cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.77 (d, J = 9.0 Hz, 1H), 7.10 – 7.20 (m, 3H), 6.65 (d, J = 2.2 Hz, 1H), 5.86 – 5.90 (m, 1H), 3.99 (q, J = 11.5 Hz, 2H), 3.34 (s, 3H), 2.77 – 2.86 (m, 2H), 2.54 – 2.68 (m, 1H), 2.31 (dt, J = 16.8 Hz, 6.4 Hz, 1H), 1.98 – 2.11 (m, 2H), 1.45 – 1.58 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.3, 137.0, 134.8, 133.6, 129.5, 127.4, 126.5, 125.1, 123.7, 117.6, 75.4, 58.1, 36.5, 31.4, 31.0, 30.3; MS (EI) m/z 224.1 (M^+, 74.9), 193.1 (64.6), 179.1 (100.0), 165.1 (54.1), 152.1 (23.2)); Exact mass calc'd. For $C_{16}H_{18}O$: 226.1355. Observed: 226.1352.



6-Methoxymethyl-1,2,3,4-tetrahydro-naphthalene (53) : Compound (**51c**) (120 mg, 0.67 mmol) was dissolved in toluene (20 mL) and placed in a sealed tube. The solution was heated to 250 ^{0}C for 16 hours. The toluene was removed under reduced pressure before purification was achieved with silica gel chromatography, employing pure pet ether as a solvent system. This afforded **53** as a colourless oil (28 mg, 23 %).

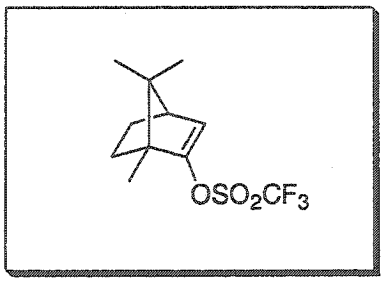
IR (neat); 2936 (s), 2852 (m), 2247 (m), 1094 (m), cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.24 (s, 3H), 4.36 (s, 2H), 3.35 (s, 3H), 2.74 (m, 4H), 1.09 (s, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 137.5, 137.0, 135.5, 129.5, 129.0, 125.4, 75.1, 58.3, 29.7, 29.5, 23.6; MS (EI) m/z 176.1 (M^+, 85.2), 145.1 (87.8), 129.1 (100.0), 115.1 (59.9), 91.1 (75.5)); Exact mass calc'd. For $C_{12}H_{16}O$: 176.1184. Observed: 176.1167.



2-Trifluoromethanesulfonyl-bicyclo[2.2.1]heptane (55a) : Prepared via **standard procedure B**. Butyl lithium (6.4 mL, 2.5 M, 16.0 mmol), diisopropylamine (2.10 mL, 16.0 mmol), norcamphor (1.6 g, 14.55 mmol) in THF (5 mL), *N*-phenyltrifluromethanesulfonimide (5.45 g, 15.3 mmol) in THF (10 mL). Purification was achieved with silica gel chromatography employing a pure pet ether solvent system. This afforded **55a** as a colourless oil (2.06 g, 59%). Characterization information was consistent with previously reported data for this compound.[51]

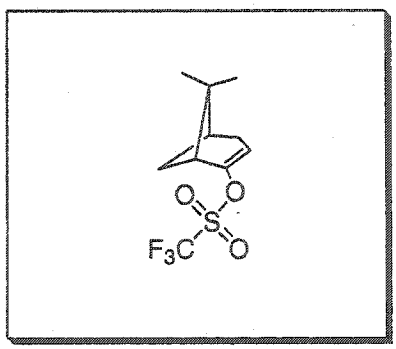
^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.65 (d, J = 3.5 Hz, 1H), 2.98 – 2.96 (m, 2H), 1.82 – 1.69 (m, 2H), 1.67 – 1.61 (m, 1H), 1.49 – 1.34 (m, 1H), 1.25 – 1.13 (m, 3H), 0.89 – 0.79 (m,

2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.3, 125.3, 121.1, 120.3, 116.8, 112.6, 48.0, 44.1, 41.7, 25.9, 24.6.



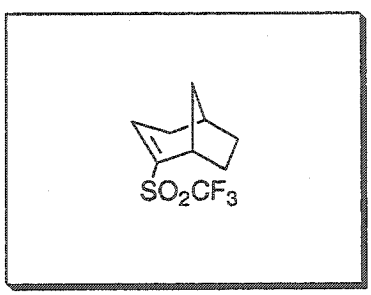
(1*R*)–Trifluoro-methanesulfonic acid 1,7,7-trimethyl-bicyclo[2.2.1]hept-2-en-2-yl ester (55b) : Prepared according to literature procedures. Characterization data and experimental yield were in line with literature values.[52]

^1H NMR ($CDCl_3$, 200 MHz): δ 5.6 (d, *J* = 3.8 Hz, 1H), 2.42 (t, *J* = 3.7 Hz, 1H), 1.95 – 1.84 (m, 1H), 1.63 (ddd, *J* = 12.1 Hz, 8.4 Hz, 3.4 Hz, 1H), 1.32 (dt, *J* = 3.4 Hz, 9.1 Hz, 1H), 1.13 (ddd, *J* = 11.9 Hz, 8.9 Hz, 3.4 Hz, 1H), 1.01 (s, 3H), 0.90 (s, 3H), 0.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 155.1, 130.1, 121.7, 117.6, 115.3, 106.9, 56.9, 53.7, 50.0, 30.7, 25.2, 19.6, 18.9, 9.3; MS (EI) m/z 284.1 (M^+ (40.7), 151.1 (55.7), 123.1 (100.0), 95.1 (59.3)); Exact mass calc'd. For $C_{11}H_{15}F_3O_3S$: 284.0685. Observed: 284.0676.



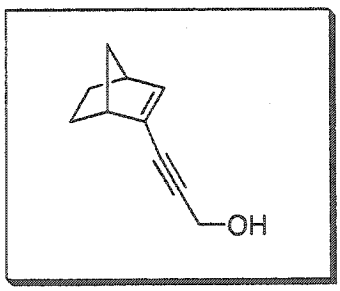
(1*R*)–Trifluoro-methanesulfonic acid 6,6-dimethyl-bicyclo[3.1.1]hept-2-en-2-yl ester (55c) : Prepared via **standard procedure B.** Butyl lithium (9.3 mL, 1.6 M, 14.8 mmol), diisopropylamine (1.94 mL, 14.8 mmol), nopinone (1.9 mL, 13.46 mmol), *N*-phenyltrifluromethanesulfonimide (5.05 g, 14.13 mmol). Purification was achieved with silica gel chromatography employing a pure per ether solvent system. This afforded **55c** as a colourless oil (1.94 g, 54%).

IR (neat); 2949 (s), 1658 (m), 1414 (s), 1224 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.51 (q, J = 3.3 Hz, 1H), 2.54 (dt, J = 9.2 Hz, 5.6 Hz, 1H), 2.22 – 2.40 (m, 3H), 2.09 – 2.13 (m, 1H), 1.35 (d, J = 9.1 Hz, 1H), 1.32 (s, 3H), 0.91 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.4, 125.2, 121.0, 116.8, 112.6, 111.8, 46.6, 40.5, 40.1, 32.1, 28.6, 25.8, 21.2; MS (EI) m/z 270.1 (M^+ (2.6), 226.0 (16.2), 162.0 (9.0), 77.0 (52.2), 55.0 (100.0); Exact mass calc'd. For $C_{10}H_{13}F_3O_3S$: 270.0517. Observed: 270.0496.



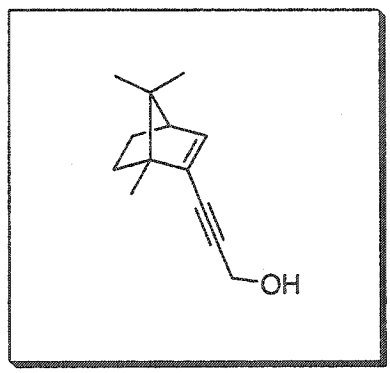
2-Trifluoromethanesulfonyl-bicyclo[3.2.1]oct-2-ene (55d) : Prepared via **standard procedure B.** Butyl lithium (7.0 mL, 2.5 M, 17.6 mmol), diisopropylamine (2.30 mL, 17.6 mmol), bicyclo [3.2.1] octanone (1.99 g, 16.0 mmol) in THF (5 mL), *N*-phenyltrifluromethanesulfonimide (6.0 g, 16.8 mmol) in THF (10 mL). Purification was achieved with silica gel chromatography employing a pure pet ether solvent system. This afforded **55d** as a colourless oil (3.55 g, 87%).

IR (neat); 2955 (s), 2865 (s), 1416 (s), 1210 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.40 - 5.38 (m, 1H), 2.53 (t, J = 4.7 Hz, 1H), 2.42 – 2.36 (m, 2H), 2.15 – 2.26 (m, 1H), 1.96 – 1.84 (m, 2H), 1.68 – 1.80 (m, 2H), 1.62 – 1.54 (m, 1H), 1.47 – 1.38 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 154.2, 125.2, 121.0, 116.8, 112.6, 114.1, 40.0, 36.0, 34.8, 34.4, 32.5, 30.3; MS (EI) m/z 256.0 (M^+ (44.2), 228.0 (20.3), 95.1 (100.0), 79.1 (57.4), 67.1 (74.8)); Exact mass calc'd. For $C_9H_{11}F_3O_3S$: 256.0379. Observed: 256.0376.



3-Bicyclo[2.2.1]hept-2-yl-prop-2-yn-1-ol (56a) : Prepared via **standard procedure C.** $Pd(PPh_3)_2Cl_2$ (269 mg, 0.38 mmol), copper (I) iodide (145 mg, 0.76 mmol), THF : DEA (50 mL), (**55a**) (1.85 g, 7.65 mmol) in THF (10 mL), propargyl alcohol (0.49 mL, 8.42 mmol). Purification was achieved with silica gel chromatography employing a 5 : 1 pet ether / ethyl acetate solvent system. This afforded **56a** as a viscous red oil (680 mg, 60%).

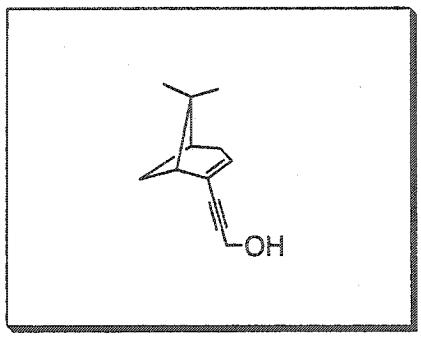
IR ($CDCl_3$); 3606 (s), 3445 (s), 2968 (s), 2865 (s), 1378 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 6.17 (d, J = 3.0 Hz, 1H), 4.32 (s, 2H), 3.24 (br s, 1H), 2.82 – 2.80 (m, 2H), 1.67 – 1.52 (m, 3H), 1.39 – 1.33 (m, 2H), 1.19 – 0.94 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.1, 129.3, 90.7, 82.4, 51.7, 48.4, 47.3, 43.0, 25.5, 24.7; MS (EI) m/z 148.1 (M^+ (37.6), 120.1 (63.9), 91.1 (100.0), 77.0 (33.8); Exact mass calc'd. For $C_{12}H_{16}O$: 176.1183. Observed: 176.1164.



(1*R*)–3-(1,7,7-Trimethyl-bicyclo[2.2.1]hept-2-en-2-yl)-prop-2-yn-1-ol (56b) : Prepared via **standard procedure C.** $Pd(PPh_3)_2Cl_2$ (317 mg, 0.45 mmol), copper (I) iodide (172 mg, 0.90 mmol), THF : DEA (50 mL), (**55b**) (2.57 g, 9.0 mmol) in THF (10 mL), propargyl alcohol (0.52 mL, 9.9 mmol). Purification was achieved with silica gel chromatography employing a 7 : 1 pet ether / ethyl acetate solvent system. This afforded **56b** as a viscous red oil (1.38 g, 81%).

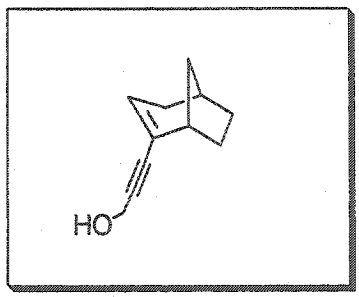
IR ($CDCl_3$); 3438 (s), 3019 (s), 2872 (s), 2400 (s), 1218 (s), 1002 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 6.27 (d, J = 3.4 Hz, 1H), 4.43 (s, 2H), 2.34 (t, J = 3.6 Hz, 1H), 1.91 – 1.85 (m, 2H), 1.55 (ddd, J = 11.9 Hz, 9.1 Hz, 3.4 Hz, 1H), 1.1.09 – 1.05 (m, 1H), 1.05 (s, 3H), 1.00 (ddd, J = 12.4 Hz, 9.1 Hz, 3.4 Hz, 1H), 0.79 (s, 3H), 0.78 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 141.0, 131.4, 91.0, 81.6, 56.3, 55.4, 51.9, 51.3, 30.9, 24.7, 19.5,

19.3, 11.8; MS (EI) m/z 190.1 (M^+ (100.0), 175.1 (69.8), 147.1 (52.0), 117.1 (50.5), 91.1 (48.8); Exact mass calc'd. For $C_{13}H_{18}O$: 190.1349. Observed: 190.1340.



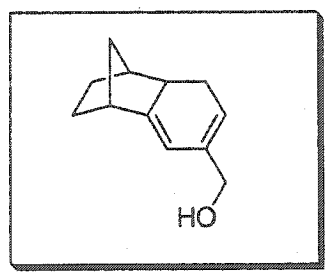
(1*R*)–3-(6,6-Dimethyl-bicyclo[3.1.1]hept-2-en-2-yl)-prop-2-yn-1-ol (56c): Prepared via **standard procedure C.** $Pd(PPh_3)_2Cl_2$ (250 mg, 0.35 mmol), copper (I) iodide (134 mg, 0.70 mmol), THF : DEA (60 mL), (**55c**) (1.90 g, 7.04 mmol) in THF (5 mL), propargyl alcohol (0.45 mL, 7.7 mmol). Purification was achieved with neutral alumina gel chromatography employing a 6 : 1 pet ether / ethyl acetate solvent system. This afforded **56c** as a viscous orange oil (1.10 g, 89%).

IR (neat); 3607 (s), 2955 (s), 1375 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.96 (t, J = 3.3 Hz, 1H), 4.36 (s, 2H), 2.38 (dt, J = 9.0 Hz, 7.7 Hz, 1H), 2.32 – 2.28 (m, 2H), 2.22 (dt, J = 1.2 Hz, 5.7 Hz, 1H), 2.10 – 2.03 (m, 1H), 1.80 (br s, 1H), 1.26 (s, 3H), 1.20 (d, J = 9.0 Hz, 1H), 0.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 131.9, 129.7, 87.3, 86.7, 52.1, 47.2, 40.5, 38.3, 32.4, 31.7, 26.3, 21.4; MS (EI) m/z 176.1 (M^+ (54.2), 161.1 (14.4), 143.1 (36.7), 128.1 (42.6), 115.1 (68.4), 103.1 (100.0), 91.1 (98.5); Exact mass calc'd. For $C_{12}H_{16}O$: 176.1191. Observed: 176.1180.



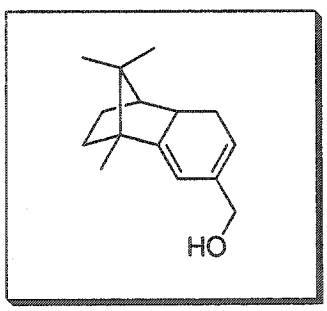
3-Bicyclo[3.2.1]oct-2-en-2-yl-prop-2-yn-1-ol (56d) : Prepared via **standard procedure C.** $Pd(PPh_3)_2Cl_2$ (344 mg, 0.49 mmol), copper (I) iodide (187 mg, 0.98 mmol), THF : DEA (80 mL), (**55d**) (2.50 g, 9.80 mmol) in THF (5 mL), propargyl alcohol (0.63 mL, 10.8 mmol). Purification was achieved with neutral alumina gel chromatography employing a 7 : 1 pet ether / ethyl acetate solvent system. This afforded **55d** as a viscous orange oil (1.03 g, 65%).

IR (neat); 3341 (s), 2942 (s), 2865 (m), 1029 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.72 (t, J = 3.1 Hz, 1H), 4.30 (s, 2H), 3.05 (br s, 1H), 2.39 – 2.23 (m, 3H), 1.89 – 1.72 (m, 3H), 1.69 – 1.61 (m, 1H), 1.56 – 1.52 (m, 1H), 1.45 – 1.30 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 132.2, 128.3, 86.9, 85.8, 51.6, 40.7, 37.7, 35.5, 35.3, 32.8 30.9; MS (EI) m/z 162.1 (M+ (100.0), 134.1 (26.9), 105.1 (33.8), 91.1 (67.7), 77.0 (45.8)); Exact mass calc'd. For $C_{11}H_{14}O$: 162.1037. Observed: 162.1030.



(1,2,3,4,8,8a-Hexahydro-1,4-methano-naphthalen-6-yl)-methanol (57a) : Prepared via **standard procedure D.** Compound (**56a**) (210 mg, 1.42 mmol) in toluene (5 mL), vinyl magnesium chloride (2.7 mL, 1.7 M, 4.54 mmol) , saturated ammonium chloride (30 mL). Purification was achieved with silica gel chromatography employing a 6 : 1 pet ether / ethyl acetate solvent system. This afforded **57a** as an orange oil (105 mg, 42%).

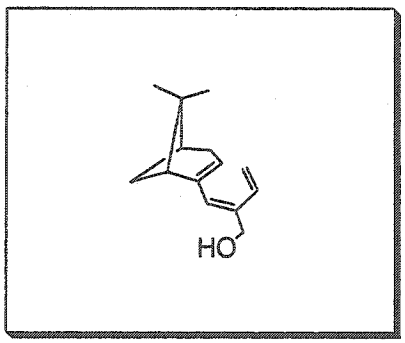
IR ($CDCl_3$); 3439 (m), 2958 (s), 2867 (s), 1469 (m), 1371 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.57 (s, 1H), 5.55 – 5.53 (m, 1H), 4.04 (q, J = 12.3 Hz, 2H), 2.71 (s, 1H), 2.15 – 2.02 (m, 3H), 1.82 – 1.59 (m, 4H), 1.47 (br s, 1H), 1.42 – 1.30 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.4, 137.8, 120.0, 110.4, 66.1, 44.4, 44.2, 42.1, 39.5, 31.0, 27.2, 26.5; MS (EI) m/z 176.1 (M^+ (26.0), 145.1 (48.3), 117.1 (87.1), 105.1 (96.9), 91.1 (100.0), 39.0 (60.7)); Exact mass calc'd. For $C_{12}H_{16}O$: 176.1183. Observed: 176.1164.



