國 立 交 通 大 學

應用化學研究所

碩士論文

Ellipticine 全合成與 Tacamonine 合成研究

Synthesis of Ellipticine & Synthetic Approach to Tacamonine

研究生：謝昇穎

指導教授：何子樂 博士

中華民國九十四年八月

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所提論文 Ellipticine全合成與Tacamonine合成研究

合於碩士資格標準、業經本委員會評審認可。

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Ellipticine 全合成與 Tacamonine 合成研究

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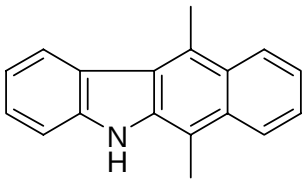
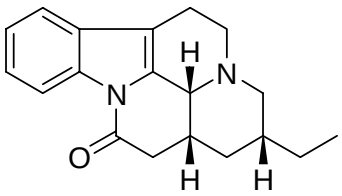
摘　　要

本論文共包含兩部分：以分子對稱性的觀點設計進行 Ellipticine 之全合成與 Tacamonine 合成研究。Ellipticine 工作已經完成：由茚烯（**39**）作為起始物經由八步可得 Ellipticine，總產率 13 %。Tacamonine 的部分則是利用雙甲酯（**83**）作為起始物，經一連串反應之後可得立體位向與 Tacamonine 相同的化合物（**91**），但此化合物無法順利脫去保護基，故需以其他的保護基替換方可繼續並結束此計畫。



Ellipticine



Tacamonine

Synthesis of Ellipticine & Synthetic Approach to Tacamonine

Student: Sheng-Ying Hsieh Advisor: Tse-Lok Ho

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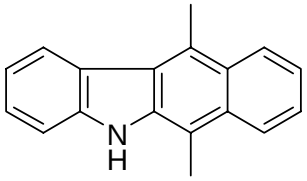
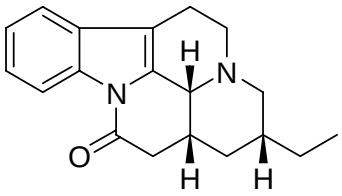
ABSTRACT

The total synthesis of ellipticine based on the concept of symmetry has been accomplished. 4,7-Dimethylindene (**39**) was used as the starting material and ellipticine was synthesized in 8 steps in 13 % overall yield. On the other hand, *cis*-1,3-dicarbomethoxycyclopent-4-ene (**83**) was chosen as the starting material for the synthesis of tacamonine. Compound **91** with the same stereochemistry of tacamonine was synthesized in 8 steps. Unfortunately, the bis-ketal of **91** could not be deprotected. Change to other protection groups is necessary for bringing this project to a successful conclusion.



Ellipticine



Tacamonine

致　　謝

首先感謝蔡蘊明老師與邱勝賢老師兩位口試委員對於本論文的建議與改進，使這本論文得以更臻完備。更感謝何子樂老師兩年來的諄諄教誨，使我在專業領域與待人接物上都有更深一層的體悟，也祝老師退休後能身心愉快身體健康。陳群貴、陳榮傑兩位學長以及稍早離開的鄭文誠學長，多謝你們在這兩年期間給予的幫助以及鼓勵，讓我成長不少獲益良多，我會懷念這段一起做實驗和每周六 meeting 的日子。也要感謝鍾文聖、陳金鑫、許千樹、吳獻仁、陳月枝、陳登銘老師實驗室的學長姐學弟妹在實驗上藥品的大力贊助。也感謝渲姝、宜錦這兩年來的幫助，借我 UV 燈與加熱器可以多作一點實驗。

兩年甘苦，如人飲水，冷暖自知。感謝老爸、老媽還有大姐二哥以及美麗可愛的女友姿利，你們是我永遠的避風港，溫暖的依靠，讓我無後顧之憂地盡情追逐自己的夢想。也感謝我的好朋友們：小 vo、小何夫婦、小儒、蘋果、耐吉、小狐狸、茂峰、阿曼、學穎、君豪、打狗、詩穎、kuwu、筱芳、逸婷…等等許許多多的人（以暱稱代替真名應該更為親切吧），多謝你們平日的關心以及適時的安慰鼓勵，以後也要保持聯絡。在交大六年要感謝的人太多了，也許，就謝天吧，也謝土地公的保佑，讓我這六年平安順利。

最後恭喜自己，能畢業的感覺真好。未來加油 :）

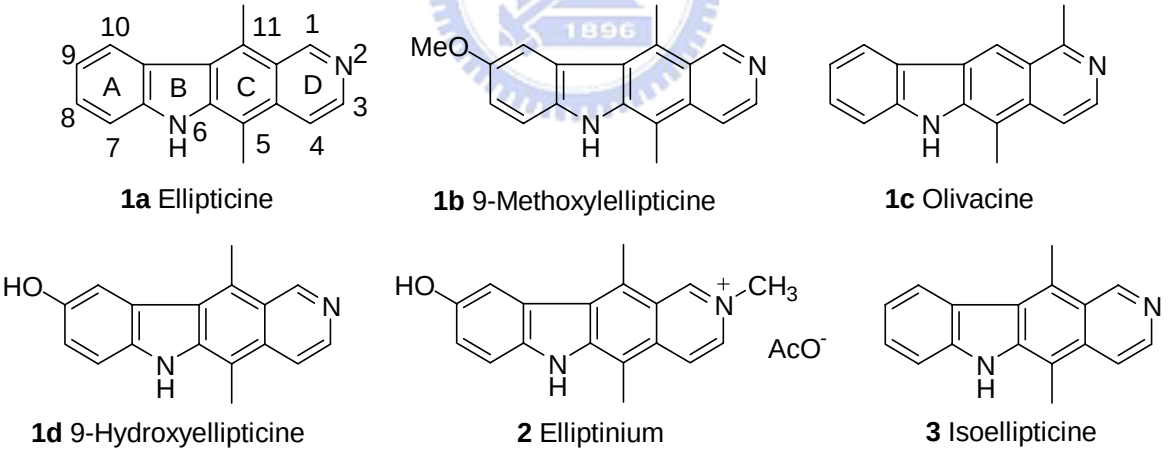
目　　錄

第一章　緒論

（一）Ellipticine全合成：

奧克羅木（Ochrosia），南美紅豆杉（Aspidosperma），馬蹄花（Tabernaemontana）與馬錢（Strychnos）這類夾竹桃科（Apocynaceae）的植物中存在某些結構為6*H*-pyrido[4,3-*b*]carbazole 的天然物（Fig. 1.1），此類天然物的結構為carbazole與pyridine的併環，例如ellipticine（**1a**，橢圓玫瑰樹鹼，在 5 與 11 碳上各有一個甲基）、9-methoxylellipticine （**1b**）、olivacine（**1c**）。在一些動物及人類身上，這些天然物已被證實具有抗癌的功效。另外，9-hydroxyellipticine （**1d**）、elliptinium（**2**，2-methyl-9-hydroxyellipticinium acetate）也於臨床上用以治療急性骨髓白血病（myeloblastic leukemia）、乳癌等疾病[1]。

Fiq. 1.1



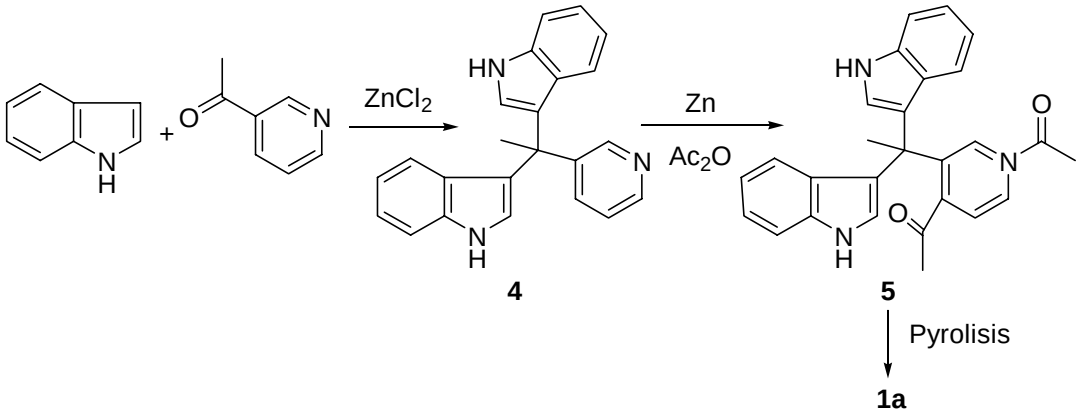
1a Ellipticine　**1b** 9-Methoxylellipticine　**1c** Olivacine

1d 9-Hydroxyellipticine　**2** Elliptinium　**3** Isoellipticine

Ellipticine學名為 5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazole，於 1959 年第一次由Goodwin教授等人從*Ochrosia elliptica* Labill植物葉片中單離出來[2]。*Ochrosia elliptica* Labill是一種小型熱帶常綠樹，屬於夾竹桃科的植物，盛產於美國佛羅里達州，在澳洲、阿達曼群島與一些太平洋島嶼中也可見其蹤跡。之後ellipticine及其衍生物也在許多其他的植物中被發現。

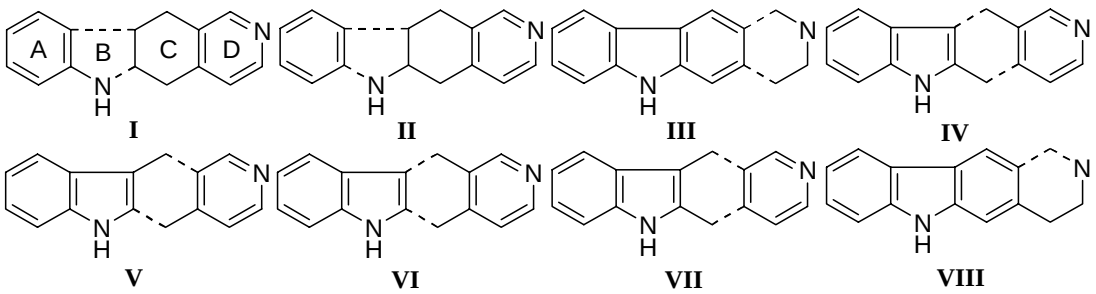
1959 年，Woodward教授等人第一次將ellipticine的結構建立出來[3]，並完成了第一篇的全合成。他們將吲哚與 3-acetylpyridine進行縮合得 **4**，接著以鋅與醋酸酐在迴流下進行反應，產物 **5** 在高溫真空下裂解而得ellipticine，但產率僅 2 %（Scheme 1.1）。

Scheme 1.1. by R. B. Woodward et al. (1959)



截至今日，關於ellipticine的全合成論文約有六十多篇，回顧性的文章約有六篇[4]，分別介紹各時期ellipticine的全合成路徑。Sainsbury教授將 1977 年以前ellipticine的全合成分為三類：一是以Fischer indolization建構B環完成ellipticine的骨架、一是以carbazole的衍生物作為前驅物再建構D環、另一則是最後完成C環（參考Fig. 1.1 的環編號）。1977 至 1982 年期間關於ellipticine的全合成則由Shannon等人分類整理，他們依循Sainsbury教授的方法並將這三個分類分別命名為B-型、C-型以及D-型合成法，代表著骨架最後完成的部分。另外， Gribble教授等人則將 1977 年至 1984 年關於ellipticine以及其部分衍生物的全合成整理分為八類，虛線代表合成pyridocarbazole骨架的關鍵鍵結（Fig. 1.2）。

Fig. 1.2. Synthesis Strategy of Ellipticine

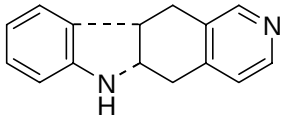


另外，Gribble 教授於 1991 年時再將其多年合成 ellipticine（**1a**）、9-methoxylellipticine（**1b**）、olivacine（**1c**）、9-hydroxyellipticine（**1d**）以及 elliptinium（**2**）的工作作一整理

並發表回顧性的文章。

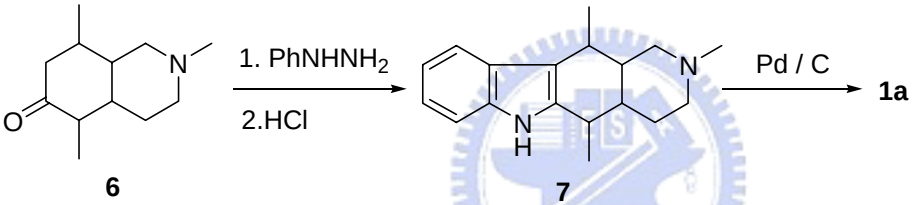
以下依 Gribble 教授所分類的方法簡介部分合成 ellipticine 的方法：

Strategy I



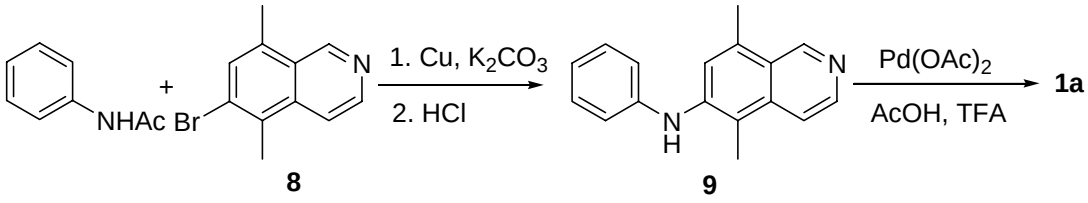
1964 年 Stillwell 與 Woodward 合成出一個傳統製 6*H*-pyrido[4,3-*b*]carbazole 骨架的方法，便是以此策略進行（Scheme 1.2）。此合成以 decahydroisoquinol-6-one（**6**） 行 Fischer indolization 而得 **7**，產率 82 %，但由於最後以 Pd / C 脫氫反應的步驟產率很低，故此法未有實際應用價值。

Scheme 1.2. by R. B. Woodward et al. (1964)



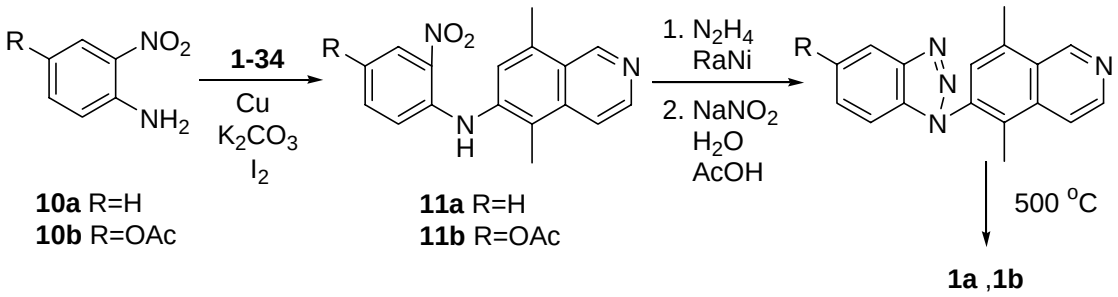
另外，Miller 等人於 1980 年利用 Ullmann coupling 作為橋聯 A 與 B 環的方法，再利用醋酸鈀進行環化反應，但此步驟產率僅 15-25 %。（Scheme 1.3）

Scheme 1.3. by R. B. Miller et al. (1980)



由於 Scheme 1.3 的結果並不理想，Miller 於 1983 年發表了改善的途徑。將 **11** 進行偶氮化再行環化，最後一步產率可提升至 70 %。（Scheme 1.4）

Scheme 1.4. by R. B. Miller et al (1983)

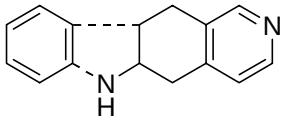


10a R=H
10b R=OAc

11a R=H
11b R=OAc

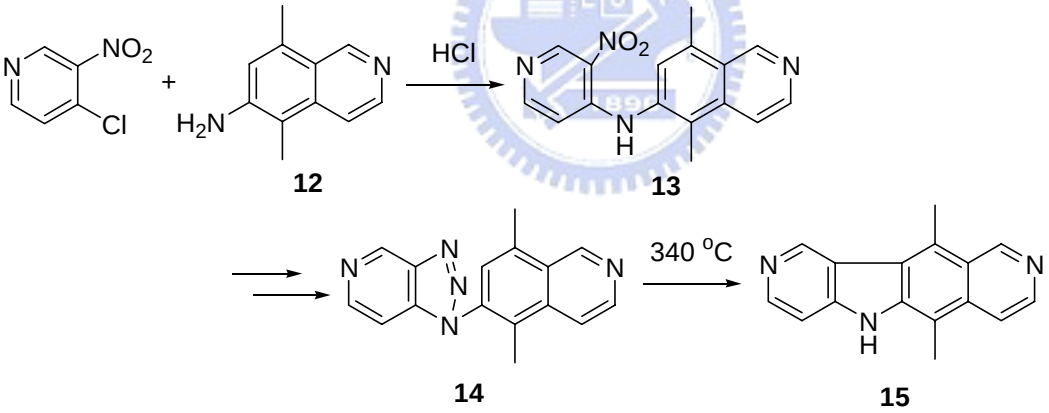
1a ,**1b**

Strategy II



利用此策略合成 ellipticine（**1a**）並未在文獻上發表過，但 6,11-dimethyl-5H-pyrido[3',4':4,5]pyrrolo[2,3-g]isoquinoline（**15**）則是以此作為合成策略。由 1979 年 Bisagni 利用前驅物 **12** 首度合成。(Scheme 1.5)

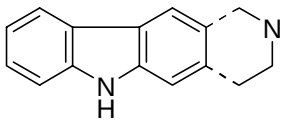
Scheme 1.5. by Bisagni et al. (1979)



12 **13**

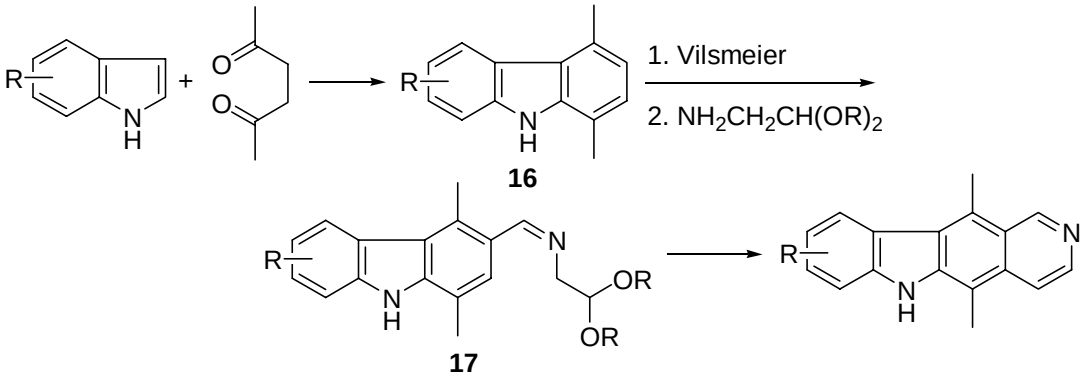
14 **15**

Strategy III

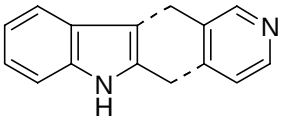


Cranwell 等人利用己二酮與吲哚生成 **16** 並進一步獲得 **17**，最後環合 D 環成 ellipticine。以此策略為合成方法最後的中間體多與 **17** 相近。

Scheme 1.6. by Cranwell et al. (1962)

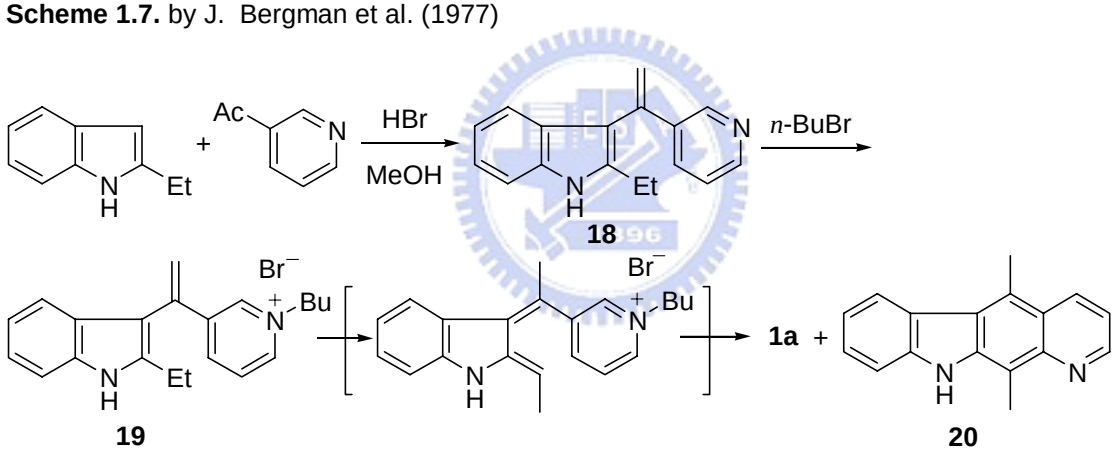


Strategy IV

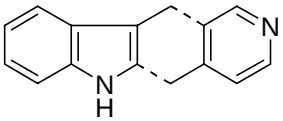


Bergman 等人於 1977 年將 1-45 於高溫下進行 C 環的環化反應，如 Scheme 1.7 所示。

Scheme 1.7. by J. Bergman et al. (1977)

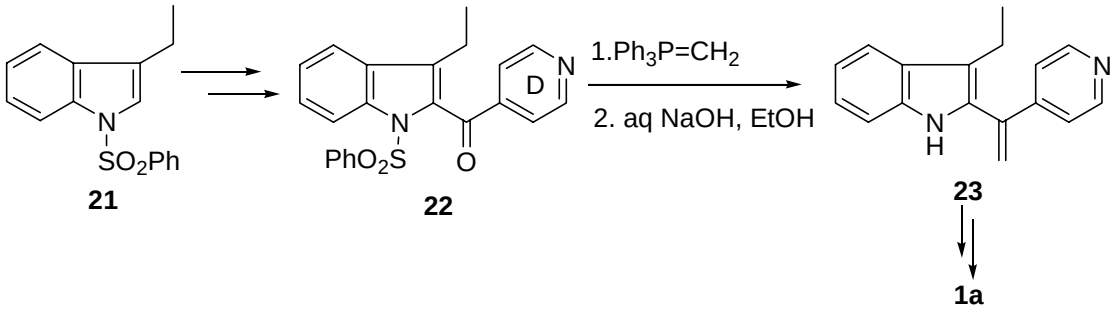


Strategy V

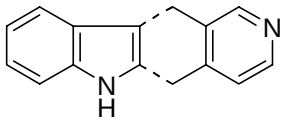


Kano 所使用的方法與 Bergman 類似（**19** 與 **22**），**23** 也是經由高溫後可得 **1a**，只是前驅物位向不同，加上利用 D 環分子內的對稱性，在環合時僅生成 **1a**。（Scheme 1.8）

Scheme 1.8. by Kano et al. (1981)

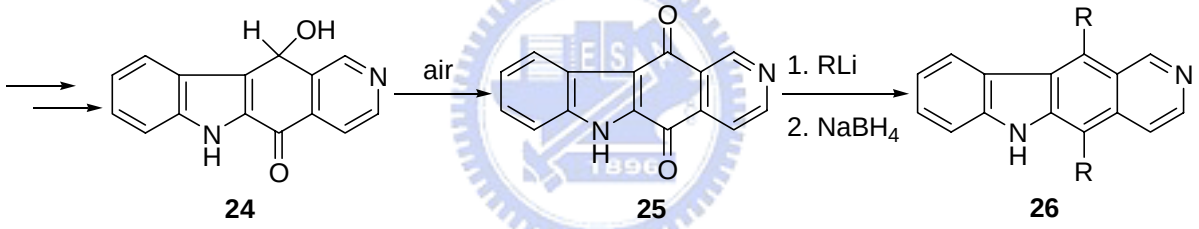


Strategy VI

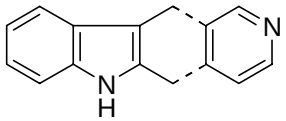


如 Scheme 1.9，Kutney 等人提供了一條便捷製 **26** 的方法。經由不同的鋰試劑，5 與 11 位上可以有不同的取代基。

Scheme 1.9. by Kutney et al. (1982)

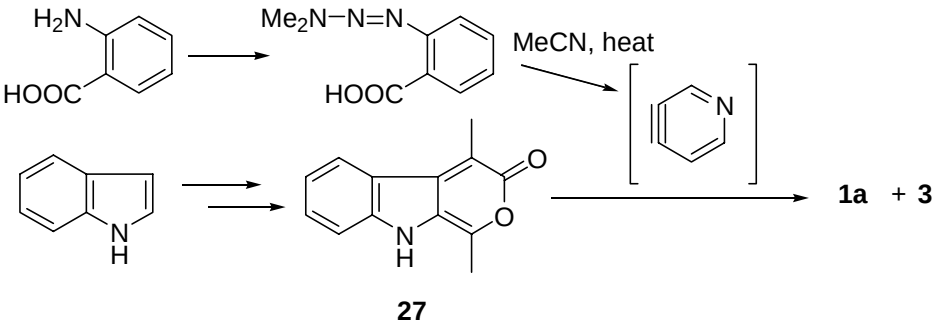


Strategy VII

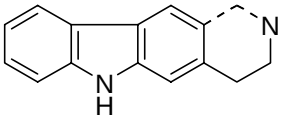


1984 年 Moody 等人利用 **27** 進行環加成反應，此結果會產生兩種異構物（ellipticine 與 isoellipticine）。（Scheme 1.10）

Scheme 1.10. by Moody et al. (1984)

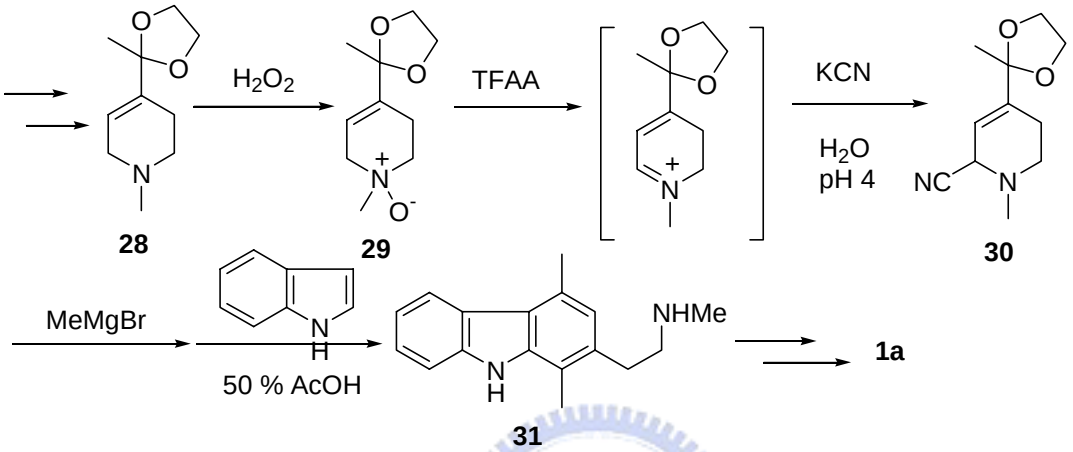


Strategy VIII



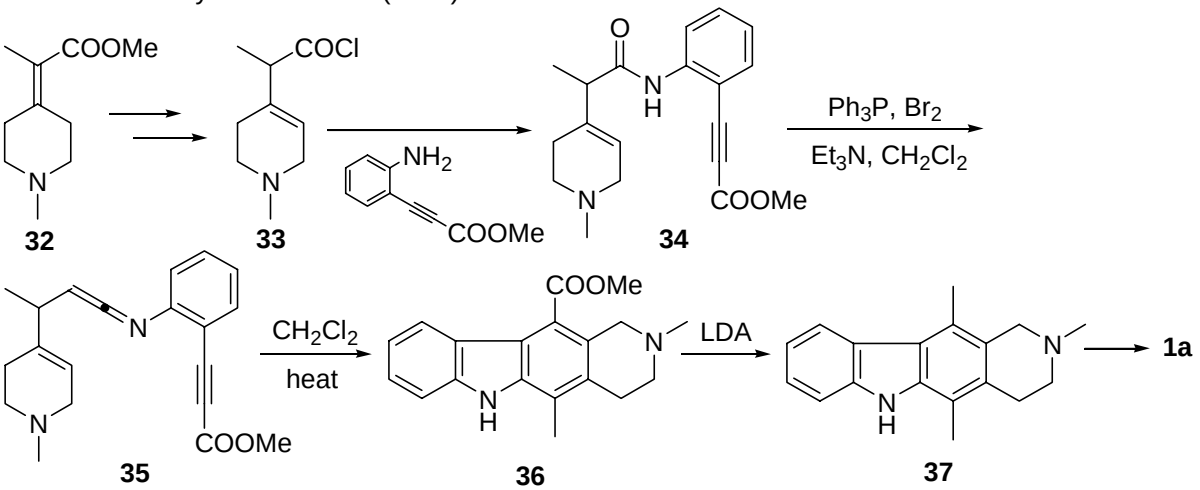
Scheme 1.11 為 Husson 利用合成 **1c** 相同的方法合成 Ellipticine。

Scheme 1.11. by Husson et al. (1981)



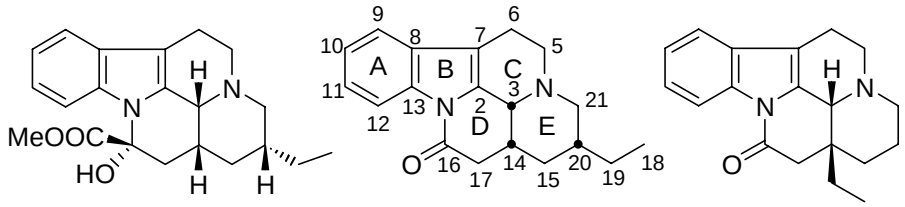
另外值得一提的是，Ghosez 教授於 1985 年以一特別的方法合成咔唑，並利用此法形式合成 Ellipticine。如 Scheme 1.12 所示，**35** 經加熱可環合成化合物 **36** 此一具 pyridocarbazole 骨架的分子。

Scheme 1.12. by Ghosez et al. (1985)



（二）Tacamonine 合成研究：

Tacamonine (**38**) 屬於 tacamine 類吲哚生物鹼，不同的是其在 D 環是一個內醯胺。另由於 E 環三個三級碳上的氫立體關係皆為同側(*cis*)，此特殊的結構使我們對於合成 tacamine 類生物鹼產生高度的興趣。

