The Synthesis of 2-Benzylisoindoline-1,3-dione and its Alkyl Derivatives

Valtýr Freyr Hlynsson

Faculty of Physical Sciences
University of Iceland
2014

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A 15 ECTS research project as a part of
Baccalaureus Scientiarum degree in chemistry

Advisor
Prof. Snorri Þór Sigurðsson

Co-Advisor
Anil Jagtap

Faculty of Physical Sciences
School of Engineering and Natural Sciences
University of Iceland
Reykjavík, May 2014

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Faculty of Physical Sciences
School of Engineering and Natural Sciences
University of Iceland
VR II, Hjarðarhaga 2-6
107 Reykjavík

Telephone: 525 4000

Registration Information:
Valtýr Freyr Hlynsson, 2014, *The synthesis of 2-benzylisoindoline-1,3-dione and its alkyl derivatives*, BS thesis, Faculty of Physical Sciences, University of Iceland, 22 p.

Print: Háskólaprent
Reykjavík, May 2014

Útdráttur

Alkýlafleiður 2-benzylisoindoline-1,3-diones voru smíðaðar með hvarfefni Grignards. Tilgangurinn var að breyta efnafræðilegum eiginleikum spunamerkja með nitroxide stakeind, sem auðvelt er að smíða úr afleiðunum sem minnst er á hér að framan. Eiginleikarnir sem hér er átt við eru meðal annars vatnsleysanleiki, sterísk hindrun og stirðleiki sameindarinnar. Enn frekar var síðan átt við eina af þessum afleiðum, þar sem vetnisbórunar-oxunarhvarf með 9-BBN var prófað.

Abstract

Alkyl derivatives of 2-benzylisoindoline-1,3-dione were synthesized with Grignard reagents. The purpose was to alter properties such as water solubility, steric hindrance and rigidity of nitroxide radical spin labels. These spin labels can easily been made out of the derivatives mentioned before. One of these derivatives was then a subject of further experiments, involving hydroboration-oxidation with 9-BBN.

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List of Abbreviations

NMR	**N**uclear **m**agnetic **r**esonance
EPR	**E**lectron **p**aramagnetic **r**esonance
SDSL	**S**ide-**d**irected **s**pin **l**abeling
MS	**M**ass **s**pectroscopy
ppm	**P**arts **p**er **m**illion
Me	**Me**thyl
Et	**Et**hyl
Bn	**B**e**n**zyl
AcOH	**Ac**etic acid
TLC	**T**hin **l**ayer **c**hromatography
9-BBN	9-**B**ora**b**icyclo[3.1.1]**n**onane
THF	**T**etra**h**ydro**f**uran
UV	**U**ltra**v**iolet
PE	**P**etroleum **e**ther
EtOAc	**Et**hyl acetate
δ	chemical shift
s	**s**inglet
d	**d**oublet
t	**t**riplet
q	**q**uartet
m	**m**ultiplet

Acknowledgements

I would like to thank my advisor, Prof. Snorri Þór Sigurðsson, for the opportunity to take on this project. I also thank him for his help and guidance over the period of this work.

My co-advisor, Anil Jagtap, has been really helpful and inspiring.

Dr. Sigríður Jónsdóttir provided all NMR and MS spectra and is thanked for that.

Working in the lab is really enjoyable, but that experience would not be the same without the fantastic co-workers at Raunó. I thank them for good times.

1 Introduction

1.1 Spin labeling and electron paramagnetic resonance

All over the world chemists are binding molecules together using wide variety of methods. One group of organic compounds are spin labels. They are radicals, having at least one unpaired electron, which is usually located at an electronegative atom like oxygen. These radicals can be detected by methods like electron paramagnetic resonance (EPR). The importance of spin labels to chemists and biochemists is largely dependent on the ability to bind to another molecule. By doing so, the spin labels can turn into a tool which can be used to study and monitor structure of molecules or regions within molecules.

A method used to study biological systems, based on this ability of spin labels, is the site-directed spin labeling (SDSL). An amino acid residue (often cysteine) is substituted for the native residue of a protein at a selected site. This exchanged residue is then spin-labelled and can then be monitored by EPR[1]. Once a spin label has been added to the target molecule, the motion of it and its local environment has significant effect on the EPR spectrum of the molecule, which is really sensitive for motion of the spin label.

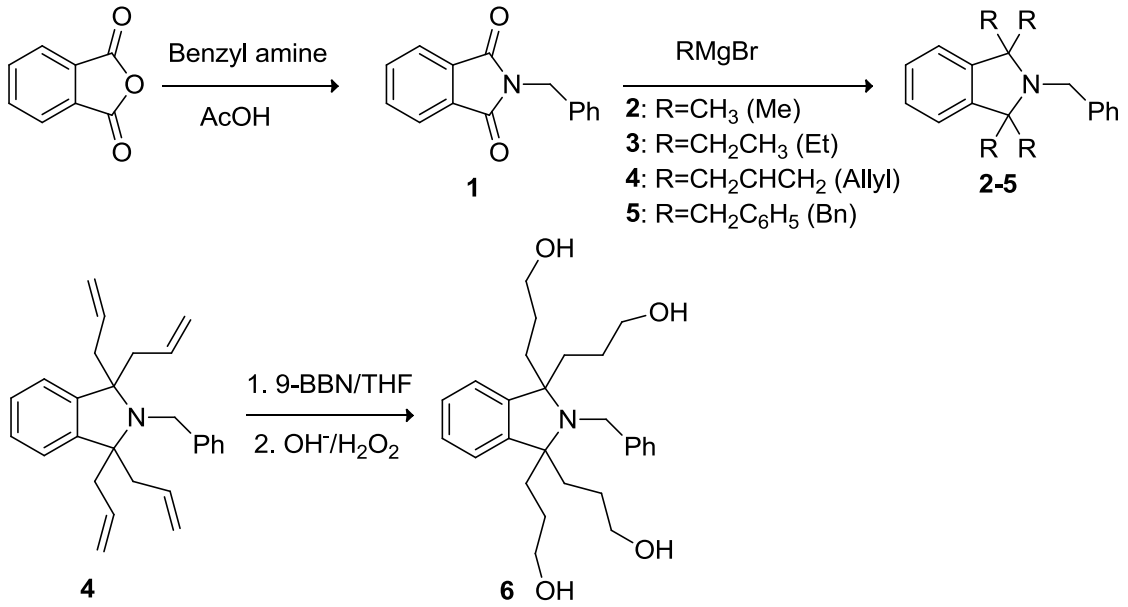
Electron paramagnetic resonance (EPR) is a technique used to study paramagnetic compounds, compounds with unpaired electrons, radicals, by exciting the lone electron. This method is analogous to nuclear magnetic resonance (NMR), with the only difference being that in EPR, the electrons are excited instead of the atomic nuclei of molecules. Because of the lack of stable molecules with unpaired electrons, the usage possibilities of EPR are limited. Despite that, in a case where they can be used, they provide key information about the structure of the molecule of interest and are an essential tool for studies of paramagnetic spin labels, like the one studied in this project. EPR amongst other low-resolution methods has provided an addition to higher-resolution methods, as it can be used to study motion and movement of biological systems[2].

1.2 Project overview

One of the biggest parts of this project is introducing various alkyl functional groups into the structure of isoindoline. The tool used to do that successfully is to use Grignard reagents. It is an organometallic compound made by reacting magnesium metal with alkyl halides and its reaction is one of the most videly used C-C bond forming method in organic synthesis. The reagent is extremely reactive towards water and oxygen and is therefore easily destroyed by moisture. The reaction and mechanism involving Grignard reagents are not fully understood, although it probably involves oxidative insertion with radical intermediates[3].

In this project, 2-benzylisoindoline-1,3-dione and few of its alkyl derivatives were synthesized, with the main goal of altering the properties of corresponding nitroxide radicals, such as water solubility, steric hindrance and rigidity. This is supposed to improve

functionality of the spin labels and detection by EPR. The alkyl derivatives were prepared with Grignard reagents. The second part of this project was altering the properties of one of the derivatives, 2-benzyl-1,1,3,3-tetraallylisoindoline, aiming for the same improvements as before.

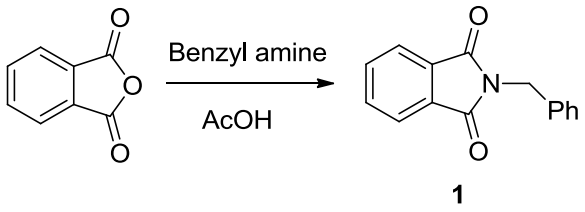


Scheme 1 Overview of the project

2 Results and Discussion

2.1 The synthesis of 2-benzylisoindoline-1,3-dione (1)

The project started by condensation of benzyl amine with phthalic anhydride to form 2-Benzylisoindoline-1,3-dione[4] **(1)**. The N-benzyl group acts as a protecting group in the alkylations, but can easily be removed by regular hydrogenation with a carbon activated palladium catalyst. After hydrogenation a nitroxide radical can be formed on that same nitrogen atom. Grignard reagents were then used to make alkyl derivatives of **1**.