(1*R*)-(4,9,9-Trimethyl-1,2,3,4,8,8a-hexahydro-1,4-methano-naphthalen-6-yl)-methanol (57b) : Prepared via **standard procedure D.** Compound (**56b**) (467 mg, 2.46 mmol) in cyclohexane (10 mL), vinyl magnesium chloride (6.15 mL, 1.6 M, 9.84 mmol) , saturated ammonium chloride (30 mL) Purification was achieved with silica gel chromatography employing a 7 : 1 pet ether / ethyl acetate solvent system. This afforded **57b** as an orange oil (391 mg, 73%).

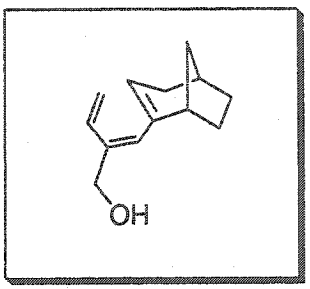
IR (neat); 3355 (s), 2952 (s), 2869 (s), 1670 (m), 1448 (m), 1045 (m) cm^{-1}; ^1H NMR (C_6D_6, 200 MHz): δ 5.59 (s, 1H), 5.52 – 5.49 (m, 1H), 4.07 (s, 2H), 2.55 – 2.39 (m, 1H), 2.20 – 2.01 (m, 2H), 1.89 – 1.71 (m, 3H), 1.31 – 1.13 (m, 1H), 1.04 (s, 3H), 0.96 (s, 3H),

0.83 (s, 3H); ^{13}C NMR (C_6D_6, 50 MHz): δ 154.3, 137.5, 118.0, 109.8, 65.5, 50.9, 50.4, 48.1, 45.5, 32.3, 30.5, 27.7, 21.8, 20.7, 11.8; MS (EI) m/z 218.0 (M^+ (17.3), 216.0 (20.9), 171.0 (34.8), 157.0 (83.0), 143.0 (100.0); Exact mass calc'd. For $C_{15}H_{22}O$: 218.1685. Observed: 218.1700.



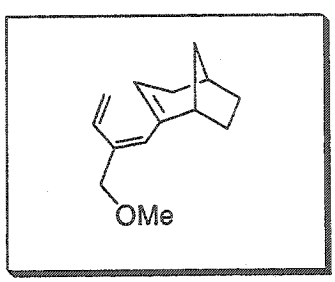
(1*R*)-2-(6,6-Dimethyl-bicyclo[3.1.1]hept-2-en-2-ylmethylene)-but-3-en-1-ol (57c) : Prepared via **standard procedure D.** Compound (**56c**) (1.0 g, 5.3 mmol) in toluene (10 mL), vinyl magnesium chloride (10 mL, 1.7 M, 16.96 mmol) , saturated ammonium chloride (30 mL) Purification was achieved with silica gel chromatography employing a 7 : 1 pet ether \ ethyl acetate solvent system. This afforded **57c** as an orange oil (830 mg, 77%).

IR (neat); 3357 (s), 2990 (s), 2920 (s), 1461 (m), 1008 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 6.75 (ddd, *J* = 0.9 Hz, 11.2 Hz, 17.9 Hz, 1H), 5.96 (s, 1H), 5.54 – 5.57 (m, 1H), 5.31 (d, *J* = 17.9 Hz, 1H), 5.10 (dt, *J* = 11.2 Hz, 1.4 Hz, 1H), 4.28 (s, 2H), 2.34 – 2.40 (m, 3H), 2.24 (dt, *J* = 1.4 Hz, 5.7 Hz, 1H), 2.05 – 2.11 (m, 1H), 1.73 (br s, 1H), 1.27 (s, 3H), 1.19 (d, *J* = 8.7 Hz, 1H), 0.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 144.8 135.3, 133.6, 131.5, 125.5, 114.4, 65.1, 46.9, 40.7, 38.2, 32.4, 31.9, 26.6, 21.5; MS (EI) m/z 204.2 (M^+ (15.2), 161.1 (24.0), 143.1 (38.8), 129.1 (52.8), 117.1 (43.9), 105.1 (100.0), 91.1 (61.3)); Exact mass calc'd. For $C_{14}H_{20}O$: 204.1501. Observed: 204.1487.



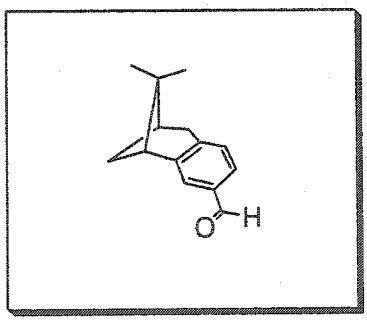
2-Bicyclo[3.2.1]oct-2-en-2-ylmethylene-but-3-en-1-ol (57d) : Prepared via **standard procedure D.** Compound (**56d**) (1.0 g, 6.17 mmol) in toluene (15 mL), vinyl magnesium chloride (11.6 mL, 1.7 M, 19.7 mmol) , saturated ammonium chloride (30 mL). Purification was achieved with silica gel chromatography employing an 8 : 1 pet ether : ethyl acetate solvent system. This afforded **57d** as a yellow oil (750 mg, 64%).

IR (neat); 3329 (s), 2936 (s), 2865 (s), 1442 (m), 1088 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 6.74 (dd, J = 17.9 Hz, 11.3 Hz, 1H), 5.97 (m, 1H), 5.34 (m, 1H), 5.31 (d, J = 17.8 Hz, 1H), 5.09 (d, J = 11.2 Hz, 1H), 4.30 (s, 2H), 2.47 – 2.31 (m, 3H), 2.01 – 1.38 (m, 8H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.5, 135.5, 133.5, 132.3, 126.1, 114.2, 65.2, 41.6, 37.8, 35.6, 35.2, 33.1, 31.1; MS (EI) m/z 190.1 (M+ (20.8), 159.1 (23.0), 129.1 (29.8), 105.1 (29.0), 91.1 (100.0), 79.1 (43.4)); Exact mass calc'd. For $C_{13}H_{18}O$: 190.1349. Observed: 190.1341.



2-(2-Methoxymethyl-buta-1,3-dienyl)-bicyclo[3.2.1]oct-2-ene (58) : **(57d)** (680 mg, 3.6 mmol) was dissolved in dry THF (20 mL). KO^{t}Bu in THF (17.9 mL, 1M, 18.0 mmol) was added via syringe and allowed to stir for 10 minutes. MeI (1.98 mL, 18.0 mmol) was added via syringe and the reaction allowed to stir at room temperature for 3 hours. The reaction was quenched with water (50 mL) and aqueous extraction was performed with diethyl ether (3 x 30 mL). This afforded **58** as a yellow oil (728 mg, 99 %).

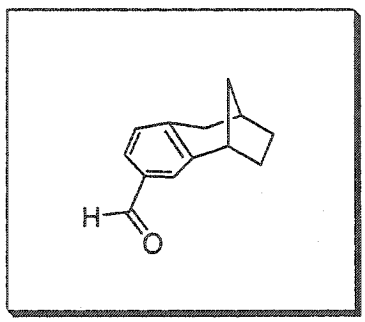
IR (neat); 2943 (s), 2865 (m), 1448 (w), 1094 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.75 (dd, *J* = 17.8 Hz, 11.2 Hz, 1H), 5.93 (m, 1H), 5.34 (m, 1H), 5.31 (d, J = 18.1 Hz, 1H), 5.06 (d, *J* = 11.2 Hz, 1H), 4.06 (s, 2H), 3.31 (s, 3H), 2.47 – 2.25 (m, 3H), 1.95 – 1.59 (m, 5H), 1.52 –1 .38 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.5, 133.6, 132.7, 131.4, 125.9, 114.4, 75.0, 58.2, 41.5, 39.8, 35.6, 35.2, 32.7, 29.2; MS (EI) m/z 204.2 (M+ (27.8), 159.1 (22.0), 129.1 (41.6), 104.1 (45.1), 91.1 (100.0), 45.0 (66.3)); Exact mass calc'd. For $C_{14}H_{20}O$: 204.1520. Observed: 204.1526.



(1*R*)–9,9-Dimethyl-1,2,3,4-tetrahydro-1,3-methano-naphthalene-7-carbaldehyde (60) : Mixture **57c** (150 mg, 0.74 mmol) was dissolved in toluene (20 mL). DDQ (500 mg, 1.85 mmol) was added and the reaction mixture refluxed for 4 hours. The DDQ was removed by filtration and the toluene removed with a rotary evaporator under reduced pressure. Purification was achieved using silica gel chromatography employing a 20 : 1

pet ether / ethyl acetate solvent system. Compound **60** was recovered as a yellow oil (82 mg, 56%).

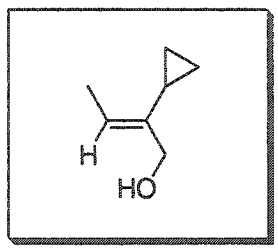
IR (neat); 2946 (m), 2840 (m), 1609 (m), 1444 (s), 1248 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 9.90 (s, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.41 (s, 1H), 7.25 (d, J = 7.2 Hz, 1H), 3.02 (s, 2H), 2.82 (t, J = 5.5 Hz, 1H), 2.69 – 2.62 (m, 1H), 2.31 – 2.27 (m, 1H), 1.38 (s, 3H), 1.20 (d, J = 9.6 Hz, 1H), 0.60 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 192.8, 148.2, 143.5, 134.2, 128.9, 128.8, 126.7, 48.0, 40.5, 39.5, 34.0, 32.1, 26.4, 21.7; MS (EI) m/z 200.1 (M^+, (6.8), 157.1 (38.4), 129.1 (100.0), 69.0 (28.7); Exact mass calc'd. For $C_{14}H_{16}O$: 200.1202. Observed: 200.1201.



6,7,8,9-Tetrahydro-5H-5,8-methano-benzocycloheptene-3-carbaldehyde (61) : Mixture **59** (90.0 mg, 0.44 mmol) was dissolved in toluene (30 mL). DDQ (245 mg, 0.88 mmol) was added and the reaction was brought to reflux and allowed to stir for 3 hours. The reaction was quenched with water (30 mL) and aqueous extraction was performed with diethyl ether (3 x 20 mL). Purification was achieved with silica gel chromatography employing a 19 : 1 pet ether / ethyl acetate solvent system. This afforded **61** as a yellow oil (52 mg, 64%).

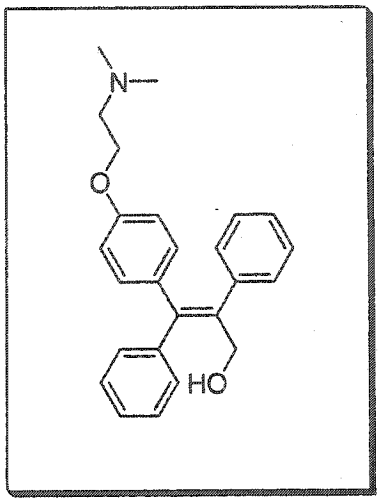
IR ($CDCl_3$); 2949 (m), 2872 (w), 1693 (s), 1609 (m), 1223 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.90 (s, 1H), 7.57 (dd, J = 7.8 Hz, 1.8 Hz, 1H), 7.49 (d, J = 7.17 (d, J = 7.8 Hz, 1H), 3.13 – 3.07 (m, 2H), 2.67 (d, J = 17.8 Hz, 1H), 2.57 – 2.54 (m, 1H), 1.98 – 1.89

(m, 2H), 1.80 – 1.72 (m, 3H), 1.48 – 1.44 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.3, 146.3, 142.8, 134.3, 130.1, 128.2, 127.4, 41.1, 40.0, 36.2, 35.3, 33.3, 29.7; MS (EI) m/z 186.1 (M^+ (42.4), 162.0 (9.0), 143.0 (7.2), 129.1 (100.0), 115.1 (20.8); Exact mass calc'd. For $C_{13}H_{14}O$: 186.1012. Observed: 186.0979.



2-Cyclopropyl-but-2-en-1-ol (62) : Copper (I) iodide (100 mg, 0.5 mmol) and 2 – butynol (0.37 mL, 5.0 mmol) were dissolved in dry THF (5 mL). Cyclopropyl magnesium bromide (21 mL, 0.75 M, 16 mmol) was added via syringe and the resulting red solution refluxed for 16 hours. The solution was cooled to 0 ^0C, and quenched with saturated ammonium chloride (20 mL) for 30 minutes. Aqueous extraction was performed with diethyl ether (3 x 20 mL) and final purification was achieved through silica gel chromatography employing a 4 : 1 pet ether / ethyl acetate solvent system. This afforded **62** as a clear yellow oil (286 mg, 51%).

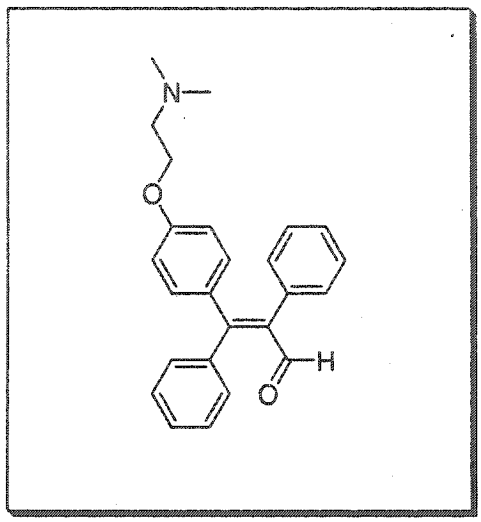
IR (neat); 3350 (s), 2929 (m), 2869 (m), 1454 (m), 994 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.53 (q, J = 6.8 Hz, 1H), 3.75 (s, 2H), 2.0 (br s, 1H), 1.69 (d, J = 6.8 Hz, 3H), 1.49 – 1.40 (m, 1H), 0.66 – 0.60 (m, 2H), 0.50 – 0.45 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.4, 124.0, 65.4, 13.5, 10.1, 5.1; MS (EI) m/z 112.0 (M^+ (12.1), 97.0 (18.0), 79.0 (100.0), 71.0 (43.0), 55.0 (47.2), 41.0 (71.1).



(2*E*)-3-{4-[2-(dimethylamino)ethoxy]phenyl}-2,3-diphenylprop-2-en-1-ol (82) : Prepared via **standard procedure A**, 3-{4-[2-(Dimethylamino)ethoxy]phenyl}prop-2-yn-1-ol (870 mg, 3.97 mmol), phenyl magnesium chloride (2 M, 6.4 mL), $Pd(Ph_3)_4$ (231 mg, 0.199 mmol), iodobenzene (1.6 mL, 14.3 mmol). Purification was achieved through silica gel chromatography, employing a 19 : 1 : 1 ethyl acetate / methanol / triethyl amine solvent system. This afforded **82** as a white solid (1.07 g, 72%).

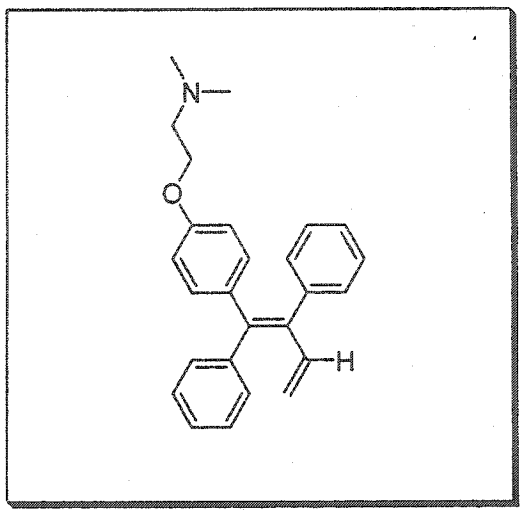
Mp = 185 °C (with decomposition)

IR ($CDCl_3$) 3601 (s), 2950 (m), 2780 (m), 1606 (m), 1467 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.32 – 7.24 (m, 5H), 7.20 – 7.07 (m, 5H), 6.79 (d, J = 8.7 Hz, 2H), 6.56 (d, J = 8.7 Hz, 2H), 4.40 (s, 2H), 3.89 (t, J = 5.5 Hz, 2H), 2.76 (br s, 1H), 2.60 (t, J = 5.5 Hz, 2H), 2.23 (s, 6H); ^{13}C NMR (C_6D_6, 75 MHz): δ 157.6, 142.9, 142.6, 141.2, 138.2, 135.1, 132.3, 130.3, 130.2, 128.6, 128.5, 127.6, 127.0, 113.9, 66.0, 65.3, 58.5, 46.2; MS (EI) m/z 373.2 (M^+(10), 343 (0.3), 297 (4), 252 (1), 226 (0.3), 191 (1), 165 (4), 133 (1), 105 (4), 72 (47), 58 (100); Exact mass cacld. For $C_{25}H_{27}NO_2$: 373.2042. Observed: 373.2079.



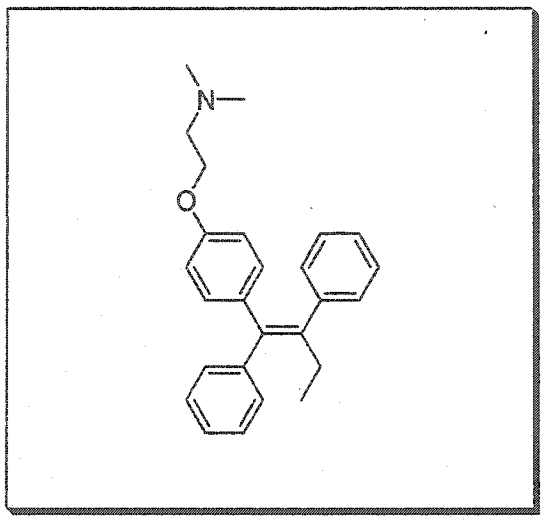
3-[4-(2-Dimethylamino-ethoxy)-phenyl]-2,3-diphenyl-propenal (83): Alkenol **82** (220 mg, 0.59 mmol) was added with Dess Martin Periodinane (752 mg, 1.77 mmol) to CH_2Cl_2 (50 mL). The suspension was stirred vigorously under air for 14 hours before being quenched with water (20 mL). 10% NaOH was added (50 mL) and the aqueous layer extracted with CH_2Cl_2 (2 x 30 mL). Removal of the solvent under reduced pressure gave **83** without further purification as a viscous yellow oil (210 mg, 96%).

IR (neat) 3056 (m), 2942 (m), 2772 (m), 1667 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 9.62 (s, 1H), 7.41 – 7.32 (m, 3H), 7.29 – 7.14 (m, 5 H), 7.07 (dd, J = 8.9 Hz, 2.0 Hz, 2H), 6.86 (d, J = 8.9 Hz, 2H), 6.63 (d, J = 8.9 Hz, 2H), 3.98 (t, J = 5.6 Hz, 2H), 2.71 (t, J = 5.5 Hz, 2H), 2.32 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 194.0, 161.0, 159.5, 139.8, 139.3, 136.9, 133.5, 133.2, 132.1, 131.6, 130.0, 128.6, 128.6, 127.7, 114.1, 66.0, 58.3, 46.1. MS (EI) m/z 371.2 (M^+ (10.6), 247.9 (11.8), 58.1 (100.0)). Exact mass cacld. For $C_{25}H_{25}NO_2$: 371.1861. Observed: 371.1836.