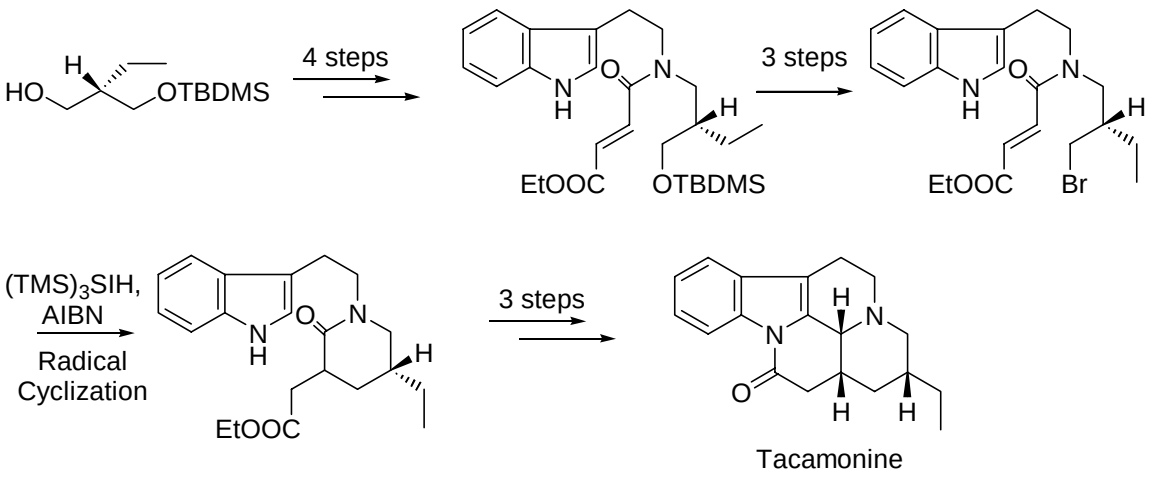


Tacamine　　**38** Tacamonine　　Eburnamonine

Tacamonine首度於 1984 年由Beek等人[5]從*T. eglandulosa*的葉子（生長在中非森林的小型藤本植物，夜晚開花，薩伊地區的住民以其根部治療毒蛇的咬傷）以乙醇萃取並單離出來，Beek當時共分離出了二十二種生物鹼，而其中十二種為新的未知物。然而較意外的是早於 1982 年Levy已經合成此化合物[6]。目前為止有五組人發表tacamonine的全合成[7]。分列如下：

1994 年，Fukumoto 教授不對稱合成 tacamonine，11 個步驟，總產率為 3 %（Scheme 2.1）。

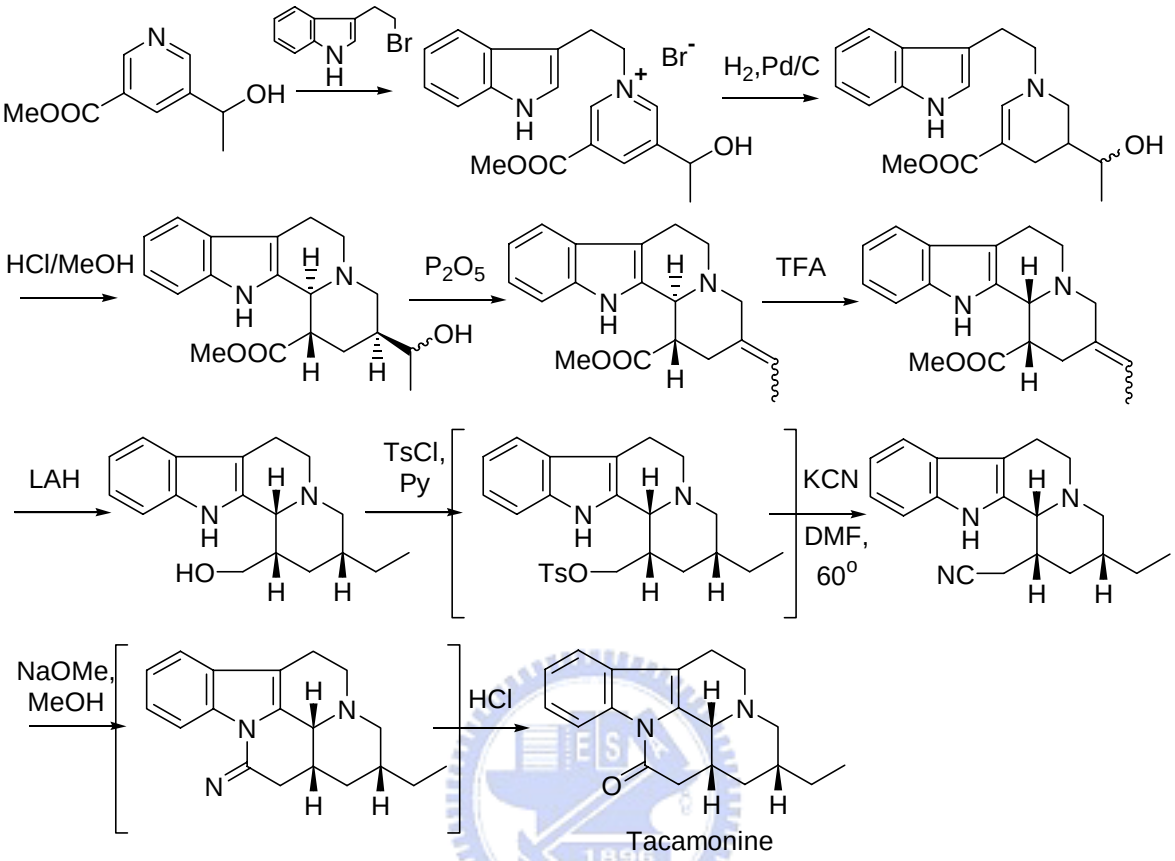
Scheme 2.1. by K. Fukumoto et al. (1994)



另外，Lounasmaa 的團隊花了數年時間合成出 tacamonine（Scheme 2.2），對於 3 位

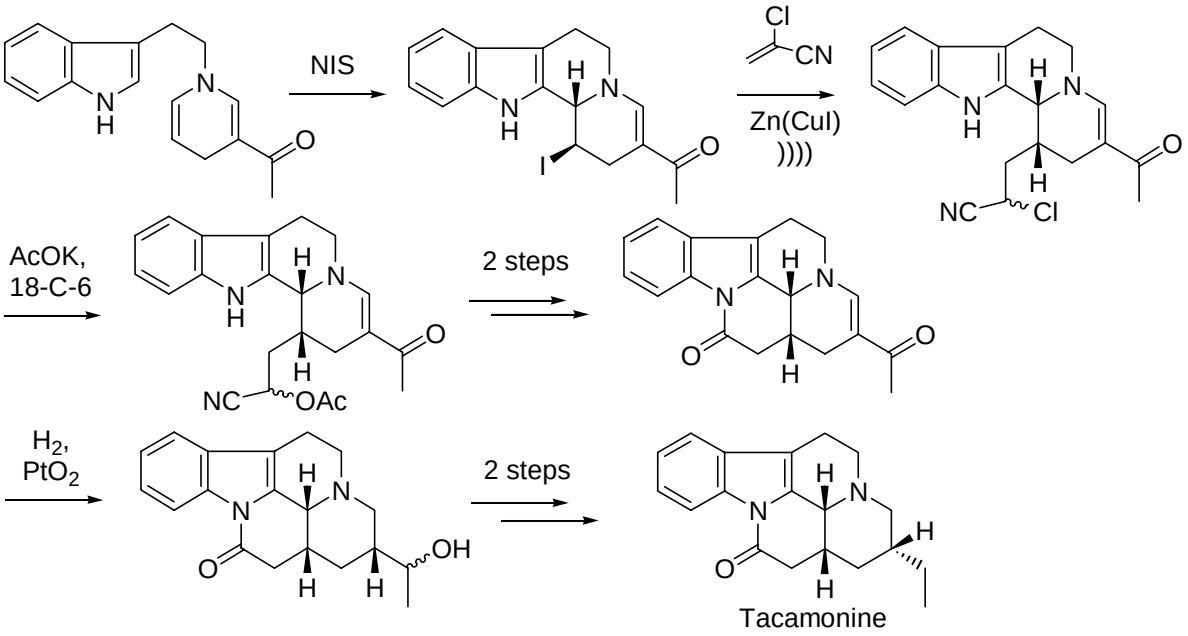
上的三極碳作了許多異構化的研究。

Scheme 2.2. by M. Lounasmaa et al. (1998)



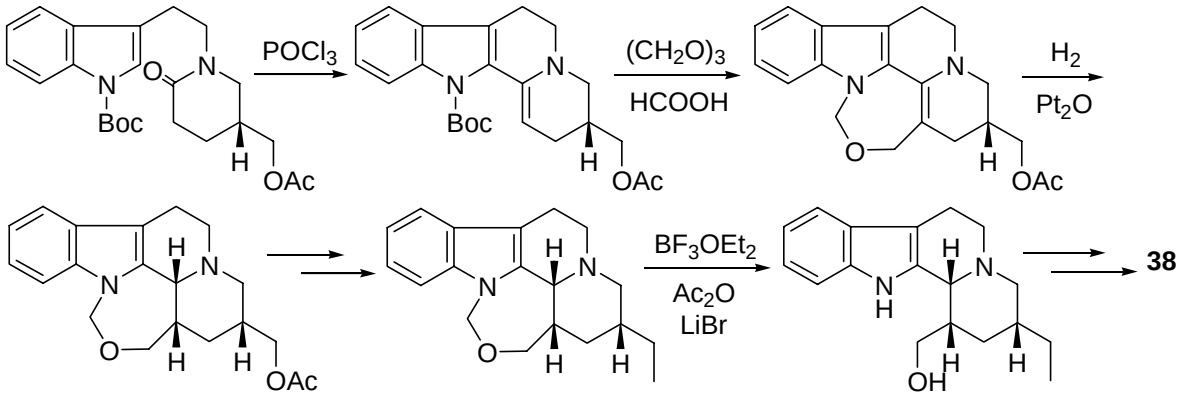
2001 年 Bosch 教授以 Lounasmaa 於 1982 年合成出的中間體為起始物，再經八個合成步驟取得 tacamonine，如 Scheme 2.3 所示。

Scheme 2.3. by J. Bosch et al. (2001)



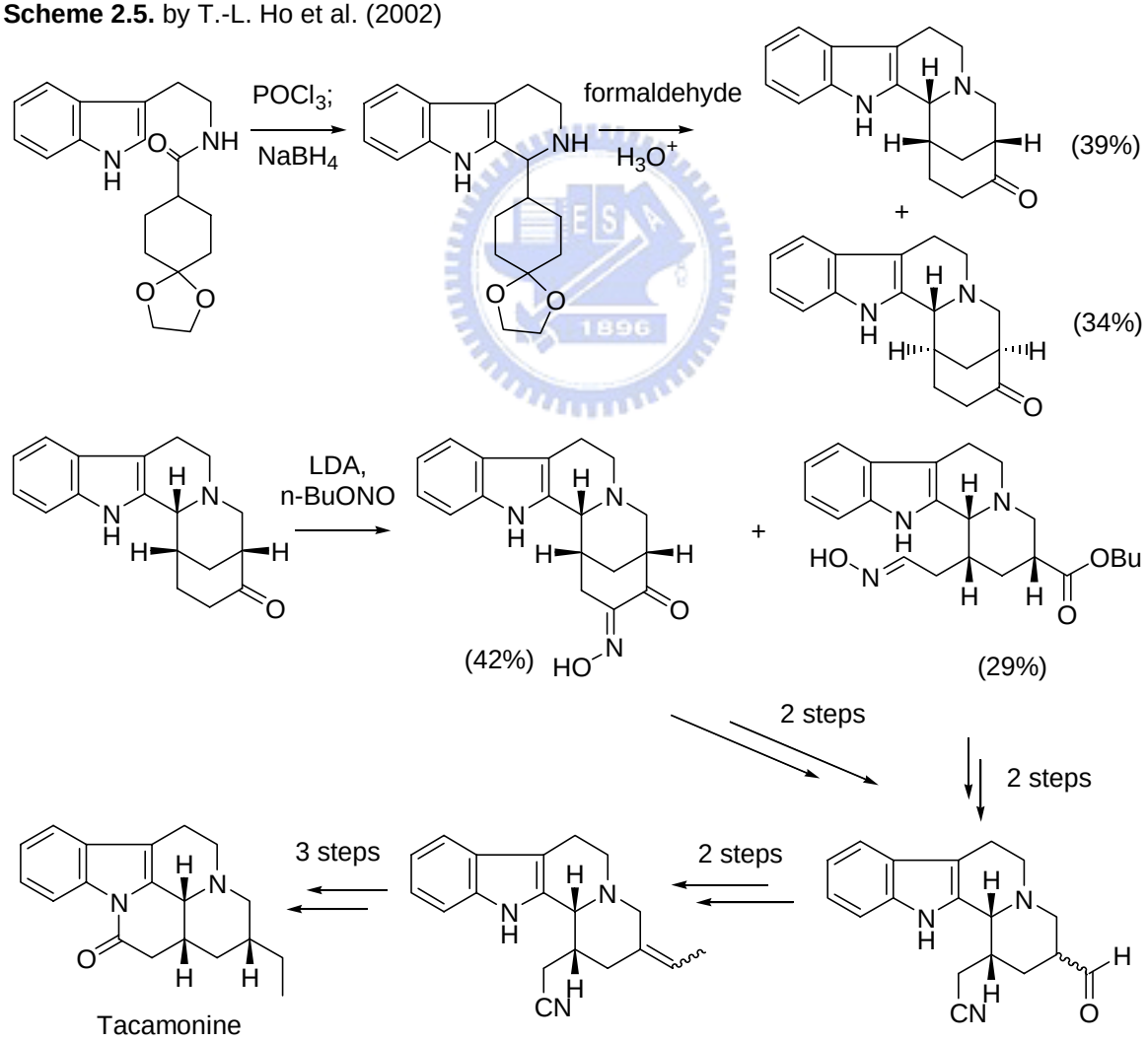
同年，Lesma教授不對稱合成tacamonine，如Scheme 2.4所示。

Scheme 2.4. by G. Lesma et al. (2001)



本實驗室於 2002 年發表 tacamonine 的全合成（Scheme 2.5）。

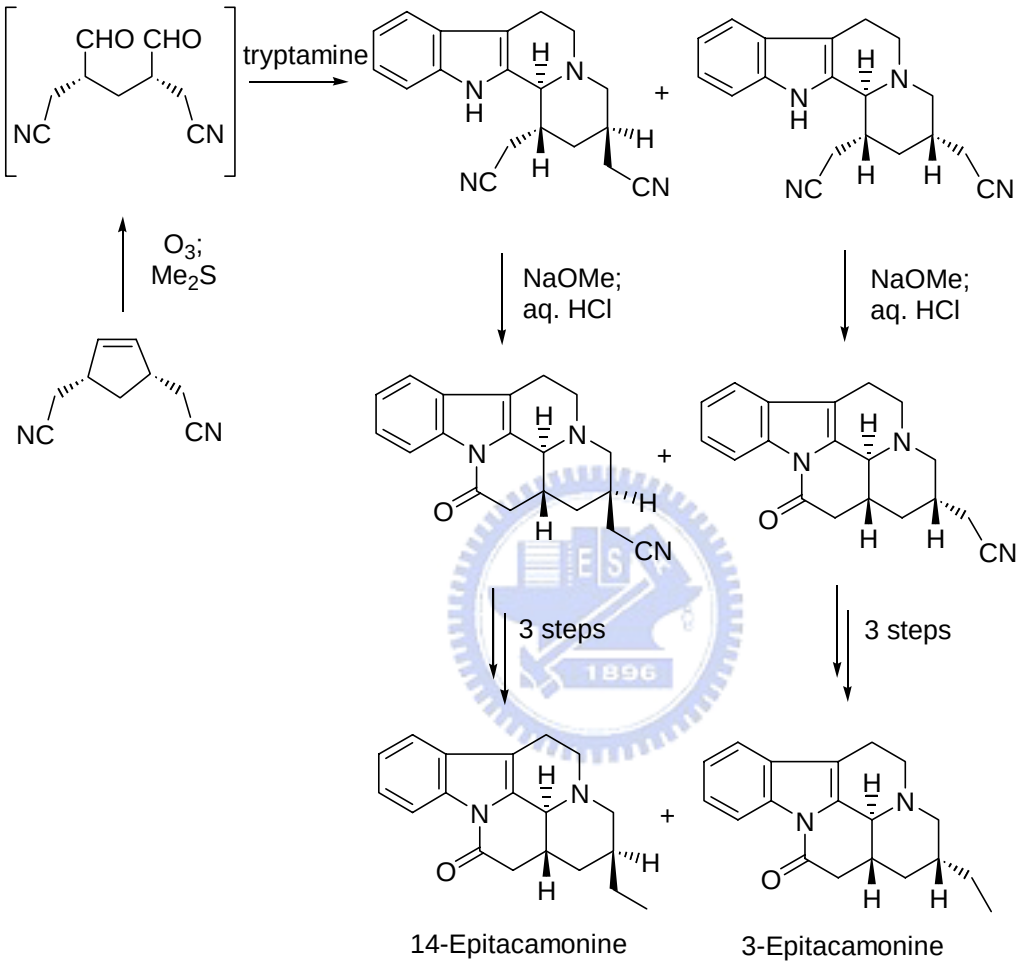
Scheme 2.5. by T.-L. Ho et al. (2002)



另外，本實驗室又嘗試以對稱的概念合成tacamonine[8]，雖得異構物 12-epitacamonine

及 3-epitacamonine（Scheme 2.6），但由此工作我們得知E環上的兩邊碳鏈不能是自由的，在一開始即必須為一個環以避免在後續的反應中造成異構化，於是我們將嘗試以其他起始物但由類似的路徑進行合成tacamonine。

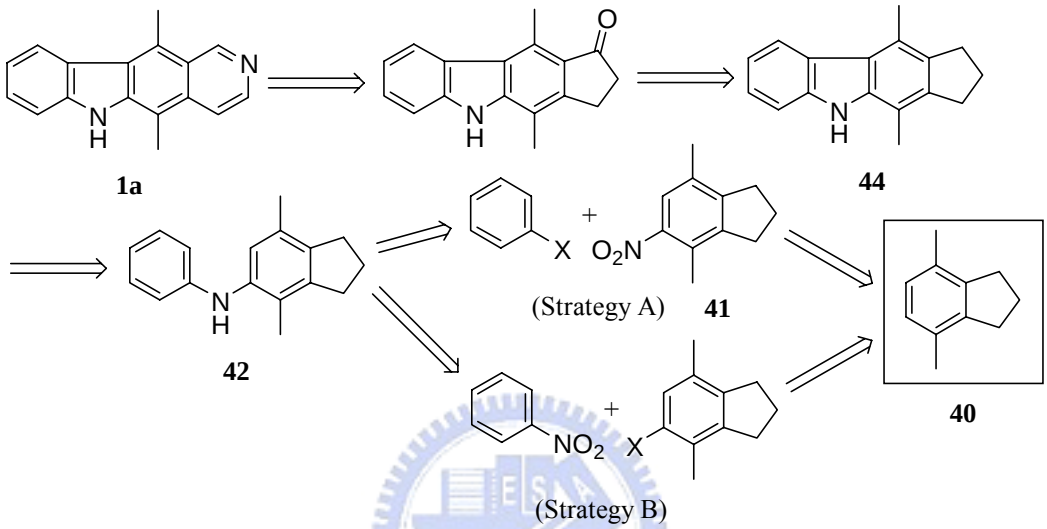
Scheme 2.6. by T.-L. Ho et al. (2001)



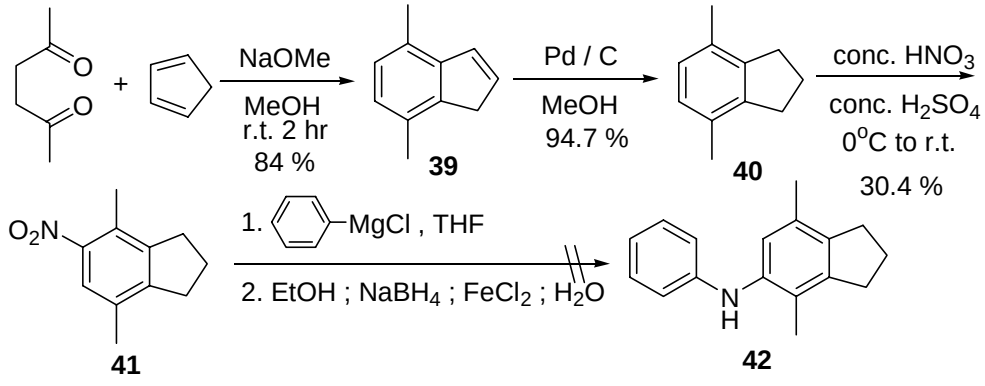
第二章 結果與討論

（一）Ellipticine 全合成：

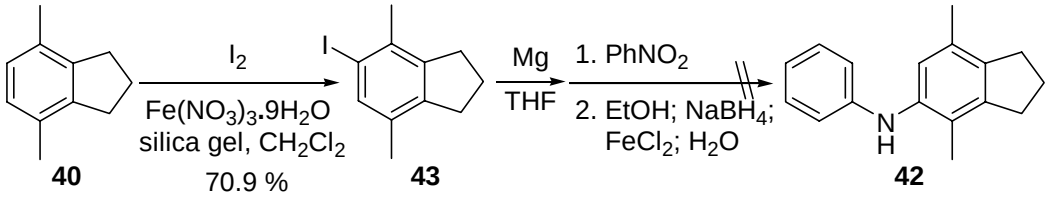
我們計畫以對稱[9]的分子作為起始物來合成ellipticine。其溯徑分析：



由P. Knochel教授所發表的文獻[10]得知$ArNO_2$可與ArMgX試劑於低溫下反應，經由氯化亞鐵與硼氫化鈉還原後得二芳胺的產物，並具有很好的產率。如果用化合物 **41** 與鹵化苯合成一二芳胺 **42**，再進行C-C成鍵則可建立一個咔唑與環己烷併環的結構 **44**，由於 **44** 的咔唑環上氮的孤對電子影響，應可選擇性氧化五員環上的碳，再經由Schmidt反應引入氮原子或在α-碳上引入OAc的官能基，則皆有機會合成出ellipticine **1a**。以下是我們的實驗結果。

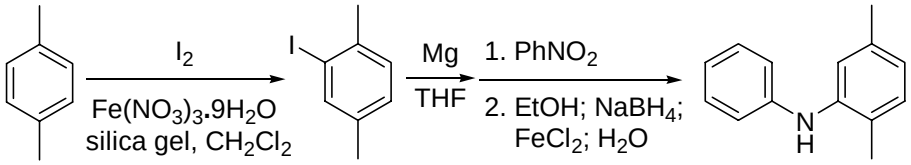


茚烯 **39**[11]可經由 2,5-己二酮與環戊二烯在甲醇鈉下反應獲得，產率 84 %。再經氫化可得indane **40**，產率 94.7 %。化合物 **40** 在濃硝酸與濃硫酸下硝化而生成化合物 **41**，但利用Knochel的方法將化合物 **41** 與PhMgCl進行反應卻失敗，所以我們嘗試先將化合物 **40** 進行鹵化再與硝基苯進行反應（Strategy B）。



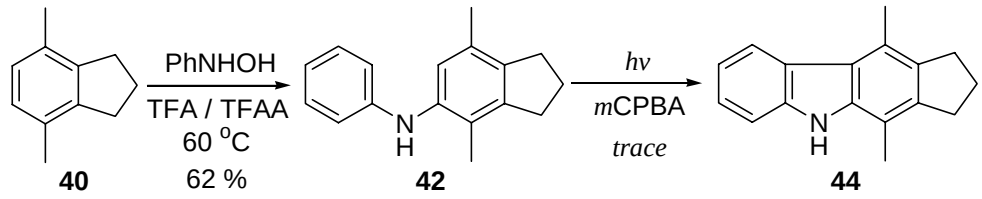
40 **43** **42**

由於化合物 **40** 經由一般溴化反應所得的結果，有單一溴化也有雙溴化，並不理想。再者，從R. Tilve提供的方法[12]，可以只碘化單一位置，且化合物 **40** 是一對稱的分子，所以不論苯環上的哪個位置被碘化都是相同的結果。故我們將化合物 **40** 依Tilve教授的方法碘化得化合物 **43**，產率 70.9 %。但將化合物 **43** 與硝基苯進行反應仍然失敗。（註：此處不採用將 **41** 還原並與鹵苯以過渡金屬鈀的催化劑進行coupling的原因在於此類反應常常需要在絕氧除水的環境下處理，也需要搭配一些配基以利反應，並不適合在我們實驗室進行。）

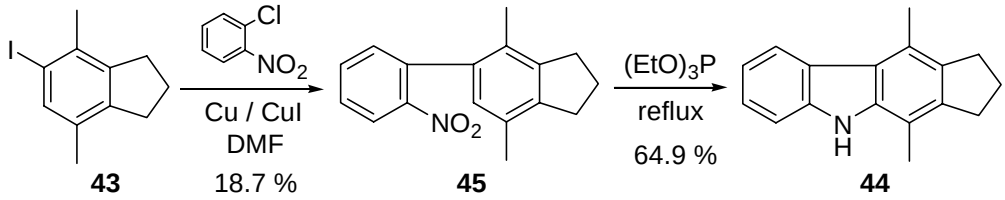


我們嘗試以碘化對二甲苯與硝基苯進行 Knochel 的模型反應，可得到預期的產物，至於無法取得化合物 **42**，原因不明。

從T. Okamoto的報告[13]得知，在三氟醋酸下PhNHOH可與苯反應得二苯胺。H. Takeuchi教授發現此反應在較高的溫度下會有較好的產率[14]，並且若存在三氟醋酸酐則產率又更高，所以我們將化合物 **40** 與PhNHOH溶於三氟醋酸與三氟醋酸酐，並將溫度提升至 60°C進行反應而得化合物 **42**（溫度高於 60°C已無太大變化，故將此定為反應溫度）。

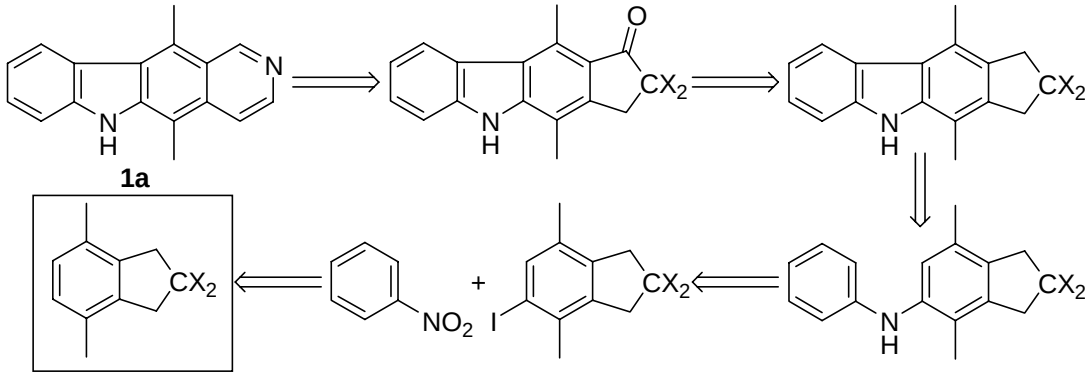


將化合物 **42** 進行光化學反應[15]可得化合物 **44**，但是此環化的產率相當低。我們嘗試使用許多方法[16]來進行此一反應，但結果都是不如理想，於是我們採取另一途徑來獲得足夠的化合物 **44**。如下所示：



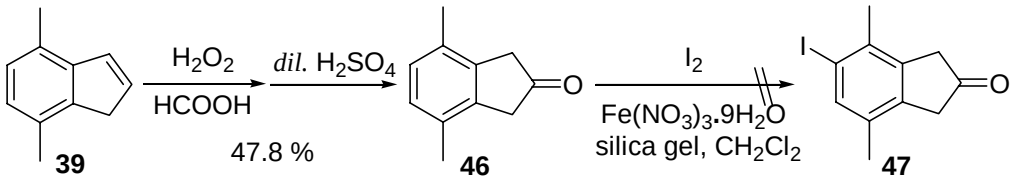
43 與對氯化硝基苯進行Ullmann coupling[17]可得化合物 **45**，但產率僅 18.7 %。接著利用J. Gadogan的方法[18]將化合物 **45** 溶於$(EtO)_3P$下迴流可得化合物 **44**，產率 64.9 %。進行此環化反應時需注意時間上的控制，時間過長則產物會部分與多餘的$(EtO)_3P$反應而使氮原子乙基化。

至此，我們希望能選擇性的氧化氮對位的碳，以利進行 Schmidt 反應或是引入一 OAc 基團。嘗試幾種氧化劑的結果都無法成功，加上 Ullmann coupling 產率並不是很高，能嘗試的反應有限。故我們希望若能一開始將環己烷環上的某個飽合碳作些改變，也許可以有利於我們在後面的合成。