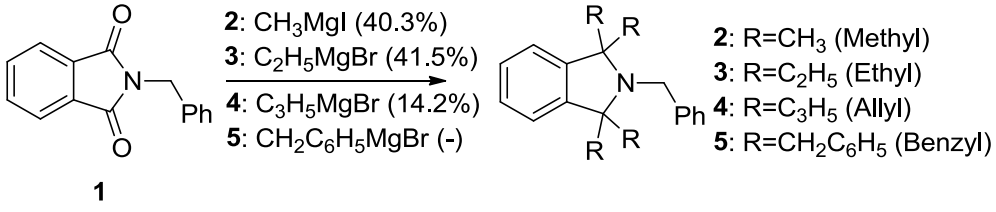


Scheme 2 Synthesis of 2-benzylisoindoline-1,3-dione **1** from phthalic anhydride

The procedure is simple and quick and gives good yields and can therefore be performed on big scale. It is really important to clean the product carefully of traces of acetic acid, despite minimal loss of yields. Yields of **1** were 92.5% and pure compound was confirmed by ^{1}H-NMR. The spectrum shows one aliphatic singlet and four peaks in the aromatic region, which correspond to 9H.

2.2 Reactions with Grignard reagents

Four different Grignard reactions were attempted. The most interesting of them are the reactions of **1** with allyl bromide and benzyl bromide, because the terminal double bonds and benzyl groups introduced allow all kinds of different chemistry to alter the properties of future nitroxide radicals. Before these reactions were carried out, **1** was reacted with iodomethane and bromoethane to give 2-benzyl-1,1,3,3-tetramethylisoindoline **(2)**, and 2-benzyl-1,1,3,3-tetraethylisoindoline **(3)** respectively. This was done to practice the general procedure for Grignard reactions, which is similar in each case.



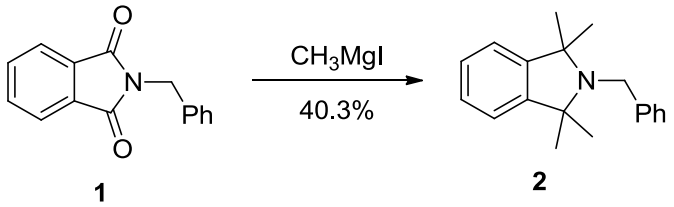
Scheme 3 Reactions of **1** with various Grignard reagents

The methyl and ethyl reactions are known and made good practice for the Grignard reactions of **1** with allyl bromide and benzyl bromide, for which simple procedures have not been found to work properly. The allyl Grignard reaction had previously been attempted by two persons in this laboratory; one failed to get any product, while the other got product in low yields. The benzyl Grignard reaction had not been attempted in this lab, although reactions of **1** with iodobenzene had been unsuccessful.

The lab recently obtained an an apparatus that has gotten the name distillation funnel. An extra exit has been added to an original dropping funnel and the stopcock has a T-like shape. This allows the user to distill and collect solvents into this distillation funnel and then discard it through the new exit. This is a simple and clever improvement, as with this introduced, the disconnection of a refluxing condenser for a distillation condenser and vice versa is avoided.

2.2.1 Iodomethane Grignard reagent

The first reaction of **1** with a Grignard reagent was with methyl magnesium bromide[4, 5] to form **2**.



1 **2**

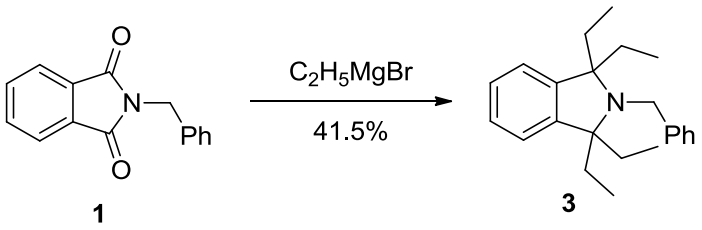
Scheme 4 Reaction of **1** with methyl magnesium iodine

The procedure is well known and has given pure compound in 20-40% yields in this laboratory. Before the starting material **1** was added to the reaction the Grignard reagent was formed by reaction of clean and dry magnesium metal with alkylhalide, in this case iodomethane. Iodine was added alongside the starting material and acts as an indicator. When the reaction mixture had been refluxed for ~18 h. it was filtrated through celite bed and filtrate bubbled with air for few hours. Then another celite bed filtration was performed and the filtrate taken to an basic alumina column to purify the product.

This reaction was performed twice and gave pure products confirmed by ^{1}H-NMR in both cases. The four new methyl groups, introduced by the Grignard reagent, give a singlet at δ 1.3 ppm. The CH_2 part of the benzyl protection group is responsible for the other singlet at δ 4.0 ppm, while the aromatic protons are measured to be nine. Three groups of peaks can be distinguished in the aromatic region, the benzyl aromatic ring giving one multiplet, while the isoindole aromat has two different types of protons. Yields were around 40% which is considered really good for this reaction.

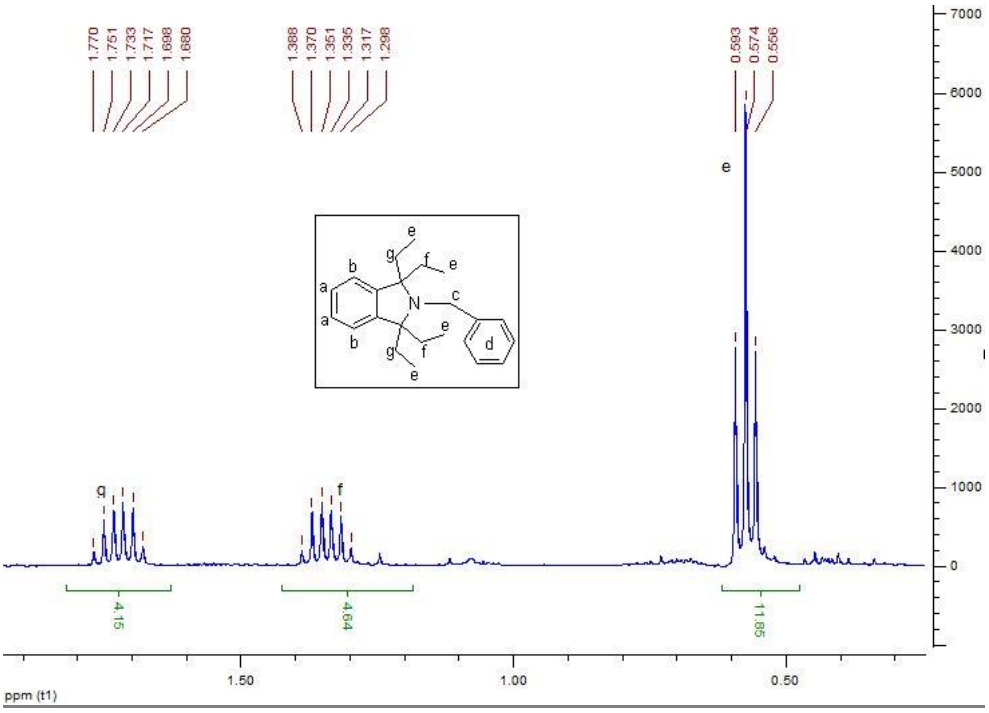
2.2.2 Bromoethane Grignard reagent

The Grignard reaction with bromoethane to give **3** was carried out only once and the procedure was very similar to the previous methyl reaction[4, 6].



Scheme 5 Reaction of **1** with ethyl magnesium bromide

It was completed without any problems and gave pure compound, confirmed by ^{1}H-NMR in excellent yields, 41.5%, since expected yields were lower than for the methyl reaction. The NMR spectrum (scheme 6) is the same as for **2** except for two changes.

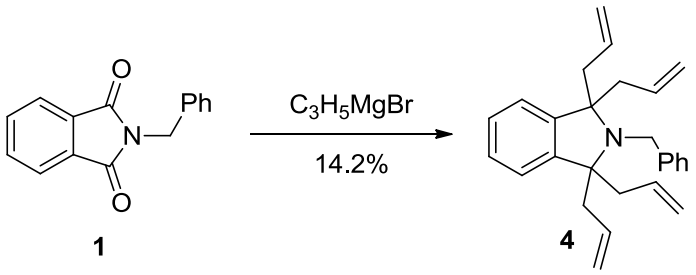


Scheme 6 Part of ^{1}H-NMR spectrum of **3**

Firstly, the big 12H aliphatic singlet has turned into triplet, which suggests that new CH_2 carbon has been placed next to these methyl carbons, as expected. Secondly, two aliphatic signals appear between 1 and 2 ppm. These are four quartets, paired two and two, confirming the presence of four CH_2 carbons, connected to terminal carbons with 3H. These four signals are different because of different chemical environment; the benzyl protecting group is closer to two of the ethyl groups. Integration of these signals confirms these suggestions.