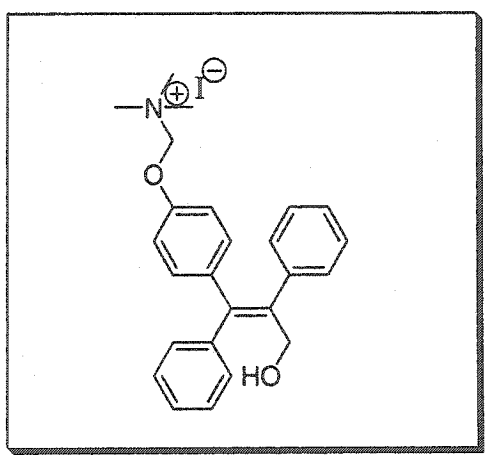


{2-[4-(1,2-Diphenyl-buta-1,3-dienyl)-phenoxy]-ethyl}-dimethyl-amine (84) : KO^{t}Bu (1M, 0.65 mL), and methyl phosphonium bromide (212 mg, 0.59 mmol) were dissolved in dry THF (15 mL). The solution was refluxed for 2 hours before aldehyde **83** (200 mg, 0.54 mmol) in THF (1 mL) was added. The solution immediately turned a bright red colour and the reaction was allowed to continue stirring at room temperature for a further 12 hours. The reaction was quenched with water (20 mL) and the aqueous layer extracted with ethyl acetate (2 x 20 mL). Purification was achieved with silica gel chromatography employing a 4 : 1 : 95 methanol / triethylamine / ethyl acetate solvent system. This afforded **84** as a yellow oil (160 mg, 81%).

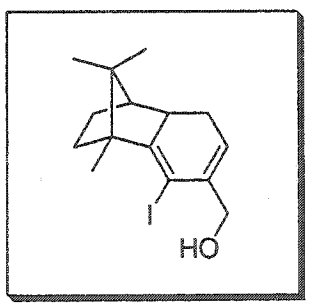
IR ($CDCl_3$) 3152 (m), 2979 (m), 2871 (m), 2778 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.49 – 7.07 (m, 10H), 6.74 (d, J = 8.9 Hz, 2H), 6.68 (dd, J = 17.3 Hz, 10.7 Hz, 1H), 5.07 (dd, J = 10.8 Hz, 1.7 Hz, 1H), 4.88 (dd, J = 17.3 Hz, 1.7 Hz, 1H), 3.92 (t, J = 5.7 Hz, 2H), 3.92 (t, J = 5.8 Hz, 2H), 2.28 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 157.3, 142.8, 142.1, 140.4, 138.8, 138.5, 135.4, 132.3, 131.6, 131.1, 128.1, 128.0, 127.3, 126.6, 117.5, 113.6, 65.9, 58.4, 46.1, 46.0. MS (EI) m/z 369.2 (M^+ (5.2), 277.1 (5.7), 215.1 (5.8), 58.1 (100.0). Exact mass cacld. For $C_{26}H_{27}NO$: 369.2099. Observed: 369.2106.



{2-[4-(1,2-Diphenyl-but-1-enyl)-phenoxy]-ethyl}-dimethyl-amine (*Z* – Tamoxifen) (66) : 84 (80 mg, 0.22 mmol) was dissolved in ethyl acetate (20 mL). Palladium on activated carbon (100 mg) was added and the reaction allowed to stir under a hydrogen atmosphere for 2 hours. The solution was filtered and solvent removed under reduced pressure. This gave compound **66** as a white solid (68 mg, 85%) without further purification. Characterization information was consistent with previously reported data for this compound.



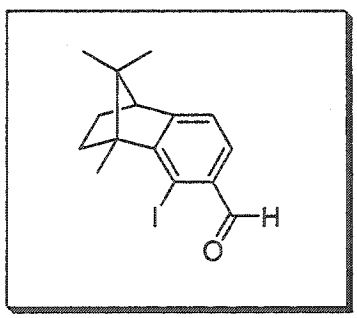
[4-(3-Hydroxy-1,2-diphenyl-propenyl)-phenoxymethyl]-trimethyl-ammonium; iodide (85) : **82** (200 mg, 0.54 mmol) was dissolved in dry THF (20 mL). NaH (30 mg, 0.75 mmol) as a 60% mineral oil dispersion and methyl iodide (0.13 mL, 2.14 mmol) were added at room temperature. The clear solution was allowed to stir at room temperature for 12 hours. Water (20 mL) was added to quench the reaction, and aqueous extraction was extracted with diethyl ether (3 x 20 mL). The organic layers were combined and washed with saturated brine solution (20 mL), and concentrated under reduced pressure. Compound **85** was recovered as a pale yellow solid (120 mg, 53%). ^{1}H NMR (DMSOD$_6$, 500 MHz): δ 7.35 (t, *J* = 7.4 Hz, 2H), 7.30 – 7.27 (m, 3H), 7.18 (s, 2H), 7.18 (d, *J* = 1.4 Hz, 2H), 7.14 – 7.07 (m, 1H), 6.81 – 6.79 (dm, *J* = 8.9 Hz, 2H), 6.71 – 6.69 (dm, *J* = 8.8 Hz, 2H), 4.66 (t, *J* = 5.0 Hz, 1H), 4.32 – 4.30 (m, 2H), 4.20 (d, *J* = 5.0 Hz, 2H), 3.69 (t, *J* = 4.7 Hz, 2H), 3.11 (s, 9H); ^{13}C NMR (DMSOD$_6$, 125 MHz): δ 155.6, 142.4, 141.4, 140.3, 139.2, 135.6, 131.4, 129.8, 129.4, 128.0, 127.6, 127.0, 126.1, 113.8, 64.2, 63.2, 61.3, 53.1.



(*1R*)-(5-Iodo-4,9,9-trimethyl-1,2,3,4,8,8a-hexahydro-1,4-methano-naphthalen-6-yl)-methanol (117) : Prepared via **standard procedure D.** Compound (**56b**) (507 mg, 2.67 mmol) in cyclohexane (10 mL), vinyl magnesium chloride (6.67 mL, 1.6 M, 8.54 mmol) , I_2 (1.49 g, 5.87 mmol) in THF (20 mL). Purification was achieved with silica gel

chromatography employing a 6 : 1 pet ether / ethyl acetate solvent system. This afforded **117** as an orange oil (790 mg, 86%).

IR (neat); 3329 (s), 2956 (s), 2870 (m), 1387 (m) cm^{-1}; ^1H NMR (C_6D_6, 500 MHz): δ 5.69 (m, 1H), 4.29 (dquintet, J = 13.6 Hz, 1.4 Hz, 1H), 4.14 (dt, J = 13.6 Hz, 1.4 Hz, 1H), 2.46 (dd, J = 18.9 Hz, 8.2 Hz, 1H), 2.04 – 1.96 (m, 1H), 1.79 – 1.73 (m, 1H), 1.68 – 1.58 (m, 2H), 1.54 – 1.48 (m, 1H), 1.42 – 1.36 (m, 1H), 1.29 (s, 3H), 1.24 (d, J = 3.8 Hz, 1H), 1.03 (m, 1H), 0.97 (s, 3H), 0.68 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 155.8, 138.6, 123.4, 79.1, 69.1, 55.7, 53.2, 52.5, 48.4, 34.0, 31.2, 28.0, 22.9, 21.7, 16.8; MS (EI) m/z 344.1 (M^+ (47.9), 257.0 (18.1), 217.2 (33.9), 143.1 (38.2), 91.1(71.3), 41.0 (100.0)); Exact mass calc'd. For $C_{15}H_{21}IO$: 344.0645. Observed: 344.0653.

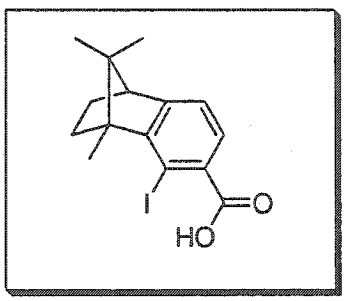


(1*R*)-(5-Iodo-4,9,9-trimethyl-1,2,3,4-tetrahydro-1,4-methano-naphthalene-6-carbaldehyde (120) : Compound **117** (183 mg, 0.538 mmol) was dissolved in toluene (20 mL) and MnO_2 (468 mg, 5.38 mmol) was added to the solution. The black suspension was refluxed for 14 hours and the MnO_2 residue was filtered off to give a yellow liquid. The solvent was removed with a rotary evaporator and purification was achieved through silica gel chromatography employing a 19 : 1 pet ether / ethyl acetate solvent system. This afforded **120** as a yellow solid (67 mg, 37%).

Mp = 75.5 – 77.5 °C.

IR (CH_2Cl_2); 3054 (s), 2987 (s), 2685 (m), 1684 (s), 1422 (s), 1258 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 10.20 (s, 1H), 7.63 (d, J = 7.4 Hz, 1H), 7.13 (d, J = 7.4 Hz, 1H),

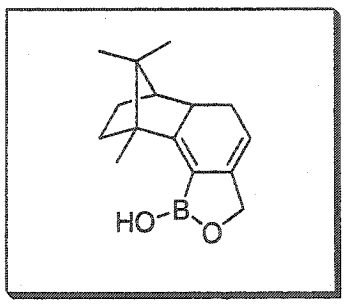
2.78 (d, J = 4.0 Hz, 1H), 2.15 – 2.05 (m, 1H), 1.84 – 1.75 (m, 1H), 1.53 (s, 3H), 1.35 – 1.20 (m, 2H), 1.12 – 1.02 (m, 1H), 0.91 (s, 3H), 0.56 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 197.4, 158.0, 151.5, 133.7, 129.8, 121.9, 95.1, 58.1, 57.8, 53.8, 32.4, 26.4, 20.4, 19.6, 15.6; MS (EI) m/z 340.0 (M^+ (100.0), 297.0 (44.4), 170.1 (30.9), 142.1 (78.8), 115.1 (42.3)); Exact mass calc'd. For $C_{15}H_{17}IO$: 340.0313. Observed: 340.0302.



(1*R*)-5-Iodo-4,9,9-trimethyl-1,2,3,4-tetrahydro-1,4-methano-naphthalene-6-carboxylic acid (118) : Compound **120** (500 mg, 1.47 mmol) was dissolved in a 5 : 2 solution of *t*-BuOH and water (50 mL). NaH_2PO_4 (706 mg, 5.88 mmol) and 2-methyl butene (1.09 mL, 10.29 mmol) were added and the solution allowed to stir for 10 min. $NaClO_2$ (798 mg, 8.82 mmol) was added and the solution allowed to stir for 3 hours at room temperature. *T*-BuOH was removed on the rotary evaporator as an azeotrope with benzene (3 x 20 mL). The resulting white solid was dried under vacuum over night. This afforded **118** as a white solid without further purification (520 mg, 99%).

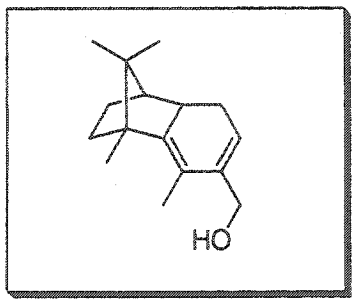
^{1}H NMR ($CDCl_3$, 300 MHz): δ7.34 (d, J = 7.3 Hz, 1H), 7.04 (d, J = 7.3 Hz, 1H), 2.71 (d, J = 3.7 Hz, 1H), 2.03 (m, 1H), 1.72 (dt, J = 4.0 Hz, 9.5 Hz, 1H), 1.47 (s, 3H), 1.25 (dt, J = 3.7 Hz, 9.2 Hz, 1H), 1.02 (dt, J = 3.9 Hz, 12.5 Hz, 1H), 0.89 (s, 3H), 0.52 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.2, 152.6, 151.3, 139.1, 127.4, 121.6, 86.9, 57.9, 57.7, 53.0, 32.6, 26.8, 20.7, 19.8, 16.0; MS (EI) m/z 356.0 (M^+, (100.0), 328.0 (33.6), 295.0

(25.7), 201.1 (32.5), 186.1 (93.2)); Exact mass calc'd.. For $C_{15}H_{17}IO_2$: 356.0286. Observed: 356.0273.



(122) : Compound **56b** (430 mg, 2.26 mmol) and magnesium chloride (323 mg, 3.39 mmol) were dissolved in dry cyclohexane (5 mL). Vinyl magnesium chloride (4.3 mL, 1.7 M, 7.23 mmol) was added via syringe at room temperature and the resulting red solution refluxed for 14 hours. The solution was cooled to 0 °C and quenched with trimethyl borate (0.76 mL, 6.78 mmol) for 1 hour. Aqueous extraction was performed with diethyl ether (3 x 25 mL) before purification was achieved through silica gel chromatography employing a 15 : 1 pet ether / ethyl acetate solvent system. This afforded **122** as a white oily solid (303 mg, 55%).

IR (neat); 3612 (m), 3296 (m), 2955 (s), 1667 (s), 1402 (s), 1255 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.22 (br s, 1H), 5.11 (s, 1H), 4.61 (s, 2H), 2.46 – 2.37 (m, 1H), 2.23 – 2.09 (m, 1H), 1.96 – 1.85 (m, 1H), 1.72 – 1.63 (m, 2H), 1.56 – 1.43 (m, 1H), 1.32 – 1.20 (m, 1H), 1.18 (s, 3H), 0.99 (s, 3H), 0.89 (s, 3H), 0.83 – 0.76 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.9, 142.4, 110.8, 70.8, 53.7, 52.7, 48.3, 48.2, 32.9, 30.6, 28.1, 22.6, 21.4, 14.0; MS (EI) m/z 244.2 (M^+, (11.6), 174.1 (68.8), 162.0 (36.3), 143.0 (31.8), 131.1 (100.0), 100.0 (65.5), 69.0 (78.7)); Exact mass calc'd. For $C_{13}H_{21}BO_2$: 244.1642. Observed: 244.1650.



(1*R*)-(4,5,9,9-Tetramethyl-1,2,3,4,8,8a-hexahydro-1,4-methano-naphthalen-6-yl)-methanol (123) : Prepared via **standard procedure D.** Compound **56b** (465 mg, 2.45 mmol) in cyclohexane (5 mL), vinyl magnesium chloride (4.6 mL, 1.7 M, 7.84 mmol) , MeI (1.5 mL, 24.5 mmol). Purification was achieved with silica gel chromatography employing a 6 : 1 pet ether / ethyl acetate solvent system. This afforded **123** as a yellow oil (520 mg, 92%).

IR (neat) 3370 (s), 2954 (s), 2872 (s), 1472 (m), 1387 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.65 (t, J = 3.9 Hz, 1H), 4.22 (d, J = 12.3 Hz, 1H), 4.02 (d, J = 12.3 Hz, 1H), 2.37 – 2.24 (m, 1H), 2.07 – 1.99 (m, 1H), 1.85 (s, 3H), 1.59 – 1.49 (m, 3H), 1.27 – 1.21 (m, 2H), 1.17 (s, 3H), 1.04 (s, 3H), 0.99 – 0.88 (m, 1H), 0.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 146.4, 140.2, 122.9, 118.5, 65.1, 53.0, 52.0, 48.1, 47.8, 34.5, 31.1, 28.2, 22.9, 21.5, 16.5, 13.0; MS (EI) m/z 232.2 (M^+ (53.1), 145.1 (87.7), 133.1 (100.0), 105.1 (67.4), 41.0 (71.9)); Exact mass calc'd. For $C_{16}H_{24}O$: 232.1804. Observed: 232.1781.

CLAIMS TO ORIGINAL RESEARCH

1. Development of a novel carbomagnesiation-palladium cross-coupling reaction for the synthesis of tetrasubstituted alkenes.

2. A short synthesis of the anti-cancer agent (*Z*)-tamoxifen (**66**).

3. Syntheses for a variety of novel (*Z*)-tamoxifen analogues (**82, 83, 84, 85**).

4. The first example for use of a cyclopropyl Grignard reagent in the carbometallation reaction.

5. Development of a novel carbometallation-annulation reaction for the synthesis of substituted polycyclic ring systems.

REFERENCES

[1] Bähr, K.; *Chem. Ber.* **1928**, 253.

[2] For use of the term "carbometallation" see (a) Negishi, E., Van Horn, D.; *J. Am. Chem. Soc.* **1978**, *100*, 2252. (b) Negishi, E., *Pure Appl. Chem.* **1981**, *53*, 2333. (c) Normant, J. F., Alexakis, A.; *Synthesis*, **1981**, 841.

[3] For reviews, see (a) Normant, J. F., Alexeaxis, A. *Synthesis*, **1981**, 841 (organo-Li, Zn, B, Al and Cu compounds). (b) Negishi, E., *Pure Appl. Chem.* **1981**, *53*, 2333 (organo-Al/Ti and Al/Zr systems). (c) Oppolzer, W.; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 38 (organo-Li, Mg, Zn (stoichiometric), and Ni, Pd, Pt (catalytic)). (d) Knochel, P., Comprehensive Organometallic Chemistry II, Able, E. W., Stone, F. G. A., Wilkinson, G. Eds.; Pergamon Press: Oxford, 1995; Vol. 11, p. 159 (organo-Li, Mg, Zn, B, Al, Cu, Hg, Pd, Ni, Mn compounds). (e) Knochel, P., In Comprehensive Organic Synthesis; Trost, B. M., Fleming, I.; Eds.; Pergamon Press: Oxford, 1991; Vol. 4, p. 865. (f) Yamamoto, Y., Asao, N.; *Chem. Rew.* **1993**, *93*, 2207 (organo-Li, Mg, Zn, B, Al compounds). (g) Negishi, E., Kondakov, D. Y.; *Chem. Rev.* **1996**, *96*, 417 (organo-Ti/Zr and Al/Zr). (h) Marek, I.; *J. Chem. Soc., Perkin Trans. I* **1999**, 535 (enantioselective organo-Mg, Al, Li, Cu, Zn). (i) Fallis, A. G., Forgione, P.; *Tetrahedron* **2001**, 5899 (organo-Mg, Zn, Cu, Zr, Li, Si, Sn, In, B, Ga, Al, Ni, Mn compounds).

[4] Eisch, J. J., Merkley, J. H., Galle, J. E.; *J. Org. Chem.* **1979**, *44*, 587

[5] Mornet, R., Gouin, L.; *Bull. Soc. Chimi. Fr.* **1977**, 737.

[6] (a) Jousseaume, B., Duboudin, J. G.; *J. Organomet. Chem.* **1975**, C1. (b) Jousseaume, B., Duboudin, J. G.; *J. Organomet. Chem.* **1979**, 1.