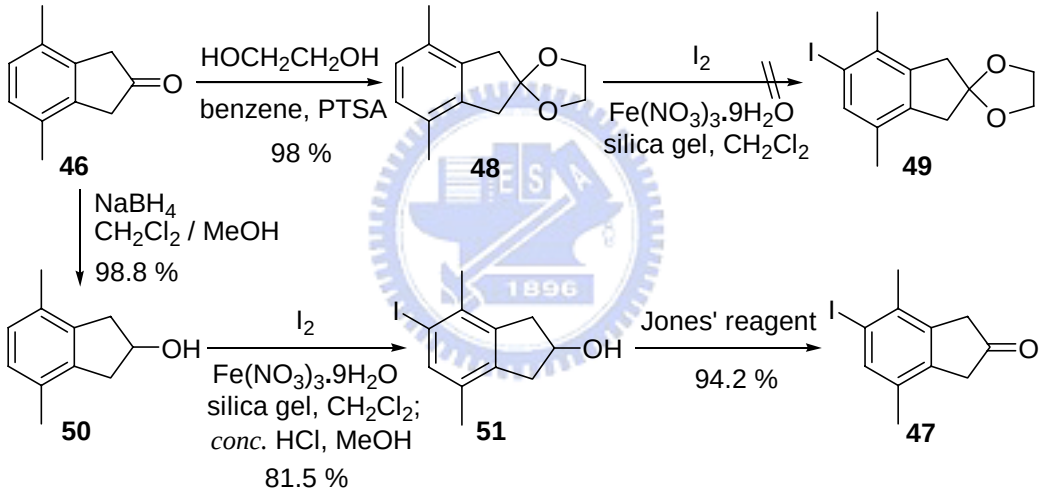


如上所示，在 indane 的 2 位上作些變化，則可以保留對稱性的優點，亦有利於未來

吡啶環的合成。故我們進行了如下的反應。



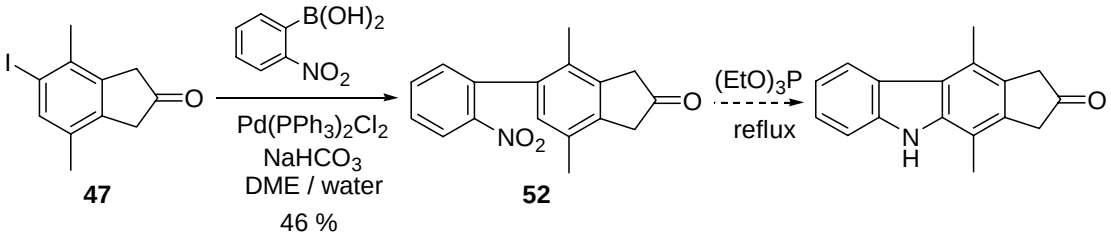
首先我們嘗試將化合物 **39** 經過氧化氫在甲酸溶液下進行反應，於稀硫酸下再利用蒸汽蒸餾而得化合物 **46**[19]。不幸的是，我們無法有效的引進單一碘原子在苯環上，懷疑酮基使α碳有所反應，經一般去碘化處理仍然無法獲得預期的產物。故我們只能將酮基以乙二醇保護後再碘化，但結果發現化合物 **48** 的結果也不好，從粗光譜可得知由於此條件下保護基被脫去。



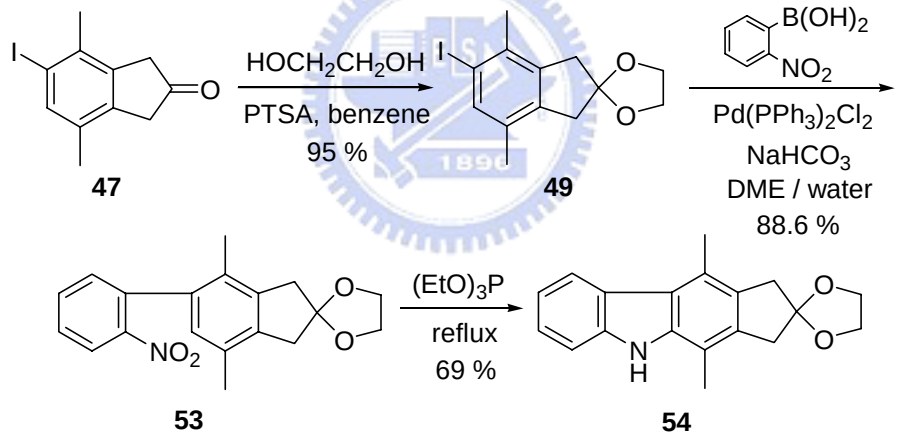
我們把酮基以硼氫化鈉還原，得產物 **50**，產率 98.8 %。此時碘化可得化合物 **51**，但我們發現除了預期的產物以外尚有一個極性較低的副產物，其光譜與 **51** 有許多相似之處，質譜所測得的分子量也與 **51** 相同。且此副產物在加熱下，或是長時間靜置都會變作 **51**。我們推測此為化合物 **51** 的-OH 官能基可能與過量的碘有弱的鍵結產生，於是我們在反應後處理上以濃鹽酸進行水解，則化合物 **51** 之產率提升到 81.6 %。將化合物 **51** 進行氧化得化合物 **47**，但 **47** 無法與對氯化硝基苯進行 Ullmann coupling，於是我們必須嘗試其他的方法。

近幾年Suzuki coupling相當熱門[20]，原因在於其優異的選擇性，又僅需少許的催化

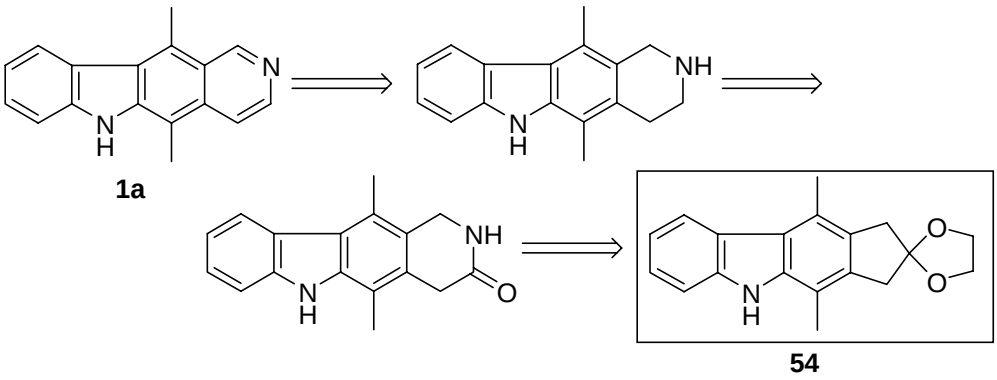
劑，並且產率普遍很高。嘗試將化合物 **47** 與鄰硝基苯硼酸（苯硼酸於醋酸酐下經發煙硝酸與尿素的混合溶液反應而得，參考W. Seamanu及M. P. Groziak的改進法[21]）進行Suzuki coupling發現以S. Labadie的方法[22]最為有效，但產率也僅 46 %。



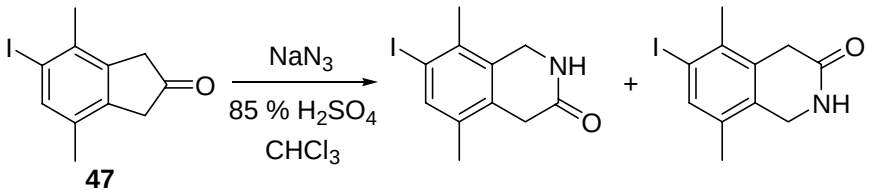
將化合物 **52** 依之前的環化方法所得的產物相當難溶於各類有機溶劑，包括苯、二氯甲烷、甲醇、丙酮、乙酸乙酯、甚至是二氯甲烷與甲醇的混溶劑或是二甲基碸，因此在蒐集光譜資料以及後續的反應大受影響。化合物 **47** 用乙二醇保護後所得的產物 **49** 可以解決這個問題。



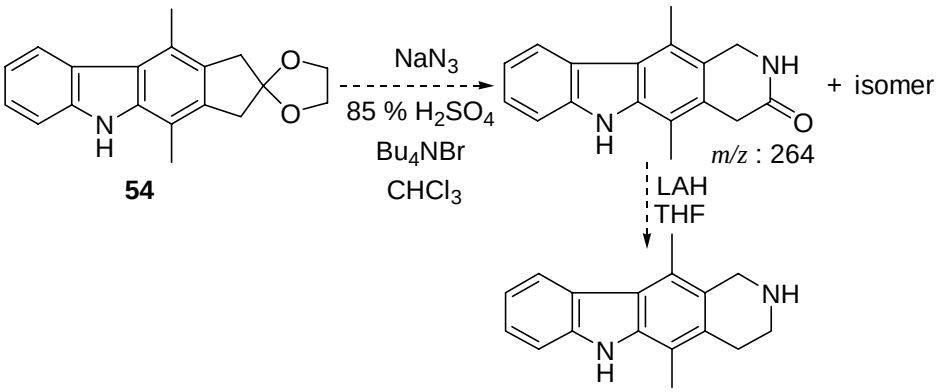
如上所示，以化合物 **49** 進行Suzuki coupling產率可接近九成，但是，要避免反應不完全，採用鄰硝基苯硼酸是過量的。將化合物 **53** 進行環化反應所得的產物極性雖大，但溶解度已較之前改善許多，又雖然多出了一步，但總產率卻是提高。



接著，我們希望可以在五員環上有選擇性的引入一個氮。我們曾作過將化合物 **47** 為模型進行Schmidt反應[23]以形成一個內醯胺的結構。

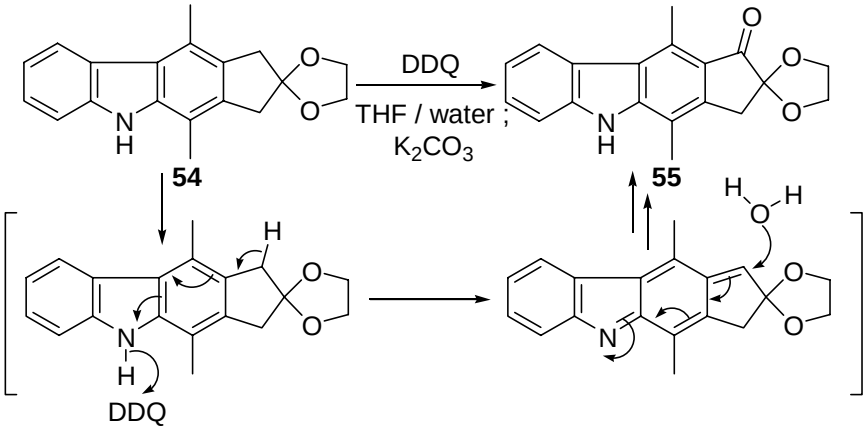


使用疊氮化鈉與濃硫酸有最好的結果，我們發現此條件下若溶劑中含有甲醇則無法成功。雖然此模型反應顯示缺乏選擇性，但我們仍認為其具有可以研究的潛能，而將化合物 **54** 進行Schmidt反應。結果發現所得到的產物多數為保護基脫去後的酮，溶解度低而造成反應性減弱，使溶解度提升不能加入甲醇。但以相轉移催化劑是解決此問題的方法。

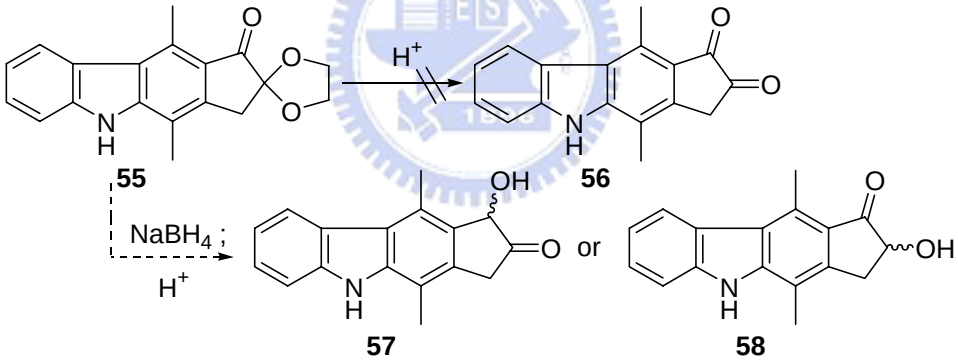


質譜檢示有Schmidt反應產物的母峰，且光譜上可以明顯發現醯胺的存在，我們卻無法將此混合物分離。由於極性很大，去除雜質極為困難，遑論單離其一產物。此時，我們將此混合物以鋰氫化鋁還原，期待生成級環胺較易處理，但所得的結果並不理想。

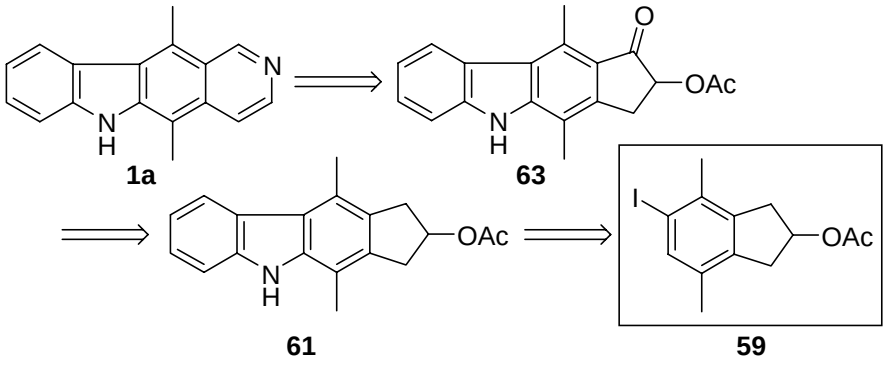
另外，我們用J. G. Rodríguez的方法[24]以二氯二氰基苯醌（DDQ）來氧化化合物 **54** 五員環上的碳，而結果是成功的。此一高度選擇性氧化，是期待氮原子發揮的效果。



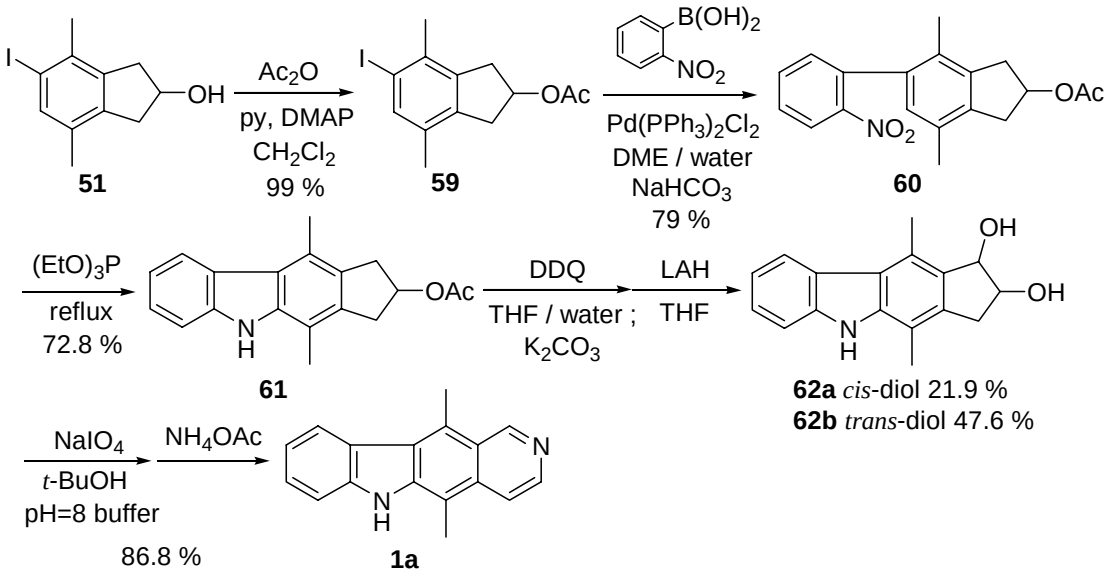
以酸水解所得的產物 **56**，結果並不甚理想；再者，把酮基以硼氫化鈉還原再進行水解，結果也是不如預期。我們推測，化合物 **56** 以及 **57** 或 **58** 在水解條件下可能並不是很穩定。



由於我們已知二氯二氰基苯醌可以選擇性的氧化五員環上的碳，較佳的合成ellipticine途徑可以改進：

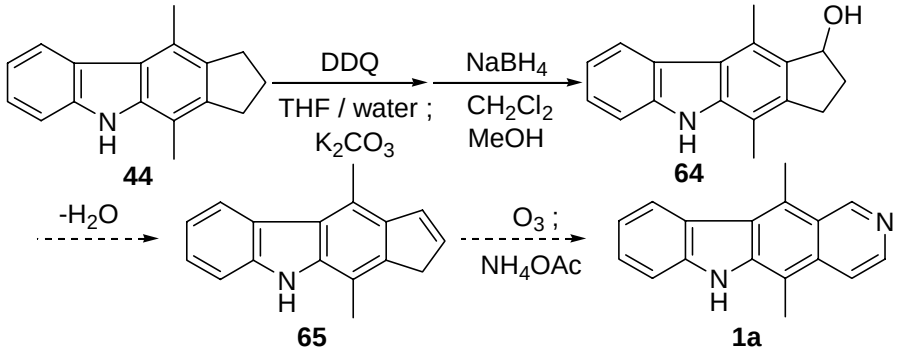


Ellipticine（**1a**）應可由化合物 **63** 還原去乙醯基而得的二醇來合成，則依循之前的途徑我們可以推得需要以化合物 **59** 作為新的起始物。以下是我們的實驗結果：



我們將化合物 **51** 乙醯化[25]（產率 99 %），**59** 再經由Suzuki coupling得化合物 **60**，再以$(EtO)_3P$環化得 **61**。化合物 **61** 利用二氯二氰基苯醌氧化後經過少許處理則直接以鋰氫化鋁進行還原並去保護，可得到順式 **62a** 與反式 **62b** 的二醇，此二醇再經過碘酸鈉氧化開環後直接以醋酸銨處理並純化即可獲得ellipticine（**1a**），各項光譜皆與文獻報導一致[26]。自化合物 **39** 至 **1a** 合成共八步，總產率為 13 %。

另值得一提的是，化合物 **45** 也可以在二氯二氰基苯醌下反應而選擇性的氧化氮對位的碳，但由於其溶解度也相當不好，直接以硼氫化鈉還原而得 **64** ，有關於化合物 **64** 的脫水反應仍需要嘗試條件，若無意外 **65** 可以臭氧切開雙鍵後以醋酸銨處理而得ellipticine，此部分的細節還需要作進一步的實驗。



光譜比對：

(本文)

2.78 (*s*, 3H); 3.25 (*s*, 3H); 7.22-7.27 (*m*, 1H); 7.49-7.57 (*m*, 2H); 7.90 (*d*, 1H, *J*=6 Hz); 8.37 (*d*, 1H, *J*=8.1 Hz); 8.42 (*d*, 1H, *J*=6 Hz); 9.68 (*s*, 1H); 11.37 (*s*, 1H)

(Ref 1)

2.80 (*s*, 3H); 3.30 (*s*, 3H); 7.25-7.30 (*m*, 1H); 7.52-7.60 (*m*, 2H); 7.93 (*d*, 1H, J=6.1 Hz); 8.40 (*d*, 1H, J=8.3 Hz); 8.44 (*d*, 1H, J=6.1 Hz); 9.70 (*s*, 1H); 11.40 (*s*, 1H)

本文 DMSO-d_6	Ref 1 DMSO-d_6	Ref 2 DMSO-d_6	Ref 3 DMSO-d_6
11.92	11.9	11.9	11.7
14.31	14.3	14.3	14.4
108.00	107.9	107.9	110.5
110.67	110.6	110.7	110.6
115.84	115.7	115.8	116.7
119.15	119.1	119.1	118.8
121.95	121.9	121.9	122.8
123.11	123.1	123.1	124.0
123.37	123.3	123.3	124.7
123.78	123.7	123.7	125.2
127.08	127.0	127.0	125.5
128.01	127.9	127.9	127.5
132.45	132.4	132.4	128.7
140.47	140.3	(lost)	138.4
140.53	140.4	140.5	143.0
142.66	142.6	142.6	143.1
149.67	149.6	149.6	148.6

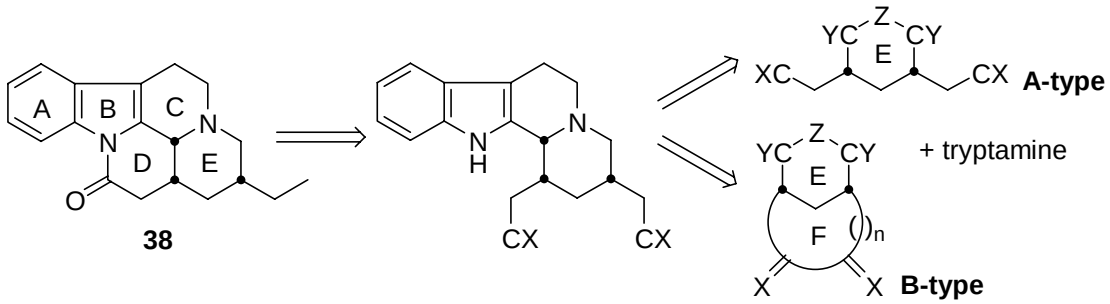
Ref 1 : *J. Org. Chem.* **1992,** *57***,** 5891-5899

Ref 2 : *J. Org. Chem.* **1982,** *47***,** 2810-2812

Ref 3 : *J. Org. Chem.* **1983**, *48*, 2690-2695 (isoellipticine)

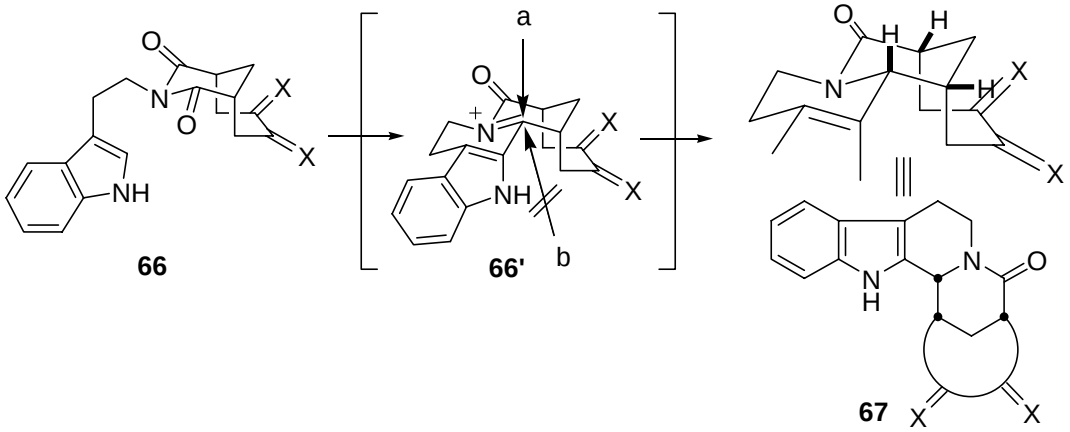
（二）Tacamonine 合成研究：

如第一部分，我們計畫以起始物為對稱[9]的分子來合成tacamonine（**38**）。其溯徑分析的示意圖如下：



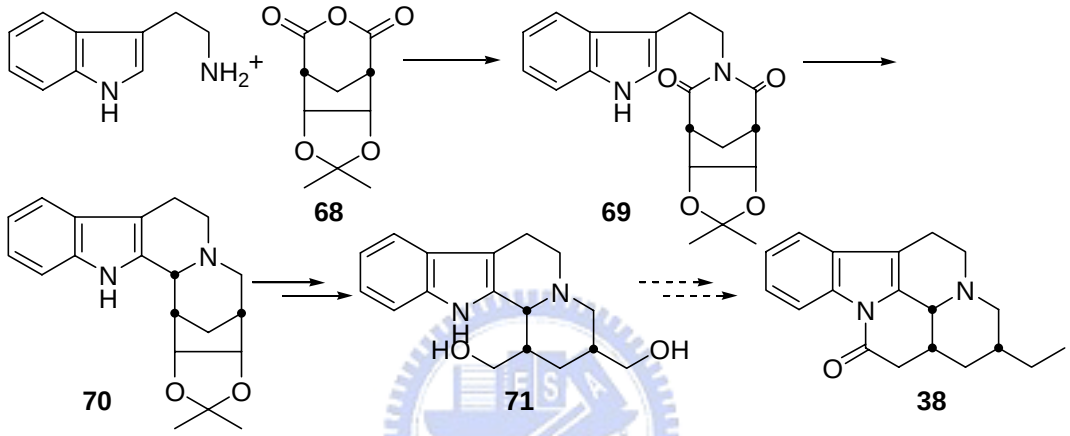
Tacamonine 的D環是一個內醯胺，由此作為拆解的開始。將D環打斷後接下來則是打斷B與E環的橋鍵，前驅物即為一對稱性的分子，此分子應可再經由色胺與A或B縮合而得。從蘇俊源學長之前的研究[8]得知，若以A類化合物作為合成的起始物，當我們將B環與E環橋聯後，很有可能在立體位向上無法進行有效的控制。故我們設計了B這類的化合物，可以有效的固定立體結構避免遭受破壞。

B 類化合物主要的特點在於 E 環的兩碳鏈是鎖起來的（假定此為 F 環），因此 E / F 併環的兩個三級碳的位向便無法輕易變動，而又由於 F 環在 C 環成環的過程中可扮演一立體阻礙的角色，使環化中傾向有利於立體效應與立體電子效應的位向，可令 E 環上的另一個三級碳在還原後也具有相同的位向，以下是我們預測反應位向的示意圖（前驅物為一 Y = Z = O 的酸酐與色胺縮合）。

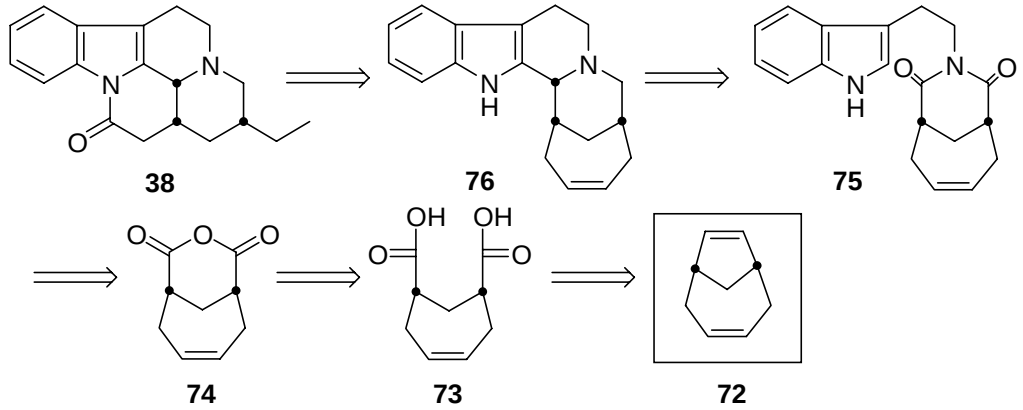


由上可知，**66** 進行環化反應時會形成一亞銨鹽的中間體，F 環會令此中間體構形停留在較穩定的狀態 **66'**，此構形進行接續的還原時有 a、b 兩個方位，b 方位因為立體阻礙且立體選擇性較差的緣故而不利進行，而 a 方位既是立體位向選擇佳也是立體選擇性佳，故還原勢必是依此方位，則預想所得的產物 **67** 即與 tacamonine 的位向相一致。

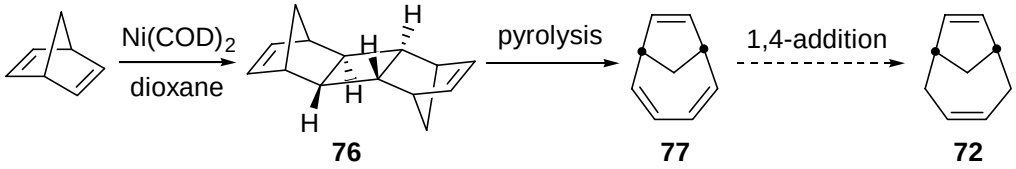
本實驗室稍早即以 B 類化合物作為起始物來進行 tacamonine 的合成，其途徑大致如下：



68 與色胺進行縮合可得化合物 **69**，經三氟甲磺酸酐反應並以硼氫化鈉反應可選擇性還原亞銨鹽而得到立體位向與 tacamonine 相同的化合物 **70**。但由於最後兩邊各延伸一個碳的結果並不理想，於是我們欲嘗試另一途徑：

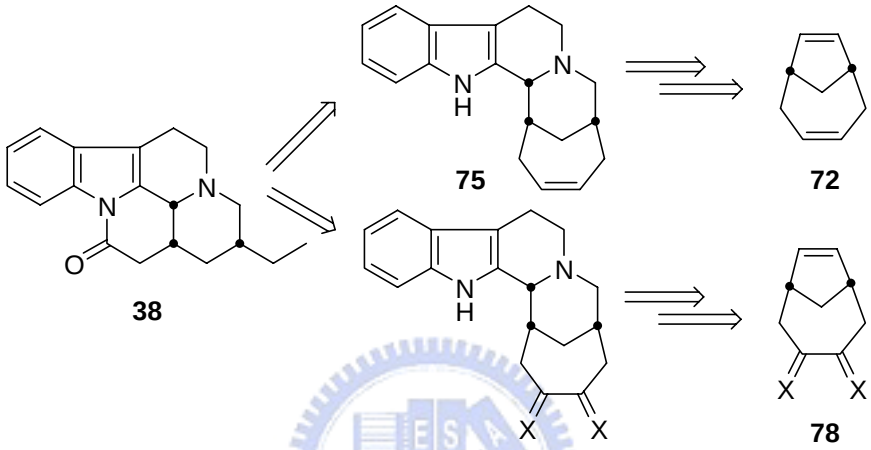


將 tacamonine 拆解，我們希望在一開始即具備足夠的碳，則不需要在合成最後延伸碳鏈造成困擾，並且應用對稱性的原則。以下是我們希望合成 **72** 的方法：



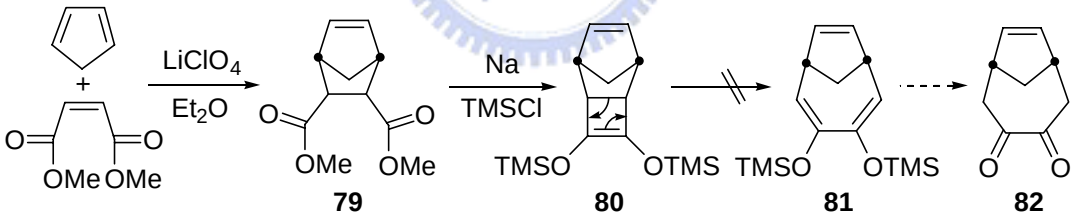
76 **77** **72**

去甲冰片二烯經由$Ni(COD)_2$催化反應可得一個雙聚體的結構 **76**[27]，經高溫裂解後可得化合物 **77**[28]，我們希望將此化合物作 1,4-加成而得化合物 **72**，但嘗試了多種還原法皆沒成功。