2.2.3 Allyl bromide Grignard reagent

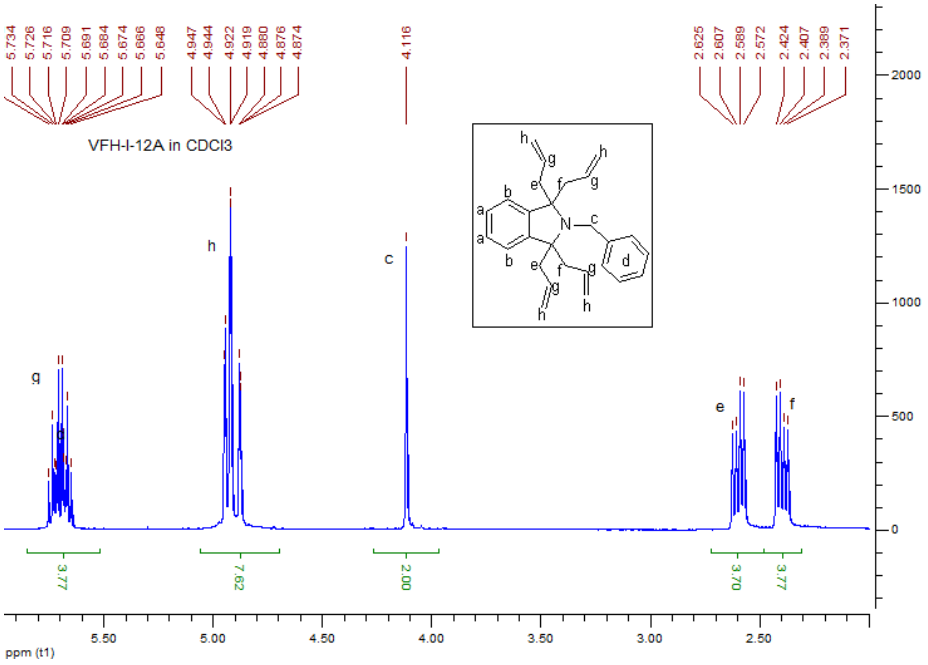
The ratio of reactants for Grignard reaction of **1** with allyl bromide is different from those with iodomethane and bromoethane, because of the tendency of allyl bromide to react with itself and form some kind of complex[7]. The procedure was based on previous Grignard reactions as well as experience from former attempts. Therefore Mg metal was used in larger excess, while the halide ratio was smaller than before.



Scheme 7 Reaction of **1** with allyl magnesium bromide

Problems were encountered after starting material **1** had been added. While refluxing the mixture, it got thicker and thicker until the magnetic stirrer used was unable to move anymore. The problem was solved by adding more solvent and disturbing the thick mud with spatula, while blowing argon powerfully through the system. This operation allowed the stirrer bar to continue its function and the problem was not encountered again throughout the rest of this procedure. Another point worth mentioning is that one filtration through celite bed was sufficient instead of two before.

The first time the reaction was performed the yields of product **4** were 10.1% and the structure was confirmed by NMR (scheme 8).



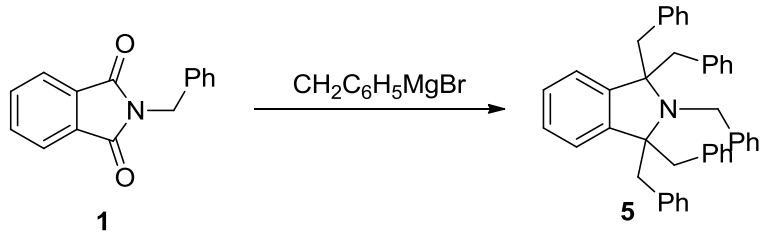
Scheme 8 Part of ^{1}H-NMR spectrum of **4**

The spectrum has the same backbone as the spectra discussed in sections 2.2.1 and 2.2.2. Still, there are some changes as expected, the most obvious being the movement of signals downfield because of the introduction of terminal double bond. In fact, the only difference in spectra of **3** and **4** is that the 12H triplet at δ 0.76 ppm in **3** has disappeared in **4** and two new peaks have appeared in the double bond region. The synthesis was repeated twice, both attempts were successful but the third attempt gave the best yields, 14.2% which can be thought of as really good. By completing this procedure three times with similar yield and

getting equivalent spectra each time, this procedure can be confirmed as working, giving around 10-15% yields.

2.2.4 Benzyl bromide Grignard reagent

The second interesting Grignard reaction was of **1** with benzyl bromide.

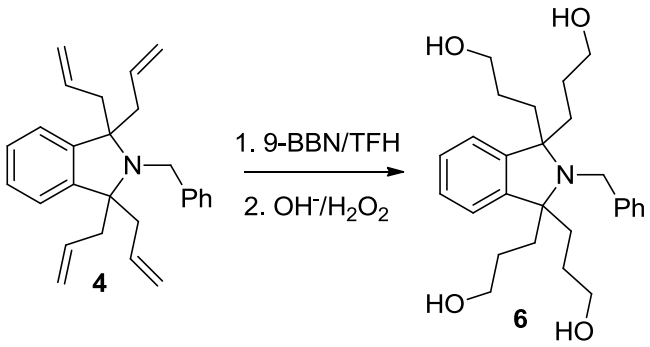


Scheme 9 Reaction of **1** with benzyl magnesium bromide

A procedure similar to the former allyl reaction procedure[7] was used in attempt to prepare a compound **5**. Compound **5** would open up possibilities of various new experiments, involving transformation of the newly introduced benzyl groups into other interesting functional groups. Unfortunately, this reaction did not work out as nicely as it did when **4** was synthesized. Interestingly, everything looked normal until the basic alumina column separation. Before that, it could not be seen that something was different, compared with previous Grignard reactions. When solvents were removed from the fractions containing the compound according to TLC, a lot of white crystals remained. A sample of these crystals was dissolved in petroleum ether and compared with a solution of benzyl bromide on TLC. The spot provided by benzyl bromide matched the R_f value of the largest spot from the reaction mixture. A sample was submitted for NMR analysis but the spectrum showed only signs of benzyl bromide. The outcome of this reaction has not been studied further.

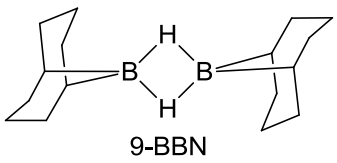
2.3 Hydroboration-oxidation on (4)

At this point in the experiments, reactions with Grignard reagents were paused for a while and the attention turned to reactions of one of earlier products, **4**. This compound was formed with reaction of allyl bromide Grignard reagent with **1** as described in section 2.2.3. The four terminal double bonds introduced provide interesting possibilities, related to the properties of spin labels. For example, the next attempted reaction, to oxidize the terminal double bonds of **4** into 1° alcohols by anti-Markovnikov addition with hydroboration-oxidation[8, 9] to get **6**, was supposed to increase the polarity of the compound significantly and if successful, make it water soluble.



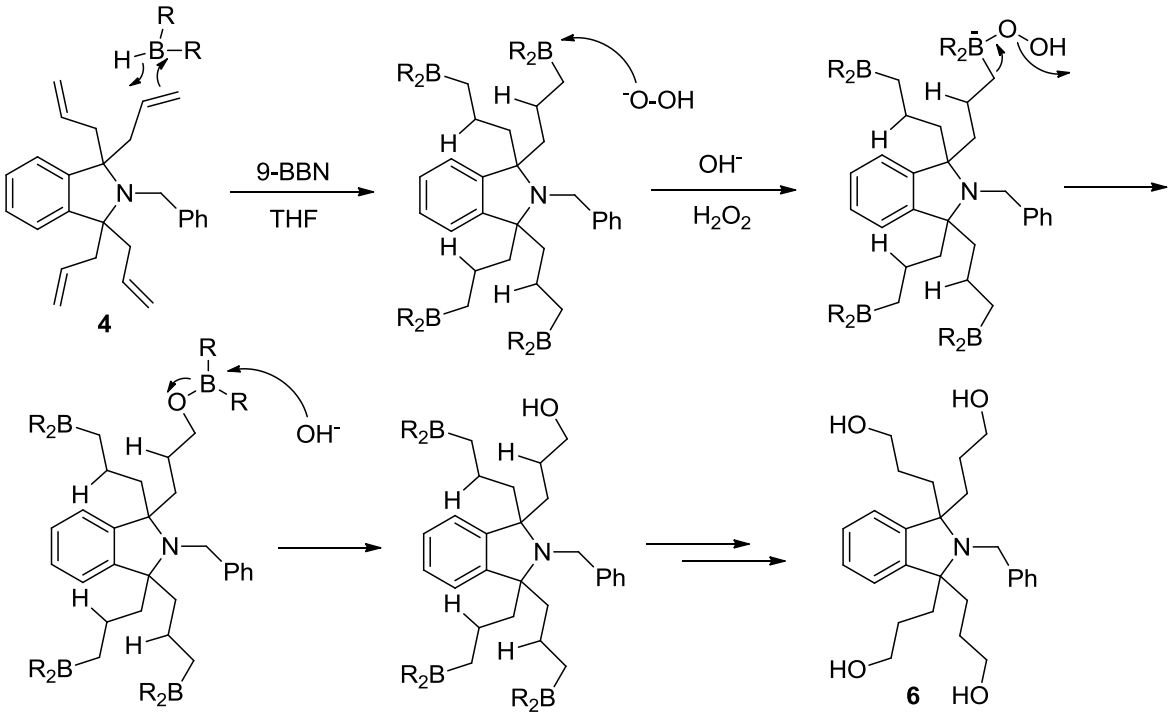
Scheme 10 Hydroboration-oxidation with 9-BBN. The motivation for this is to increase water solubility.