[7] (a) Richey, H. G., Erickson, W. E., Heyn, A. S.; *Tetrahedron Lett.* **1971**, 2183. (b) Mauze, B., Nivert, L., Miginiac, L.; *J. Organomet. Chem.* **1972**, 69.

[8] Mkryan, G. M., Gasparyan, S. M., Avetisyan, E. A., Mndzhoyan, S.; *Arm. Khim. Zh.* **1968**, 124. (b) Nelson, D. J., Miller, W. J.; *J. Chem. Soc. Chem. Commun.* **1973**, 444. (c) Moreau, J. L., Gaudemar, M.; *J. Organomet. Chem.* **1976**, 159.

[9] Forgione, P. Fallis, A.G.; *Tetrahedron Lett.*, **2000**, *41*, 11

[10] Forgione, P.; Wilson, P. D.; Fallis, A. G.; *Tetrahedron Lett.*, **2000**, *41*, 17

[11] Forgione, P. Fallis, A.G.; *Tetrahedron Lett.*, **2000**, *41*, 11

[12] Forgione, P.; Wilson, P. D.; Yap, G. P. A.; Fallis, A. G.; *Synthesis*, **2000**, *7*, 921

[13] Duboudin, J. G., Jousseaume, B.; *J. Organomet. Chem.* **1979**, 227.

[14] Examples performed by Dr. Fabio Souza

[15] Example performed by Andrea Penwell

[16] Fürstner, A., Leitner, A., Mendez, M., Krause, H.; *J. Am. Chem. Soc.* **2002**, *124*, 13856

[17] Pal, K., *Synthesis* **1995**, *12*, 1485

[18] (a) Shields, T. C., Billups, W. E., Lepler, A. P.; *J. Am. Chem. Soc.* **1968**, *90*, 4749 (b) Marvel, E. N., Lin, C.; *J. Am. Chem. Soc.* **1978**, *100*, 877 (c) Hudlicky, T., Kutchan, T. M., Wilson, S. R., Mao, D. T.; *J. Am. Chem. Soc.* **1980**, *102*, 6351 (d) Paquette, L. A., Wells, G. J., Horn, K. A., Yan, T. H.; *Tetrahedron Lett.* **1982**, 263 (e) Hudlicky, T., Kutchan, T. M., Naqvi, S. M.; *Org. Reactions* **1985**, *33*, 247

[19] Henderson, B. E., Ross, R. K., Bernstein, L.; *Cancer Res.* **1988**, *48*, 246

[20] (a) Smith, E. P., Boyd, J., Frank, G. R., Takahashi, H., Cohen, R. M., Specker, B., Williams, T. C., Lugahn, D. B., Karach, K. S.; *N. Engl. J. Med.* **1994**, *331*, 1056 (b) Ciocca, D. R., Vargas Roig, L. M.; *Endocr. Rev.* **1995**, *16*, 35

[21] Lindsat, R.; Sex Steroids in the pathogenesis and prevention of osteoporosis. In *Osteoporosis: Etiology, Diagnosis, and Management;* Riggs, B. L, Melton, L. J, Eds,; Raven: New York, **1988**, 333

[22] Colditz, G. A., Hankinson, S. E., Hunter, D. J., Willett, W. C., Manson, J. E., Stampfer, M. J., Hennekens, C., Rosner, B., Speizer, F. E.; *N. Engl. J. Med.* **1995**, *332*, 1589

[23] For reviews, see: (a) Grese, T. A., Dodge, J. A.; *Annu. Rep. Med. Chem.* **1996**, *31*, 181 (b) Kauffman, R. F., Bryant, H. U.; *Drug News Perspect.* **1995**, *8*, 531 (c) Evans, G. L., Turner, R. T.; *Bone* **1995**, *17*, 181S

[24] Harper, M. J. K., Walpole, A. L.; *Nature (London)* **1966**, *212*, 87

[25] Jordan, V. C., *J. Steroid Biochem. Mol. Biol.* **2000**, *74*, 269.

[26] Jordan, V. C., Haldeman, B., Allen, K. E.; *Endocrinology* **1981**, *108*, 1353

[27] Katznellenbogen, B. S., Carlson, K. E.; *J. Steroid Biochem.* **1985**, *22*, 589

[28] (a) Jones, C. D., Jevnikar, M. G., Pike, A. J., Peters, M. K., Black, L. J., Thompson, A. R., Falcone, J. F., Clemens, J. A.; *J. Med. Chem.* **1984**, *27*, 1057 (b) Draper, M. W., Flowers, D. E., Huster, W. J., Neild, J. A., Harper, K. D., Arnaud, C. A.; *J. Bone Miner. Res.* **1996**, *11*, 835

[29] Bouhoute, A.; Leclerq, G.; *Biochem. Pharmacol.* **1994**, *47*, 748.

[30] (a) McCauge, R.; *J. Chem. Res. Synop.* **1986**, 58 (b) Potter, G. A., McCauge, R.; *J. Org. Chem.* **1990**, *55*, 6184 (c) Olier-Reuchet, C., Aitken, D. J., Bucourt, R., Husson, H. P.; *Tetrahedron Lett.* **1995**, *36*, 8221 (d) Gauthier, S., Mailhot, J.; Labrie, F.; *J. Org. Chem.* **1996**, *61*, 3890 (e) Detsi, A., Koufaki, M., Calogeropoulou, T.; *J. Org. Chem.* **2002**, *67*, 4300

[31] Miller, R. B., Al-Hassan, R. I.; *J. Org. Chem.* **1985**, *50*, 2121

[32] Knochel, P., Studemann, T.; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 93

[33] Hunter, D. H.; Ponce, Y. Z. *Can. J. Chem.* **1984**, *62*, 2015

[34] Reaction performed by Andrea Penwell

[35] Barton D.H.R., Godfrey C.R.A., Morzycki, J.W., Motherwell, W.B., Stobie A.; *Tetrahedron Lett.* **1982**, 957

[36] Dess, D. B., Martin, J. C.; *J. Org. Chem.* **1983**, *48*, 4155

[37] Dess, B. D., Martin J. C.; *J. Am. Chem. Soc.* **1991**, *113*, 7277

[38] Frigerio, M., Santagostino, M.; *Tetrahedron Lett.* **1994**, 8019

[39] Frigerio, M., Santagostino, M., Sputore, S., Palmisano, G.; *J. Org. Chem.* **1995**, *60*, 7272

[40] Kocienski, P.J.; *Protecting Groups*; Thieme Verlang: Stuttgart, **1994**, Chapters 1 and 6.

[41] Nicalaou, K.C., Baran, P. S., Zhong, Y.-L., Vega, J. A.; *Angew. Chem. Int. Ed.* **2000**, *39*, 2525 – 2529

[42] Nicolaou, K.C., Zhong, Y.-L., Baran, P.S; *Angew. Chem. Int. Ed.* **2000**, *39*, 625-628

[43] Nicalaou, K.C., Baran, P. S., Zhong, Y.-L., Barluenga, S., Hunt, K. W., Kranich, R., Vega, J. A.; *J. Am. Chem. Soc.* **2002**, *124*, 2233

[44] Nicalaou, K. C., Baran, P. S., Zhong, Y.-L.; *J. Am. Chem. Soc.*, **2001**, *123*, 3183 – 3185

[45] Nicalaou, K. C.; Zhong, Y.-L.; Baran, P. S.; *J. Am. Chem. Soc.*, **2000**, *122*, 7596 - 7597

[46] Thottumkara, A. P.; Vinod, T. K., *Tetrahedron Lett.* **2002,** *43,* 569 – 572

[47] Comins D. L.; Dehghani, A.; *Tetrahedrom Lett.* **1997**, *74*, 77

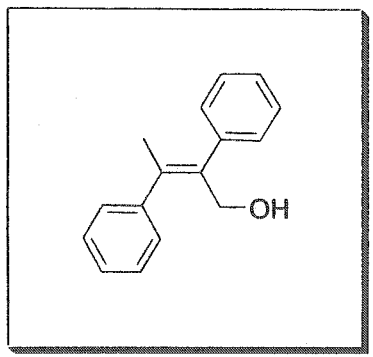
[48] Dueber, T. E.; Stang, P. J.; Pfeifer, W. D.; Summerville, R. H.; Imhoff, M. A.; Schleyer, P. R.; Hummel, K.; Bocher, S.; Harding, C. E.; Hanack, M. *Angew. Chem. Int. Ed. Engl.* **1970**, *9*, 521

[49] Nimkar, S. K.; Anderson, A.; Rimoldi, J. M.; Stanton, M.; Castagnoli, K. P.; Mabic, S.; Wang, Y. X.; Castagnoli, N., *Chemical Research in Toxicology*, **1996**, *9*, 1013

[50] Fukuyama, T.; Shinmen, T.; Nishitani, S.; Sato, M.; Ryu, I., *Org. Lett.* **2002**, *10*, 1691

[51] Bentz, H., etal.; *Tetrahedron Lett.* **1977**, *1*, 9 – 12

[52] McMurray, J. E.; Scott, W. J. *Tetrahedron Lett.* Vol. 24, 979, **1983**



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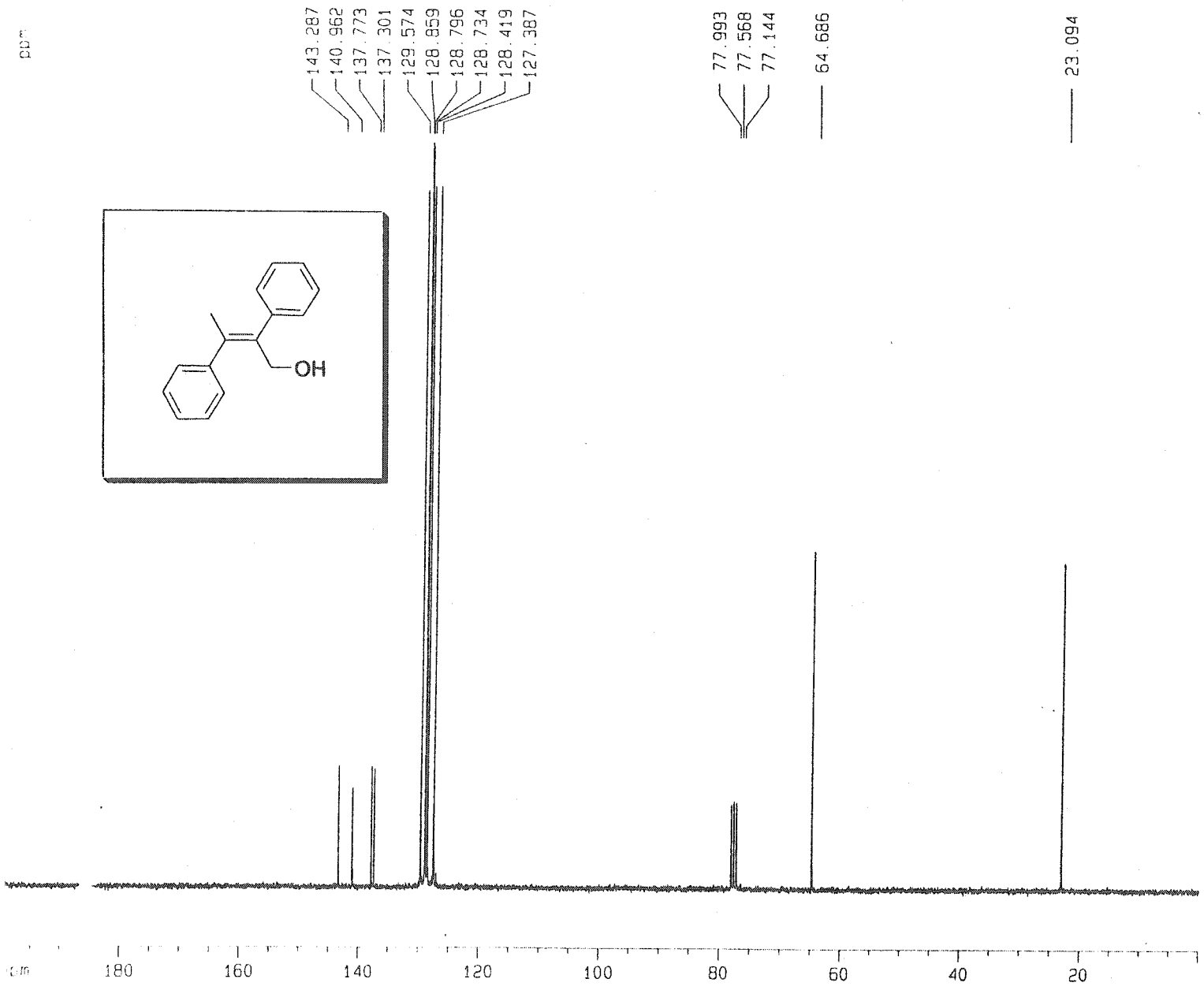

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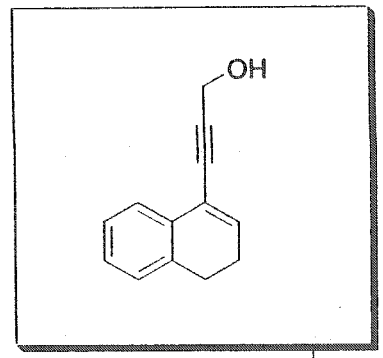
SEP 2 4 2001



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TD 65536
NS 8
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LB 0.00 Hz
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1D NMR plot parameters
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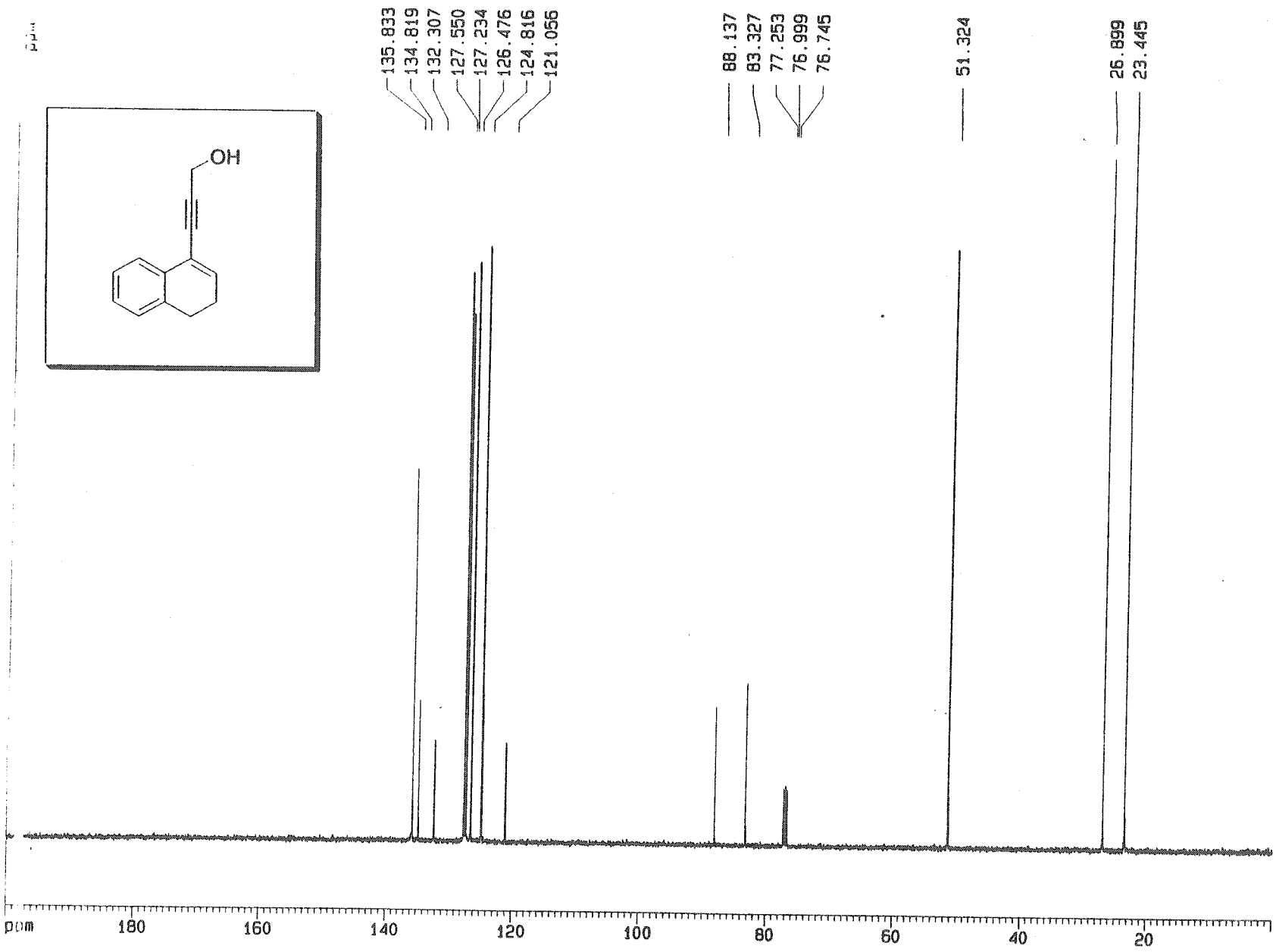