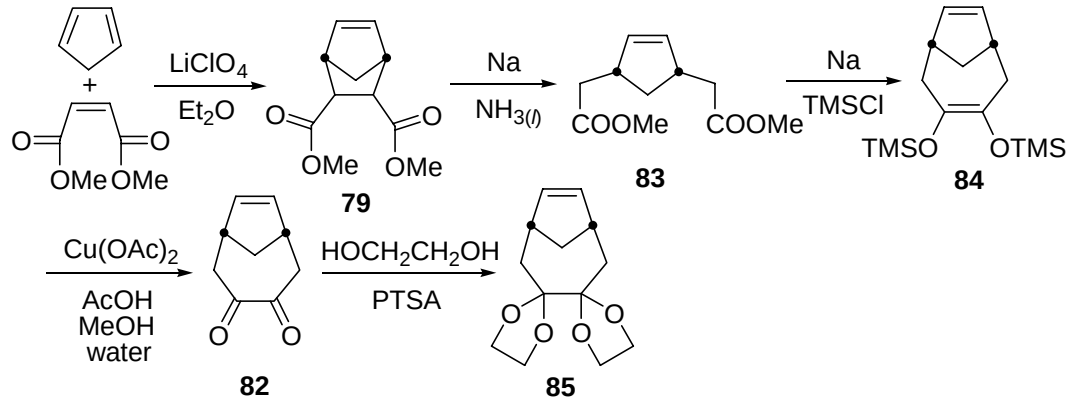
38 **75** **72** **78**

可以代替化合物 **72** 的是 **78**，可是從熱裂 **80** 以取得 **81** 有實驗上的困難。



79 **80** **81** **82**

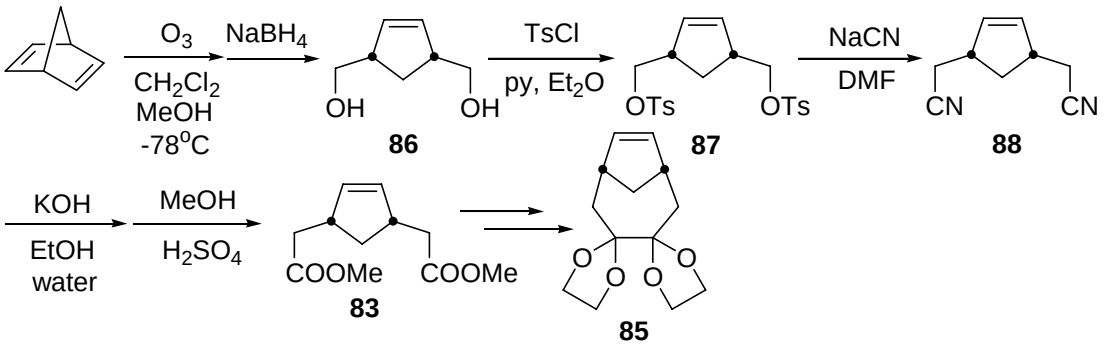
於是我們嘗試利用下面的途徑得到 **82**：



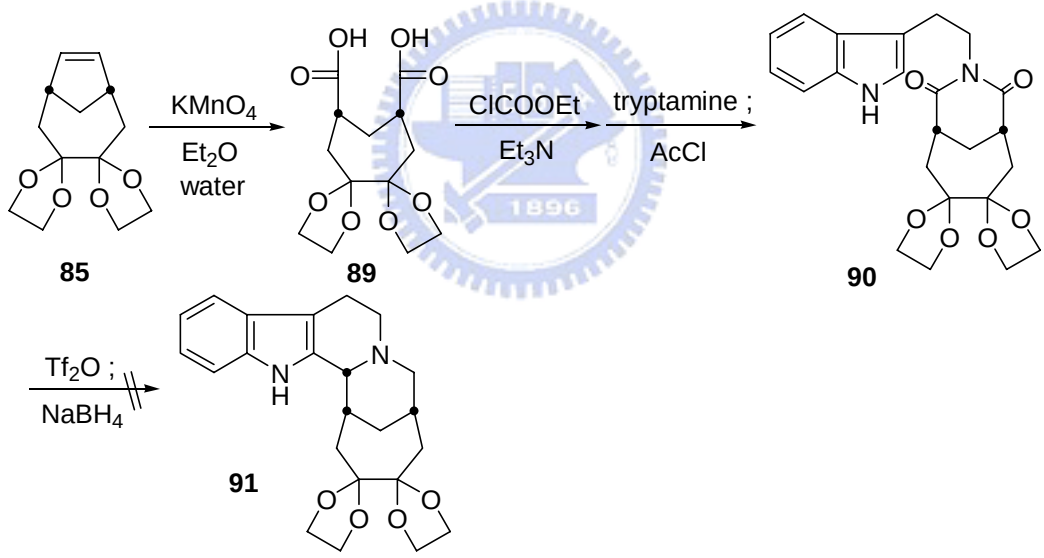
79 **83** **84** **82** **85**

我們將化合物 **79** 進行還原可得化合物 **83**；接著利用Acyloin縮合[29]可得化合物

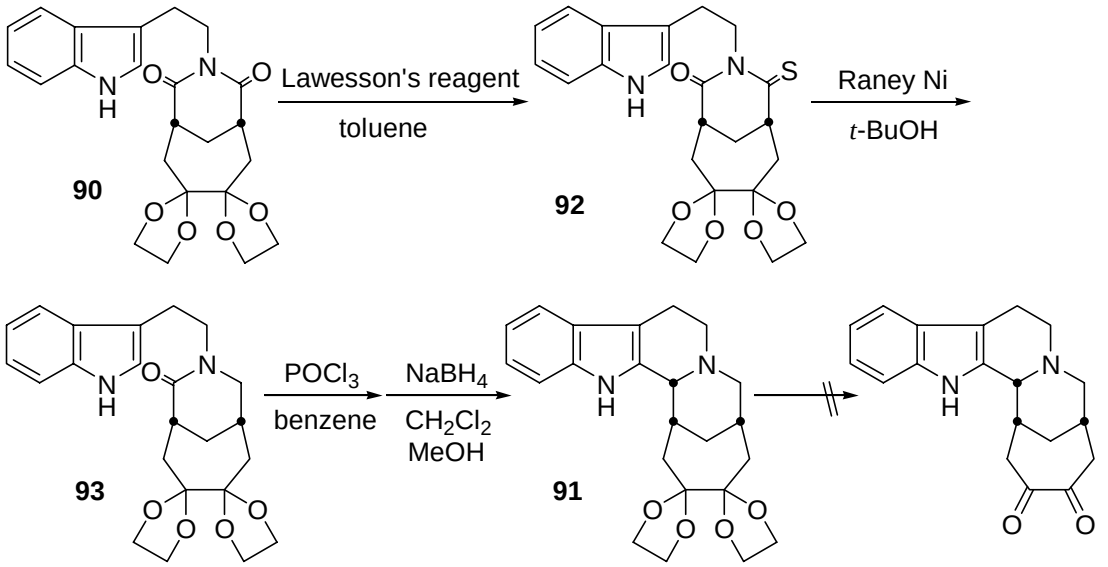
84，由於為七員環的縮合，兩步的產率不高。至於 **84** 進行水解並氧化[30]則可以得到期望的 **82** 這樣對稱的分子，將 **82** 進行保護得 **85** 以避免後階段引起副反應。



為了要獲得大量的 **83** 我們先將去甲冰片二烯進行臭氧裂解並還原得一二醇 **86**，再與對甲基苯磺醯氯反應得 **87** 後進行取代反應得 **88**[8]，此化合物以強鹼水解後續進行酯化反應可得化合物 **83**。此途徑雖較之前為長，但有利於大量製備。



接著我們將 **85** 以過錳酸鉀進行雙鍵氧化[31]得化合物 **89**，將 **89** 經氯甲酸乙酯在三乙胺下處理後直接與色胺進行縮合[32]可得化合物 **90**。我們嘗試將 **90** 依之前的環化方法（三氟甲磺酸酐然後以硼氫化鈉還原）失敗，推其原因可能是 **90** 的雙縮酮保護基之影響，先將保護基脫去的反應也不順利，所得到的產物至多只脫一邊的保護基，造成不對稱分子，故我們必須嘗試其他的方法進行環化。

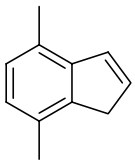


採用Milewska的方法[33]將 **90** 的亞胺以Lawesson試劑進行硫化單逼可得 **92**，再用Raney鎳處理可得到一個內醯胺 **93**，此化合物可利用三氯氧磷進行環化後以硼氫化鈉還原亞胺鹽[7e]得立體位向與tacamonine相同的化合物 **91**。

但 **91** 的脫保護基反應卻遭遇到困難，嘗試多種水解條件皆無法完成，實在使人失望。至此，我們可能需要把 **82** 改變成其他有利於回復為二酮的結構，才能完成 tacamonine 之合成

第三章 實驗步驟

General. Column chromatography (CC): *Merck* silica-gel (63-200 mesh). TLC: *Merck* silica-gel *60 F 254* plates. M.p.: uncorrected; *Laboratory Devices.* IR Spectra: *Bio-Rad FTS 3100*; ν in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Varian Unity-300*; $CDCl_3$ unless otherwise indicated; δ in ppm, *J* in Hz (reference peak: δ^H 7.24, δ^C 77). EI-MS: *Trio-2000* and *Jeol SX-102A*; ionization potential 70 eV. EA: *Heraeus CHN-O Rapid*. THF and ether were distilled from sodium-benzophenone, and DMF from Mg_2SO_4, while dicholomethane and toluene from calcium hydride.

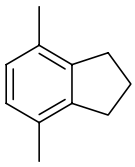


4,7-dimethylindene[11] **(39)**

Sodium (5 g, 0.22 mol) was dissolved in dry methanol (60 ml). The NaOMe solution was cooled at 0^{o} and freshly distilled cyclopentadiene (6.5 g, 0.10 mol) and 2,5-hexandione (11.41 g, 0.10 mol) were added dropwise. The ice bath was removed, and the mixture was stirred at room temperature for 2 hr. After quenching with water, the mixture was evaporated. The residue was extracted with hexane, and the extracts were washed with brine and dried over Na_2SO_4. Solvent was removed *in vacuo* and the product was isolated by fractional distillation (b.p. 45^{o}C, 0.05 torr) to afford **39** as a pale yellow oil, 12.18 g (84 %).

^{1}H NMR: δ 2.43 (*s*, 3H); 2.53 (*s*, 3H); 3.37-3.38 (*m*, 2H); 6.63-6.67 (*m*, 1H); 7.01-7.03 (*m*, 1H); 7.08-7.12 (*m*, 2H)

^{13}C NMR: δ 18.24 (*q*); 18.39 (*q*); 38.22 (*t*); 125.77 (*d*); 127.53 (*d*); 127.66 (*s*); 130.10 (*s*); 130.48 (*d*); 130.18 (*d*); 142.12 (*s*); 143.18 (*s*)

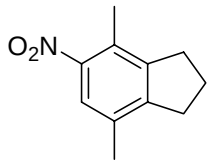


4,7-dimethylindane[34] (40)

A mixture of 4,7-dimethylindene (1 g, 6.9 mmol) and 10 % Pd/C (20 mg) in methanol (2 ml) was stirred under H_2. After absorption of hydrogen ceased, the catalyst was removed by filtration and the solvent was evaporated to provide indane **40** (0.96 g, 94.7 %).

^{1}H NMR: δ 2.20 (*quintet*, 2H, *J*=7.5 Hz); 2.36 (*s*, 6H); 2.98 (*t*, 4H, *J*=7.5 Hz); 7.02 (*s*, 2H)

^{13}C NMR: δ 18.88 (*q*); 24.16 (*t*); 31.61 (*t*); 126.98 (*d*); 130.85 (*s*); 142.54 (*s*)



4,7-dimethyl-5-nitroindane (41)

A mixture of conc. HNO_3 (1 ml), conc. H_2SO_4 (1 ml) and 4,7-dimethylindane (1 g, 6.85 mmol) was stirred at 0^o for 10 min. and at room temperature for 30 min. The reaction product was poured into 20 ml of ice water and extracted with CH_2Cl_2. The combined organic extracts were washed with water, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography to afford **41** (0.40 g, 30.4 %), m.p. 61-62^{o}C

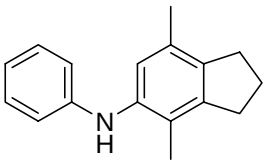
^{1}H NMR: δ 2.10 (*tt*, 2H, J_1=7.5 Hz, J_2=7.5 Hz); 2.21 (*s*, 3H); 2.35 (*s*, 3H); 2.85 (*t*, 2H, *J*=7.5 Hz); 2.88 (*t*, 2H, *J*=7.5 Hz); 7.51 (*s*, 1H)

^{13}C NMR: δ 16.14 (*q*); 18.53 (*q*); 23.93 (*t*); 31.88 (*t*); 32.08 (*t*); 123.46 (*d*); 126.24 (*s*); 131.61 (*s*); 145.27 (*s*); 148.03 (*s*); 148.38 (*s*)

IR (neat): ν 3441; 3433; 2958; 2918; 1645; 1514; 1458; 1433; 1378; 1333; 1265; 1212; 1004; 898

EI-MS: 192 (M^++1, 27.35); 191 (M^+, 22.06); 175 (61.18); 174 (55.59); 147 (32.06); 146 (43.53); 128 (100); 115 (47.65); 91 (20.59)

EA: Anal. calcd. for $C_{11}H_{13}O_2N$**: C:** 69.09; **H:** 6.85; **N:** 7.32; Found: **C:** 69.25; **H:** 7.03; **N:** 7.28



_N_-phenyl-4,7-dimethyl-5-indanamine (42)

TFA (3.42 g, 30 mmol) and TFAA (1.05 g, 5mmol) were mixed, stirred and warmed to 60°. 4,7-Dimethylindane (3.65 g, 25 mmol) and *N*-phenylhydroxyamine (0.55 g, 5 mmol) were added slowly. After 3 hr the reaction mixture was basified with aqueous Na_2CO_3 to pH>7, and extracted with CH_2Cl_2. The combined extracts were washed with 30% HCl and water, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography (CH_2Cl_2/Hex=1/20) to afford **44** (0.74 g, 62 % based on *N*-phenylhydroxyamnie). Approximately 80 % of indene **42** was recovered.

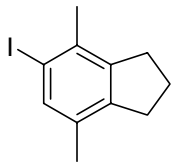
^{1}H NMR: δ 2.23 (*s* ,3H); 2.24 (*tt*, 2H, J_1=7.5 Hz, J_2=7.5 Hz); 2.31 (*s*, 3H); 2.96 (*t*, 2H, *J*=7.5 Hz); 3.00 (*t*, 2H, *J*=7.5 Hz); 5.32 (*br*, 1H); 6.90-6.94 (*m*, 3H); 7.01 (*s*, 1H); 7.28-7.34 (*m*, 2H)

^{13}C NMR: δ 14.08 (*q*); 18.91 (*q*); 24.47 (*t*); 31.37 (*t*); 32.23 (*t*); 115.61 (*d*); 118.97 (*d*); 121.05 (*d*); 124.03 (*s*); 129.12 (*d*); 131.26 (*s*); 137.78 (*s*); 138.63 (*s*); 144.07 (*s*); 145.66 (*s*)

IR (neat): ν 3389; 3046; 2939; 2841; 1652; 1599; 1496; 1479; 1405; 1323; 1308; 1247; 1175; 748; 693

EI-MS: 237 (M^+, 100); 222 (14.18); 220 (3.77); 145 (2.97); 144 (2.13); 91 (2.72); 77 (2.72)

HR-MS: Anal. calcd. for $C_{17}H_{19}N$: 237.1519; Found: 237.1523



5-iodo-4,7-dimethylindane (43)

$Fe(NO_3)_3.9H_2O$ (4 g, 10 mmol) was grinded with silica gel (8 g) in an agate mortar to furnish a pale yellow powder "silfen". It was used directly.

To a stirred solution of 4,7-dimethyindane (4.38 g, 30 mmol) in CH_2Cl_2 (45 ml), iodine (4.20 g, 16.5 mmol) and silfen (18 g) were added. After 12 hr at room temperature, the reaction mixture was filtered, and the filter cake was washed with CH_2Cl_2. The combined organic solution was washed with aqueous sodium thiosulfate and water, dried over Na_2SO_4 and evaporated. The residue was purified by column chromatography to give **43** (5.83 g, 70.9 %).

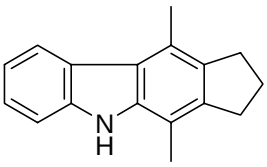
^{1}H NMR: δ 2.08 (*tt*, 2H, J_1=7.5 Hz, J_2=7.5 Hz); 2.19 (*s*, 3H); 2.34 (*s*, 3H); 2.82 (*t*, 2H, *J*=7.5 Hz); 2.91 (*t*, 2H, *J*=7.5 Hz); 7.47 (*s*, 1H)

^{13}C NMR: δ 18.29 (*q*); 24.26 (*t*); 24.42 (*q*); 31.61 (*t*); 33.31 (*t*); 98.57 (*s*); 133.05 (*s*); 133.98 (*s*); 137.30 (*d*); 142.98 (*s*); 143.50 (*s*)

IR (neat): ν 2941; 2916; 2842; 2360; 2342; 1710; 1637; 1593; 1570; 1459; 1377; 1174; 949; 859; 746

EI-MS: 272 (M+, 100); 145 (18.82); 130 (9.48); 115 (4.16)

HR-MS: Anal. calcd. for $C_{11}H_{13}I$: 272.0063; Found: 272.0069



4,10-dimethyl-1,2,3,5-tetrahydrocyclopentano[2,3-*b*]carbazole (44)

A mixture of **45** (70 mg, 0.26 mmol) and triethyl phosphite (0.5 ml) was heated at 150°C under nitrogen for 5 hr. Excess $(EtO)_3P$ and $(EtO)_3P=O$ were distilled at reduced pressure to leave a brown residue which was purified by column chromatography over silica gel to give product **44** (40 mg, 64.9 %).

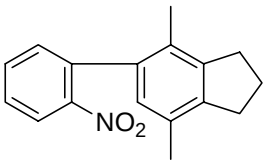
^{1}H NMR: δ 2.20 (*tt*, 2H, J_1=7.8 Hz, J_2=7.8 Hz); 2.43 (*s*, 3H); 2.79 (*s*, 3H); 3.05 (*t*, 2H, *J*=7.8 Hz); 3.08 (*t*, 2H, *J*=7.8 Hz); 7.21-7.27 (*m*, 1H); 7.36-7.46 (*m*, 2H); 7.80 (*br*, 1H); 8.18-8.21 (*m*, 1H)

^{13}C NMR: δ 13.51 (*q*); 16.97 (*q*); 25.25 (*t*); 31.22 (*t*); 31.81 (*t*); 110.29 (*d*); 112.04 (*s*); 118.95 (*d*); 120.42 (*s*); 122.19 (*d*); 124.17 (*d*); 124.69 (*s*); 125.34 (*s*); 134.44 (*s*); 138.41 (*s*); 139.70 (*s*); 140.79 (*s*)

IR (neat): ν 3476; 3413; 2947; 2841; 1609; 1511; 1455; 1386; 1344; 1305; 1251; 1225; 1145; 1114; 744; 730

EI-MS: 235 (M^+, 100); 220 (90.98); 204 (42.29); 117 (7.85); 108 (12.22); 102 (14.10)

HR-MS: Anal. calcd. for $C_{17}H_{17}N$: 235.1362; Found: 235.1362



4,7-dimethyl-5-(2-nitrophenyl)indane (45)

5-Iodo-4,7-dimethylindane (0.27 g, 1 mmol) and *o*-chloronitrobenzene (0.16 g, 1.1 mmol) were dissolved in dry DMF (6 ml). The mixture was heated in a N_2 atmosphere, then Cu powder (0.64 g, 10 mmol) and CuI (0.76 g, 40 mmol) were added at reflux. After 20 hr the cooled reaction mixture was filtered, washed with CH_2Cl_2, and the organic solutions were combined, washed with water, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel to give product **45** (0.05 g, 18.7 %).

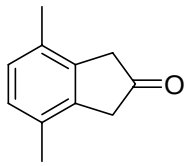
^{1}H NMR: δ 1.99 (*s*, 3H); 2.13 (*tt*, 2H, J_1=7.5 Hz, J_2=7.5 Hz); 2.24 (*s*, 3H); 2.88-2.93 (*m*, 4H); 6.76 (*s*, 1H); 7.34 (*d*, 1H, *J*=7.5 Hz); 7.45-7.50 (*m*, 1H); 7.57-7.62 (*m*, 1H); 7.94 (*d*, 1H, *J*=8.1 Hz)

^{13}C NMR: δ 16.36 (*q*); 18.81 (*q*); 24.02 (*t*); 31.08 (*t*); 32.09 (*t*); 123.76 (*d*); 127.37 (*d*); 127.77 (*d*); 128.53 (*s*); 130.66 (*s*); 132.15 (*d*); 132.54 (*d*); 135.19 (*s*); 136.95 (*s*); 142.70 (*s*); 143.15 (*s*); 149.49 (*s*)

IR (neat): ν 3392; 3062; 2940; 2921; 2867; 2845; 1704; 1608; 1571; 1526; 1487; 1467; 1437; 1349; 1292; 1194; 1119; 959; 871; 854; 786; 757; 722; 695

EI-MS: 267 (M^+, 90.20); 250 (93.14); 236 (94.12); 205 (43.87); 189 (28.92); 178 (29.41); 165 (26.23); 152 (9.99)

HR-MS: Anal. calcd. for $C_{17}H_{17}O_2N$: 267.1260; Found: 267.1255

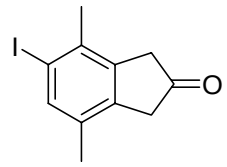


4,7-dimethyl-2-indanone[19] **(46)**

To an ice-cooled solution of 30 % H_2O_2 (5.5 g) in 98 % formic acid (24 ml), 4,7-dimethylindene (4.8 g, 33 mmol) was added dropwise. After addition was completed, the reaction mixture was stirred overnight at room temperature. The excess formic acid was removed *in vacuo*, and the remaining brown oil was mixed with 140 ml of 7% H_2SO_4. Steam distillation gave an off-white solid. The product was collected by dissolving in CH_2Cl_2 and dried over Na_2SO_4. On evaporation, **46** (2.55 g, 47.8 %) was obtained.

^{1}H NMR: δ 2.22 (*s*, 6H); 3.42 (*s*, 4H); 7.01 (*s*, 2H)

^{13}C NMR: δ 18.87 (*q*); 43.15 (*t*); 128.03 (*d*); 131.19 (*s*); 136.47 (*s*); 215.21 (*s*)



5-iodo-4,7-dimethyl-2-indanone (47)

To an ice-cooled, stirred solution of 5-iodo-4,7-dimethyl-2-indanol (8 g. 27.8 mmol) in acetone (50 ml) was added slowly Jones' reagent (16 ml). After 1 hr, excess oxidant was destroyed by isopropanol. Addition of water (100 ml) was followed by evaporation of acetone under reduced pressure. The residue was filtered and redissolvd with CH_2Cl_2. The organic phase was washed with water, dried over Na_2SO_4, and evaporated to afford product **47** (7.48 g, 94.2 %), m.p. 124-125^{o}C.

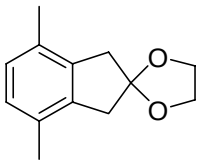
^{1}H NMR: δ 2.15 (*s*, 3H); 2.28 (*s*, 3H); 3.37 (*s*, 2H); 3.46 (*s*, 2H); 7.56 (*s*, 1H)

^{13}C NMR: δ 18.43 (*q*); 24.68 (*q*); 43.26 (*t*); 44.46 (*t*); 99.47 (*s*); 133.45 (*s*); 134.57 (*s*); 136.79 (*s*); 137.01 (*s*); 138.44 (*d*); 213.84 (*s*)

IR (neat): ν 2912; 2859; 1749; 1577; 1462; 1376; 1182; 1147; 938; 863; 796; 761; 729; 576

EI-MS: 286 (M^+, 100); 272 (5.10); 258 (83.67); 131 (15.43); 115 (10.84); 91 (21.30); 77 (20.28)

HR-MS: Anal. calcd. for $C_{11}H_{11}OI$: 285.9855; Found: 285.9855



4,7-dimethyl-2-(1,3-dioxolan-2-yl)indane (48)

A mixture of 4,7-dimethyl-2-indanone (0.20 g, 1.25 mmol), ethlylene glycol (0.62 g, 10 mmol), and *p*-toluenesufonic acid (10 mg) in benzene (10 ml) was heated under a Dean-Stark apparatus at reflux overnight. Benzene was distilled as much as possible. The residue was basified with sat. K_2CO_3 and extracted with CH_2Cl_2. The organic phase was washed with water and brine, dried over Na_2SO_4 and evaporated. The residue was purified by short column chromatography over silica gel to afford product **48** (0.25 g, 98 %), m.p. 65-66^{o}C.

^{1}H NMR: δ 2.31 (*s*, 6H); 3.22 (*s*, 4H); 4.09 (*d*, 4H, *J*=1.2 Hz); 7.01 (*s*, 2H)

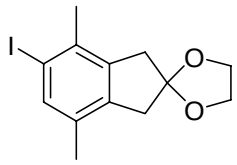
^{13}C NMR: δ 18.56 (*q*); 42.09 (*t*); 64.17 (*t*); 116.91 (*s*); 127.39 (*d*); 130.50 (*s*); 138.03 (*s*)

IR (neat): ν 2979; 2938; 2892; 1496; 1442; 1333; 1290; 1274; 1203; 1188; 1175; 1164; 1139; 1108; 1051; 1012; 947; 836; 806; 735; 578; 540

EI-MS: 204 (M^+, 100); 159 (8.2); 145 (22.95); 132 (59.77); 117 (25.00); 91 (14.36)

HR-MS: Anal. calcd. for $C_{13}H_{16}O_2$: 204.1151; Found: 204.1149

EA: Anal. calcd. for $C_{13}H_{16}O_2$: **C:** 76.44; **H:** 7.89; Found: **C:** 76.62; **H:** 7.77



5-iodo-4,7-dimethyl-2-(1,3-dioxolan-2-yl)indane (49)

A mixture of 5-iodo-4,7-dimethyl-2-indanone (0.50 g, 1.75 mmol), ethlylene glycol (0.86 g, 8 eq.), and *p*-toluenesufonic acid (50 mg) in benzene (30 ml) was heated under a Dean-Stark apparatus at reflux overnight. Benzene was distilled as much as possible. The residue was basified with sat. K_2CO_3 and extracted with CH_2Cl_2. The organic phase was washed with water and brine, dried over Na_2SO_4 and evaporated. The residue was purified by short column chromatography over silica gel to afford product **49** (0.55 g, 95.3 %), m.p. 89-90^oC.

^{1}H NMR: δ 2.13 (*s*, 3H); 2.27 (*s*, 3H); 3.05 (*s*, 2H); 3.14 (*s*, 2H); 4.01 (*s*, 4H); 7.48 (*s*, 1H)

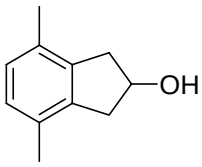
^{13}C NMR: δ 18.21 (*q*); 24.39 (*q*); 42.25 (*t*); 43.71 (*t*); 64.45 (*t*); 99.18 (*s*); 116.66 (*s*); 133.03 (*s*); 133.97 (*s*); 137.91 (*d*); 138.62 (*s*); 138.94 (*s*)

IR (neat): ν 2946; 2883; 1576; 1462; 1417; 1378; 1328; 1280; 1220; 1114; 1061; 1012; 948; 859; 798; 742; 579; 504; 464; 451

EI-MS: 330 (M^+, 87.30); 258 (100); 131 (48.36); 115 (50.82); 91 (23.26)

HR-MS: Anal. calcd. for $C_{13}H_{15}O_2I$: 330.0118; Found: 330.0113

EA: Anal. calcd. for $C_{13}H_{15}O_2I$**: C:** 47.29; **H:** 4.58; Found: **C:** 47.17; **H:** 4.70



4,7-dimethyl-2-indanol (50)

Sodium borohydride (0.2 g, 5.28 mmol) was added slowly to a stirred solution of 4,7-dimethyl-2-indanone (0.60 g, 3.75 mmol) in CH_2Cl_2 (10 ml) and methanol (10 ml) in an ice bath. After 3 hr, water was added and the solvents were evaporated. The residue was extracted with CH_2Cl_2, the organic layer was washed with brine, dried over Na_2SO_4 and evaporated to furnish product **50** (0.6 g, 98.8 %), m.p. 58-59^oC.

^{1}H NMR: δ 2.32 (*s*, 6H); 2.87 (*dd*, 2H, J_1=16.5 Hz; J_2=3.3 Hz); 3.16 (*dd*, 2H, J_1=16.5 Hz, J_2=6.6 Hz); 3.19 (*br*, 1H); 4.69 (*tt*, 1H, J_1=3.3 Hz, J_2=6.6 Hz); 7.00 (*s*, 2H)

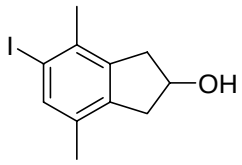
^{13}C NMR: δ 18.64 (*q*); 41.08 (*t*); 71.97 (*d*); 131.03 (*s*); 139.21 (*s*)

IR (neat): ν 3321; 3036; 3009; 2918; 1867; 1743; 1607; 1497; 1417; 1328; 1295; 1266; 1219; 1200; 1020; 948; 832; 805

EI-MS: 162 (M^+, 43.93); 144 (20.27); 133 (100); 129 (11.61); 119 (16.61); 91 (19.20); 77 (19.29); 65 (14.02); 51 (20.80)

HR-MS: Anal. calcd. for $C_{11}H_{14}O$: 162.1045; Found: 162.1051

EA: Anal. calcd. for $C_{11}H_{14}O$**: C:** 81.44; **H:** 8.70; Found: **C:** 81.80; **H:** 8.73



5-iodo-4,7-dimethyl-2-indanol (51)

To a stirred solution of 4,7-dimethyl-2-indanol (6.26 g, 38.6 mmol) in CH_2Cl_2 (60 ml), iodine (5.60 g, 22 mmol) and then silfen (24 g) were added. The reaction mixture was allowed to proceed for 12 hr at room temperature, filtered, and washed with CH_2Cl_2. The organic solution was washed with aqueous sodium thiosulfate and water. The extracts were dried over Na_2SO_4 and evaporated. The residue dissolved in methanol (20 ml) was cooled in an ice bath and conc. HCl (10 ml) was added slowly. The mixture was stirred for 2 hr and water (200 ml) was added. Solids that appeared were filtered and redissolved in CH_2Cl_2. The organic solution was washed with water, dried over Na_2SO_4, and evaporated to afford product **51** (8.97 g, 81.6 %), m.p. 85-86^{o}C.