The hydroboration-oxidation reaction of **4** also proved to be more problematic than had been hoped for. On a small scale, **4** was dissolved in THF before 9-borabicyclo [3.1.1]nonane (9-BBN), dissolved in THF, was added (see scheme 11 for structure).



Scheme 11 Structure of dimer 9-borabicyclo[3.1.1]nonane (9-BBN)

The 9-BBN is a hydroboration reagent, chosen ahead of borane (BH_3) because of several reasons, for example does the bulkiness of 9-BBN increase regioselectivity towards the terminal carbon atom[9]. Its function is to add hydrogen atom to the more substituted carbon of the double bond, while it attaches to the more accessible, less substituted carbon atom. After that, water solutions of hydrogen peroxide (H_2O_2) and sodium hydroxide (NaOH) were added to the mixture. This is supposed to replace the terminal borane with a hydroxyl functional group, giving the 1° alcohol desired (see scheme 12 for mechanism).



Scheme 12 Hydroboration-oxidation mechanism

This however, seems not to be the case. In the first attempt of this reaction the hydroboration step was started after about one hour of stirring at room temperature. The oxidized product mixture that was produced was complex, with at least 6 new spots visible on TLC. It should though be noted that although the product mixture was complex, the relatively non-polar starting material disappeared completely from TLC in the hydroboration step, while all the compounds formed were much more polar than the starting material. This suggests that something polar, most likely hydroxyl groups are present in the product mixture, with compounds having 1-4 hydroxyl groups.

The same reaction was simultaneously performed on a model compound, styrene, which is a benzene ring with one allyl group. This effort however did not give any significant insight into the reaction because of solubility problems that occurred of styrene in THF.

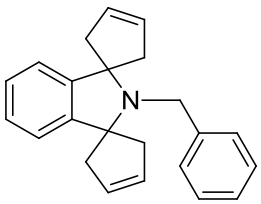
In another attempt to perform this reaction, it was made a priority to decrease the number of different compounds formed in this reaction by making sure that the hydroboration step had come to an end before starting the oxidation step. In an attempt to accomplish this goal, the mixture was heated to reflux and when TLC still showed multiple spots, extra amount of 9-BBN was added and reflux continued for a while. The product after the oxidation showed four nicely separated bands on TLC that were isolated by prep-TLC. Two of these bands gave more compound than the other and were separately driven through another prep-TLC. Major spots were then submitted to ^{1}H-NMR and MS. Mass spectrum of one of these purified compounds showed exact mass of the product that was expected, with four hydroxyl groups instead of double bonds, although another much bigger signal was observed. Despite that, this mass spectrum indicates that the wanted product was formed to some extent.

3 Conclusion and Future Outlook

The synthesis of **1** was done on large scale, large enough to supply starting material for the whole project. Three of four attempted reactions with Grignard reagents were successful, confirmed by ^{1}H-NMR, ^{13}C-NMR and MS, each one in excellent yield. One of these successfully synthesized compounds, **4**, was then a subject of further experiments where its properties were altered. These reactions did not give any pure product, although the desired product **6** is most likely present to some extent. Further experiments are required, as this compound seems to have really interesting properties.

When the project was started, the author had minimal experience of working in the laboratory and of the techniques used there. Although much time was spent trying to figure out the small things that weren‘t working as expected, when looking out of the rear window, it can be seen that personal milestones have been reached and hopefully some that will be useful for others.

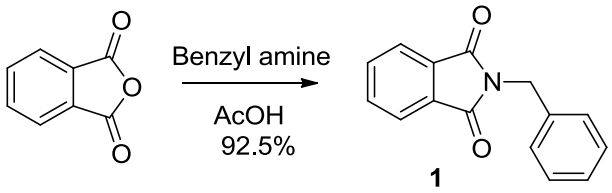
If not for time limits, this project would have been almost endless, because the possibilities that lie ahead are interesting and diverse. Firstly, the fourth attempted Grignard reaction, with benzyl bromide, did not prove successful in this project, but great efforts weren‘t put into solving the problem that came up. It is likely that with some alteration that reaction could be completed successfully. If completed, further modifications of the benzyl functional groups would be possible. Another branch of future possibilities lies in further experiments with the allyl compound **4** which was successfully synthesized. For example it was initially a part of this project to use second generation Grubb‘s catalyst to connect the allyl groups together, two and two, to form 5-membered rings. That would increase rigidity of the future spin label dramatically. Because of limited time these reactions were not attempted.



Scheme 13 Hopeful product of a possible reaction of **4** with Grubb‘s catalyst

4 Experimental Section

Chemicals were purchased primarily from Sigma-Aldrich Chemical Company and Acros, Belgium, and were used without further purification. TLC was carried out using glass plates pre-coated with silica gel (Kieselgel 60 F254, 0.2mm, Merck). Visualisation was by UV light and/or iodine unless stated otherwise. Silica gel was purchased from Silicycle and used for column chromatography. ^{1}H-NMR and ^{13}C-NMR spectra were recorded at the frequencies stated, using deuterated solvents as internal standards. 400 MHz spectra were recorded on a Bruker Advance 400 spectrometer. Residual proton signal from the deuterated chloroform [7.26 ppm for ^{1}H spectra and 77.0 ppm for ^{13}C spectra] were used as references. All coupling constants were measured in Hertz. All moisture sensitive reactions were carried out using argon gas from standard BOC industrial cylinders, dried through an activated silica column.



1

4.1 2-Benzylisoindoline-1,3-dione (1)

Over the period of 20 min. benzyl amine (81 mL, 740 mmol) was added drop-wise to an acetic acid (600 mL) solution of phthalic anhydride (100 g, 670 mmol) in a 2 L boiling flask. The reaction mixture was heated and refluxed for 12 h. The reaction mixture was cooled to 40 °C before it was poured into ice water to give white solid material, which was filtered out through celite bed and washed with ice water and cold ethanol. It was then allowed to dry in hood before it was dissolved in 150 mL of ethanol and refluxed for 10 min. After cooling, solid was again filtered out and traces of ethanol removed under high vacuum and the white compound allowed to stand for 2 d. in the fume hood (148 g, 92.5% yield).

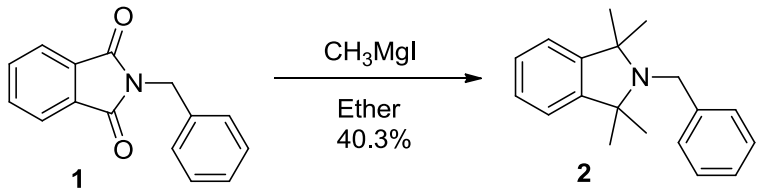
Notebook reference: VFH-I-03

TLC (Silica gel, 100% PE), R_f (Phthalic anhydride) = 0.2, R_f (**1**) = 0.3

^{1}H-NMR ($CDCl_3$): δ 4.85 (s, 2H, CH_2^c), δ 7.30 (m, 5H, 5x CH^d), δ 7.70 (2x d, 2H, 2x CH^b, J=3.2Hz), δ 7.84 (2x d, 2H, 2x CH^c, J=3.2Hz).

^{13}C-NMR ($CDCl_3$): δ 41.39, 123.11, 127.59, 128.38, 128.44, 131.91, 133.74, 136.14, 167.81 ppm.

MS: Calculated for $C_{15}H_{11}NO_2$ 237.079 amu, found 260.0682 amu (M+Na).



4.2 2-Benzyl-1,1,3,3-tetramethylisoindoline (2)

To a 3-neck round-bottom flask with argon flow was added clean, dried magnesium metal (12.3 g, 505 mmol) and diethyl ether added. Iodomethane (89.6 g, 631.5 mmol) was then dissolved in diethyl ether (78 mL in whole) along with a pinch of iodine. This solution was now added drop-wise to the magnesium metal, which caused the ether to reflux gently. After addition, the mixture was allowed to reflux for 3 h, before distilling off solvents at 80 °C. Then the diketone **1** (10 g, 42.2 mmole) was dissolved in 100 mL of toluene and added drop-wise to the reaction mixture between 70-80 °C. Toluene was now distilled off at 120 °C before the remaining reaction mixture was refluxed for 18 h. The hot reaction mixture was now filtered through celite bed and washed with ~500 mL of petroleum ether. The ether filtrate was bubbled with air for 8 h. before second filtration through another celite bed. This filtrate was passed through basic alumina column to obtain oily product **2** (4.52 g, 40.3% yield).

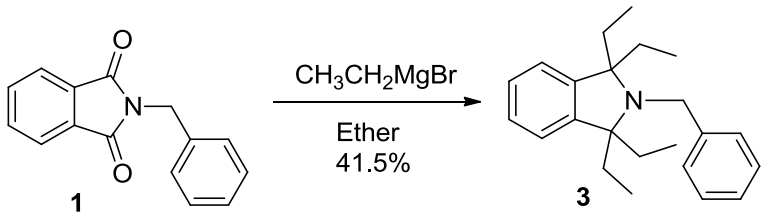
Notebook reference: VFH-I-01

TLC (Silica gel, 100% PE), R_f (**2**) = 0.4

^{1}H-NMR ($CDCl_3$): δ 1.31 (s, 12H, 4x CH_3^e), 4.00 (s, 2H, CH_2^c), 7.14 (2x d, 2H, 2x CH^b, J=3.2Hz), 7.24 (2x d, 2H, 2x CH^a, J=3.2Hz), 7.3-7.5 (m, 5H, 5x CH^d) ppm.