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F1 - Processing paramet

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1D NMR plot parameters

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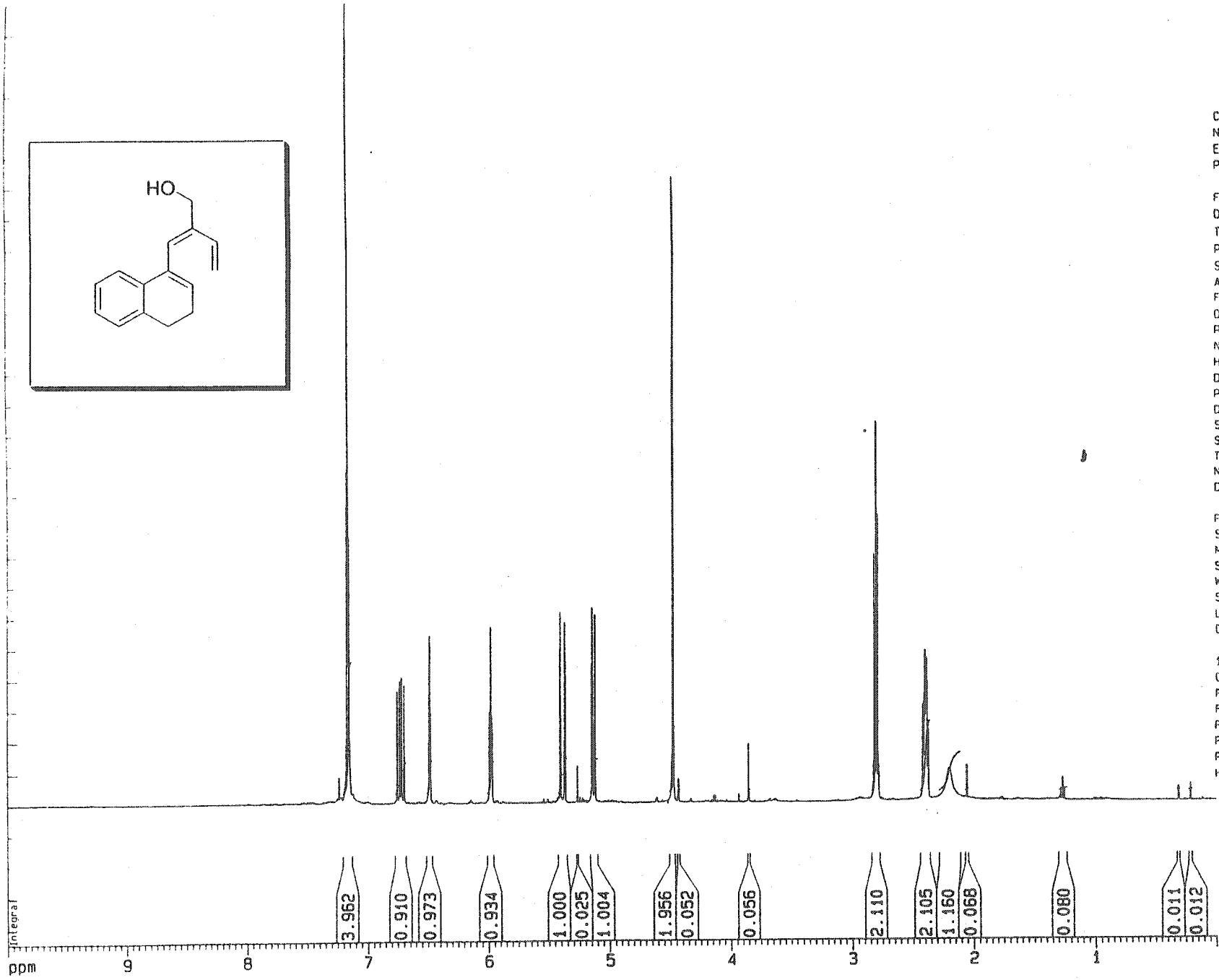

OCT 1 6 2001

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P1 3.0 usec
DE 88.8 usec
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SWH 7042.25 Hz
TD 65536
NS 16
DS 0

F1 - Processing parameters
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WDW EM
SSB 0
LB 0.00 Hz
GB 0

1D NMR plot parameters
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F2P 0.000 ppm
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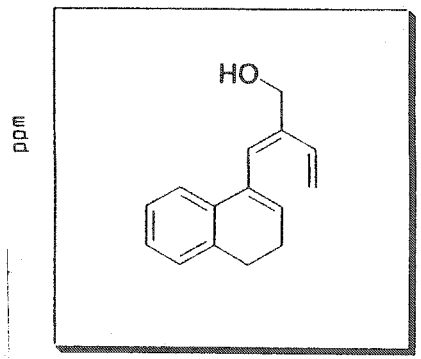
PPMCM 0.45455 ppm/
HZCM 227.33429 Hz/



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1D NMR plot parameters

CX	22.00
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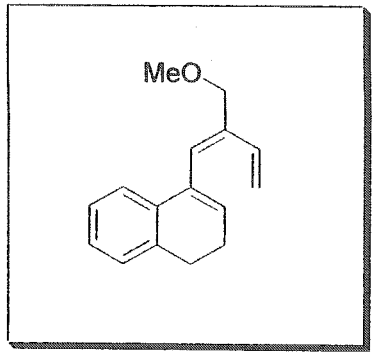
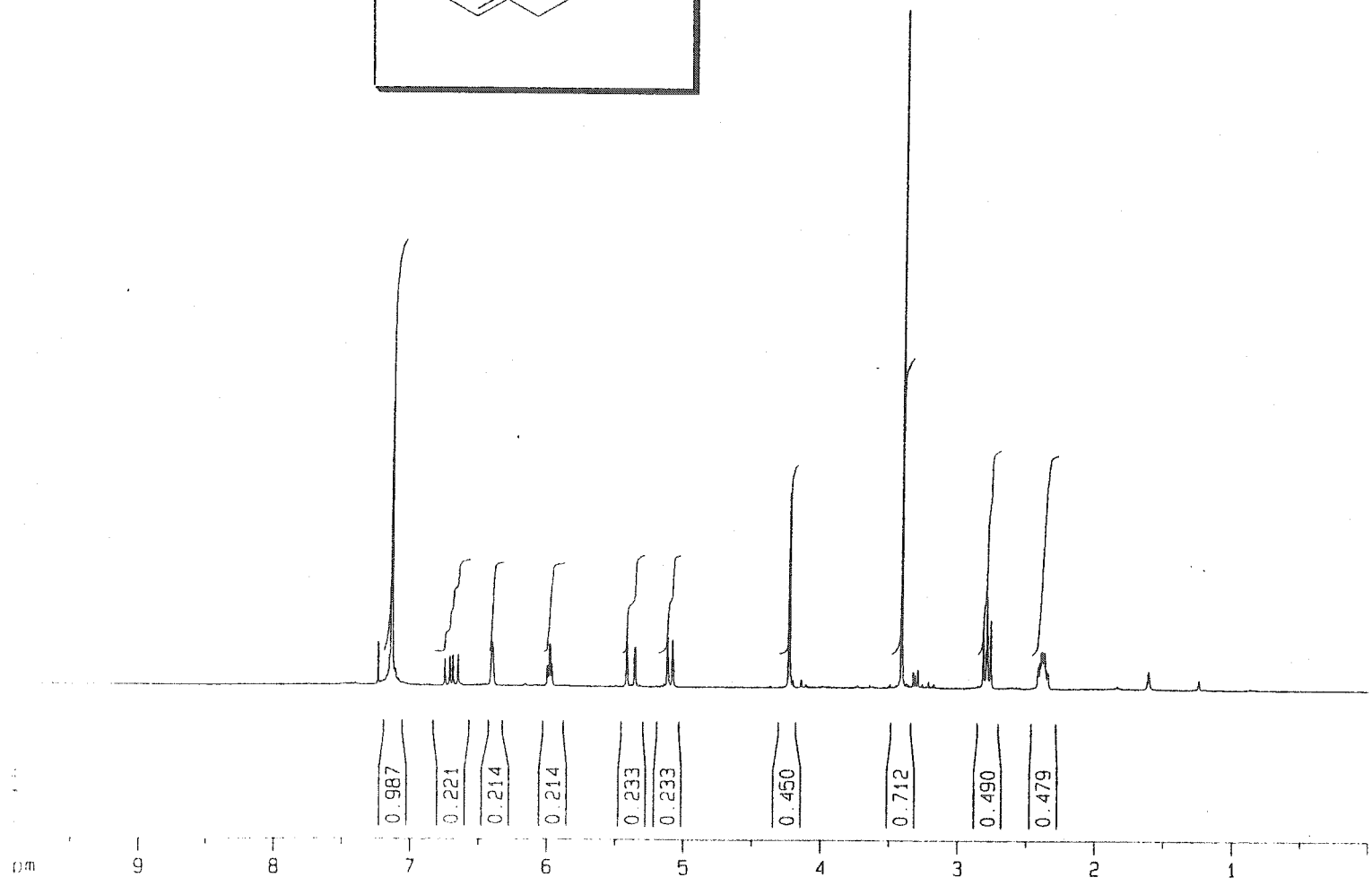
F1	25151.83
F2P	0.000
F2	0.00
PPMCM	9.09091
HZCM	1143.26514





Current Data Parameters

NAME	pt-2-33
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020802
Time	14.54
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	143.7
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

NUC1	1H
P1	8.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

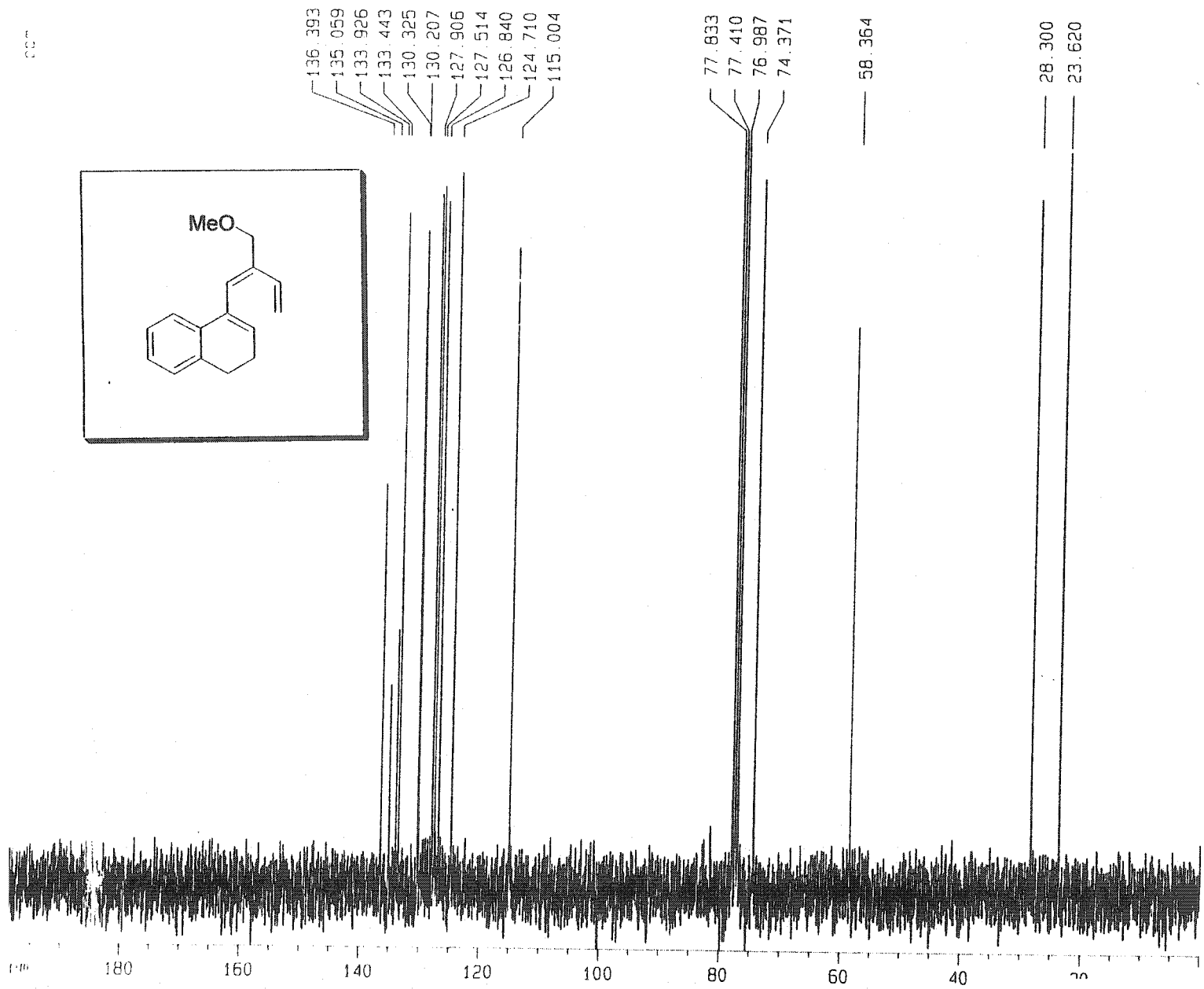
F2 - Processing parameters

SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	pt-2-33
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20020802
Time	15.07
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	128
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	2048
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

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

NUC1	13C
P1	6.50 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

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

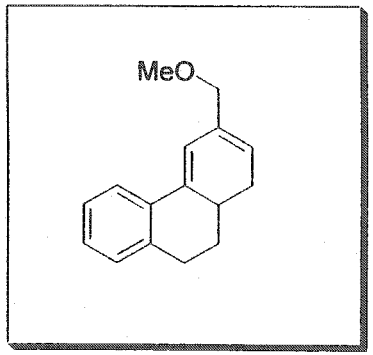
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	15.84 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

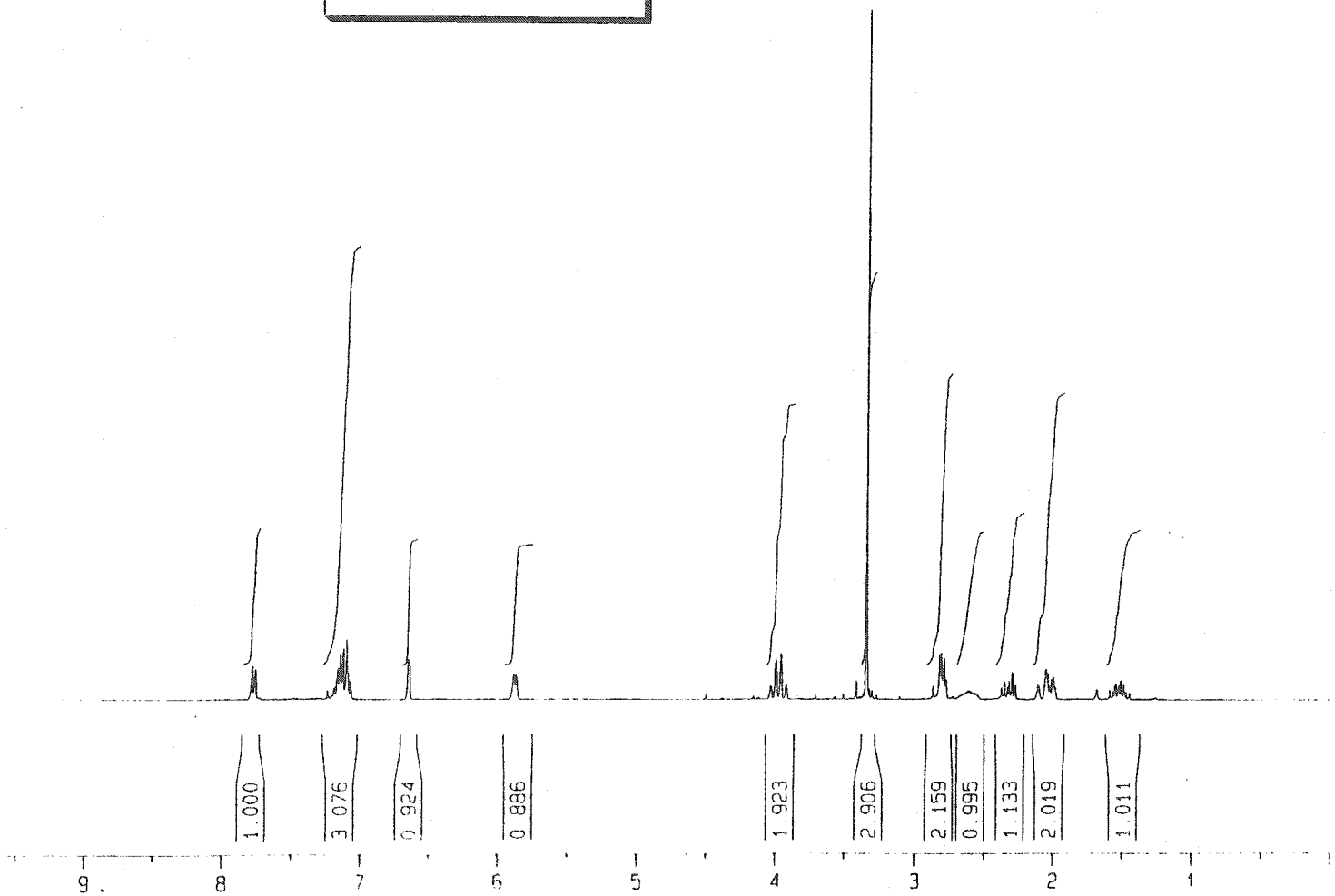
F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	200.000 ppm
F1	15093.54 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	10.00000 ppm/cm





Current Data Parameters

NAME	pt-2-34
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020802
Time	14.30
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	80.6
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

NUC1	1H
P1	8.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

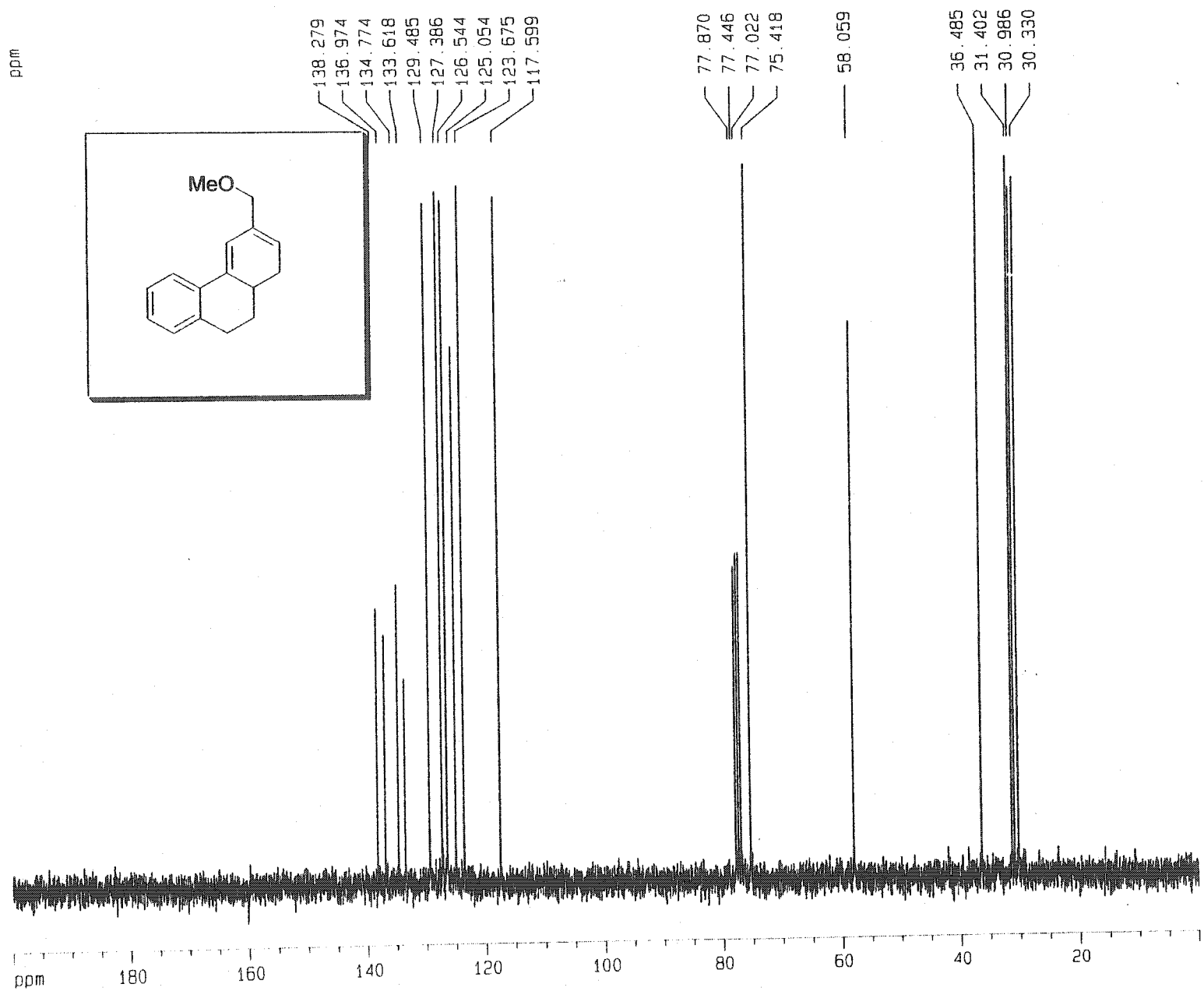
F2 - Processing parameters

SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	pt-2-34
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20020802
Time	14.43
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	128
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	2580.3
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