^{1}H NMR: δ 2.15 (*s*, 3H); 2.94 (*s*, 3H); 2.67-2.83 (*m*, 2H); 2.89 (*br*, 1H); 2.96-3.14 (*m*, 2H); 4.52-4.58 (*m*, 1H); 7.47 (*s*, 1H)

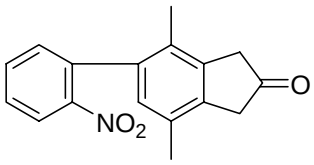
^{13}C NMR: δ 18.25 (*q*); 24.36 (*q*); 41.16 (*t*); 42.75 (*t*); 71.80 (*d*); 99.06 (*s*); 133.37 (*s*); 134.28 (*s*); 137.77 (*d*); 139.65 (*s*); 140.09 (*s*)

IR (neat): ν 3305; 2917; 1573; 1459; 1417; 1331; 1299; 1263; 1201; 1177; 1017; 955; 934; 859; 797; 743

EI-MS: 288 (M^+, 100); 270 (15.67); 259 (96.48); 245 (9.02); 161 (11.14); 143 (38.73); 128 (22.71); 115 (28.17); 91 (12.15)

HR-MS: Anal. calcd. for $C_{11}H_{13}OI$: 288.0012; Found: 288.0013

EA: Anal. calcd. for $C_{11}H_{13}OI$**: C:** 45.86; **H:** 4.55; Found: **C:** 45.82; **H:** 4.78



4,7-dimethyl-5-(2-nitrophenyl)-2-indanone (52)

5-Iodo-4,7-dimethyl-2-indanone (0.57 g, 2 mmol), 2-nitrophenylboronic acid (0.40 g, 2.4 mmol), $NaHCO_3$ (0.50 g, 6 mmol), and $Pd(PPh_3)_2Cl_2$ (30 mg, 2 mol %) were placed in a two-necked round-bottomed flask filled with N_2. A mixture of DME and water (1:1 v/v, 16 ml) was added through syringe. The reaction was heated at 80°C for 18 hr, solvents were evaporated and the residue was extracted with CH_2Cl_2. The extracts were combined, washed with water, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel to give product **52** (0.26 g, 46 %).

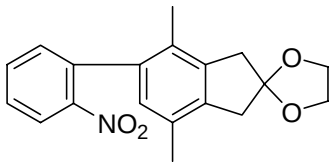
^{1}H NMR: δ 1.95 (*s*, 3H); 2.22 (*s*, 3H); 3.49 (*s*, 2H); 3.50 (*s*, 2H); 6.87 (*s*, 1H); 7.29-7.32 (*m*, 1H); 7.53-7.48 (*m*, 1H); 7.60-7.65 (*m*, 1H); 7.95-7.98 (*m*, 1H)

^{13}C NMR: δ 16.58 (*q*); 18.87 (*q*); 43.40 (*t*); 43.67 (*t*); 124.00 (*d*); 128.24 (*d*); 128.26 (*d*); 129.12 (*s*); 131.30 (*s*); 132.25 (*d*); 132.48 (*d*); 136.19 (*s*); 136.56 (*s*); 136.59 (*s*); 137.10 (*s*); 149.15 (*s*); 214.78 (*s*)

IR (neat): ν 3447; 2920; 1748; 1647; 1608; 1524; 1470; 1388; 1351; 1287; 1199; 1165; 1141; 950; 876; 854; 786; 758

EI-MS: 281 (M^+, 44.13); 253 (100); 206 (16.90); 191 (15.34); 115 (5.65); 89 (11.38)

HR-MS: Anal. calcd. for $C_{17}H_{15}O_3N$: 281.1053; Found: 281.1054



4,7-dimethyl-5-(2-nitrophenyl)-2-(1,3-dioxolan-2-yl)indane (53)

49 (2.90 g, 8.8 mmol), 2-nitrophenylboronic acid (2.50 g, 15 mmol), $NaHCO_3$ (2.58 g, 30.7 mmol), and $Pd(PPh_3)_2Cl_2$ (0.25 g, 4 mol %) were placed in a two-necked round-bottomed flask filled with N_2. A mixture of DME and water (1:1 v/v, 40 ml) was added through syringe. The reaction was heated at 80°C for 18 hr, solvents were evaporated and the residue was extracted with CH_2Cl_2. The extracts were combined, washed with water, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel to give product **53** (2.53 g, 88.6 %), m.p. 155-156°C.

^{1}H NMR: δ 1.91 (*s*, 3H); 2.18 (*s*, 3H); 3.07-3.21 (*m*, 4H); 4.03 (*s*, 4H); 6.74 (*s*, 1H); 7.26-7.29 (*m*, 1H); 7.43-7.48 (*m*, 1H); 7.54-7.60 (*m*, 1H); 7.90-7.93 (*m*, 1H)

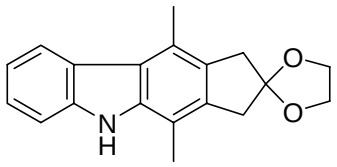
^{13}C NMR: δ 16.32 (*q*); 18.67 (*q*); 42.34 (*t*); 42.69 (*t*); 64.25 (*t*); 64.56 (*t*); 117.02 (*s*); 123.76 (*d*); 127.83 (*d*); 127.87 (*d*); 128.50 (*s*); 130.67 (*s*); 132.20 (*d*); 132.44 (*d*); 135.75 (*s*); 136.62 (*s*); 138.31 (*s*); 138.78 (*s*); 149.29 (*s*)

IR (neat): ν 2946; 2890; 2361; 2341; 2252; 1526; 1454; 1417; 1350; 1284; 1209; 1115; 1059; 1013; 948; 911; 854; 786; 758; 730; 709

EI-MS: 325 (M^+, 100); 308 (27.30); 294 (19.14); 278 (32.43); 234 (25.90); 222 (26.58); 207 (34.91); 189 (36.26); 178 (49.55); 165 (35.14); 152 (24.10); 88 (20.05)

HR-MS: Anal. calcd. for $C_{19}H_{19}O_4N$: 325.1315; Found: 325.1308

EA: Anal. calcd. for $C_{19}H_{19}O_4N$**: C:** 70.14; **H:** 5.89; **N:** 4.31; Found: **C:** 69.85; **H:** 5.87; **N:** 4.55



4,10-dimethyl-2-(1,3-dioxolan-2-yl)-

1,2,3,5-tetrahydrocyclopentano[2,3-*b*]carbazole (54)

A mixture of **53** (80 mg, 0.25 mmol) and triethyl phosphite (2 ml) was heated at 150°C under nitrogen for 5 hr. Excess $(EtO)_3P$ and $(EtO)_3P=O$ were distilled at reduced pressure to leave a brown residue which was purified by column chromatography over silica gel to give product **54** (50 mg, 69.3 %), m.p. 219-220°C.

^{1}H NMR ($CDCl_3$+CD_3OD): δ 2.31 (*s*, 3H); 2.55 (*s*, 3H); 2.90 (*br*, 1H); 3.24 (*s*, 4H); 4.05 (*s*, 4H); 7.11-7.16 (*m*, 1H); 7.27-7.39 (*m*, 2H); 8.04-8.07 (*m*, 1H)

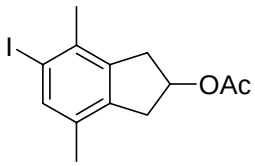
^{13}C NMR ($CDCl_3$+CD_3OD): δ 13.31 (*q*); 16.64 (*q*); 41.58 (*t*); 42.03 (*t*); 64.36 (*t*); 110.23 (*d*); 112.39 (*s*); 117.42 (*s*); 118.59 (*d*); 120.40 (*s*); 122.04 (*d*); 124.11 (*d*); 124.29 (*s*); 125.47 (*s*); 129.19 (*s*); 135.46 (*s*); 138.42 (*s*); 139.58 (*s*)

IR (neat): ν 3359; 2936; 2904; 2882; 2359; 2337; 1296; 1136; 1120; 1050; 1008; 952; 738

EI-MS: 293 (M^+, 100); 265 (7.88); 248 (20.28); 221 (56.12); 204 (26.66); 102 (19.52)

HR-MS: Anal. calcd. for $C_{19}H_{19}O_2N$: 293.1417; Found: 293.1415

EA: Anal. calcd. for $C_{19}H_{19}O_2N$**: C:** 77.79; **H:** 6.53; **N:** 4.77; Found: **C:** 77.50; **H:** 6.67; **N:** 5.11



5-iodo-4,7-dimethyl-2,3-dihydro-1*H*-2-indentyl acetate (59)

5-Iodo-4,7-dimethyl-2-indanol (0.36 g, 1.25 mmol), acetic anhydride (0.64 g, 6.27 mmol), pyridine (0.50 g, 6.33 mmol) and DMAP (20 mg) were dissolved in CH_2Cl_2 (10 ml). The reaction mixture was stirred at room temperature overnight and then evaporated *in vacuo*. The residue was purified by column chromatography over silica gel to afford **59** (0.41 g, 99.4 %), m.p. 63-64^{o}C.

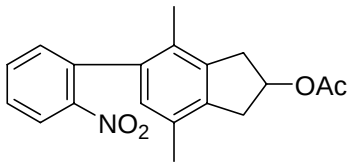
^{1}H NMR: δ 2.02 (*s*, 3H); 2.16 (*s*, 3H); 2.29 (*s*, 3H); 2.85-3.00 (*m*, 2H); 3.14-3.31 (*m*, 2H); 5.46-5.50 (*m*, 1H); 7.48 (*s*, 1H)

^{13}C NMR: δ 18.22 (*q*); 21.21 (*q*); 24.34 (*q*); 38.52 (*t*); 40.05 (*t*); 74.41 (*d*); 99.30 (*s*); 133.24 (*s*); 134.25 (*s*); 138.08 (*d*); 139.32 (*s*); 139.70 (*s*); 170.79 (*s*)

IR (neat): ν 2942; 2916; 2860; 1732; 1574; 1462; 1373; 1312; 1242; 1199; 1015; 973; 860; 744

EI-MS: 330 (M^{+}); 286; 270; 259; 244; 210; 195; 178; 160; 143; 128; 115; 105; 91; 77; 65; 51

HR-MS: Anal. calcd. for $C_{13}H_{15}O_2I$: 330.0118; Found: 330.0115



5-(2-nitrophenyl)-4,7-dimethyl-2,3-dihydro-1*H*-2-indentyl acetate (60)

59 (0.41 g, 1.24 mmol), 2-nitrophenylboronic acid (0.33 g, 1.98 mmol), $NaHCO_3$ (0.42 g, 5 mmol), and $Pd(PPh_3)_2Cl_2$ (20 mg, 2 mol %) were placed in a two-necked round-bottomed flask filled with N_2. A mixture of DME and water (1:1 v/v, 8 ml) was added through syringe. The reaction was heated at 80°C for 18 hr, solvents were evaporated and the residue was extracted with CH_2Cl_2. The extracts were combined, washed with water, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel to give product **60** (0.32 g, 79.2 %).

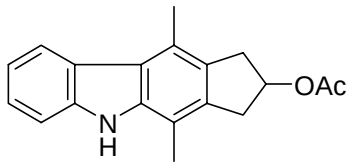
^{1}H NMR: δ 1.95 (*s*, 3H); 2.04 (*d*, 3H, *J*=6.9 Hz); 2.20 (*s*, 3H); 2.95-3.02 (*m*, 2H); 3.24-3.35 (*m*, 2H); 5.54-5.58 (*m*, 1H); 6.78 (*s*, 1H); 7.27-7.32 (*m*, 1H); 7.43-7.49 (*m*, 1H); 7.56-7.61 (*m*, 1H); 7.90-7.31 (*m*, 1H) **(conformation isomer)**

^{13}C NMR: δ 16.18 (*q*); 16.19 (*q*); 18.53 (*q*); 21.12 (*q*); 38.50 (*t*); 38.61 (*t*); 38.84 (*t*); 38.98 (*t*); 74.48 (*d*); 74.62 (*d*); 123.69 (*d*); 123.72 (*d*); 127.88 (*d*); 127.99 (*d*); 128.70 (*s*); 130.77 (*s*); 132.15 (*d*); 132.17 (*s*); 132.29 (*s*); 135.93 (*s*); 136.41 (*s*); 138.89 (*s*); 139.39 (*s*); 139.42 (*s*); 149.25 (*s*); 170.83 (*s*); 170.99 (*s*) **(conformation isomer)**

IR (neat): ν 2943; 2920; 1734; 1609; 1571; 1527; 1469; 1437; 1350; 1244; 1194; 1021; 977; 873; 854; 786; 758; 708

EI-MS: 325 (M^+); 295; 282; 265; 248; 234; 218; 203; 178; 165; 152; 146; 115; 101; 91; 77

HR-MS: Anal. calcd. for $C_{19}H_{19}O_4N$: 325.1315; Found: 325.1316



4,10-dimethyl-1,2,3,5-tetrahydrocyclopentano[2,3-*b*]carbazol-2-yl acetate (61)

A mixture of **60** (0.32 g, 0.98 mmol) and triethyl phosphite (5 ml) was heated at 150°C under nitrogen for 5 hr. Excess $(EtO)_3P$ and $(EtO)_3P=O$ were distilled at reduced pressure to leave a brown residue which was purified by column chromatography over silica gel to give product **61** (0.21 g, 72.8 %).

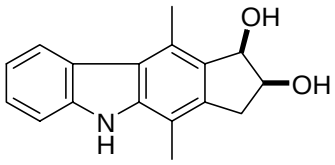
^{1}H NMR: δ 1.97 (*s*, 3H); 2.33 (*s*, 3H); 2.66 (*s*, 3H) 3.01-3.11 (*m*, 2H); 3.29-3.38 (*m*, 2H); 5.51-5.57 (*m*, 1H); 7.11-7.16 (*m*, 1H); 7.26-7.37 (*m*, 2H); 7.88 (*br*, 1H); 8.06-8.09 (*m*, 1H)

^{13}C NMR: δ 13.51 (*q*); 16.93 (*q*); 21.38 (*q*); 38.07 (*t*); 38.57 (*t*); 75.44 (*d*); 110.37 (*d*); 112.48 (*s*); 119.15 (*d*); 120.98 (*s*); 122.27 (*d*); 124.51 (*d*); 125.85 (*s*); 130.52 (*s*); 136.73 (*s*); 138.69 (*s*); 139.66 (*s*); 171.33 (*s*) **(one C_q peak was not found)**

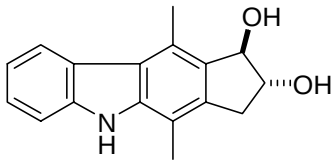
IR (neat): ν 3280; 2740; 1707; 1610; 1517; 1368; 1304; 1263; 1194; 1014; 976; 839; 773; 730

EI-MS: 293 (M^+, 15.25); 234 (24.20); 233 (100); 218 (47.80); 117 (5.63)

HR-MS: Anal. calcd. for $C_{19}H_{19}O_2N$: 293.1417; Found: 293.1421



***cis*-4,10-dimethyl-1,2,3,5-tetrahydrocyclopentano [2,3-*b*]carbazole-1,2-diol (62a)**



***trans*-4,10-dimethyl-1,2,3,5-tetrahydrocyclopentano [2,3-*b*]carbazole-1,2-diol (62b)**

To a mixture of **60** (0.30 g, 1 mmol) and H_2O (0.15 g, 8.0 mmol) in THF (5 ml), a solution of DDQ (0.93 g, 4.1 mmol) in THF (10 ml) was added dropwise at 0^oC during 10 min. The reaction mixture was stirred at room temperature for 8 hr. 50 % K_2CO_3 (10 ml) was added and the mixture was stirred for another 1 hr. THF was evaporated. The residue was extracted with CH_2Cl_2 / MeOH (10 : 1), the organic extracts were combined, washed with sat. K_2CO_3, dried over Na_2SO_4 and evaporated.

The residue (0.26 g) was dissolved in dry THF (10 ml) and added to LAH (0.26 g, 6.8 mmol) in dry THF (5 ml) dropwise. The reaction mixture was stirred at room temperature for 10 hr, excess LAH was destroyed by water. The mixture was filtered, and washed with CH_2Cl_2. The combined organic extracts were washed with sat. K_2CO_3, dried over Na_2SO_4 and evaporated. The residue was purified by column chromatography over silica gel to afford *cis*-diol **62a** (0.06 g, 21.9 %) and *trans*-diol **62b** (0.13 g, 47.6 %).

***cis*-diol (62a):**

^{1}H NMR (CD_3OD): δ 2.40 (*s*, 3H); 2.82 (*s*, 3H); 2.96 (*dd*, 1H, J_1=15 Hz, J_2=8.7 Hz); 3.19 (*dd*, 1H, J_1=15 Hz, J_2=7.2 Hz); 4.31 (*ddd*, 1H, J_1=8.7 Hz, J_2=7.2 Hz, J_3=5.4 Hz); 5.09 (*d*, 1H, *J*=5.4 Hz); 7.09-7.14 (*m*, 1H); 7.27-7.33 (*m*, 1H); 7.43-7.46 (*m*, 1H); 8.07-8.10 (*m*, 1H)

^{13}C NMR (CD_3OD): δ 13.53 (*q*); 16.63 (*q*); 37.37 (*t*); 74.39 (*d*); 74.49 (*d*); 111.59 (*d*); 113.99 (*s*); 119.59 (*d*); 121.94 (*s*); 123.00 (*d*); 125.33 (*d*); 125.57 (*s*); 129.05 (*s*); 132.72 (*s*); 138.25 (*s*); 141.58 (*s*); 141.75 (*s*)

IR (neat): ν 3419; 2923; 2085; 1645; 1519; 1456; 1338; 1297; 1235; 1118; 1085; 1002; 740

EI-MS: 268 (M^{+1}, 10.20); 267 (M^{+}, 46.84); 249 (74.56); 221 (100); 206 (31.86); 204 (36.55); 191 (14.75); 111 (10.88)

HR-MS: Anal. calcd. for $C_{17}H_{17}O_2N$: 267.1260; Found: 267.1262

***trans*-diol (62b):**

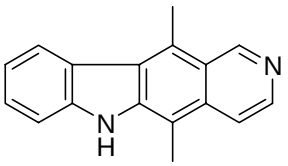
^{1}H NMR (CD_3OD): δ 2.43 (*s*, 3H); 2.82 (*m*, 1H); 2.86 (*s*, 3H); 3.44 (*dd*, 1H, J_1=16.8 Hz, J_2=5.4 Hz); 4.40-4.42 (*m*, 1H); 5.16 (*s*, 1H); 7.09-7.14 (*m*, 1H); 7.27-7.32 (*m*, 1H); 7.44-7.46 (*m*, 1H); 8.09-8.12 (*m*, 1H)

^{13}C NMR (CD_3OD): δ 13.50 (*q*); 16.72 (*q*); 38.73 (*t*); 80.24 (*d*); 81.84 (*d*); 111.58 (*d*); 114.17 (*s*); 119.54 (*d*); 122.20 (*s*); 123.00 (*d*); 125.25 (*d*); 125.58 (*s*); 129.23 (*s*); 133.13 (*s*); 139.48 (*s*); 141.79 (*s*); 141.87 (*s*)

IR (neat): ν 3314; 2918; 1685; 1609; 1559; 1518; 1457; 1381; 1340; 1296; 1250; 993; 731

EI-MS: 268 (M^{+1}, 11.66); 267 (M^{+}, 55.19); 249 (77.36); 235 (19.34); 234 (20.80); 221 (100); 218 (13.62); 217 (11.38); 206 (30.86); 204 (35.42); 194 (10.52); 191 (13.30); 165 (10.56); 111 (10.26)

HR-MS: Anal. calcd. for $C_{17}H_{17}O_2N$: 267.1260; Found: 267.1259



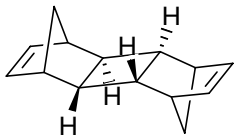
5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazole; Ellipticine[26] (1a)

To a stirred solution of the diol (*cis* + *trans*, 0.10 g, 0.37 mmol) and pH=8 phosphate buffer (2 ml) in *t*-BuOH (6 ml), $NaIO_4$ (0.16 g, 7.5 mmol) was added. At the end of 6 hr, ammonium acetate (0.29 g, 3.6 mmol) was added, stirring was continued for 1 hr and then the solvent was evaporated. The residue was extracted with CH_2Cl_2 / MeOH (10 : 1), washed with sat. K_2CO_3, dried over Na_2SO_4 and evaporated. The residue was purified by column chromatography over silica gel to afford **1a** (0.08 g, 86.8 %).

^{1}H NMR (DMSO-d_6): δ 2.78 (*s*, 3H); 3.25 (*s*, 3H); 7.22-7.27 (*m*, 1H); 7.49-7.57 (*m*, 2H); 7.90 (*d*, 1H, *J*=6 Hz); 8.37 (*d*, 1H, *J*=8.1 Hz); 8.42 (*d*, 1H, *J*=6 Hz); 9.68 (*s*, 1H); 11.37 (*s*, 1H)

^{13}C NMR (DMSO-d_6): δ 11.92 (*q*); 14.31 (*q*); 108.00 (*s*); 110.67 (*d*); 115.84 (*d*); 119.15 (*d*); 121.95 (*s*); 123.11 (*s*); 123.37 (*s*); 123.78 (*d*); 127.08 (*d*); 128.01 (*s*); 132.45 (*s*); 140.47 (*d*); 140.53 (*s*); 142.66 (*s*); 149.67 (*s*)

HR-MS: Anal. calcd. for $C_{17}H_{14}N_2$: 246.1158; Found: 246.1152

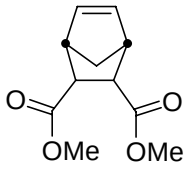


pentacyclo[8.2.1.1^{4,7}.0^{2,9}.0^{3,8}]tetradeca-5,11-diene[27] (76)

Norbornadiene (42.7 g, 50 ml, 463.5 mmol) was added to a stirring solution of nickel bis(cyclooctadiene) (0.65 g, 2.37 mmol) in 1,4-dioxane through syringe. The resulting dark red solution was allowed to stir at room temperature for 22 hr, resulting in formation of a white precipitate. A second portion of norbornadiene (42.7 g, 50 ml, 463.5 mmol) was then added to the reaction mixture, which was heated at 50-55^{o}C for 48 hr and at 40^{o}C for an additional 16 hr. The reaction mixture was then allowed to cool to room temperature and concentrated *in vacuo* to give a solid residue. The white solid was treated by flash column chromatography (100 % Hex) over silica gel (81.55 g). On evaporation of solvent, the residue was purified by sublimation to afford dimer **76** (46 g, 53.9 %).

^{1}H NMR: δ 1.23 (*d*, 2H, *J*=9 Hz); 1.34 (*s*, 4H); 1.69 (*d*, 2H, *J*=9 Hz); 2.62 (*s*, 4H); 6.01 (*s*, 4H)

^{13}C NMR: δ 39.76 (*d*); 42.20 (*t*); 44.17 (*d*); 136.13 (*d*)

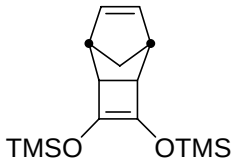


dimethyl (2R,3S)-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate[35] **(79)**

Freshly distilled cyclopentadiene (10.2 g, 153 mmol) was added slowly to an ice-cooled solution of dimethyl maleate (21.6 g, 150 mmol) and lithium perchlorate (6 g) in dry ether (30 ml). The mixture was stirred at room temperature for 10 hr and water was added. The aqueous layer was extracted with CH_2Cl_2, and the organic extracts were combined, washed with water and brine, dried over Na_2SO_4, and evaporated. The resulting oil was purified by column chromatography over silica gel to afford **79** (30.5 g, 96.8 %).

^{1}H NMR: δ 1.23-1.26 (*m*, 1H); 1.35-1.39 (*m*, 1H); 3.06-3.07 (*m*, 2H); 3.19-3.20 (*m*, 2H); 3.51 (*s*, 6H); 6.15-6.16 (*m*, 2H)

^{13}C NMR: δ 46.01 (*d*); 47.79 (*d*); 48.42 (*t*); 51.23 (*q*); 134.65 (*d*); 172.66 (*s*)

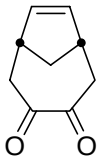


endo-3,4-bis(trimethylsiloxy)tricyclo[4.2.1.0^{2,5}]nona-3,7-diene[36] (80)

To a vigorously stirred suspension of sodium (1.84 g, 80 mmol) in dry toluene (40 ml) at reflux was added a solution of diester **79** (3.74 g, 17.8 mmol) and freshly distilled chlorotrimethylsilane (9.12 g, 84 mmol) in dry toluene (10 ml) during 2 hr. The resulting mixture was heated at reflux for an additional 10 hr, cooled, filtered through Celite, and washed with dry ether. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography over silica gel (Hex : EA = 10 :1) to provide **80** (4.43 g, 96.4 %).

^{1}H NMR: δ 0.19 (*s*, 18 H); 1.56 (*d*, 1H, *J*=8.1 Hz); 1.94 (*d*, 1H, *J*=8.1 Hz); 2.57 (*s*, 2H); 2.72-2.73 (*m*, 2H); 5.90-5.91 (*m*, 2H)

^{13}C NMR: δ 0.40 (*q*); 41.11 (*d*); 42.27 (*d*); 54.22 (*t*); 125.97 (*s*); 131.54 (*d*)



bicyclo[4.2.1]non-7-ene-3,4-dione (82)

A mixture of 3,4-bis(trimethylsiloxy)bicycle[4.2.1]nona-3,7-diene (6.18 g, 20.9 mmol) and $Cu(OAc)_2 \cdot H_2O$ (8.34 g, 2 eq.) in methanol (10 ml) and 50 % aqueous acetic acid was heated at 75°C for 12 hr. The reaction mixture was cooled, filtered though Celite, and washed with CH_2Cl_2. The solution was separated on addition of water, the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2, and the organic extracts were combined, washed with water and 10 % K_2CO_3, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel to afford **82** (1.97 g, 62 %).

^{1}H NMR: δ 1.42-1.46 (*d*, 1H, *J*=13.8 Hz); 2.20-2.29 (*m*, 1H); 2.25-2.32 (*m*, 2H); 2.47 (*dd*, 2H, J_1=14.4 Hz, J_2=5.4 Hz); 2.92-2.97 (*m*, 2H); 5.72 (*s*, 2H)

^{13}C NMR: δ 35.47 (*t*); 37.14 (*d*); 42.26 (*t*); 134.53 (*d*); 207.49 (*s*)

IR (neat): ν 3410; 2938; 1698; 1653; 1541; 1457; 1380; 1215; 1139; 1103; 1049; 991; 871; 812; 739

EI-MS: 150 (M^+, 14.89); 122 (8.78); 107 (10.45); 91 (11.07); 79 (100); 66 (26.72)

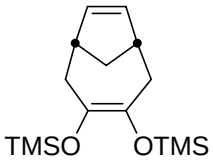
HR-MS: Anal. calcd. for $C_9H_{10}O_2$: 150.0681; Found: 150.0681

cis-1,3-dicarbomethoxycyclopent-4-ene[37] (83)

88 (8.86 g, 60 mmol) was hydrolyzed with KOH (13.6 g, 24.3 mmol) in 70 % ethanol (50 ml) by heating the solution at reflux for 10 hr. After addition of water (30 ml), ethanol was evaporated. The solution was then acidified, and extracted with EA. The combined extracts were dried over Na_2SO_4 and evaporated. The residue was dissolved in methanol (30 ml) and several drops of conc. H_2SO_4 were added. The solution was heated at reflux overnight and the methanol was evaporated after addition of water (20 ml). The residue was extracted with CH_2Cl_2, and the organic extracts were washed with water, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel to afford **83** (9.2 g, 71.5 %).

^{1}H NMR: δ 0.97 (*dt*, 1H, J_1=7.5 Hz, J_2=13.2 Hz); 2.19-2.41 (*m*, 5H); 2.95-3.05 (*m*, 2H); 3.59 (*s*, 6H); 5.60 (*s*, 2H)

^{13}C NMR: δ 36.71 (*t*); 40.54 (*t*); 41.85 (*d*); 51.29 (*q*); 134.24 (*d*); 172.83 (*s*)



3,4-bis(trimethylsiloxy)bicyclo[4.2.1]nona-3,7-diene (84)

A dispersion of sodium (0.30 g, 13 mmol) was placed in dry toluene (15 ml) at reflux and with rapidly stirring for 1 hr. After cooling to room temperature, diester **83** (0.50 g, 2.4 mmol) was added followed by freshly distilled chlorotrimethylsilane (1.36 g, 12.6 mmol) in dry toluene (4 ml) in a dropwise manner at temperature below 50^{o}C during 0.5 hr. The resulting mixture was heated at reflux for 1 d, cooled, filtered through Celite, and washed with dry ether. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography over silica gel (Hex : EA = 10 :1) to provide **84** (0.30 g, 43 %).

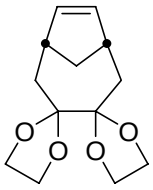
^{1}H NMR: δ 0.10 (*s*, 18H); 1.442 (*d*, 1H, *J*=11.7 Hz); 1.99-2.09 (*m*, 1H); 2.13-2.14 (*m*, 2H); 2.41-2.51 (*m*, 2H); 2.72-2.76 (*m*, 2H); 5.68 (*s*, 2H)

^{13}C NMR: δ 0.99 (*q*); 37.26 (*t*); 38.33 (*t*); 39.43 (*d*); 133.48 (*d*); 133.72 (*s*)

IR (neat): ν 3052; 2956; 2907; 2832; 2360; 1718; 1667;1558; 1507; 1448; 1435; 1410; 1340; 1250; 1178; 1082; 1025; 972; 888; 842; 757; 718; 687; 650

EI-MS: 296 (M^{+}, 51.11); 281 (10.56); 230 (99.11); 215 (31.56); 147 (39.56); 73 (100); 45 (27.33)

HR-MS: Anal. calcd. for $C_{15}H_{28}O_2Si_2$: 296.1628; Found: 296.1627



3,4-bis(1,3-dioxolan-2-yl)-bicyclo[4.2.1]non-7-ene (85)

A mixture of bicyclo[4.2.1]non-7-ene-3,4-dione (0.25 g, 1.67 mmol), ethlylene glycol (1.60 g, 25.8 mmol), and *p*-toluenesufonic acid (30 mg) in benzene (20 ml) was heated under a Dean-Stark apparatus at reflux overnight. Benzene was distilled as much as possible. The residue was basified with sat. K_2CO_3 and extracted with CH_2Cl_2. The organic phase was washed with water and brine, dried over Na_2SO_4 and evaporated. The residue was purified by short column chromatography over silica gel to afford bisketal product **85** (0.21 g, 53 %).