^{13}C-NMR ($CDCl_3$): δ 28.25, 46.11, 65.05, 99.82, 121.17, 126.26, 126.62, 127.77, 128.18, 128.67, 147.71 ppm.

MS: Calculated for $C_{19}H_{23}N$ 265.183 amu, found 266.1898 amu (M+H).



4.3 2-Benzyl-1,1,3,3-tetraethylisoindoline (3)

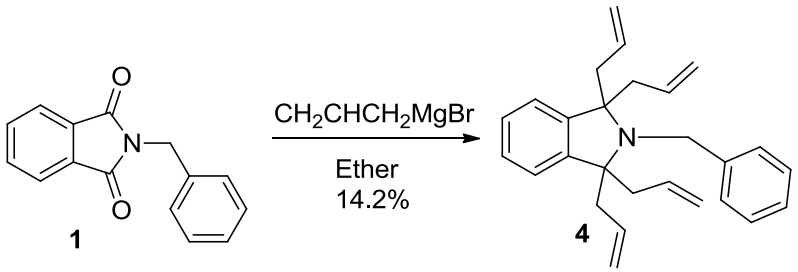
Along with 35 mL of diethyl ether, clean magnesium metal (12.3 g, 505.8 mmol) was added to 3-necked round-bottom flask. Ethyl bromide (68.9 g, 632.3 mmol) and pinch of iodine were dissolved in 40 mL of diethyl ether and added drop-wise to the Mg metal. The mixture started refluxing and was allowed to reflux for 3 h before heating to 80 °C and distillation. After that, **1** (10 g, 42.2 mmol) was dissolved in 100 mL of toluene and added drop-wise, before refluxing for 18 h. Mixture was heated to 110 °C and fractions collected, before celite bed filtration was performed at ~80 °C, followed by thorough washing with petroleum ether. The deeply orange filtrate was bubbled with air for ~1 h or until all solvents had evaporated. After that, another filtration through celite bed with petroleum ether was performed to give clear yellow filtrate. To isolate the product, the yellow filtrate was passed through basic alumina column with petroleum ether as mobile phase. After removal of solvents, a thick, yellow, oily compound **3** remained which solidified in freezer (5.63 g, 41.5% yield).

Notebook reference: VFH-I-09

^{1}H-NMR ($CDCl_3$): δ 0.76 (t, 12H, 4x CH_3^e, J=7.2Hz), 1.53 (m (2x q), 4H, 2x CH_2^f, J=7.2Hz), 1.91 (m (2x q), 4H, 2x CH_2^g, J=7.2Hz), 4.00 (s, 2H, CH_2^c), 7.04 (2x d, 2H, 2x CH^b, J=3.2Hz), 7.19 (2x d, 2H, 2x CH^a, J=3.2Hz), 7.22-7.45 (m, 5H, 5x CH^d) ppm.

^{13}C-NMR ($CDCl_3$): δ 9.58, 30.36, 46.73, 71.29, 123.39, 125.58, 126.51, 127.75, 129.24, 142.41, 144.57 ppm.

MS: Calculated for $C_{23}H_{31}N$ 321.246 amu, found 322.2529 amu (M+H).



4.4 2-Benzyl-1,1,3,3-tetraallylisoindoline (4)

Clean, dry magnesium metal (12.3 g, 505.8 mmol) was added to a 3-necked round-bottom flask and 100 mL of diethyl ether added. Allyl bromide (14.6 mL, 169 mmol) was dissolved in 15 mL of diethyl ether along with a pinch of iodine and the solution added drop-wise through dropping funnel. Reflux started and addition was continued to maintain reflux. After addition, stirring was continued overnight, without heating. The mixture was then heated to 50 °C and refluxed for 30 min, before solvents were collected in distillation funnel. Starting material **1** (5 g, 21.2 mmol) was now dissolved in 50 mL of toluene and added drop-wise to the 50 °C hot reaction mixture. Then, the temperature was raised to 115 °C and the mixture allowed to reflux. Another 50 mL portion of toluene was added and temperature raised to 120°C over night. The thick mixture was heated to 70 °C and another 30 mL of toluene added before filtration through celite bed and washing with petroleum ether was performed. The orange filtrate was bubbled with air overnight and then passed through basic alumina column to give the white product, **4** (1.11 g, 14.2% yield).

Notebook reference: VFH-I-20

TLC (Silica gel, 5% EtOAc / PE), R_f (**4**) = 0.3

^{1}H-NMR ($CDCl_3$): δ 2.39 (2x d, 4H, 2x CH_2^f, J=7.2Hz), 2.60 (2x d, 4H, 2x CH_2^e, J=7.2Hz), 4.11 (s, 2H, CH_2^c), 4.87-4.98 (m, 8H, 4x CH_2^h), 5.69 (m, 4H, 4x CH^g), 7.03 (2x d, 2H, 2x CH^b, J=3.2Hz), 7.19 (2x d, 2H, 2x CH^a, J=3.2Hz), 7.24-7.49 (m, 5H, 5x CH^d) ppm.

^{13}C-NMR ($CDCl_3$): δ 43.65, 47.13, 70.89, 116.95, 123.57, 126.23, 126.92, 128.00, 129.43, 136.03, 141.43, 143.67 ppm.

MS: Calculated for $C_{27}H_{32}N$ 369.25 amu, found 370.2523 amu (M+H).

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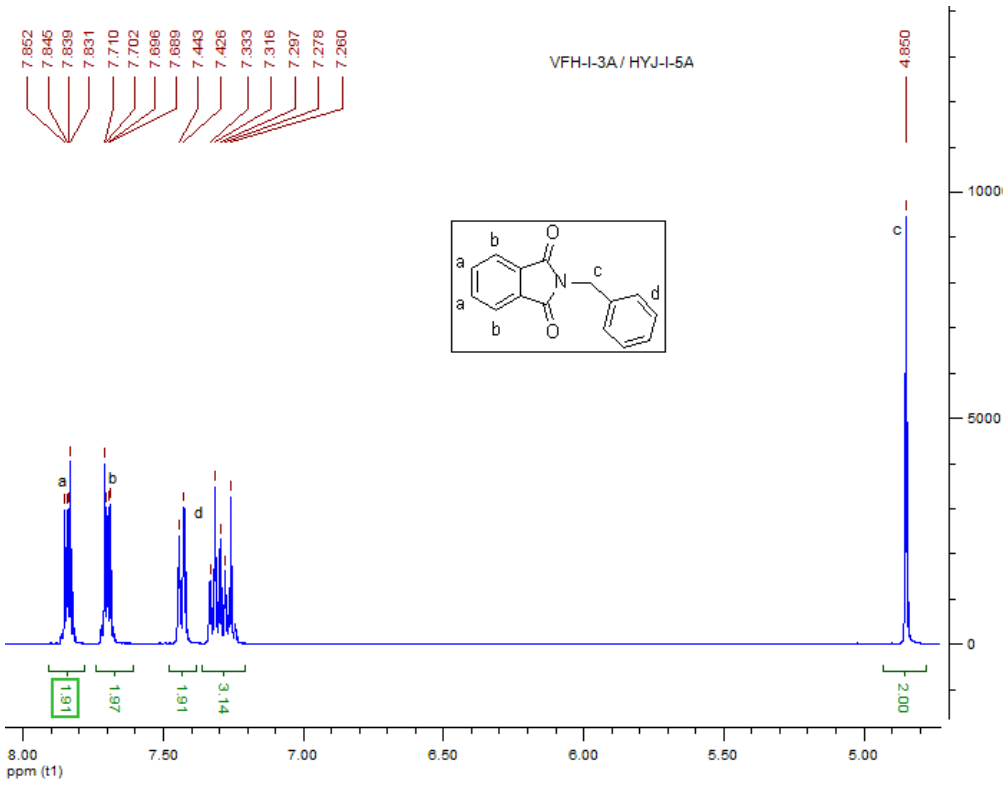
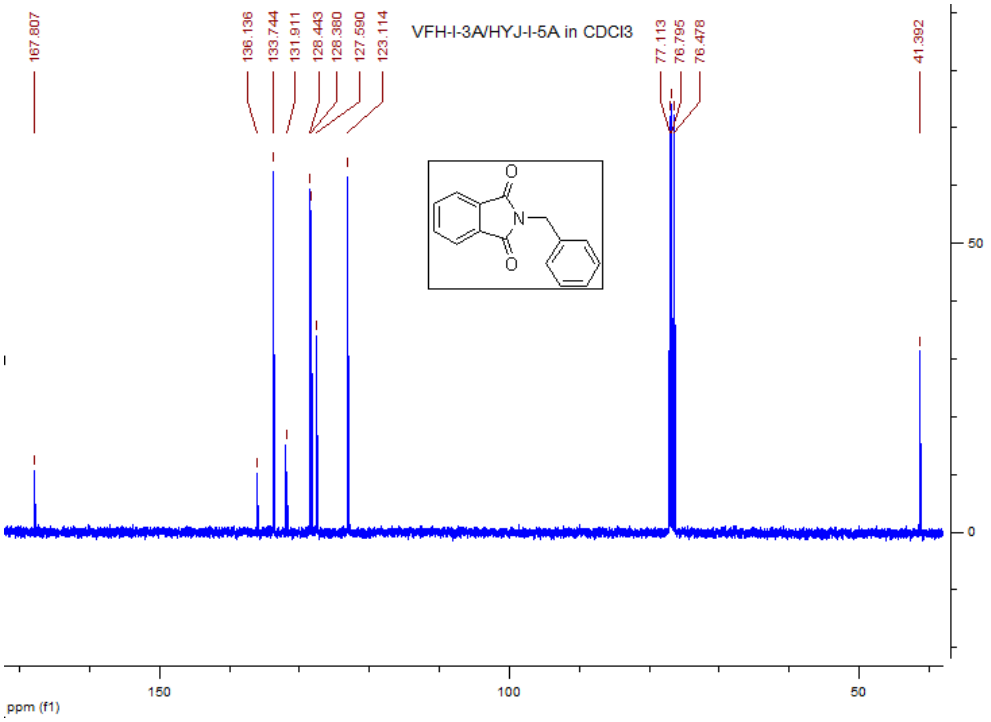
Appendix