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

NUC1	13C
P1	6.50 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

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

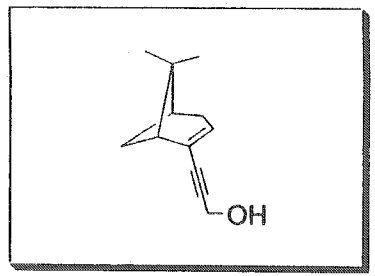
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	15.84 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

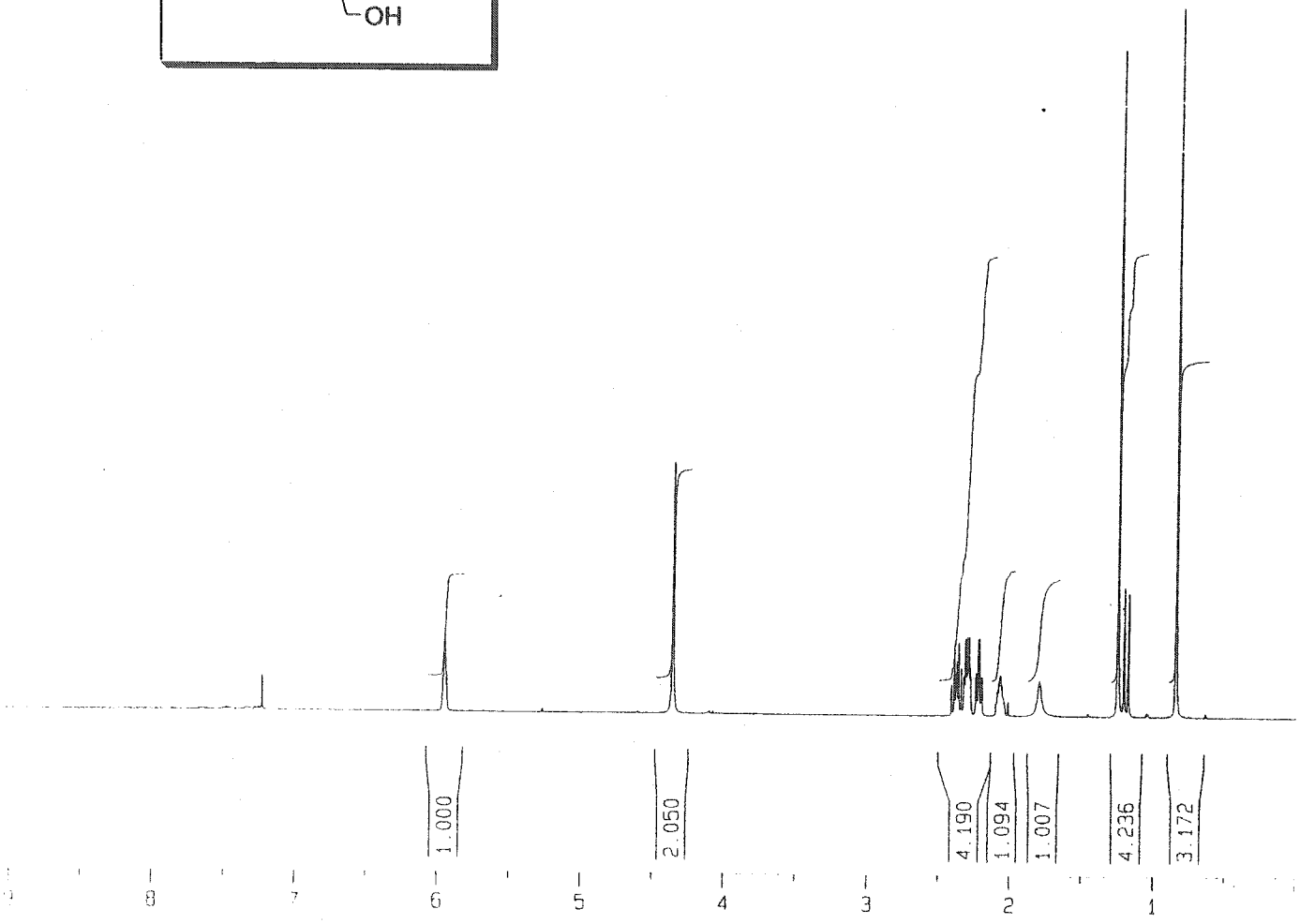
F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	200.000 ppm
F1	15093.54 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	10.00000 ppm/cm
HZCM	754.67719 Hz/cm





Current Data Parameters

NAME	pt-2-94
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20030109
Time	9.12
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	114
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

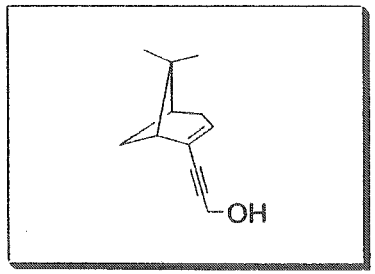
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

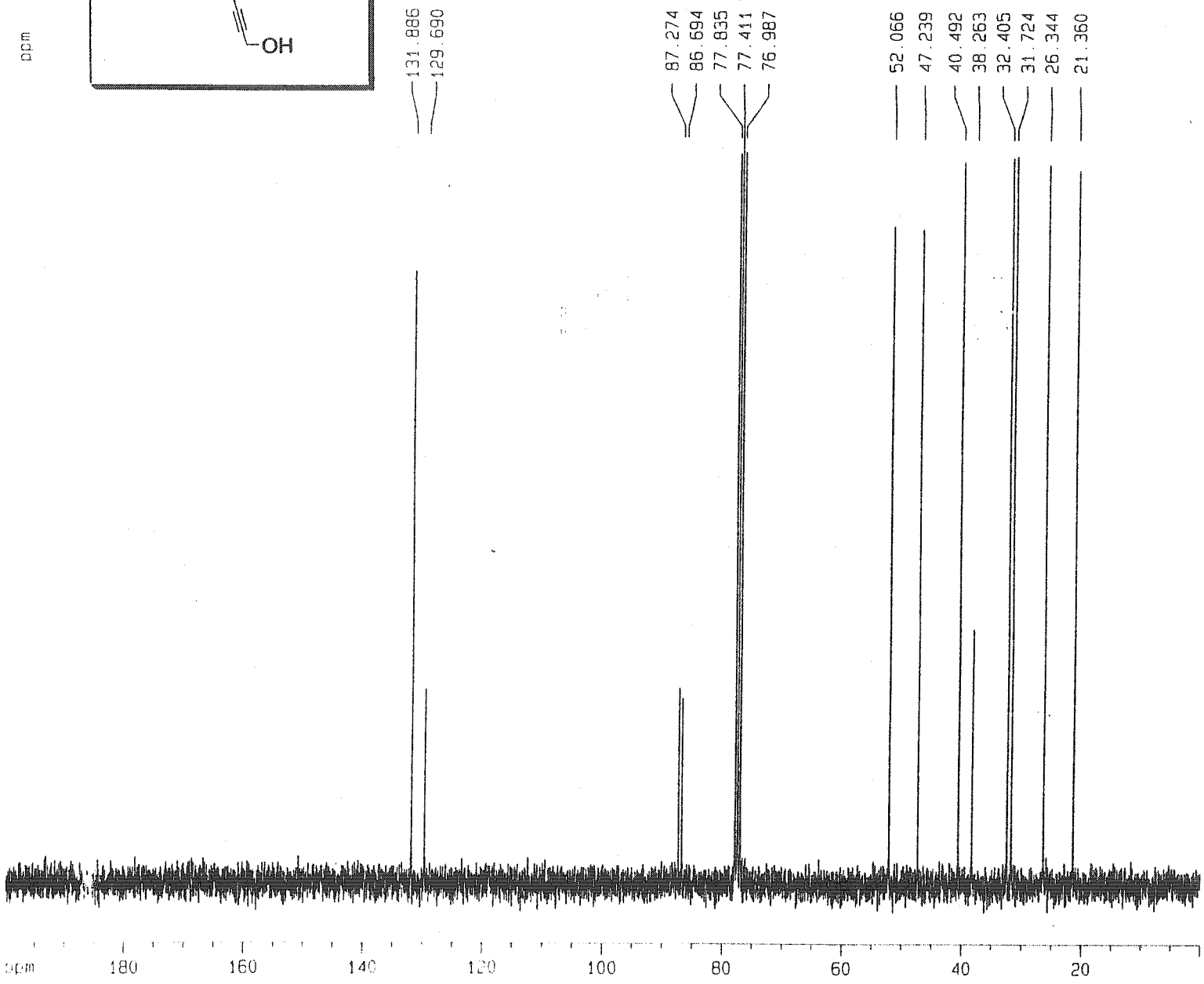
SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm



13C with proton decoupling



Current Data Parameters

NAME	pt-2-94
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20030109
Time	9.19
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	128
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	812.7
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

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

NUC1	13C
P1	5.00 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

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

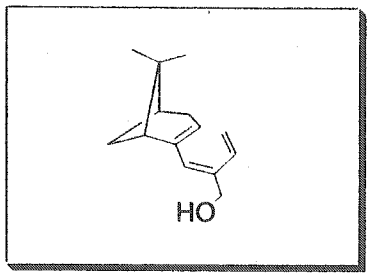
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	14.12 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	200.000 ppm
F1	15093.54 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	10.00000 ppm/cm
HZCM	754.67719 Hz/cm



Current Data Parameters

NAME	pt-2-95
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20030109
Time	8.55
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	45.3
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

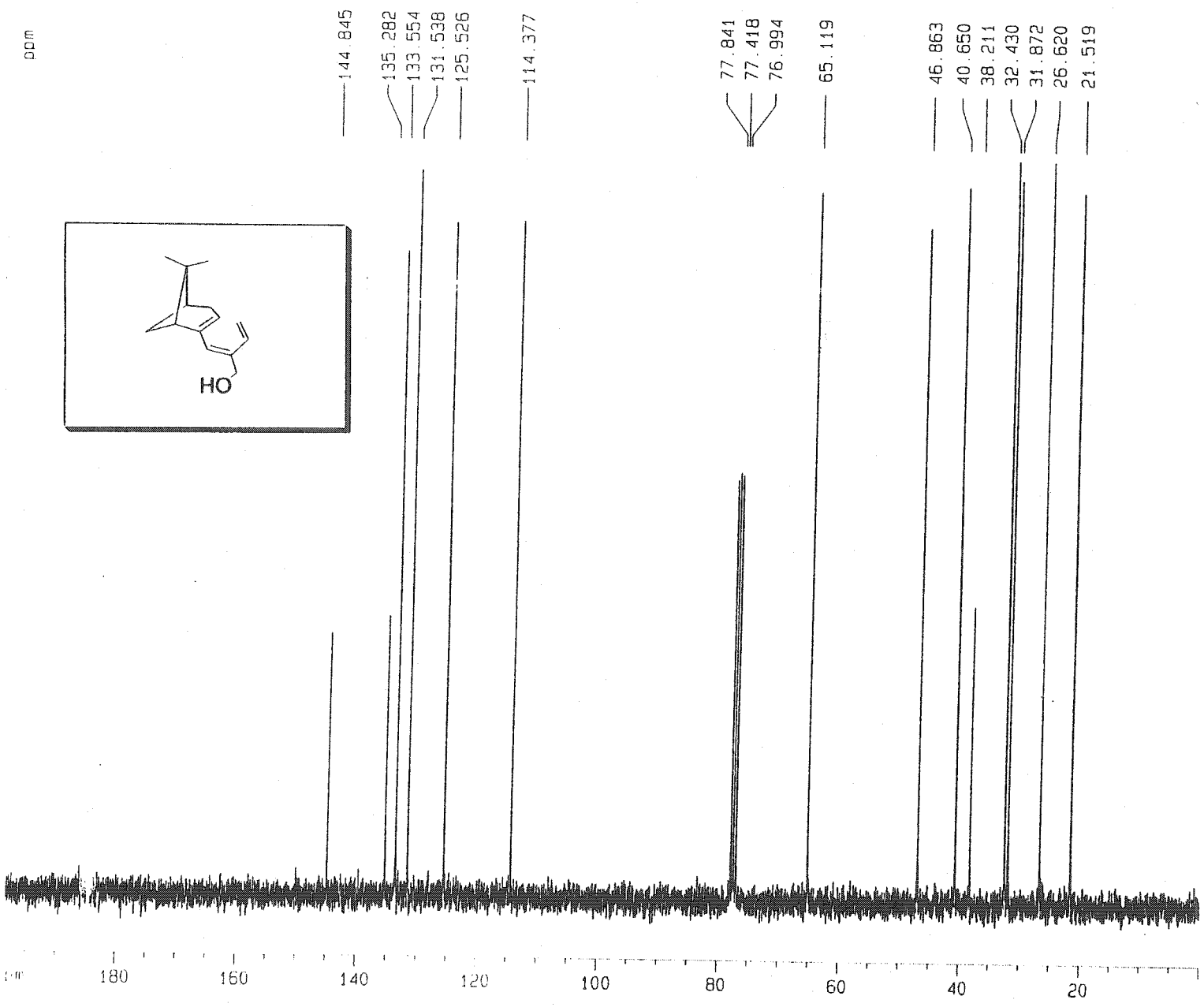
F2 - Processing parameters

SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	pt-2-95
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20030109
Time	9.06
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	128
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	574.7
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

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

NUC1	13C
P1	5.00 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

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

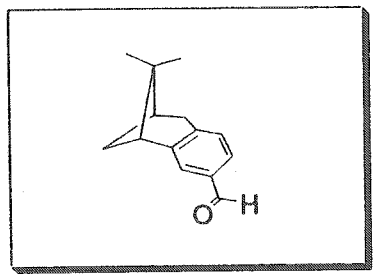
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	14.12 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

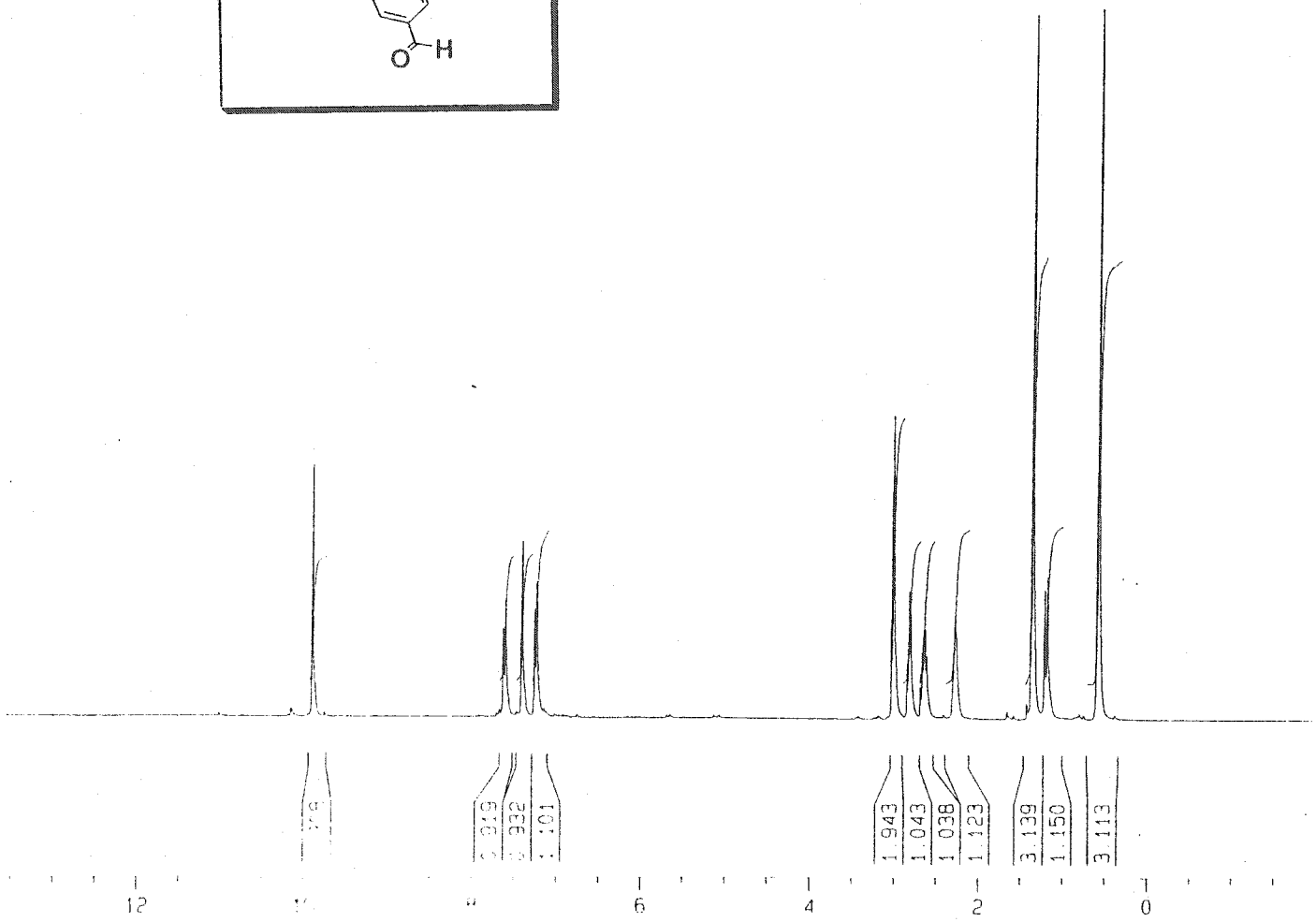
F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	200.000 ppm
F1	15093.54 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	10.00000 ppm/cm
HZCM	754.67719 Hz/cm