^{1}H NMR: δ 1.49-1.60 (*m*, 3H); 1.62-1.77 (*m*, 2H); 2.18 (*d*, 1H, *J*=11.7 Hz); 2.46-2.51 (*m*, 2H); 3.71-3.82 (*m*, 8H); 5.62 (*s*, 2H)

^{13}C NMR: δ 35.47 (*t*); 37.14 (*d*); 42.26 (*t*); 134.53 (*d*); 207.49 (*s*)

IR (neat): ν 3481; 2952; 2895; 1724; 1427; 1404; 1367; 1314; 1156; 1070; 1030; 1002; 953; 867; 849; 830; 717

EI-MS: 238 (M^+, 5.47); 165 (37.34); 150 (18.67); 137 (25.31); 86 (100); 79 (34.02); 41 (28.63)

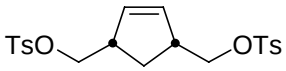
HR-MS: Anal. calcd. for $C_{13}H_{18}O_4$: 238.1205; Found: 238.1206

cis-1,3-bis-hydroxymethyl-cyclopent-4-ene[8] (86)

Ozone was bubbled into a solution of norbornadiene (20.00 g, 217.1 mmol) in a mixture of methanol (280.0 ml) and CH_2Cl_2 (160 ml) at -78°C. When all starting material had been consumed, the solution was purged with N_2, and $NaBH_4$ (8.20 g, 216.6 mmol) was added very slowly to the reaction mixture while keeping the temperature below -60°C. After 1 hr, the reaction mixture was warmed to room temperature, and sat. K_2CO_3 was added. Solvents were evaporated under reduced pressure, and the residue was extracted with EA. The product was isolated by distillation to give the product **86** (15.70 g, 56.4%) as a clear oil.

^{1}H NMR: δ 1.32 (*dt*, 1H, J_1=5.4 Hz, J_2=13.5 Hz); 2.13 (*dt*, 1H, J_1=9.3 Hz, J_2=13.5 Hz); 2.79-2.87 (*m*, 2H); 3.49 (*d*, 4H, *J*=4.8 Hz); 3.94 (*s*, 2H); 5.64 (*s*, 2H)

^{13}C NMR: δ 28.80 (*t*); 47.93 (*d*); 65.92 (*t*); 133.31 (*d*)



cis-1,3-bis(toluenesulfonyloxymethyl)-cyclopent-4-ene[8] (87)

To a solution of diol **86** (6.40 g, 50.0 mmol), *p*-toluenesulfonyl chloride (28.6 g, 150 mmol) in dry ether (50 ml), pyridine (25.0 ml) was added dropwise at 0°C. The reaction mixture was stirred for another 2 hr after removal of the ice bath. The mixture was poured into ice water and ether was evaporated carefully. The residue was added more ice water and excess *p*-toluenesulfonyl chloride was consumed after 3 hr. The white solid was filtered and washed with water and methanol. The solid was dried under reduced pressure to give the product **87** (18.7 g, 86%) without further purification.

^{1}H NMR: δ 1.09 (*dt*, 1H, J_1=6.3 Hz, J_2=13.5 Hz); 2.13 (*dt*, 1H, J_1=8.7 Hz, J_2=13.5 Hz); 2.42 (*s*, 6H); 2.93-3.02 (*m*, 2H); 3.84 (*d*, 4H, *J*=4.5 Hz); 5.57 (*s*, 2H); 7.31-7.34 (*m,* 4H); 7.72-7.76 (*m,* 4H)

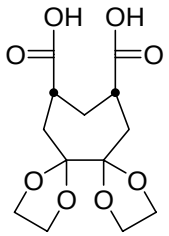
^{13}C NMR: δ 21.60 (*q*); 29.11 (*t*); 44.96 (*d*); 72.91 (*t*); 127.83 (*d*); 129.86 (*d*); 132.46 (*d*); 132.76 (*s*); 144.86 (*s*)

cis-1,3-bis(cyanomethyl)-cyclopent-4-ene[8] (88)

A solution of ditosylate **87** (10.0 g, 22.9 mmol) and NaCN (4.5 g, 91.8 mmol) in DMF (50.0 ml) was heated at 60°C for 30 hr. The reaction mixture was evaporated under reduced pressure and the residue was triturated with EA, washed with water and 0.5N HCl. The organic solutions were dried over Na_2SO_4 and evaporated. The residue was purified by column chromatography over silica gel to give the product **88** (3.1 g, 93%) as a colorless oil.

^{1}H NMR ($CDCl_3$): δ 1.19 (*dt*, 1H, J_1=6.9 Hz, J_2=13.5 Hz); 2.42 (*d*, 4H, *J*=6.6 Hz); 2.50 (*dt*, 1H, J_1=8.4 Hz, J_2=13.5 Hz); 3.00-3.09 (*m*, 2H); 5.73 (*s*, 2H)

^{13}C NMR ($CDCl_3$): δ 23.19 (*t*); 32.73 (*t*); 41.93 (*d*); 118.34 (*s*); 133.82 (*t*)



(12RS,14SR)-1,4,7,10-tetraoxadispiro[4.0.4.5]pentadecane-12,14-dicarboxylic acid (89)

A mixture of **85** (0.21, 0.88 mmol), ether (20 mL), and water (20 mL) was cooled in an ice bath. Solid $KMnO_4$ (0.50 g, 3.16 mmol) was added in small portions with efficient stirring and cooling within 30 min. The mixture was then stirred at room temperature for 6 h. Solid Na_2SO_3 (0.30 g, 2.38 mmol) was added, MnO_2 was filtered off, and the cake was washed several times with 5% $NaHCO_3$. The clear filtrate was adjusted to pH 7 with conc. HCl and the insoluble solid was extracted with EA. The solution was cooled in an ice bath then acidified with conc. HCl to ~pH 3 and extracted immediately with EA. The extracts were combined, dried over Na_2SO_4, and evaporated to furnish diacid **89** (0.20 g, 75 %).

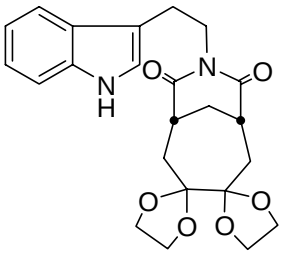
^{1}H NMR (CD_3OD): δ 1.87-2.00 (*m*, 2H); 2.09-2.11 (*m*, 3H); 2.25 (*dt*, 1H, J_1=11.4 Hz, J_2=3.3 Hz); 2.58-2.67 (*m*, 2H); 3.88-4.02 (*m*, 8H); 5.00 (*br*)

^{13}C NMR (CD_3OD): δ 32.33 (*t*); 37.97 (*t*); 40.5 (*d*); 66.79 (*t*); 66.91 (*t*); 112.01 (*s*); 179.15 (*s*)

IR (neat): ν 3369; 2969; 2889; 2362; 2337; 1695; 1456; 1431; 1363; 1295; 1165; 1117; 1064; 1036; 955; 900; 654

EI-MS: 302 (M^+); 284; 256; 240; 216; 212; 198; 185; 157; 143; 112; 99; 86

HR-MS: Anal. calcd. for $C_{13}H_{18}O_8$: 302.1001; Found: 302.1002



3,4-bis(1,3-dioxolan-2-yl)-8-[2-(1*H*-indol-3-yl)ethyl]-

8-azabicyclo[4.3.1]decane-7,9-dione (90)

To an ice-cooled solution of diacid **89** (0.30 g, 1 mmol) in dry THF (10 ml) was added triethylamine (0.25 g, 2.5 mmol), and a solution of ethyl chloroformate (0.27 g, 2.4 mmol) in dry THF (5 ml) dropwise. The reaction mixture was stirred overnight at room temperature, and then evaporated *in vacuo* below 20^{o}C. The residue (0.28 g) and tryptamine (0.16 g , 1 mmol) were dissolved in THF (10 ml) and the mixture was heated at reflux for 8 hr. On cooling, acetyl chloride (1 ml) was added, and then the mixture was heated at reflux for 10 hr. Volatile materials were evaporated and the residue was purified by column chromatography over silica gel to afford **90** (0.40 g, 95 %).

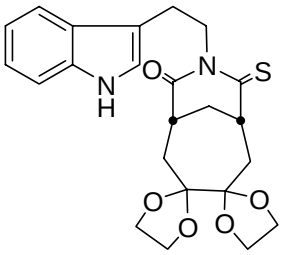
^{1}H NMR: δ 2.03-2.14 (*m*, 2H); 2.21-2.28 (*m*, 4H); 2.90-2.99 (*m*, 4H); 3.80-4.02 (*m*, 10H); 7.06 (*s*, 1H); 7.10-7.24 (*m*, 2H); 7.32-7.34 (*m*, 2H); 7.85-7.88 (*m*, 2H); 8.03 (*br*, 1H)

^{13}C NMR: δ 22.40 (*t*); 22.59 (*t*); 35.40 (*d*); 37.16 (*t*); 40.99 (*t*); 65.54 (*t*); 65.73 (*t*); 110.95 (*d*); 111.53 (*s*); 113.42 (*s*); 119.38 (*d*); 121.94 (*d*); 121.96 (*d*); 127.59 (*s*); 136.19 (*s*); 176.17 (*s*) **(one $CH_{(Ar)}$ peak was not found)**

IR (neat): ν 3406; 3057; 2969; 2895; 1716; 1663; 1456; 1430; 1357; 1278; 1177; 1145; 1117; 1078; 1044; 951; 904; 744

EI-MS: 426 (M^{+}, 4.11); 340 (2.27); 212 (7.43); 143 (100); 130 (17.34)

HR-MS: Anal. calcd. for $C_{23}H_{26}O_6N_2$: 426.1798; Found: 426.1795



(1RS,6SR)-3,4-bis(1,3-dioxolan-2-yl)-8-[2-(1*H*-indol-3-yl)ethyl]-9-thioxo-8-azabicyclo[4.3.1]decan-7-one (92)

A mixture of imide **90** (0.50 g, 1.2 mmol) and Lawesson's reagent (0.95 g, 2.35 mmol) was reflux in dry toluene (15 ml) for 10 hr. Evaporation left a residue which was purified by column chromatography over silica gel to afford **92** (0.35 g, 67.5 %).

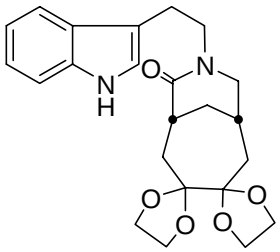
^{1}H NMR: δ 2.15-2.58 (*m*, 6H); 2.95-3.05 (*m*, 2H); 3.13-3.23 (*m*, 1H); 3.56-3.58 (*m*, 1H); 3.77-4.07 (*m*, 8H); 4.34-4.44 (*m*, 1H); 4.63-4.73 (*m*, 1H); 7.06 (s, 1H); 7.10-7.20 (*m*, 2H); 7.31-7.33 (*d*, 1H, *J*=5.4 Hz); 7.90-7.93 (*m*, 1H); 8.18 (*br*, 1H) **(one CH_2 (ketal) peak was not found)**

^{13}C NMR: δ 21.18 (*t*); 23.08 (*t*); 35.14 (*d*); 37.95 (*t*); 40.20 (*t*); 45.52 (*d*); 47.44 (*t*); 65.29 (*t*); 65.63 (*t*); 65.75 (*t*); 110.93 (*d*); 111.30 (*s*); 113.43 (*s*); 119.94 (*s*); 119.23 (*d*); 119.42 (*d*); 121.85 (*d*); 122.14 (*d*); 127.51 (*s*); 136.14 (*s*); 172.66 (*s*); 214.59 (*s*)

IR (neat): ν 3405; 2963; 2932; 2889; 1698; 1456; 1427; 1386; 1362; 1315; 1283; 1231; 1176; 1141; 1095; 1071; 1043; 948; 906; 734

EI-MS: 442 (M^+, 2.19); 143 (100); 130 (7.33)

HR-MS: Anal. calcd. for $C_{23}H_{26}O_5N_2S$: 442.1564; Found: 442.1565



(1RS,6RS)-3,4-bis(1,3-dioxolan-2-yl)-8-[2-(1*H*-indol-3-yl)ethyl]-8-azabicyclo[4.3.1]decan-7-one (93)

A suspension of Raney nickel (*ca.* 2 g) in absolute *t*-BuOH (8 ml) added to a hot solution of **92** (0.40 g, 0.9 mmol) in abs. *t*-BuOH (30 ml). The mixture was stirred for 3 hr at 60°C. The catalyst was separated by filtration and then washed with CH_2Cl_2. The filtrate was dried over Na_2SO_4 and evaporated to afford product **93** (0.35 g, 94 %).

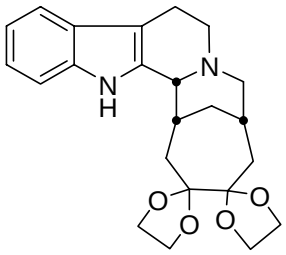
^{1}H NMR: δ 1.88-1.95 (*m*, 1H); 2.05-2.19 (*m*, 3H); 2.32-2.37 (*m*, 1H); 2.43 (*dd*, 1H, J_1=3.3 Hz, J_2=14.4 Hz); 2.58-2.60 (*m*, 1H); 2.88-3.14 (*m*, 3H); 3.29-3.41 (*m*, 2H); 3.83-4.14 (*m*, 10H); 7.00 (*s*, 1H); 7.04-7.16 (*m*, 2H); 7.33 (*d*, 1H, J=7.8 Hz); 7.65 (*d*, 1H, 7.8 Hz); 8.69 (*br*, 1H)

^{13}C NMR: δ 22.30 (*t*); 24.79 (*d*); 27.64 (*t*); 34.97 (*d*); 36.65 (*t*); 37.75 (*t*); 48.40 (*t*); 56.44 (*t*); 65.20 (*t*); 65.28 (*t*); 65.68 (*t*); 66.05 (*t*); 111.18 (*d*); 111.79 (*s*); 112.13 (*s*); 113.02 (*s*); 118.69 (*d*); 118.97 (*d*); 121.64 (*d*); 122.18 (*d*); 127.41 (*s*); 136.32 (*s*); 171.45 (*s*)

IR (neat): ν 3258; 3053; 2959; 2931; 2893; 2694; 1614; 1494; 1455; 1428; 1340; 1297; 1167; 1169; 1110; 1084; 1046; 1010; 951; 893; 741; 700

EI-MS: 412 (M^+, 4.19); 270 (9.88); 210 (14.22); 198 (15.27); 143 (100); 130 (25.9)

HR-MS: Anal. calcd. for $C_{23}H_{28}O_5N_2$: 412.1999; Found: 412.2008



Bisketal (91)

Freshly distilled $POCl_3$ (0.6 ml) was added to a boiling solution of lactam **93** (0.15 g, 0.36 mmol) in benzene (5 ml) with vigorous stirring. After refluxing for 3 hr, the excess of $POCl_3$ and benzene were removed in vacuo and the residue was dissolved in CH_2Cl_2 / MeOH (8 ml, 1:1), then $NaBH_4$ (0.10 g) was added in protions. After stirring for 2 hr at room temperature, solvent was evaporated and water was added to the residue. Extraction with CH_2Cl_2 followed by standard workup provided a solid which could be purified chromatographically (0.13 g, 90.2 %), *dec.* ~200°C

^{1}H NMR ($CDCl_3$+CD_3OD): δ 1.33-1.41 (*m*, 1H); 1.56-1.61 (*m*, 1H); 1.75-1.96 (*m*, 4H); 2.20 (*m*, 1H); 2.35-2.49 (*m*, 3H); 2.62-2.66 (*m*, 1H); 2.76-2.82 (*m*, 2H); 3.13 (*m*, 1H); 3.32-3.39 (*m*, 1H); 3.77-3.88 (*m*, 8H); 6.86-6.95 (*m*, 2H); 7.15 (*d*, 1H, *J*=7.5 Hz); 7.30 (*d*, 1H, *J*=7.5 Hz)

^{13}C NMR ($CDCl_3$+CD_3OD): δ 21.37 (*t*); 28.58 (*d*); 29.99 (*t*); 31.07 (*d*); 32.88 (*t*); 39.96 (*t*); 52.66 (*t*); 61.20 (*t*); 63.81 (*d*); 64.42 (*t*); 65.14 (*t*); 65.32 (*t*); 65.50 (*t*); 110.00 (*s*); 110.45 (*d*); 113.15 (*s*); 113.45 (*s*); 117.52 (*d*); 118.53 (*d*); 120.50 (*d*); 127.18 (*s*); 134.37 (*s*); 136.18 (*s*)

IR (neat): ν 3419; 2955; 2897; **2796; 2744** (Wenkert-Bohlmann bands)**;** 2529; 2244; 2088; 1645; 1456; 1346; 1266; 1172; 1081; 1045; 952; 852; 737

EI-MS: 396 (M^+, 45.20); 251 (23.48); 211 (39.65); 184 (100); 169 (79.8); 156 (32.58); 143 (29.8); 112 (37.63)

HR-MS: Anal. calcd. for $C_{23}H_{28}O_4N_2$: 396.2050; Found: 396.2047

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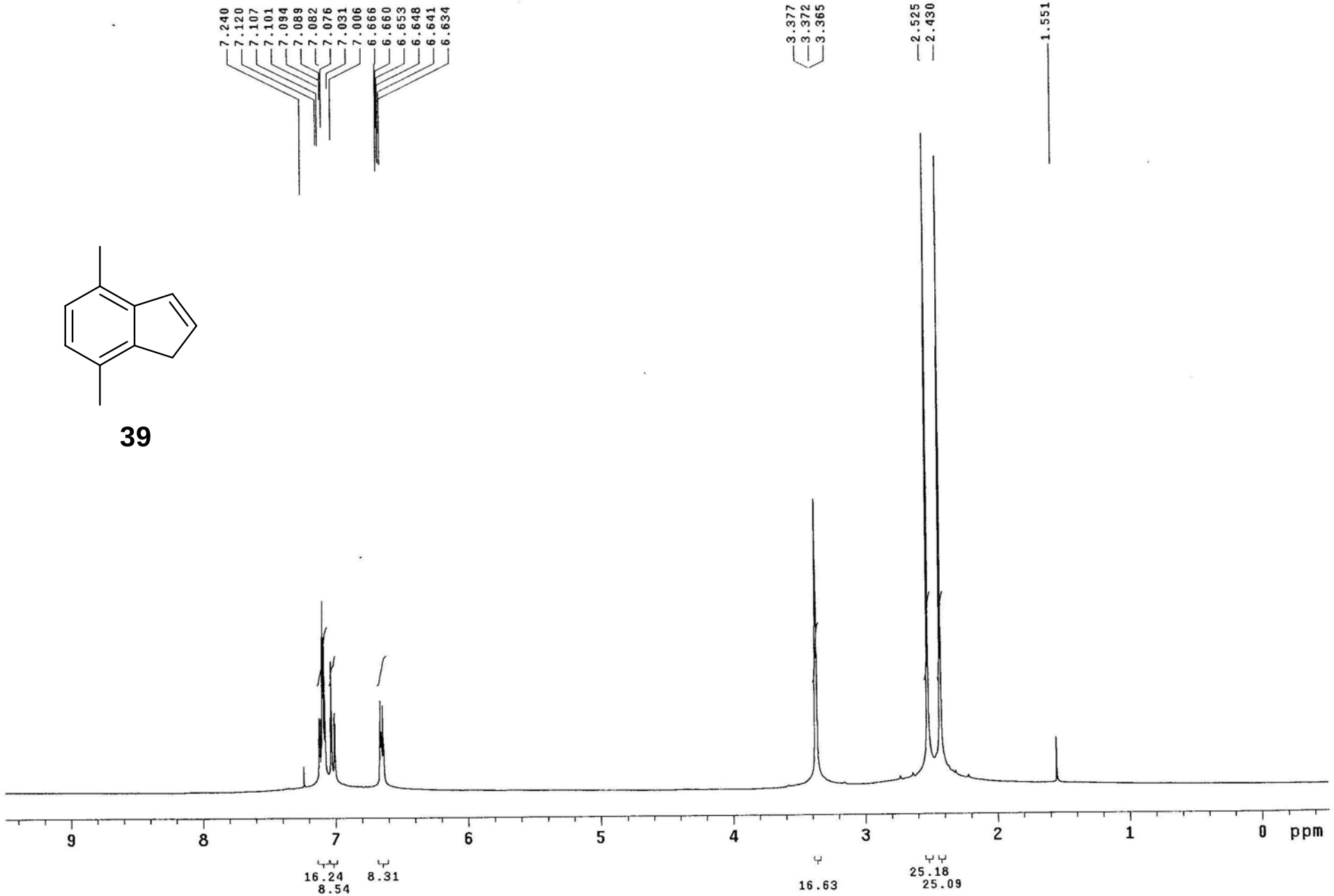
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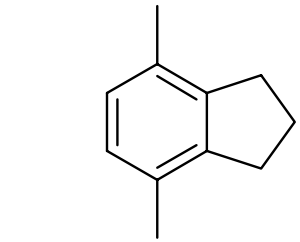

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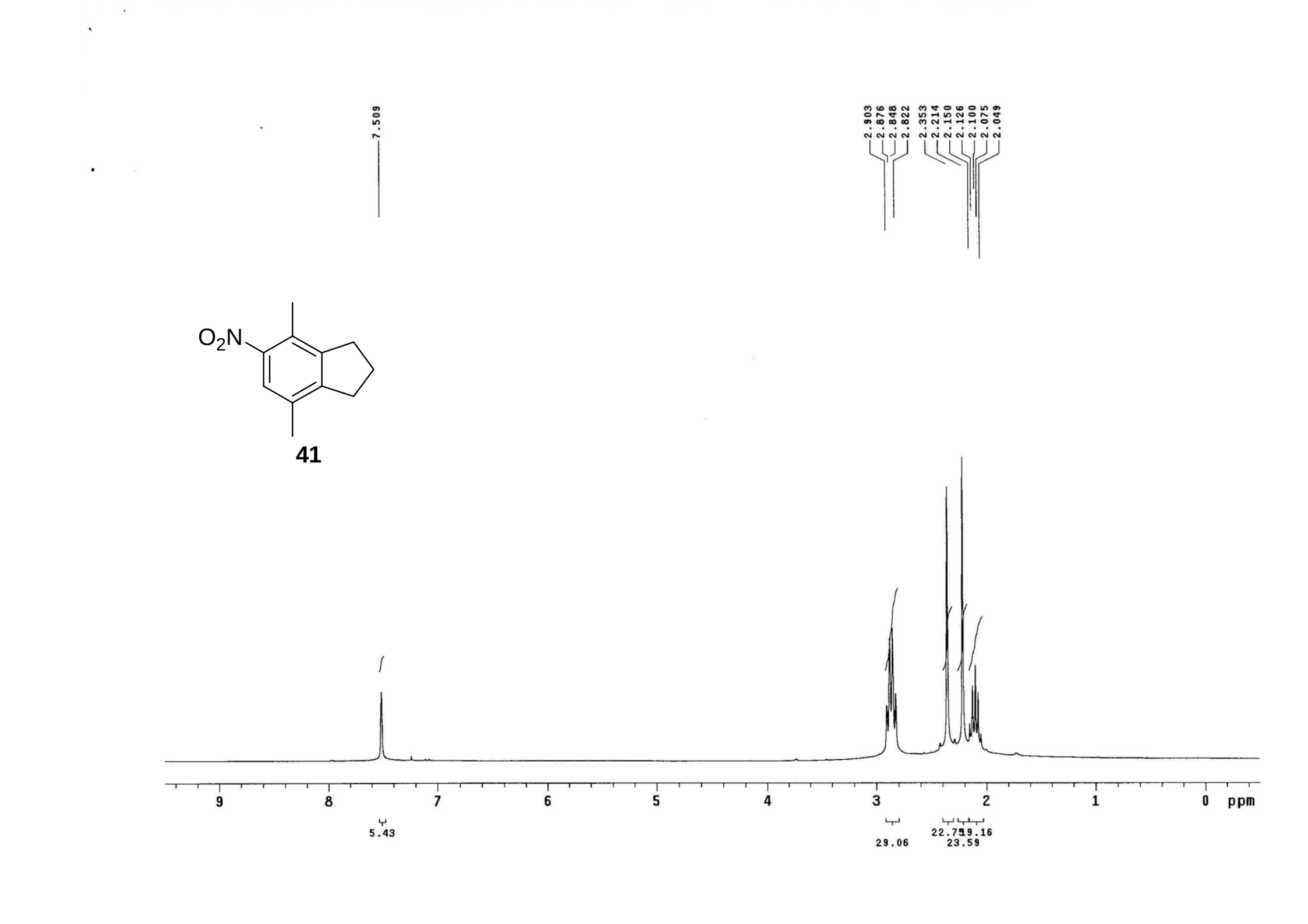
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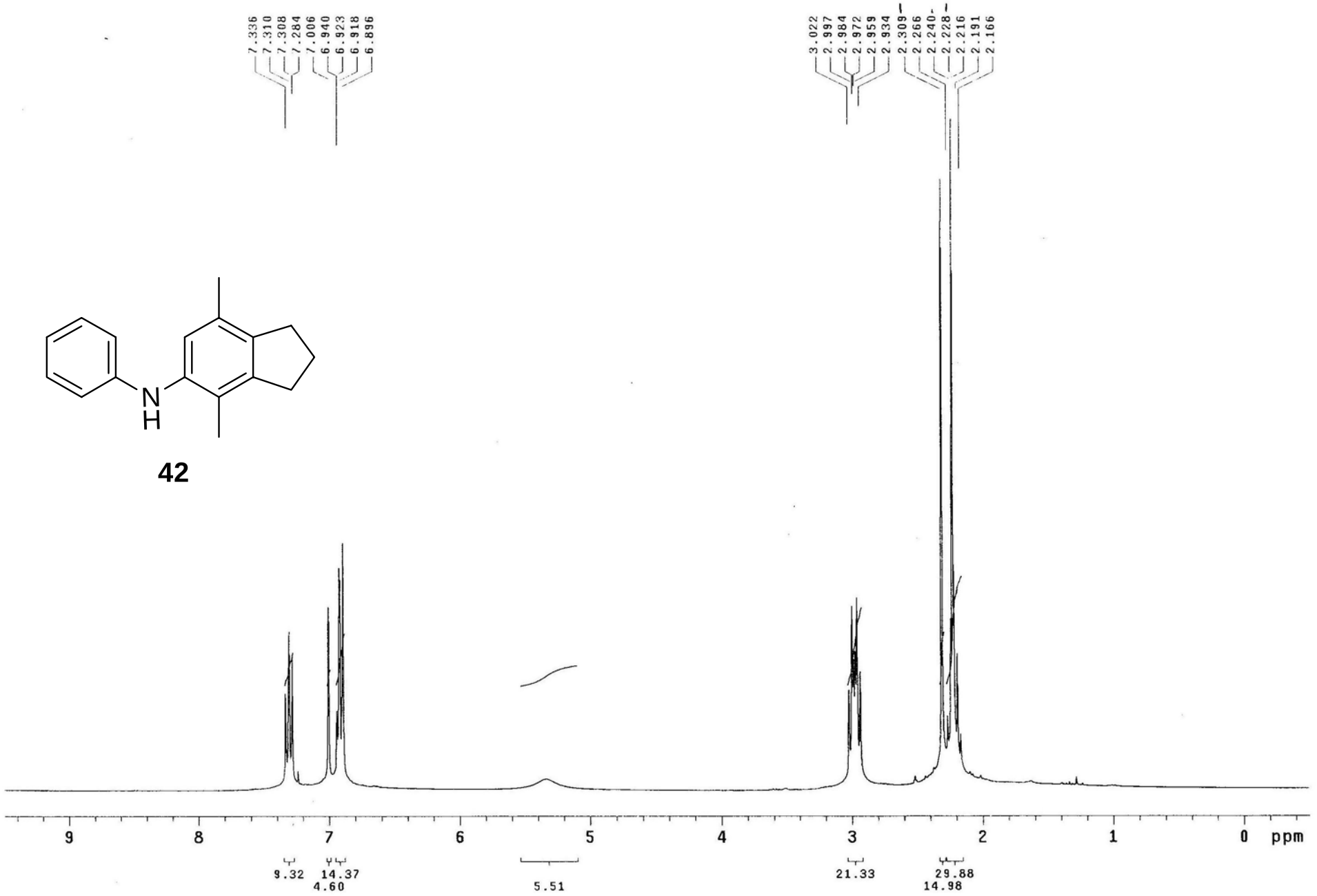
2.903
2.876
2.848
2.822
2.353
2.214
2.150
2.126
2.100
2.075
2.049
O2N
41
9
8
7
6
5
4
3
2
1
0
ppm
5.43
29.06
22.75
19.16
23.59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7.310
7.308
7.284
7.006
6.940
6.923
6.918
6.896
3.022
2.997
2.984
2.972
2.959
2.934
2.309
2.266
2.240
2.228
2.216
2.191
2.166
N
H
9
8
7
6
5
4
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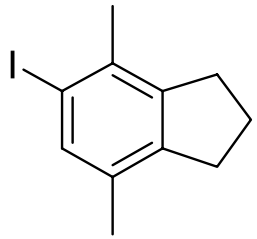
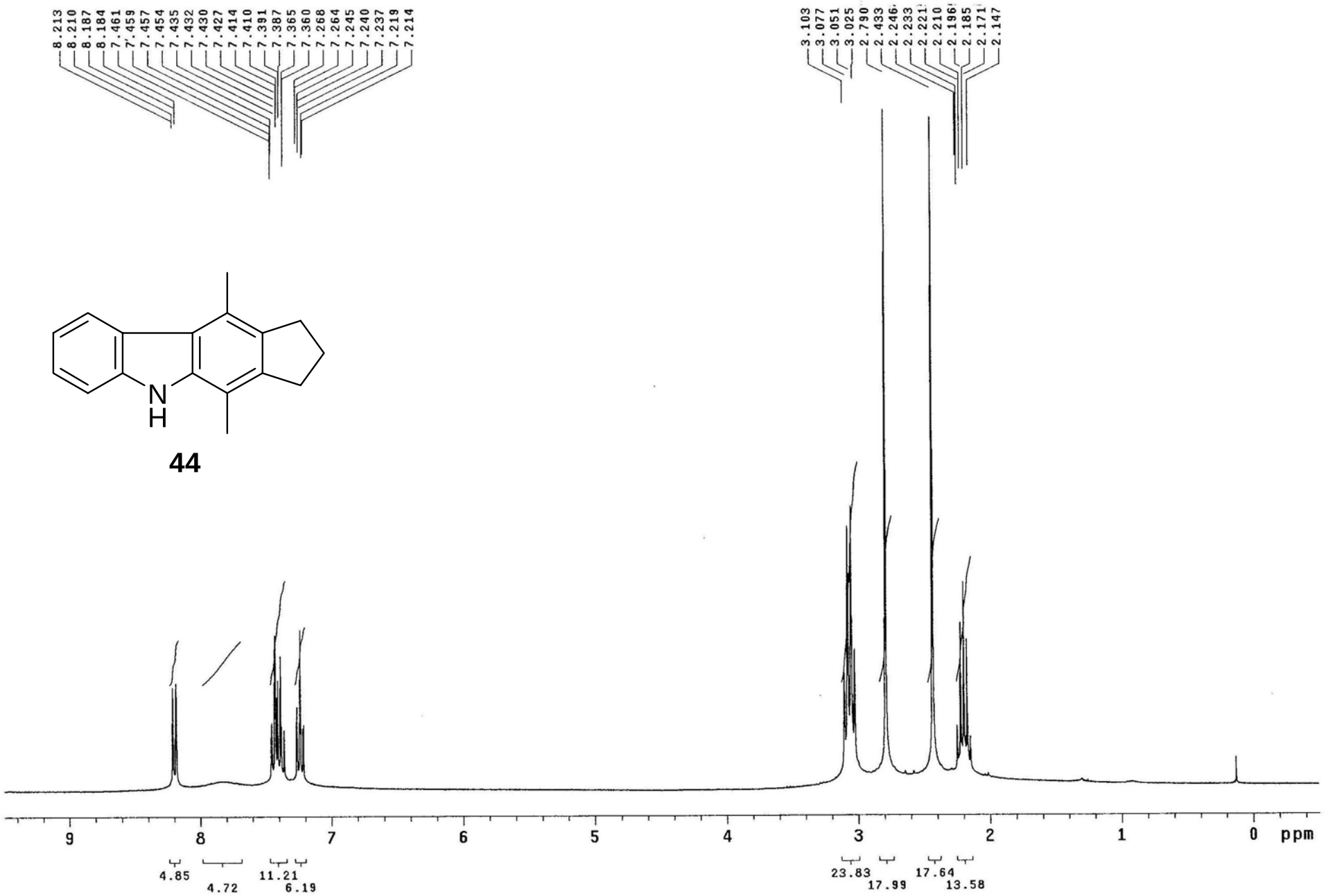
2
1
0
ppm
9.32
14.37
4.60
5.51
21.33
29.88
14.98