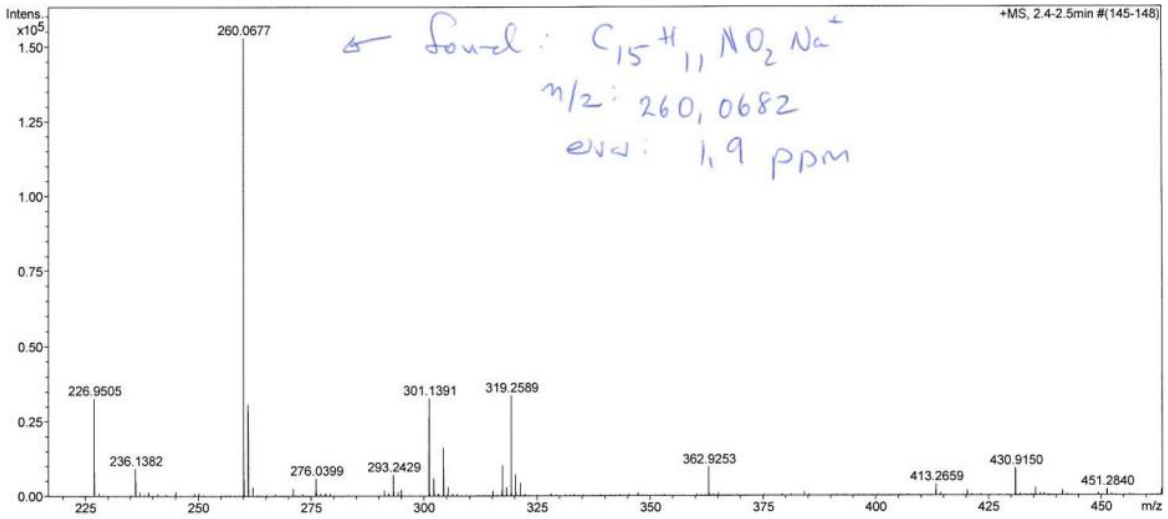
400 MHz ^{1}H-NMR spectrum of 2-benzylisoindoline-1,3-dione (1)



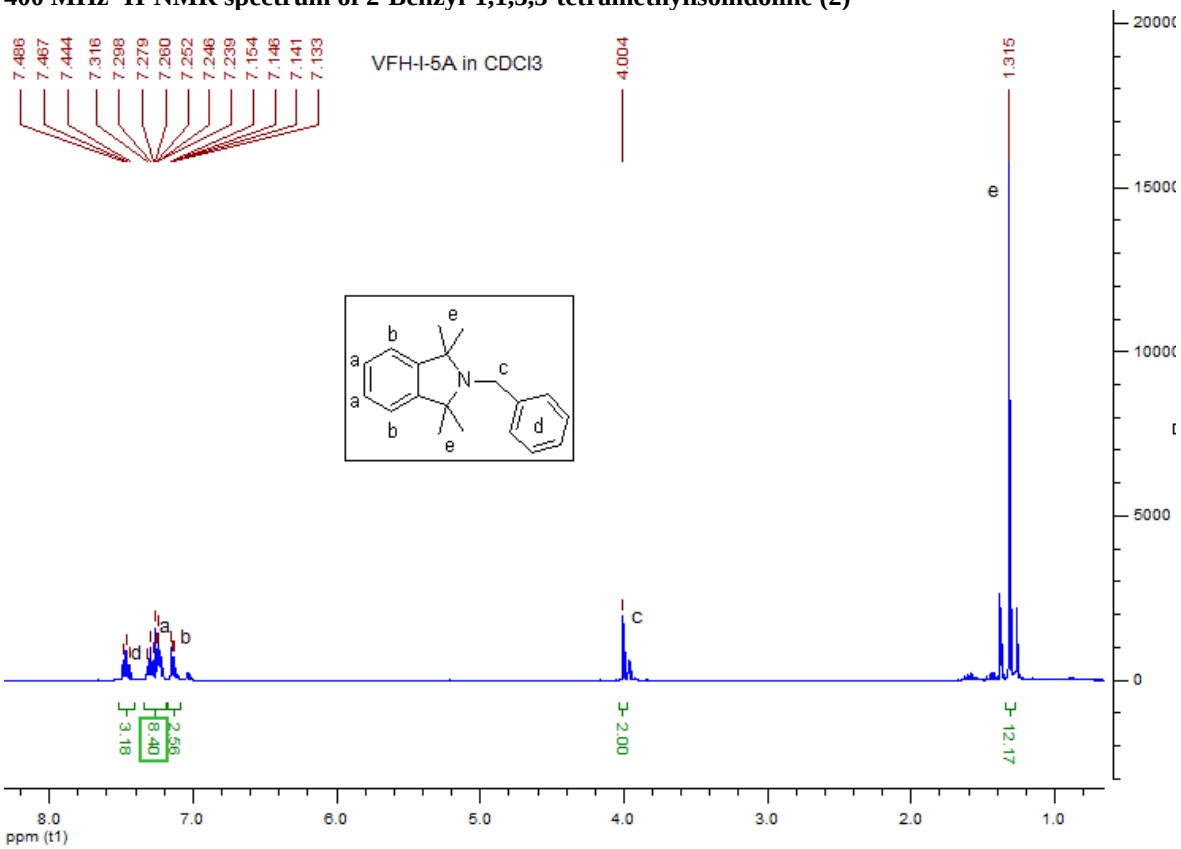
400 MHz ^{13}C-NMR spectrum of 2-benzylisoindoline-1,3-dione (1)



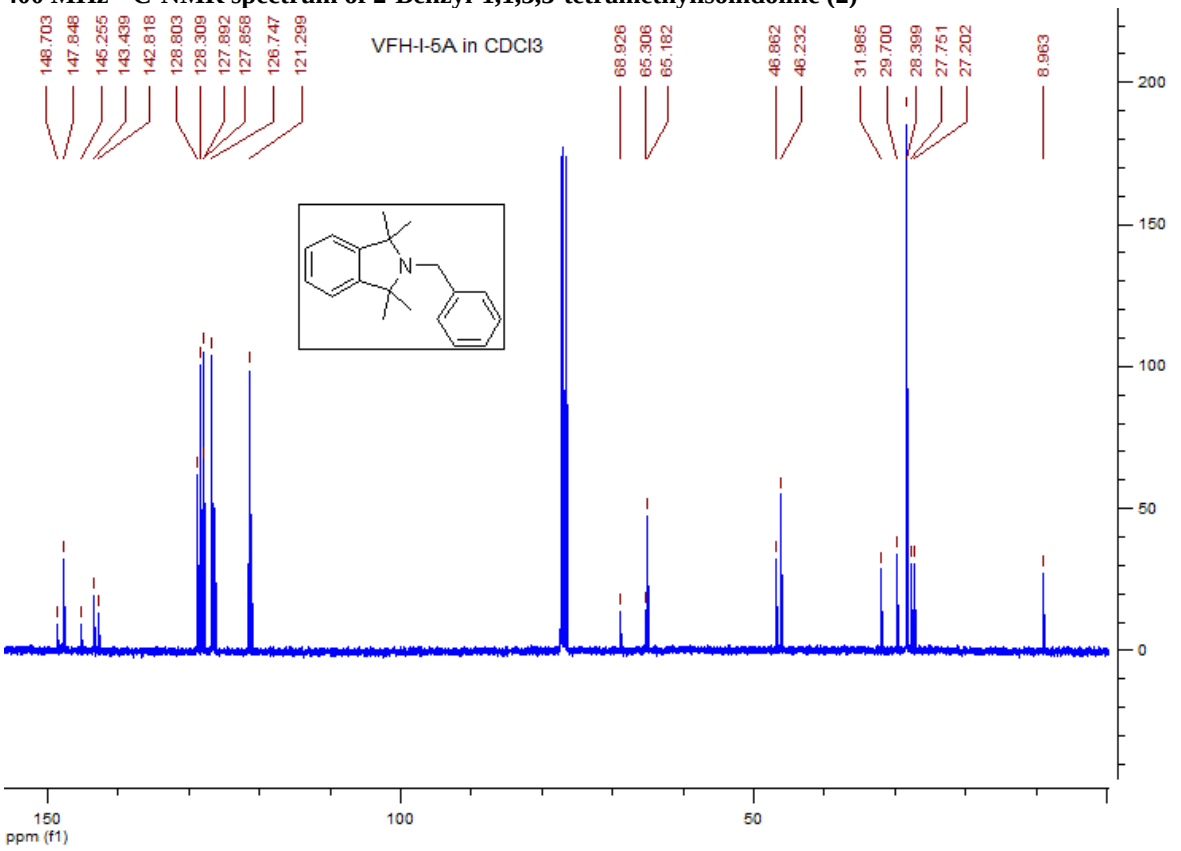
Mass Spectrum of 2-benzylisoindoline-1,3-dione (1)