Current Data Parameters
NAME pt-2-104
EXPNO 1
PROCNO 1

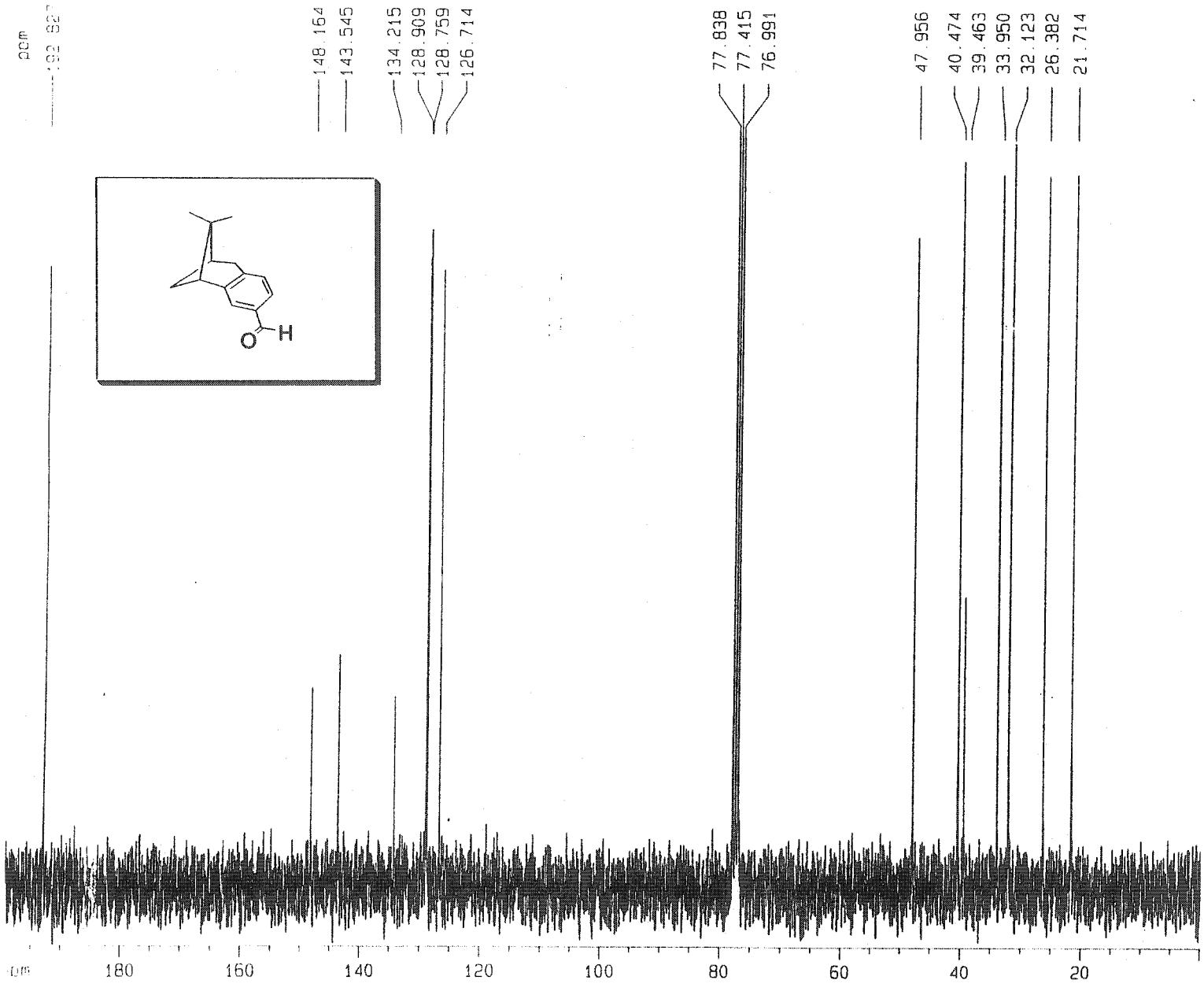
F2 - Acquisition Parameters
Date 20030123
Time 10.06
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 128
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
NUC1 1H
P1 9.75 usec
PL1 -3.00 dB
SFO1 300.1319477 MHz

F2 - Processing parameters
SI 65536
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 14.955 ppm
F1 4488.36 Hz
F2P -1.976 ppm
F2 -592.94 Hz
PPMCM 0.84652 ppm/cm
HZCM 254.06506 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	pt-2-104
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20030123
Time	10.11
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	128
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	724.1
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

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

NUC1	13C
P1	5.00 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

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

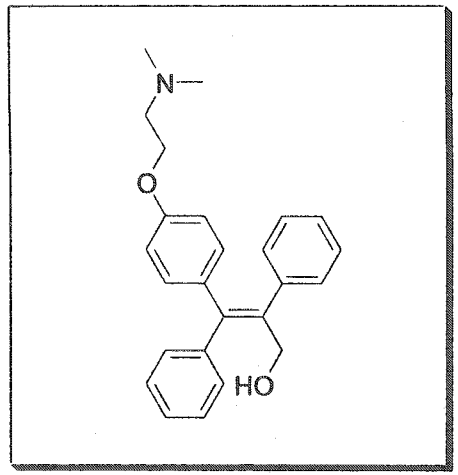
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	14.12 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

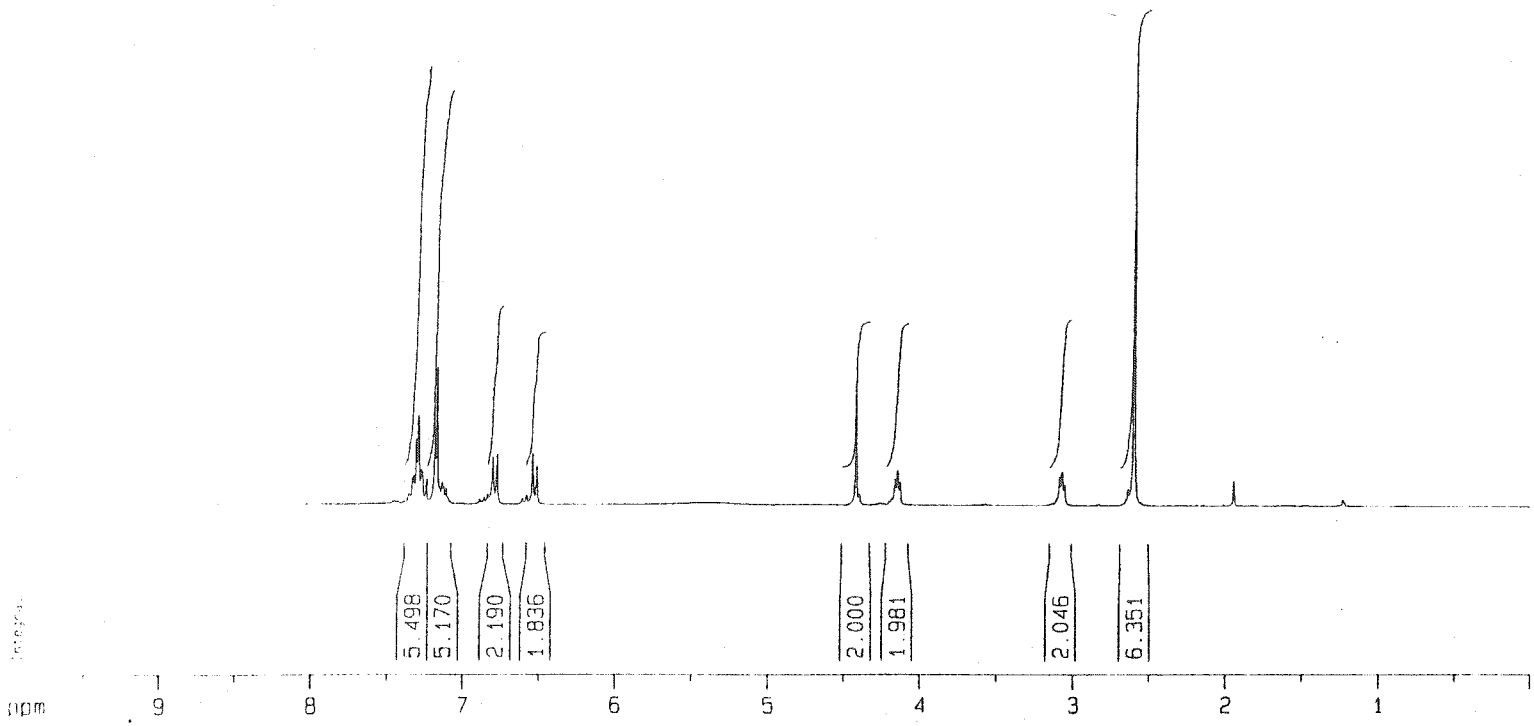
F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	200.000 ppm
F1	15093.54 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	10.00000 ppm/cm
HZCM	754.67719 Hz/cm





Current Data Parameters

NAME	pt-2-70
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20021106
Time	8.47
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	181
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SF01	300.1319477 MHz

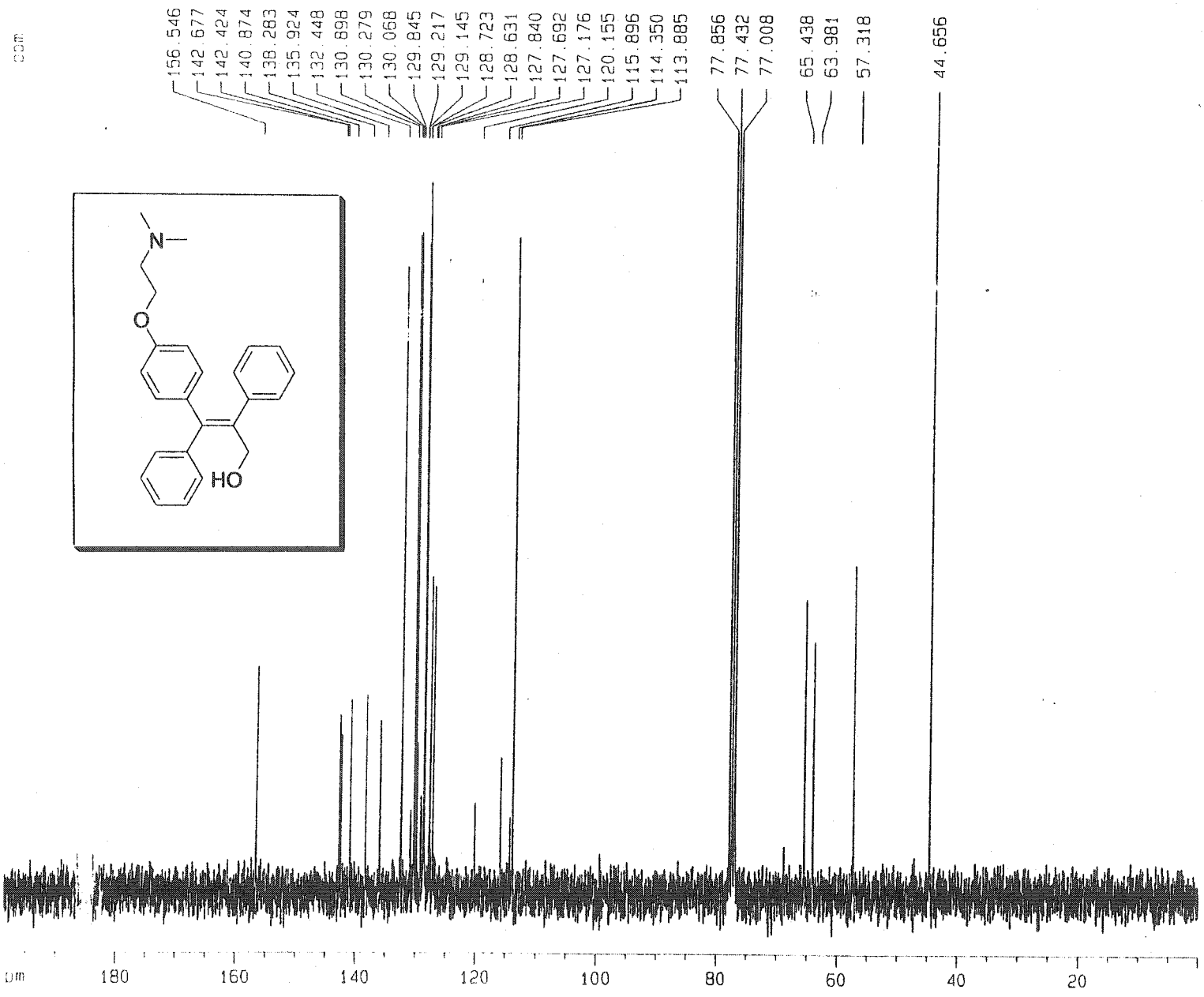
F2 - Processing parameters

SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	4.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	pt-2-70
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Date_	20021106
Time	9.10
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	256
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	2298.8
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

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

NUC1	13C
P1	5.00 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

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

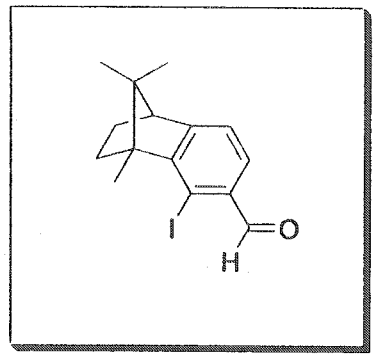
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	14.12 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

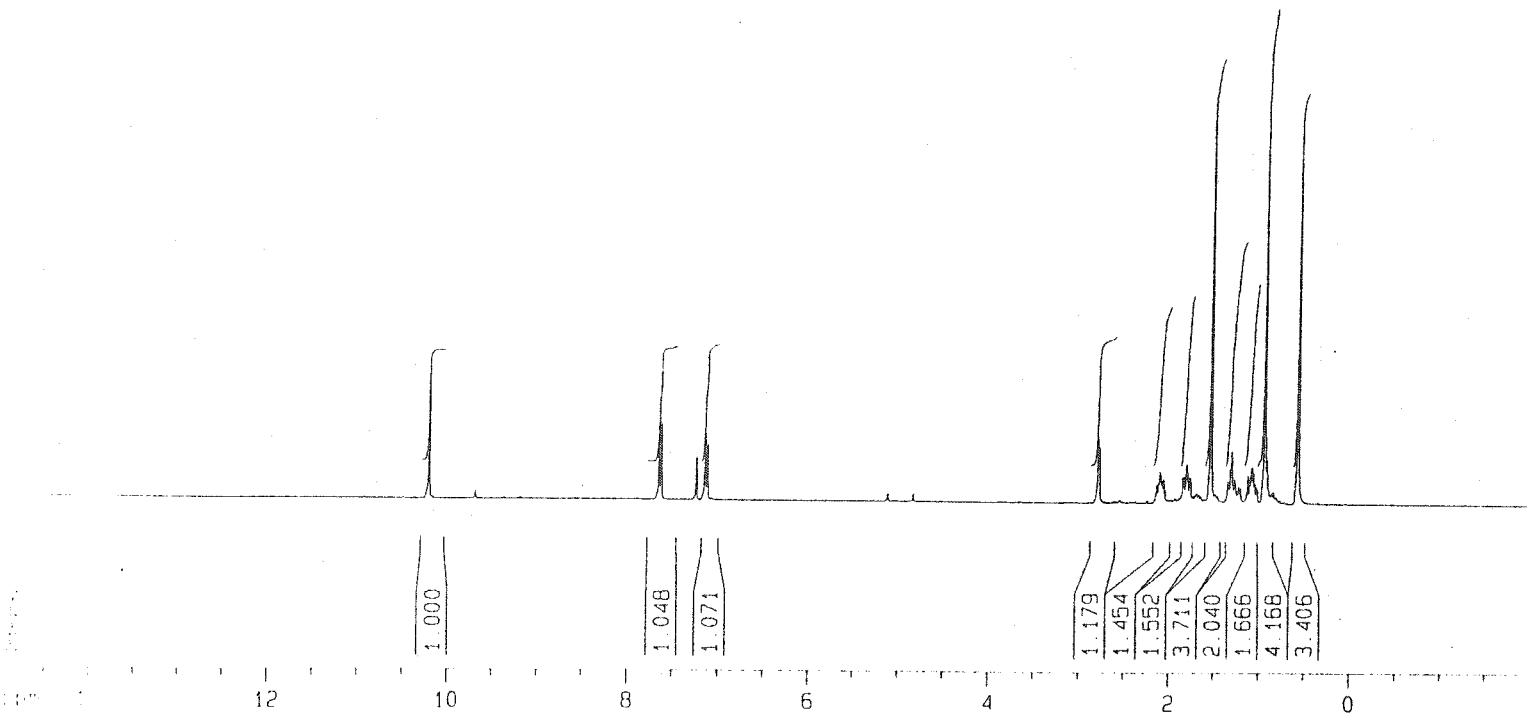
F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	200.000 ppm
F1	15093.54 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	10.00000 ppm/cm
HZCM	754.67719 Hz/cm





Current Data Parameters

NAME	pt1133b
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020116
Time	12.43
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	8
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	228.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

NUC1	1H
P1	11.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

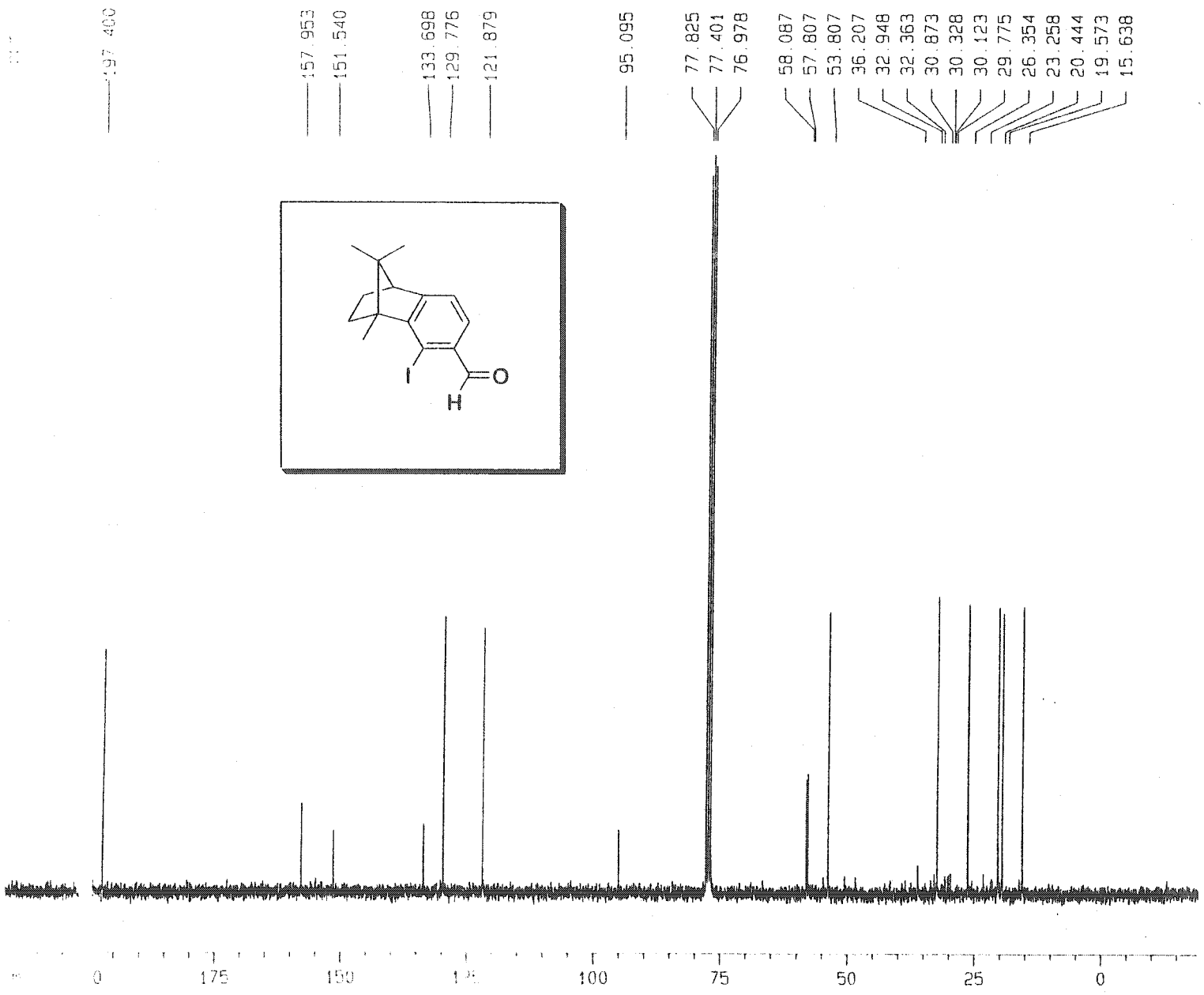
F2 - Processing parameters

SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	5.00 cm
F1P	14.955 ppm
F1	4488.36 Hz
F2P	-1.976 ppm
F2	-592.94 Hz
PPMCM	0.84652 ppm/cm
HZCM	254.06506 Hz/cm