42


I

43

7.471
2.938
2.913
2.888
2.845
2.820
2.795
2.342
2.192
2.130
2.104
2.095
2.080
2.067
2.054
2.029
9
8
7
6
5
4
3
2
1
0
ppm
5.32
15.51
15.73
22.69
22.82
7.93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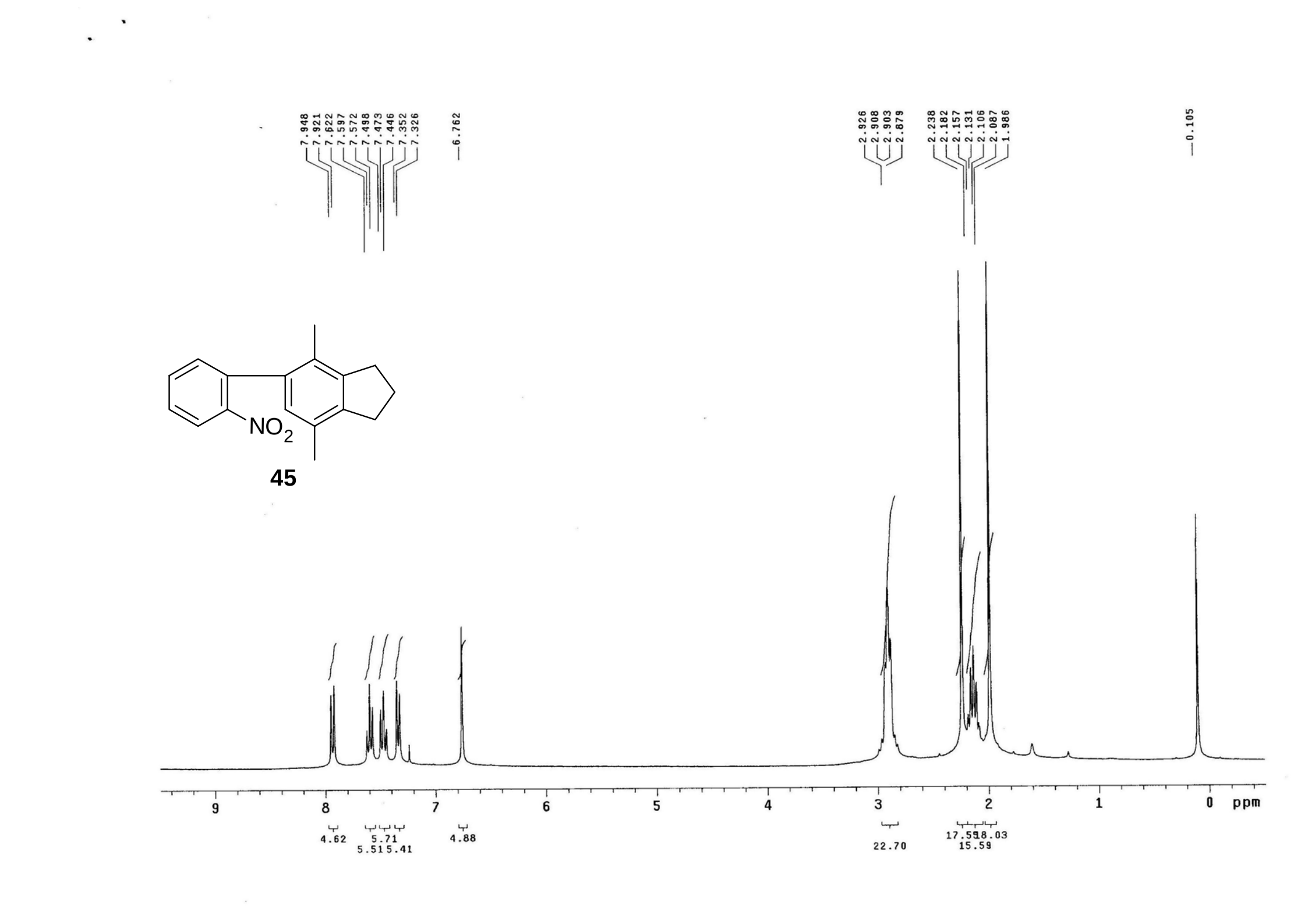
8.210
8.187
8.184
7.461
7.459
7.457
7.454
7.435
7.432
7.430
7.427
7.414
7.410
7.391
7.387
7.365
7.360
7.268
7.264
7.245
7.240
7.237
7.219
7.214
3.103
3.077
3.051
3.025
2.790
2.433
2.246
2.233
2.221
2.210
2.196
2.185
2.171
2.147
N
H
9
8
7
6
5
4
3
2
1
0
ppm
4.85
4.72
11.21
6.19
23.83
17.99
17.64
13.58

44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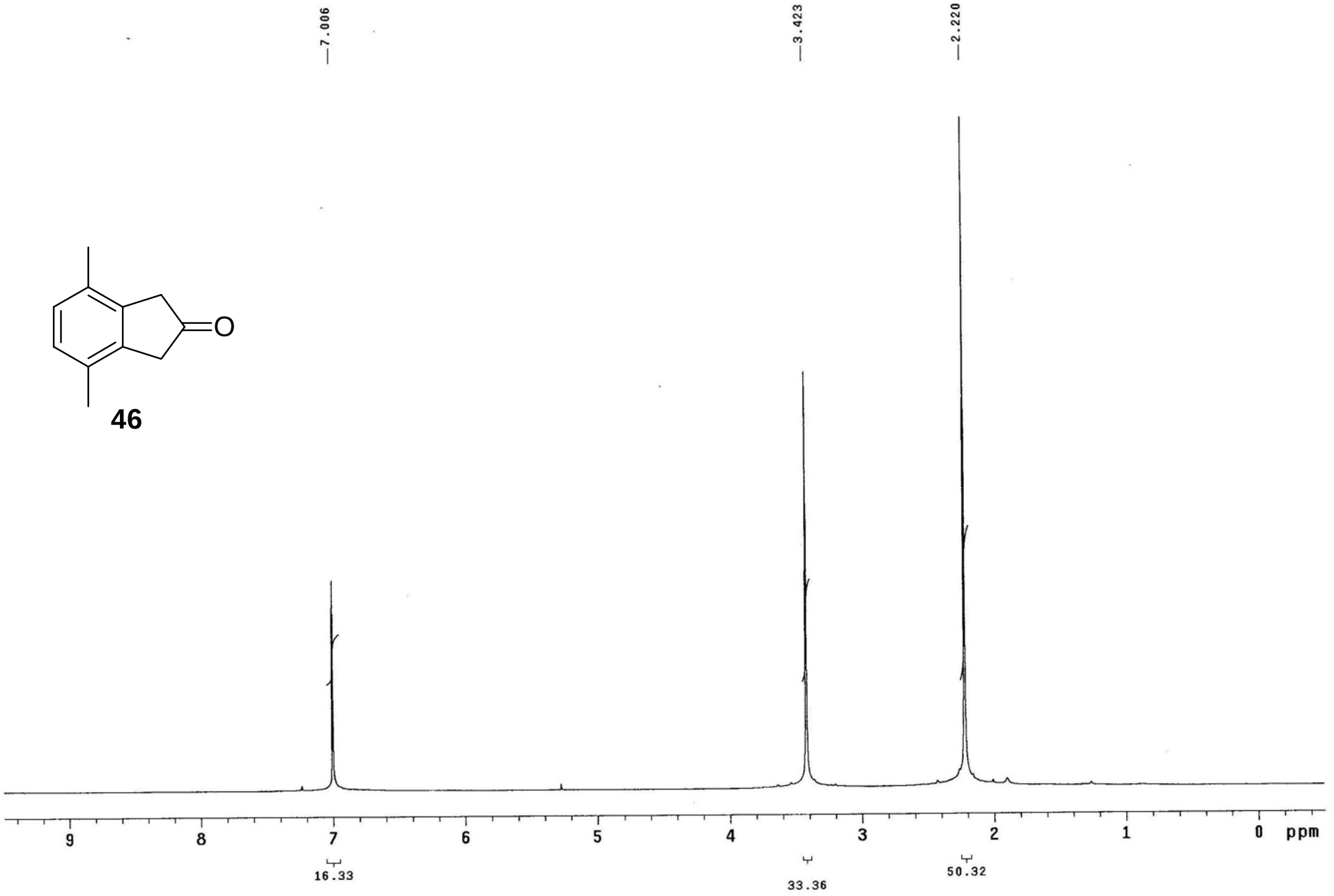
7.921
7.622
7.597
7.572
7.498
7.473
7.446
7.352
7.326
6.762
2.926
2.908
2.903
2.879
2.238
2.182
2.157
2.131
2.106
2.087
1.986
0.105
NO2
45
9
8
7
6
5
4
3
2
1
0
ppm
4.62
5.71
5.51
5.41
4.88
22.70
17.55
18.03
15.59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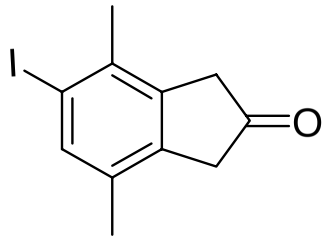
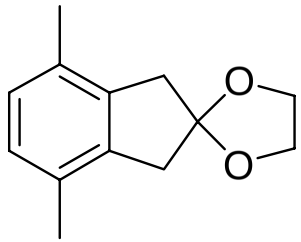
3.423
2.220
O
46
9
8
7
6
5
4
3
2
1
0
ppm
16.33
33.36
50.32


I
O

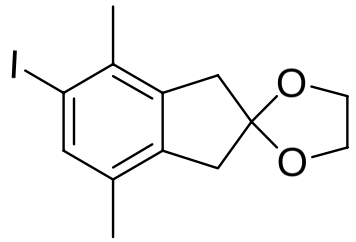
47

7.560
3.460
3.365
2.275
2.153
9
8
7
6
5
4
3
2
1
0
ppm
9.01
18.62
18.24
27.23
26.89


O
O

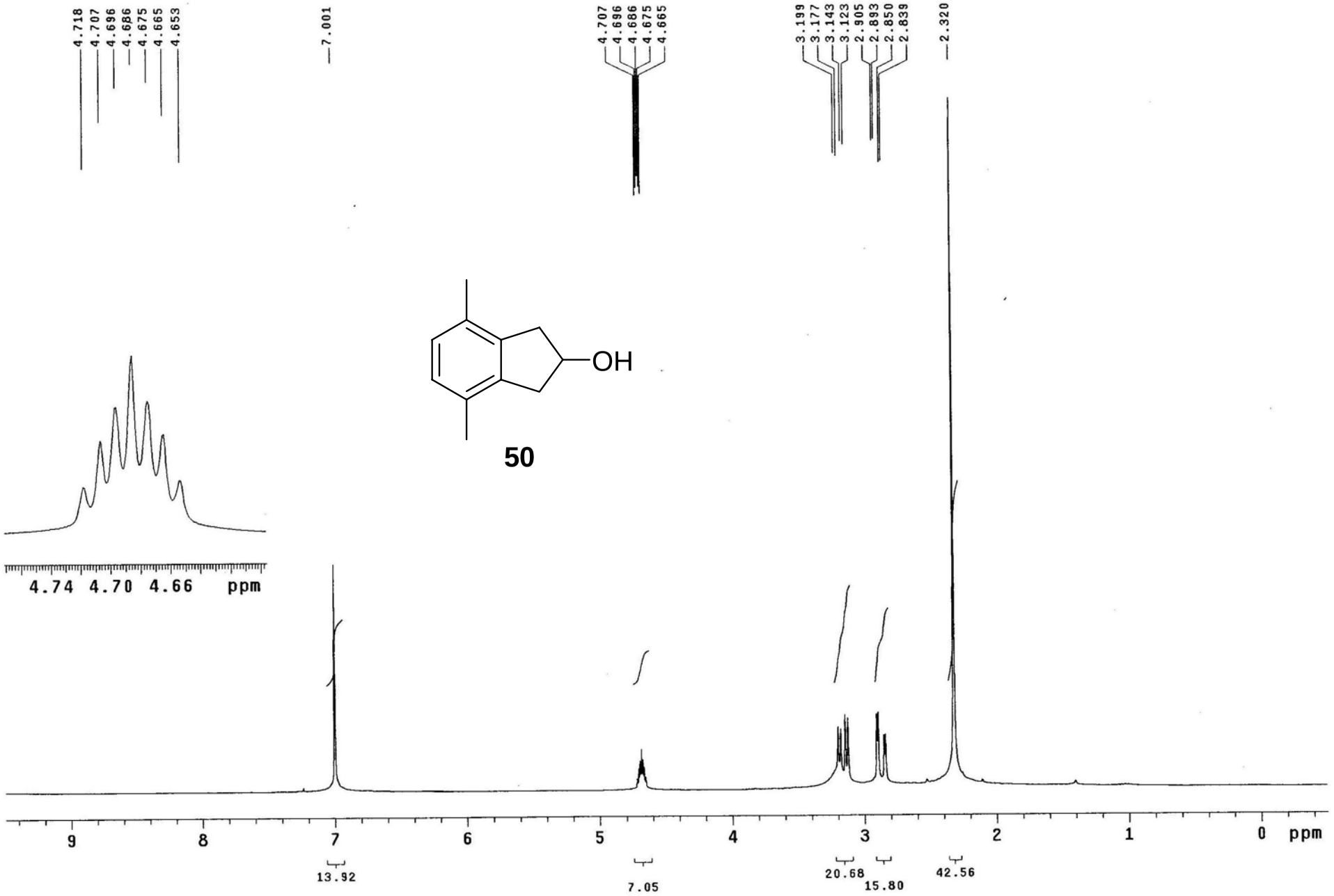
48

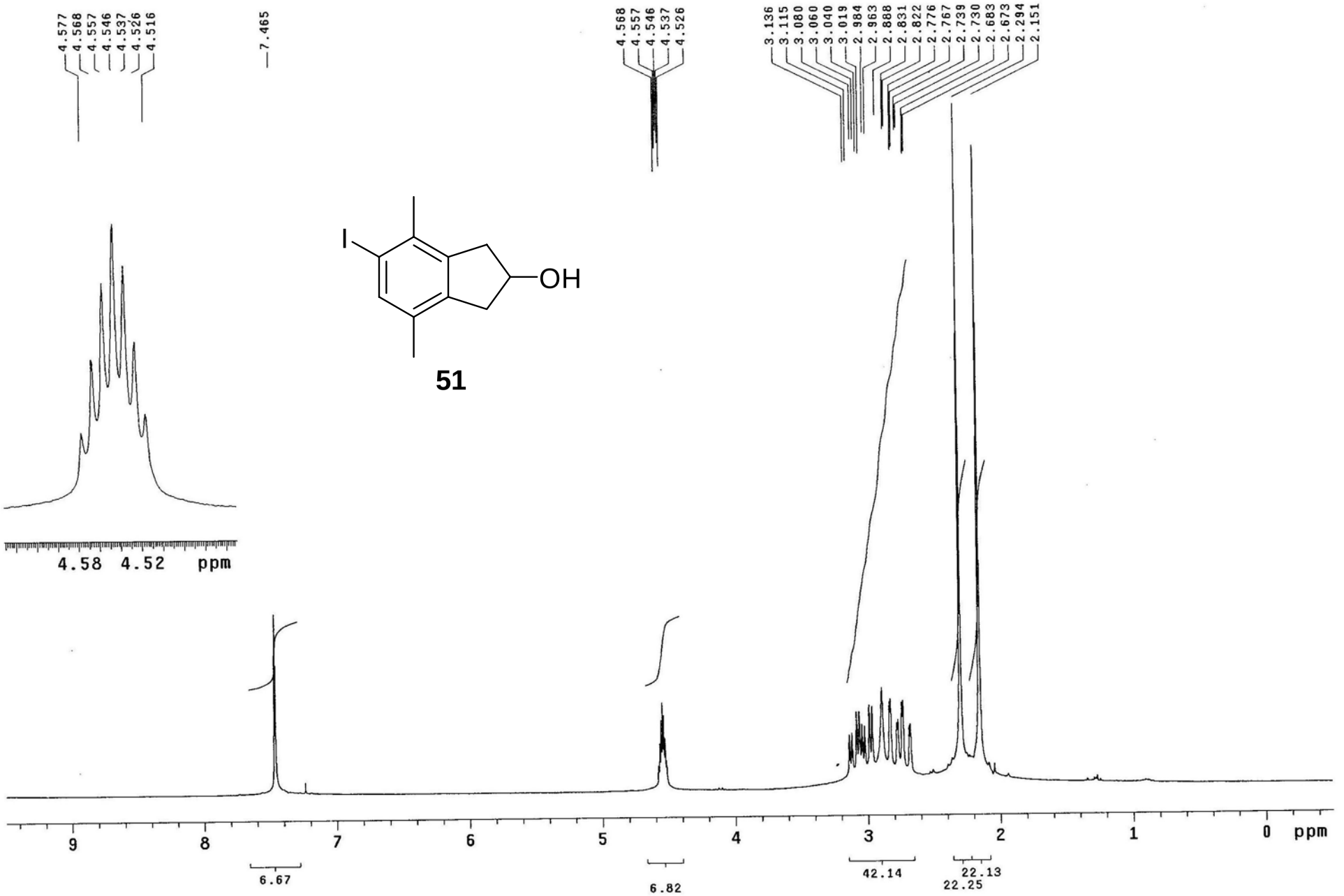
7.011
4.096
4.092
3.222
2.305
9
8
7
6
5
4
3
2
1
0
ppm
12.21
25.09
25.28
37.42

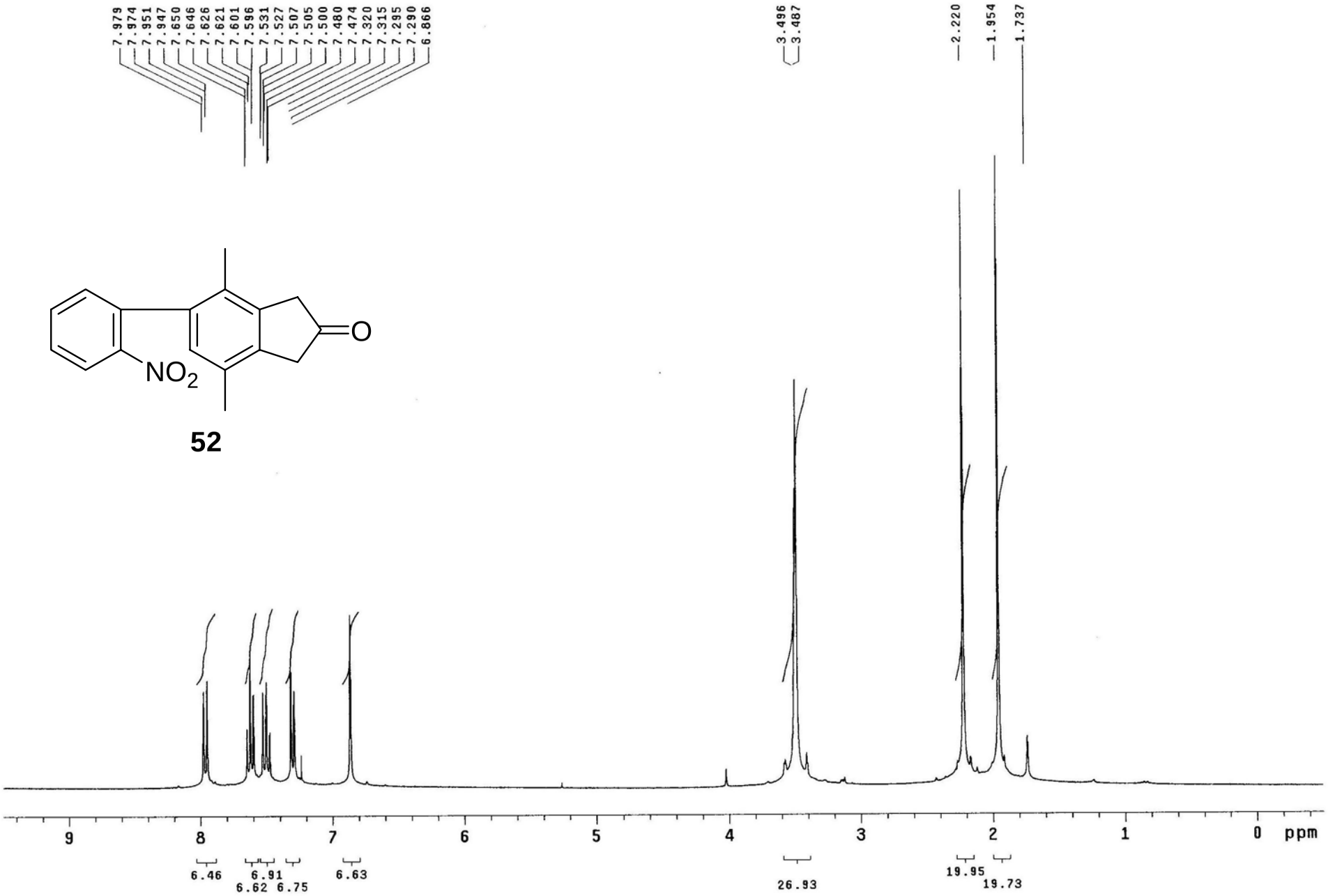

I
O
O

49

4.005
3.144
3.045
2.274
2.132
9
8
7
6
5
4
3
2
1
0
ppm
6.61
25.24
13.09
13.87
20.40
20.79


4.718
4.707
4.696
4.686
4.675
4.665
4.653
7.001
4.707
4.696
4.686
4.675
4.665
3.199
3.177
3.143
3.123
2.905
2.893
2.850
2.839
2.320
OH
50
4.74 4.70 4.66 ppm
9 8 7 6 5 4 3 2 1 0 ppm
13.92
7.05
20.68
15.80
42.56


4.577
4.568
4.557
4.546
4.537
4.526
4.516
7.465
4.568
4.557
4.546
4.537
4.526
3.136
3.115
3.080
3.060
3.040
3.019
2.984
2.963
2.888
2.831
2.822
2.776
2.767
2.739
2.730
2.683
2.673
2.294
2.151
I
OH
51
4.58 4.52 ppm
9 8 7 6 5 4 3 2 1 0 ppm
6.67
6.82
42.14
22.13
22.25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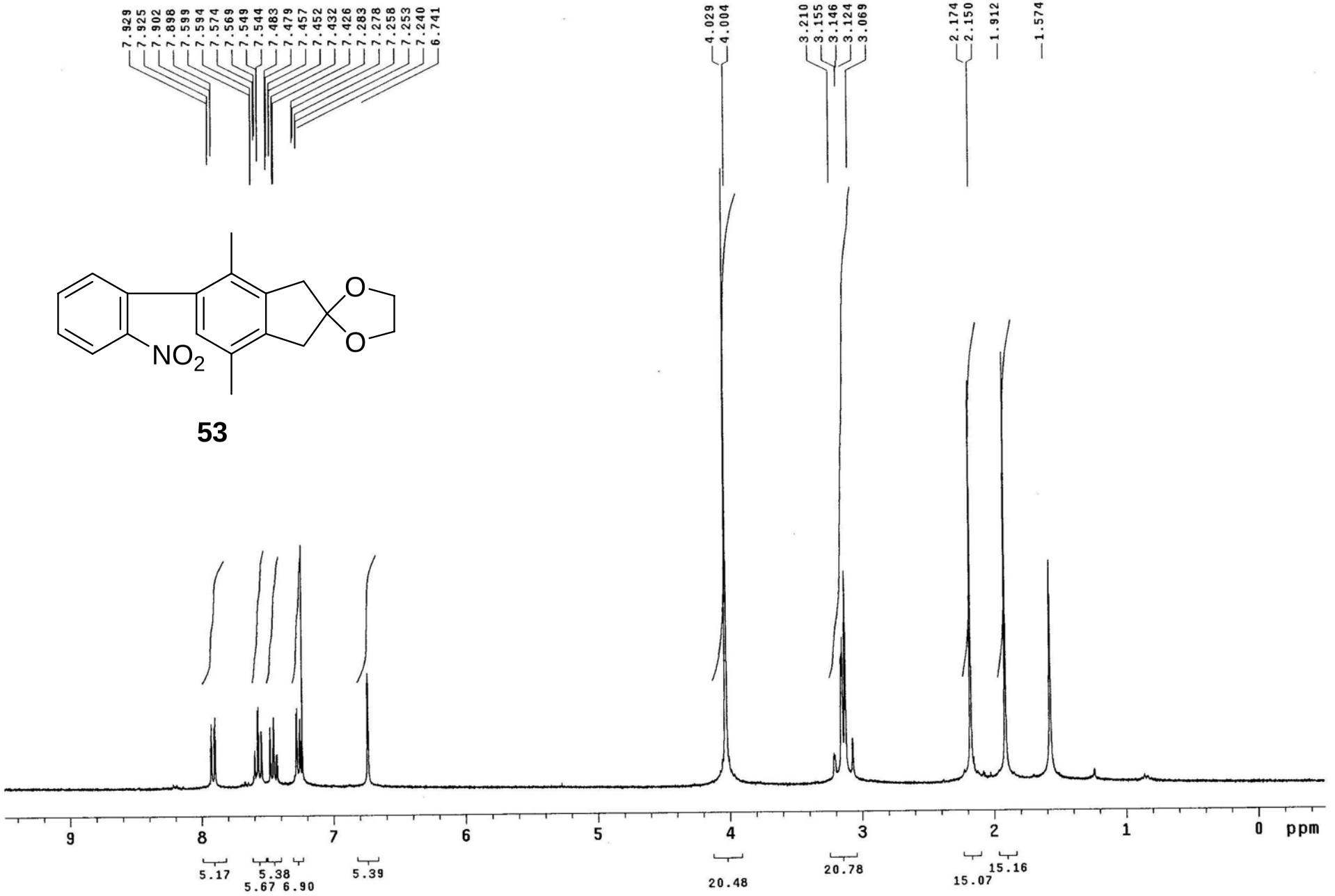
7.974
7.951
7.947
7.650
7.646
7.626
7.621
7.601
7.596
7.531
7.527
7.507
7.505
7.500
7.480
7.474
7.320
7.315
7.295
7.290
6.866
3.496
3.487
2.220
1.954
1.737
O
NO2
9
8
7
6
5
4
3
2
1
0
ppm
6.46
6.91
6.62
6.75
6.63
26.93
19.95
19.73

52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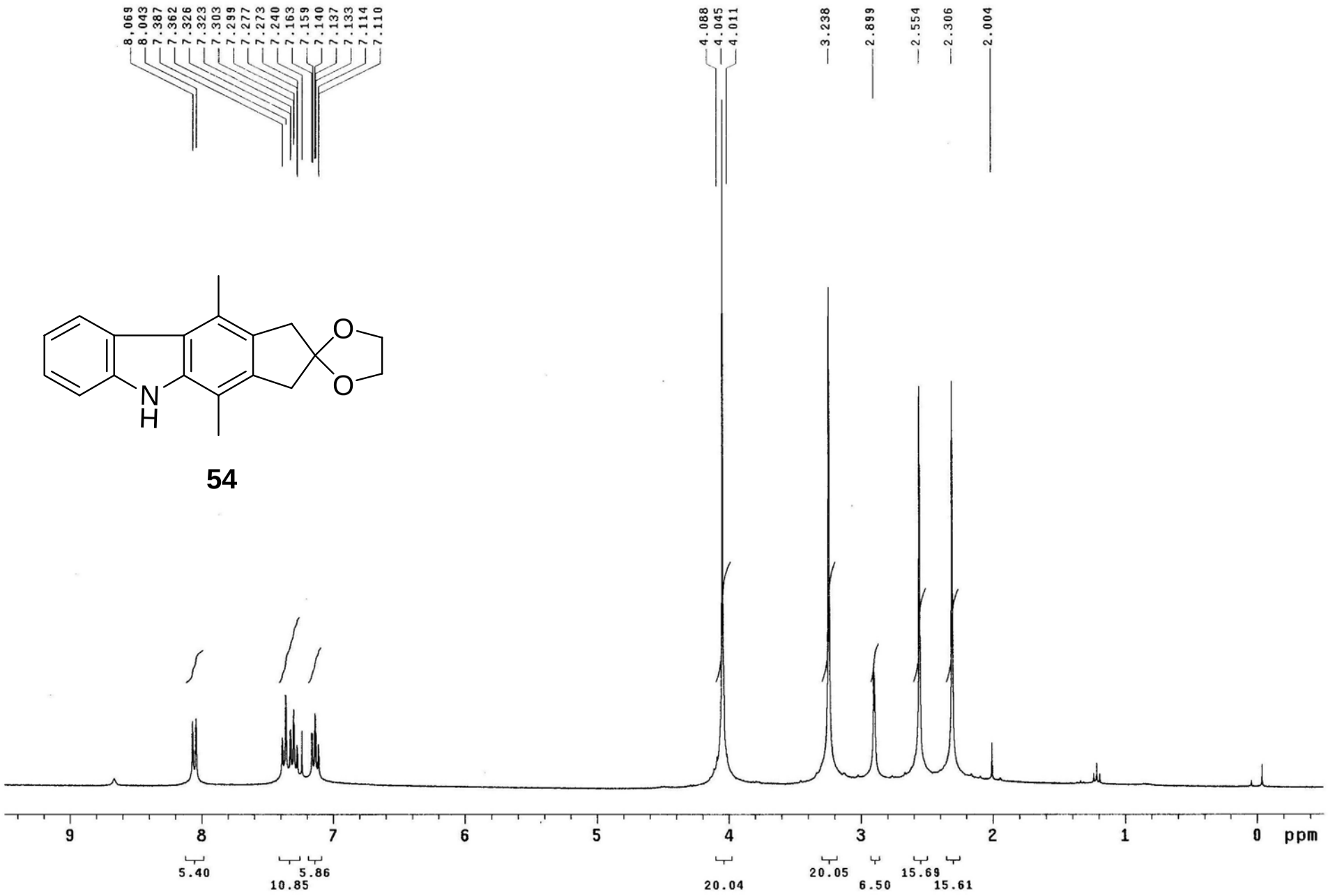
7.925
7.902
7.898
7.599
7.594
7.574
7.569
7.549
7.544
7.483
7.479
7.457
7.452
7.432
7.426
7.283
7.278
7.258
7.253
7.240
6.741
4.029
4.004
3.210
3.155
3.146
3.124
3.069
2.174
2.150
1.912
1.574
O
O
NO2
9
8
7
6
5
4
3
2
1
0 ppm
5.17
5.38
5.67 6.90
5.39
20.48
20.78
15.07
15.16