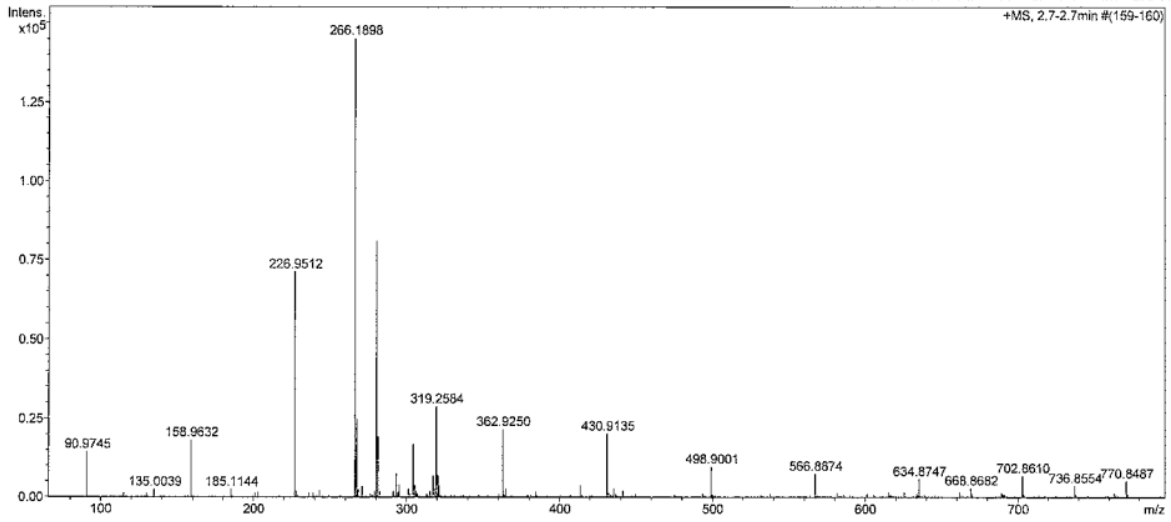
400 MHz ^{1}H-NMR spectrum of 2-Benzyl-1,1,3,3-tetramethylisoindoline (2)



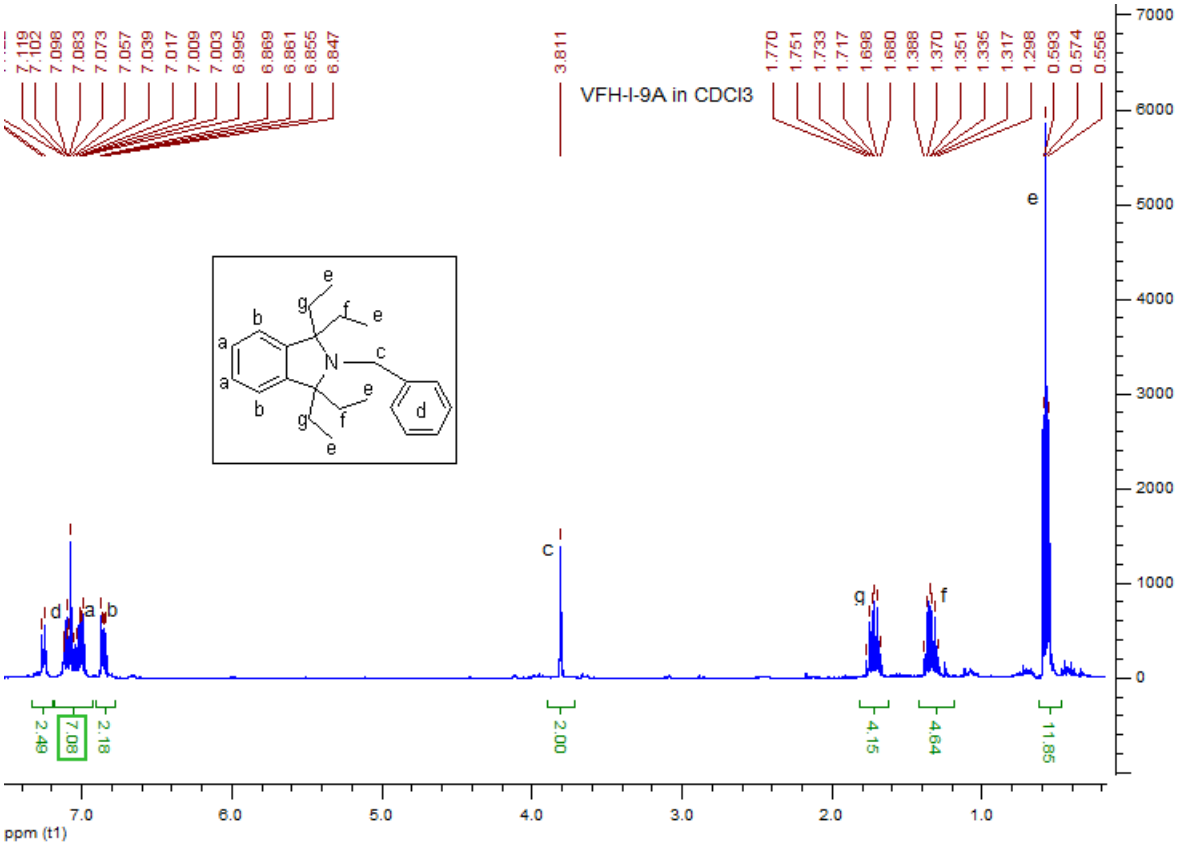
400 MHz ^{13}C-NMR spectrum of 2-Benzyl-1,1,3,3-tetramethylisoindoline (2)



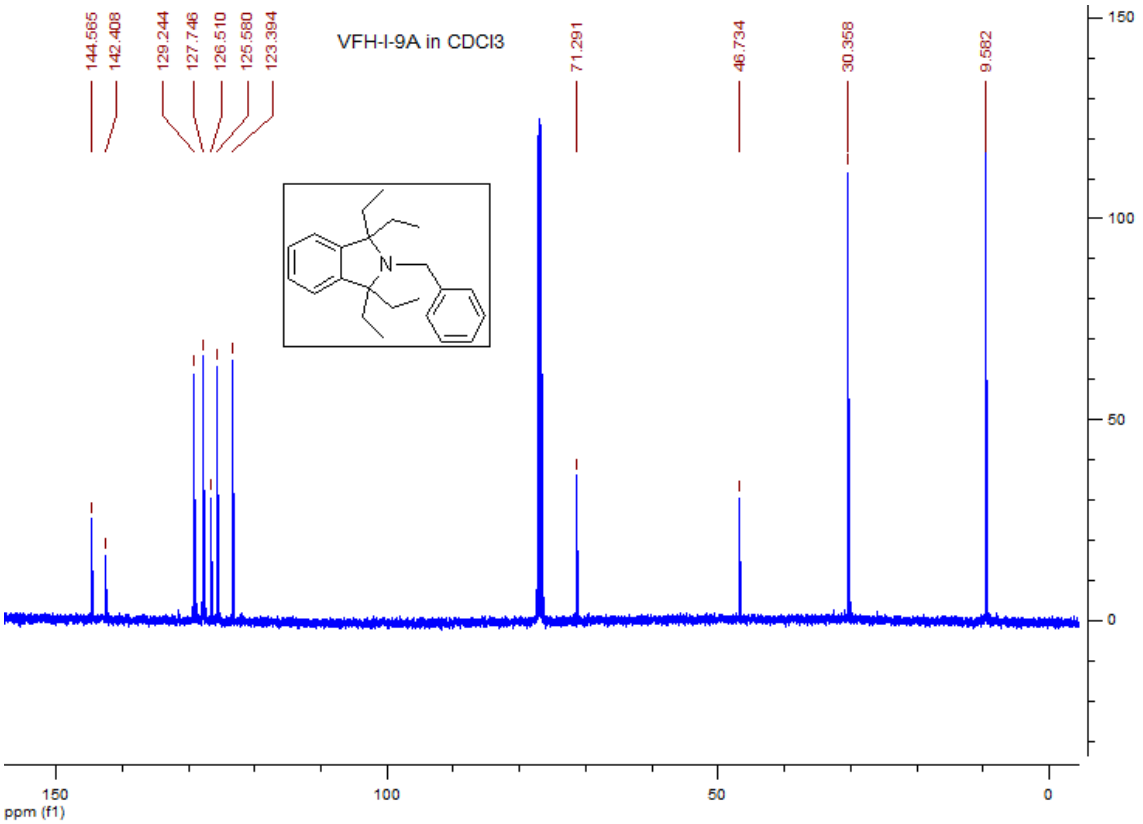
Mass Spectrum of 2-Benzyl-1,1,3,3-tetramethylisoindoline (2)