13C



Current Data Parameters

NAME	pt1133b
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20020116
Time	12.51
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	1071
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	9195.2
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

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

NUC1	13C
P1	5.10 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

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

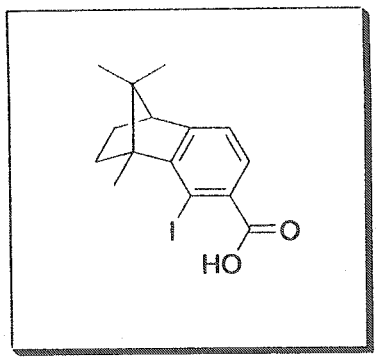
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	13.48 dB
PL13	15.00 dB
SFO2	300.1314860 MHz

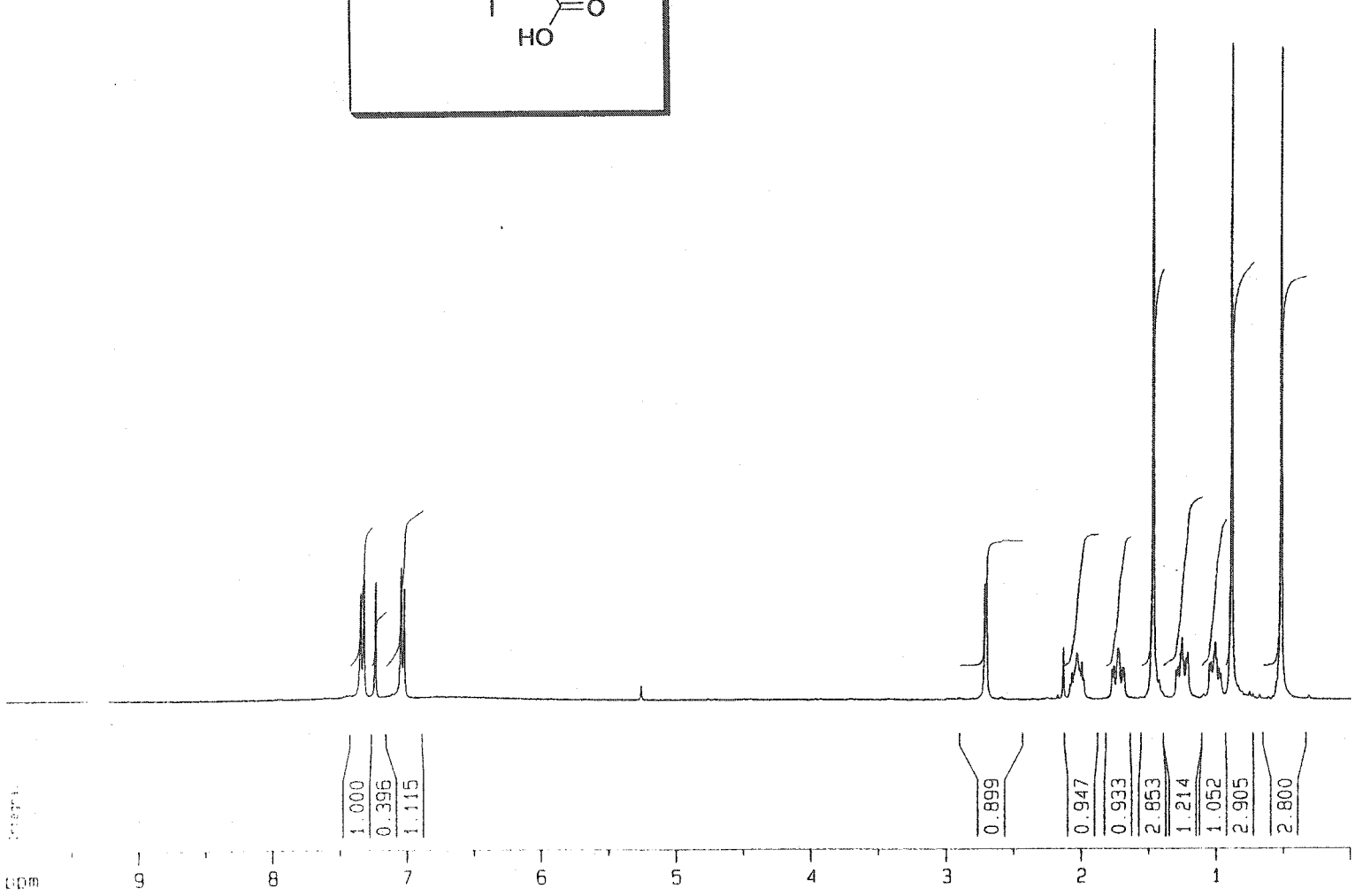
F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	5.00 cm
F1P	219.154 ppm
F1	16539.09 Hz
F2P	-19.167 ppm
F2	-1446.52 Hz
PPMCM	11.91610 ppm/cm
HZCM	899.28058 Hz/cm





Current Data Parameters

NAME	Pt-1-159
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Date_	20020502
Time	14.22
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	456.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

NUC1	1H
P1	10.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

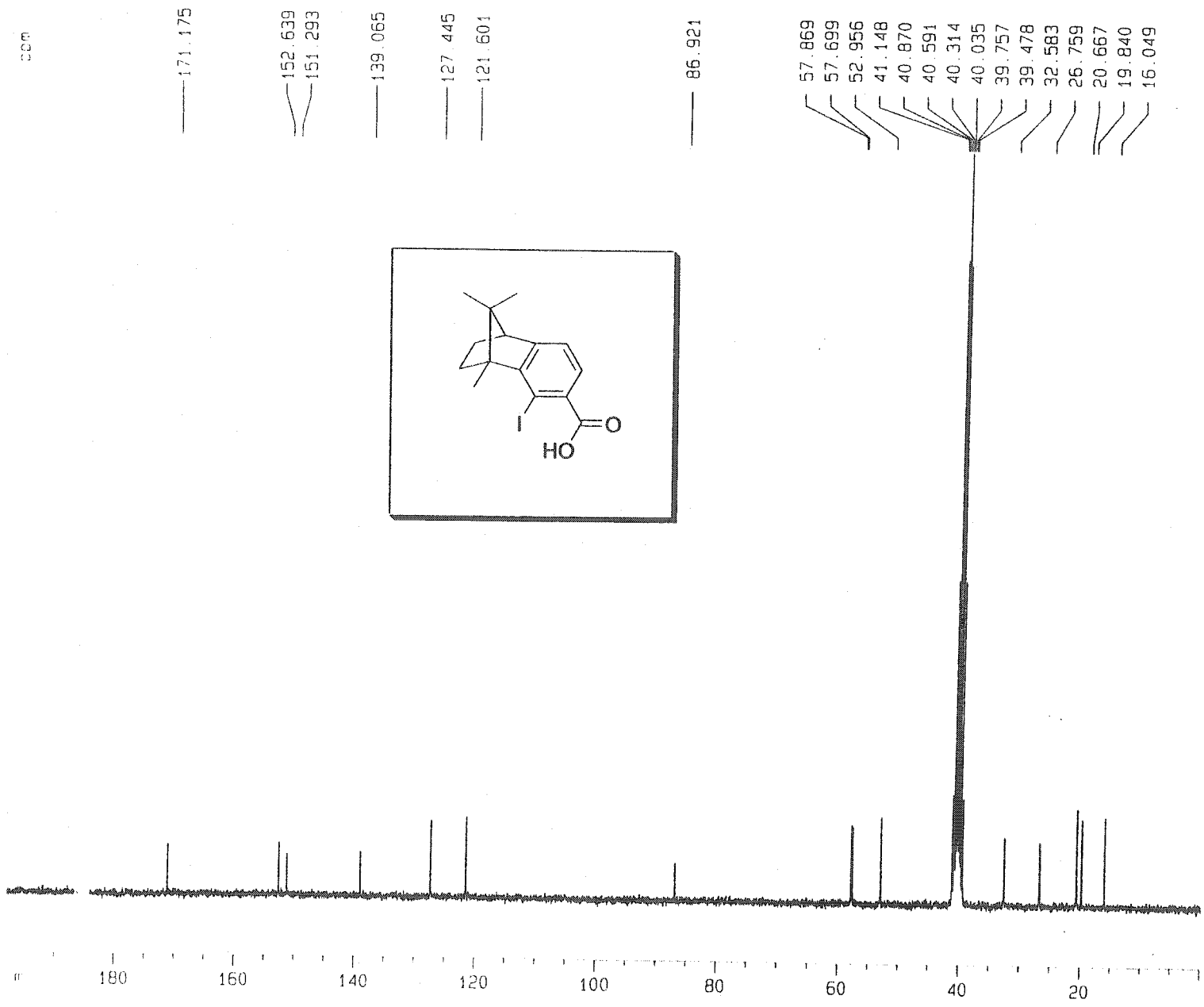
F2 - Processing parameters

SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	pt-1-159
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20020501
Time	14.45
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	1024
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	3649.1
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

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

NUC1	13C
P1	5.10 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

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

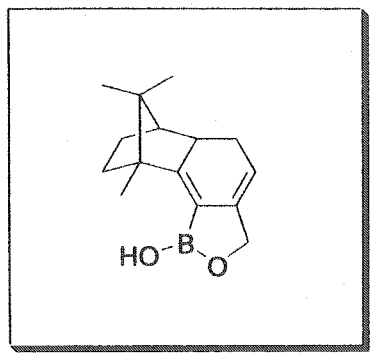
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	13.90 dB
PL13	13.90 dB
SFO2	300.1314860 MHz

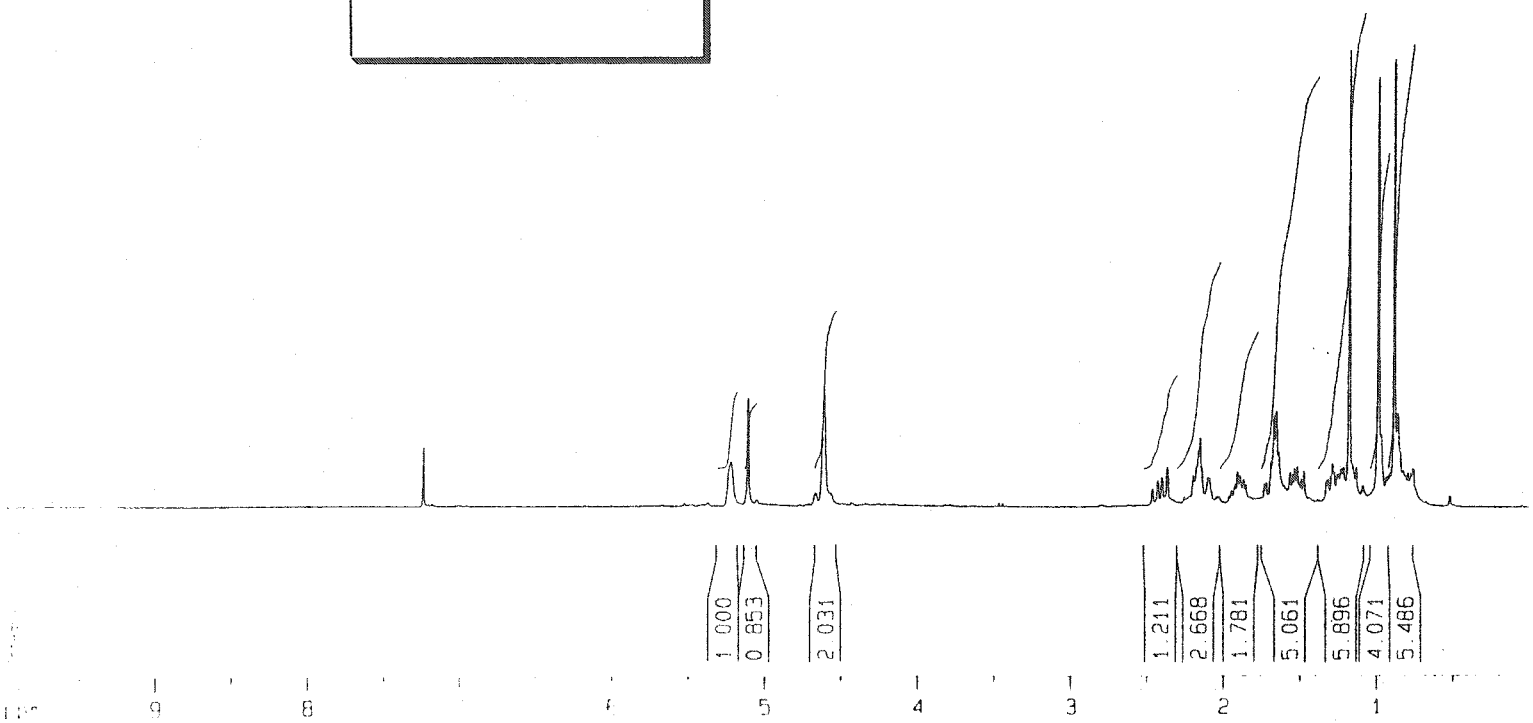
F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	200.000 ppm
F1	15093.54 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	10.00000 ppm/cm
HZCM	754.67719 Hz/cm





Current Data Parameters

NAME	pt-2-49
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020828
Time	11.39
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	228.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

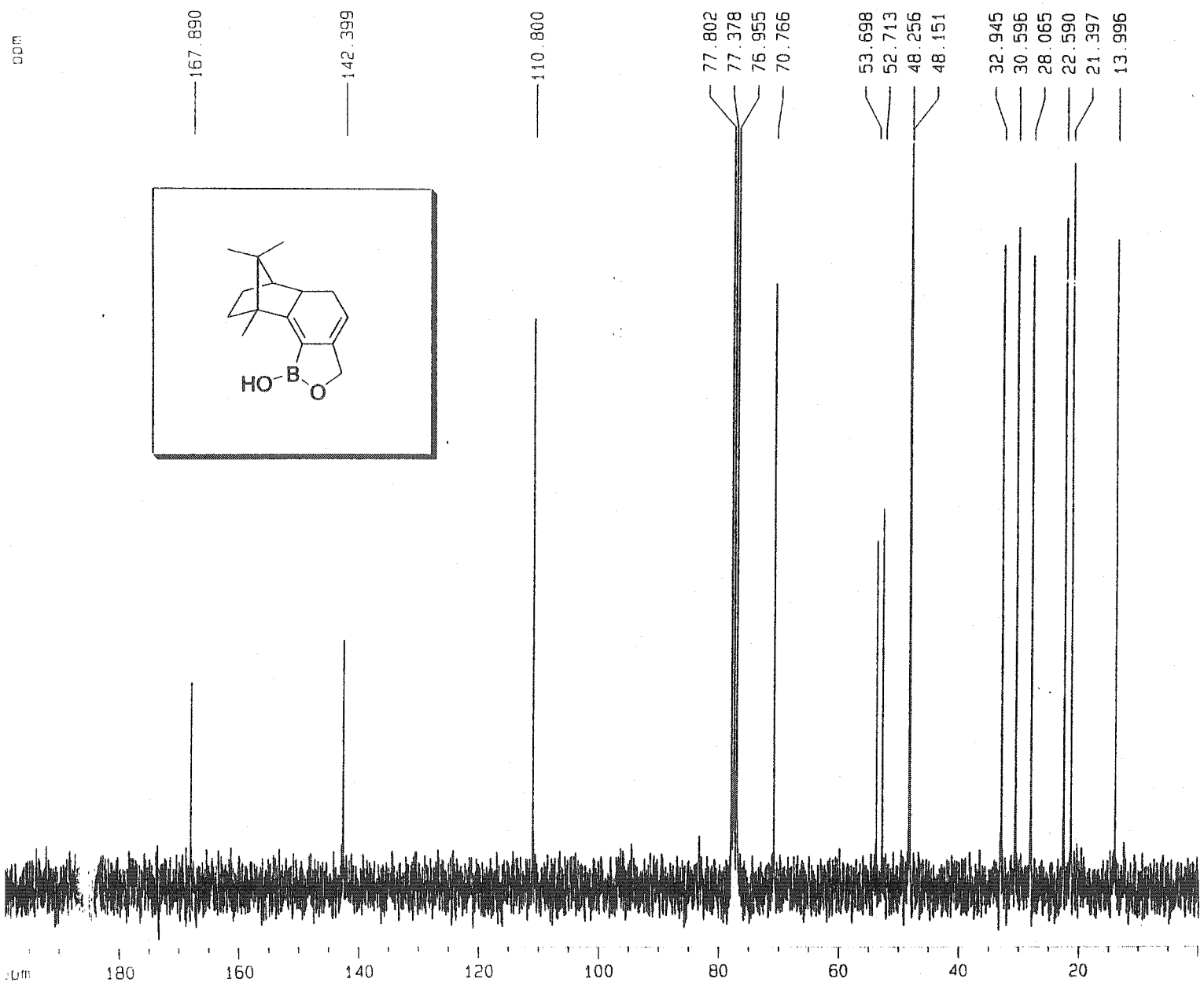
F2 - Processing parameters

SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	6.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	pt-2-49
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20020828
Time	11.54
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	1024
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	3649.1
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

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

NUC1	13C
P1	5.00 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

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

CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	14.12 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	200.000 ppm
F1	15093.54 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	10.00000 ppm/cm
HZCM	754.67719 Hz/cm