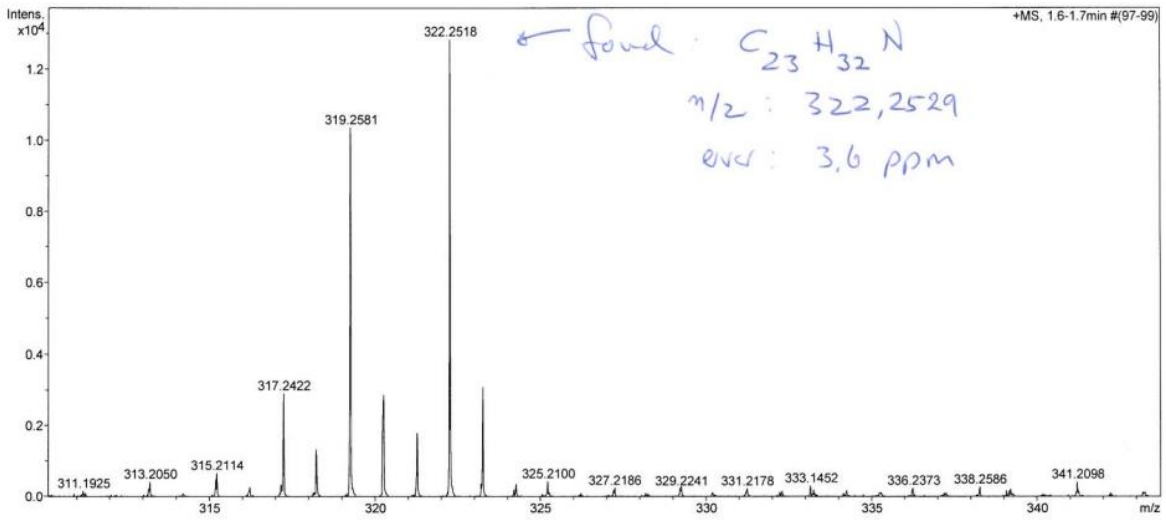
400 MHz ^{1}H-NMR spectrum of 2-Benzyl-1,1,3,3-tetraethylisoindoline (3)



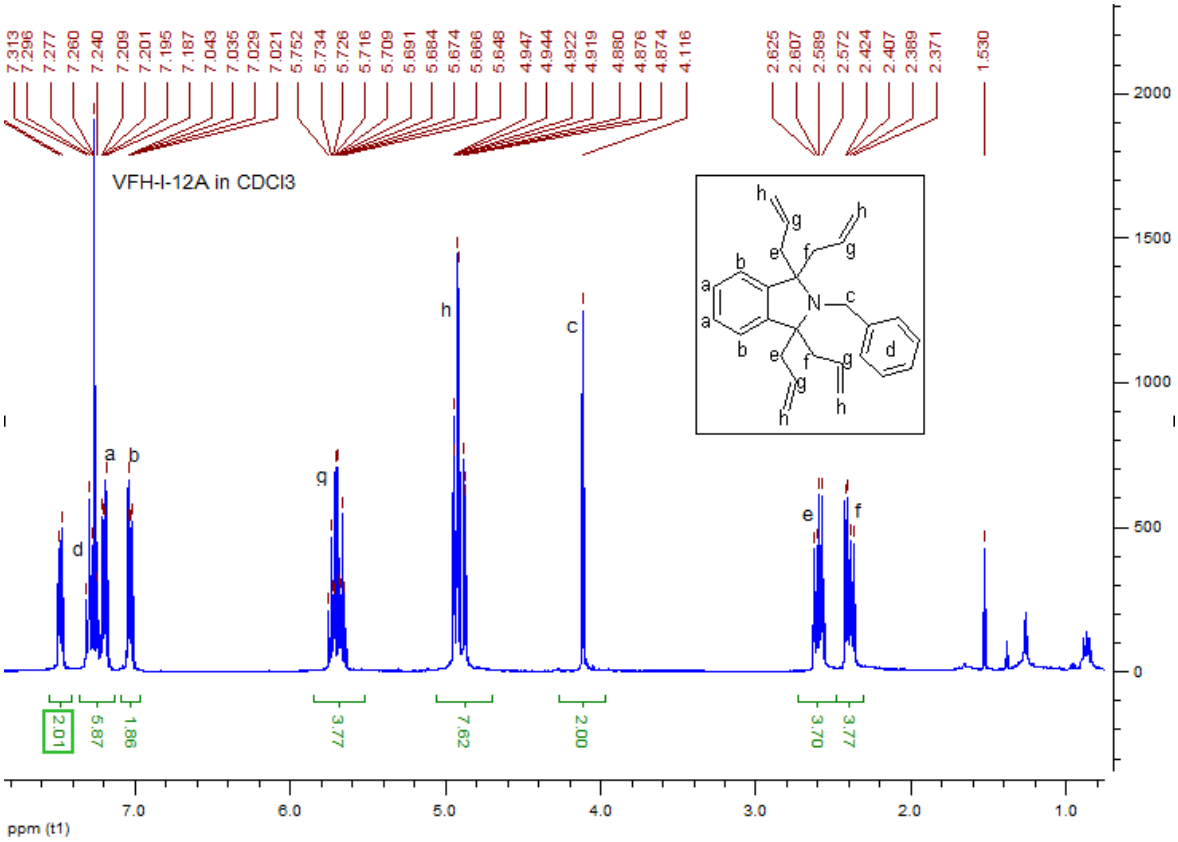
400 MHz ^{13}C-NMR spectrum of 2-Benzyl-1,1,3,3-tetraethylisoindoline (3)



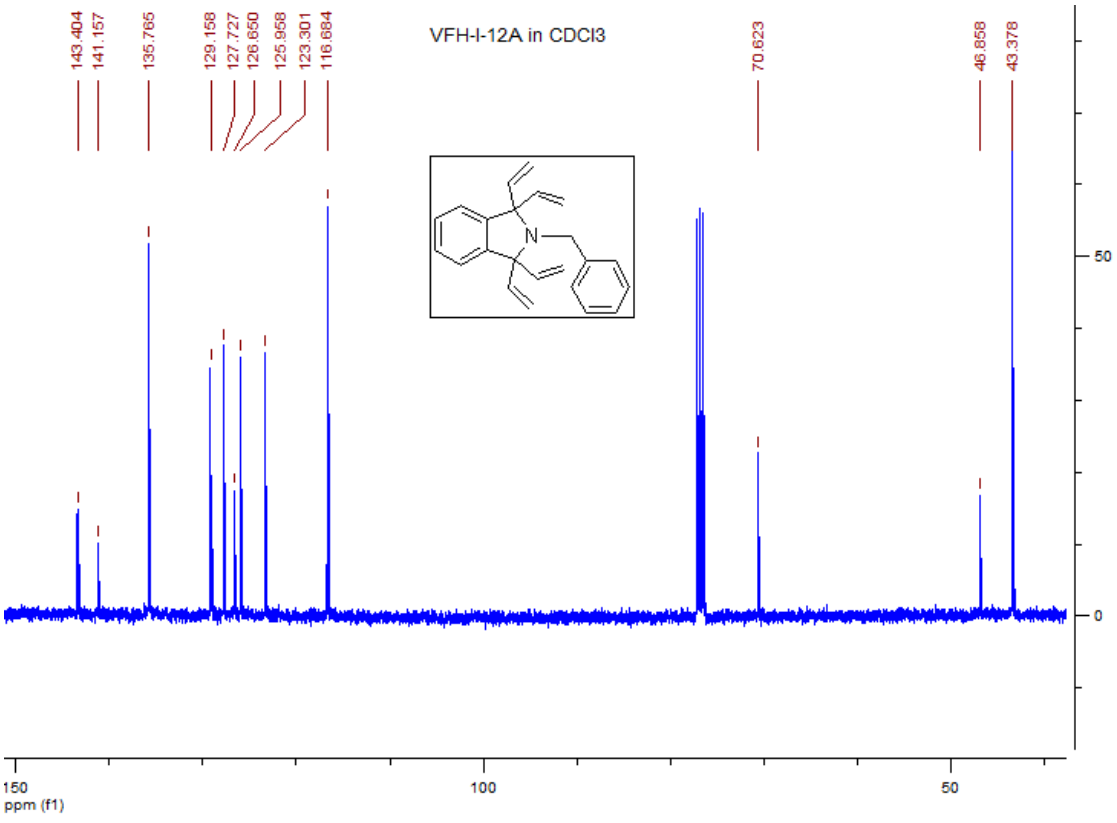
Mass Spectrum of 2-Benzyl-1,1,3,3-tetraethylisoindoline (3)



400 MHz ^{1}H-NMR spectrum of 2-Benzyl-1,1,3,3-tetraallylisoindoline (4)



400 MHz ^{13}C-NMR spectrum of 2-Benzyl-1,1,3,3-tetraallylisoindoline (4)



Mass Spectrum of 2-Benzyl-1,1,3,3-tetraallylisoindoline (4)