53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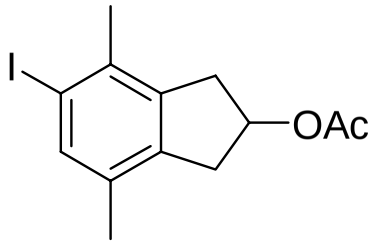
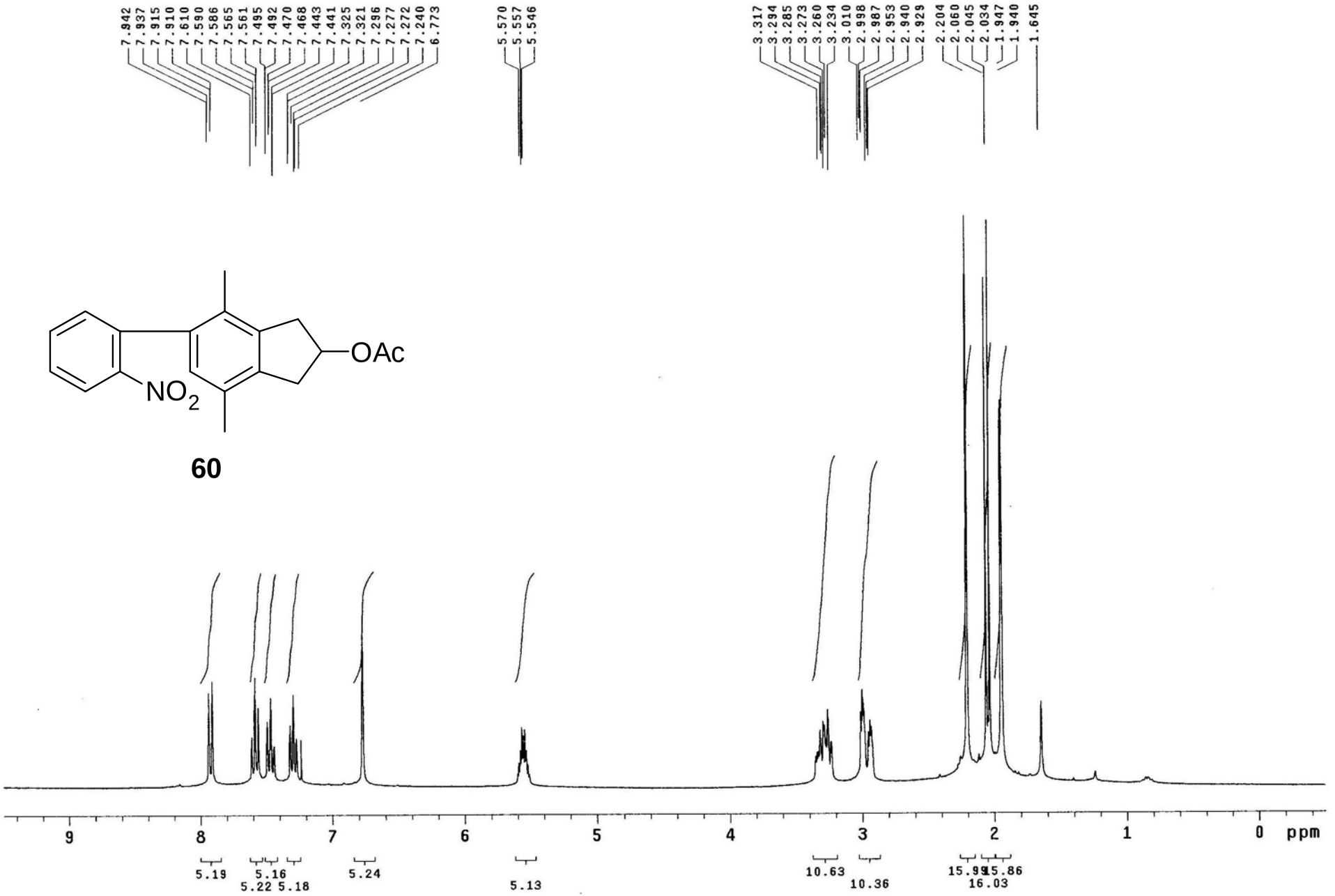
8.043
7.387
7.362
7.326
7.323
7.303
7.299
7.277
7.273
7.240
7.163
7.159
7.140
7.137
7.133
7.114
7.110
4.088
4.045
4.011
3.238
2.899
2.554
2.306
2.004
O
O
N
H
9
8
7
6
5
4
3
2
1
0
ppm
5.40
10.85
5.86
20.04
20.05
6.50
15.69
15.61

54


I
OAc

59

7.479
5.502
5.489
5.479
5.470
5.457
3.313
3.292
3.256
3.234
3.218
3.195
3.160
3.137
3.002
2.945
2.905
2.853
2.848
2.292
2.236
2.207
2.156
2.090
2.021
1.956
9
8
7
6
5
4
3
2
1
0
ppm
6.61
6.58
13.14
13.12
19.90
19.99
20.65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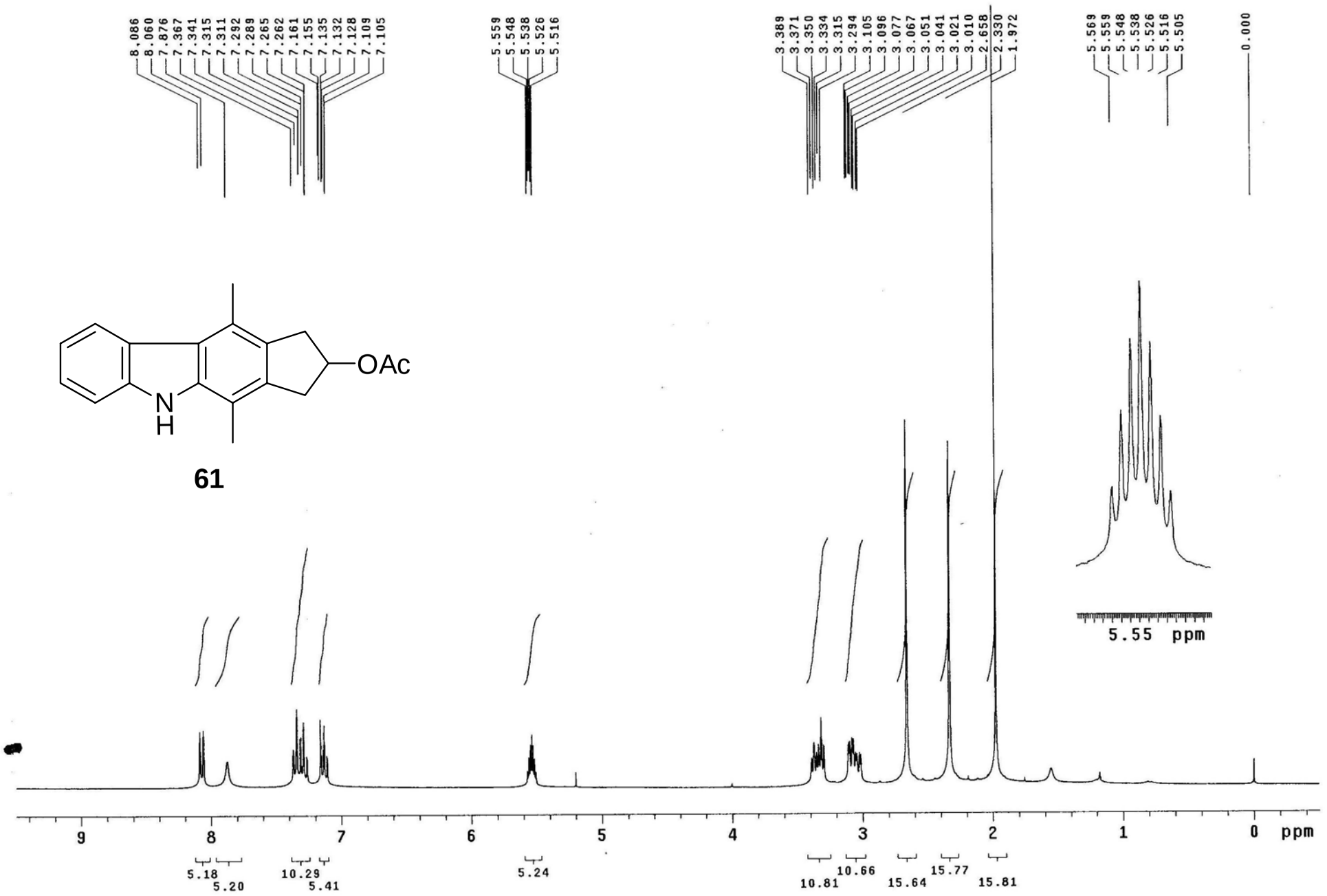
7.937
7.915
7.910
7.610
7.590
7.586
7.565
7.561
7.495
7.492
7.470
7.468
7.443
7.441
7.325
7.321
7.296
7.277
7.272
7.240
6.773
5.570
5.557
5.546
3.317
3.294
3.285
3.273
3.260
3.234
3.010
2.998
2.987
2.953
2.940
2.929
2.204
2.060
2.045
2.034
1.947
1.940
1.645
OAc
NO2
9
8
7
6
5
4
3
2
1
0
ppm
5.19
5.16
5.22
5.18
5.24
5.13
10.63
10.36
15.99
15.86
16.03

60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8.060
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7.367
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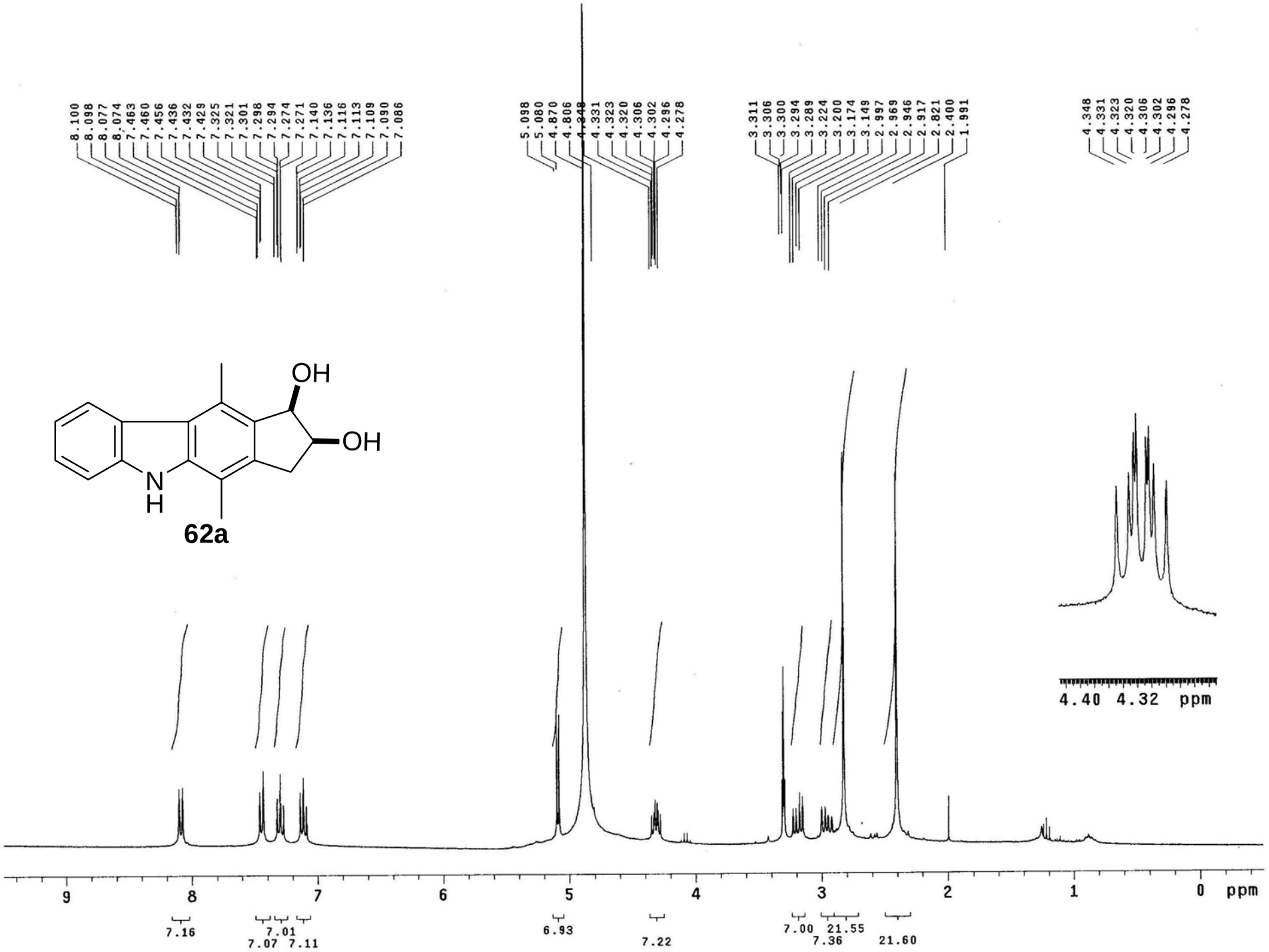
7.315
7.311
7.292
7.289
7.265
7.262
7.161
7.155
7.135
7.132
7.128
7.109
7.105
5.559
5.548
5.538
5.526
5.516
3.389
3.371
3.350
3.334
3.315
3.294
3.105
3.096
3.077
3.067
3.051
3.041
3.021
3.010
2.658
2.330
1.972
5.569
5.559
5.548
5.538
5.526
5.516
5.505
0.000
OAc
N
H
5.55 ppm
9
8
7
6
5
4
3
2
1
0 ppm
5.18
5.20
10.29
5.41
5.24
10.81
10.66
15.64
15.77
15.81

61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8.074
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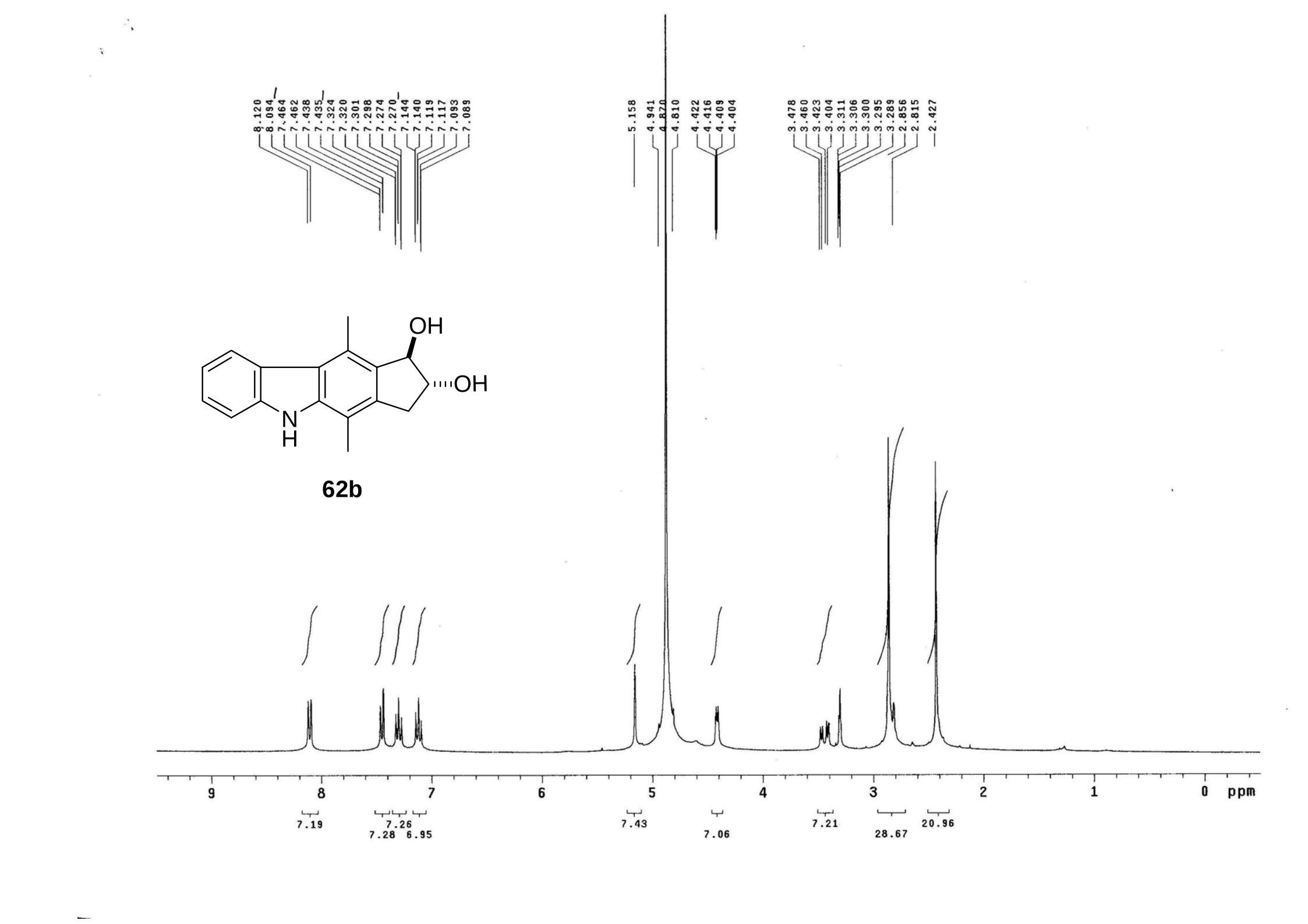
7.460
7.456
7.436
7.432
7.429
7.325
7.321
7.301
7.298
7.294
7.274
7.271
7.140
7.136
7.116
7.113
7.109
7.090
7.086
5.098
5.080
4.870
4.806
4.348
4.331
4.323
4.320
4.306
4.302
4.296
4.278
3.311
3.306
3.300
3.294
3.289
3.224
3.200
3.174
3.149
2.997
2.969
2.946
2.917
2.821
2.400
1.991
OH
OH
N
H
62a
4.40 4.32 ppm
9
8
7
6
5
4
3
2
1
0 ppm
7.16
7.01
7.07 7.11
6.93
7.22
7.00
21.55
7.36
21.60


8.120
8.094
7.464
7.462
7.438
7.435
7.324
7.320
7.301
7.298
7.274
7.270
7.144
7.140
7.119
7.117
7.093
7.089
5.158
4.941
4.870
4.810
4.422
4.416
4.409
4.404
3.478
3.460
3.423
3.404
3.311
3.306
3.300
3.295
3.289
2.856
2.815
2.427
OH
OH
N
H
9
8
7
6
5
4
3
2
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0
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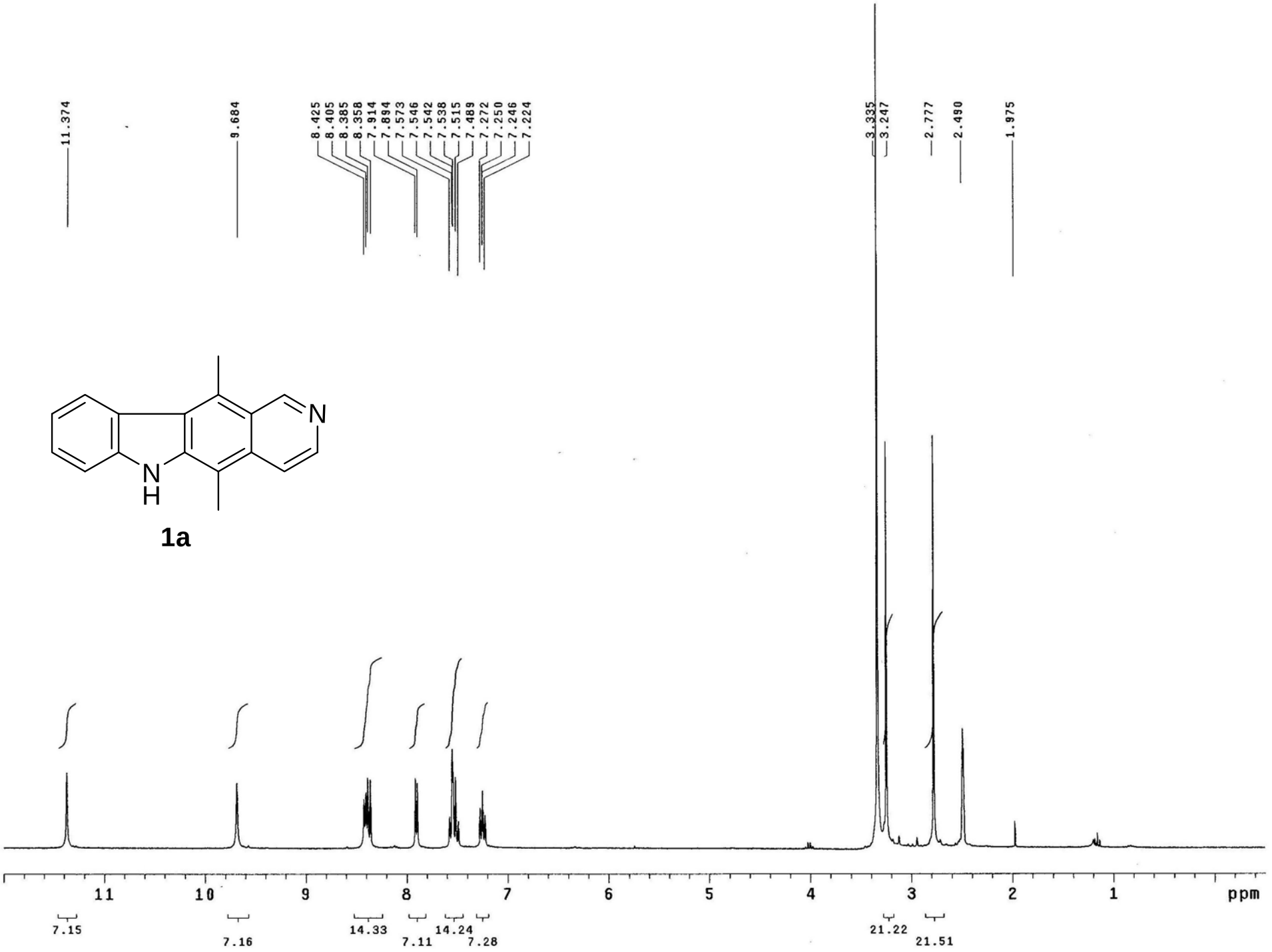
7.19
7.26
7.28
6.95
7.43
7.06
7.21
28.67
20.96

62b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8.425
8.405
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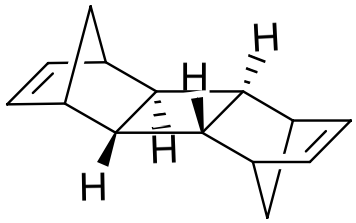
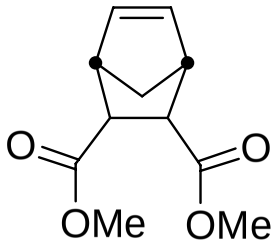
8.358
7.914
7.894
7.573
7.546
7.542
7.538
7.515
7.489
7.272
7.250
7.246
7.224
3.335
3.247
2.777
2.490
1.975
N
N
H
11
10
9
8
7
6
5
4
3
2
1
ppm
7.15
7.16
14.33
7.11
14.24
7.28
21.22
21.51

1a


H
H
H
H

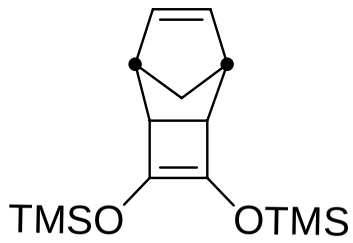
76

6.014
6.009
6.004
2.625
2.620
1.702
1.672
1.342
1.247
1.217
9
8
7
6
5
4
3
2
1
0 ppm
24.44
24.71
12.97
13.61
24.27


O
O
OMe
OMe

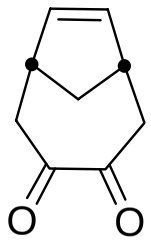
79

6.178
6.161
6.155
6.149
3.697
3.508
3.204
3.198
3.194
3.071
3.066
3.060
3.055
1.389
1.366
1.361
1.354
1.257
1.256
1.229
1.227
9
8
7
6
5
4
3
2
1
0
ppm
13.96
41.99
14.44
13.94
7.79
7.88


TMSO
OTMS

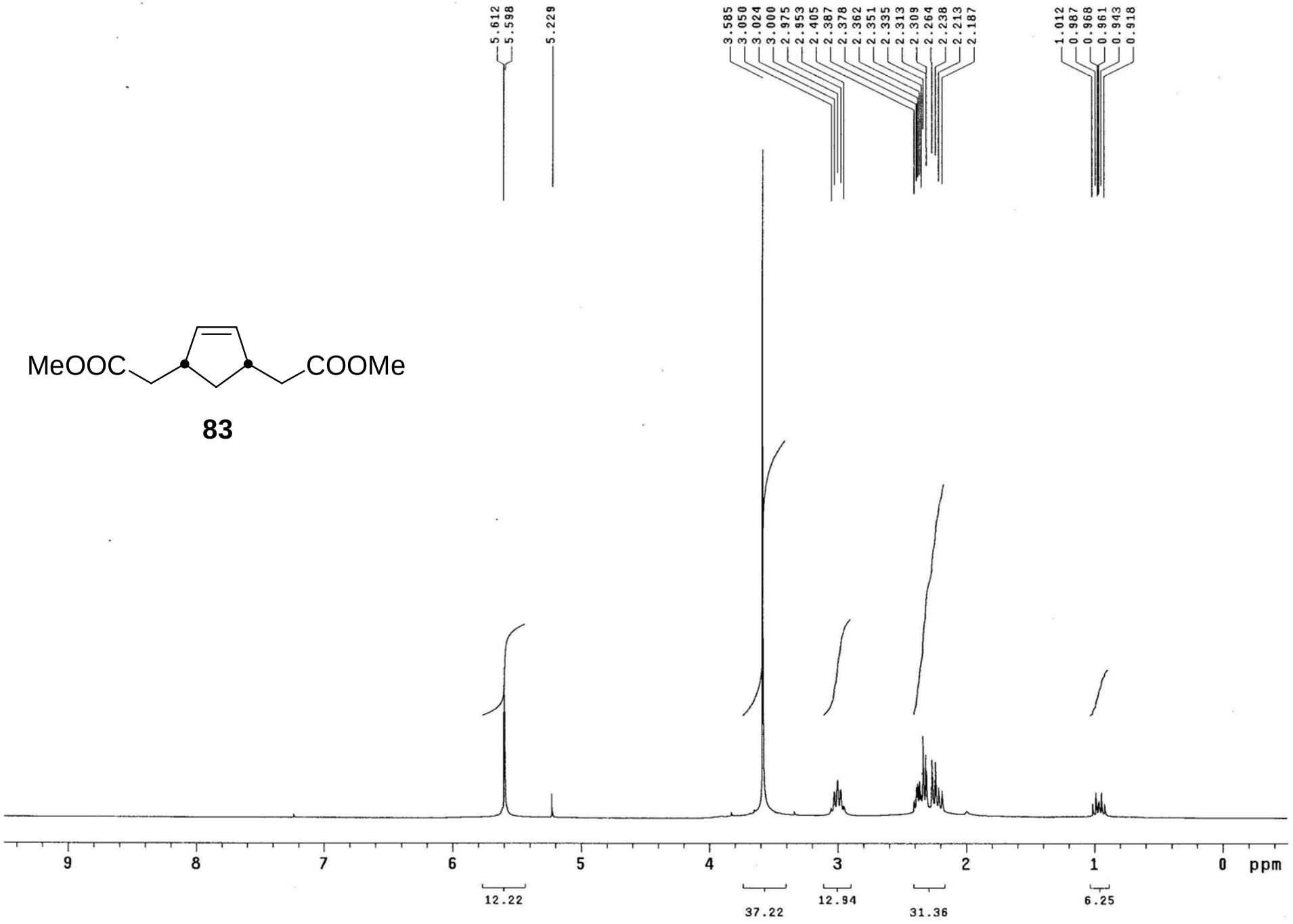
80

5.907
5.901
5.896
5.287
2.734
2.725
2.569
1.957
1.929
1.573
1.546
0.389
0.342
0.327
0.286
0.264
0.255
0.248
0.240
0.233
0.219
0.203
0.193
0.164
0.149
0.128
0.111
0.000
0.081
0.059
0.038
0.000
-0.024
9
8
7
6
5
4
3
2
1
0
ppm
6.64
7.81
7.67
4.13
4.43
69.32

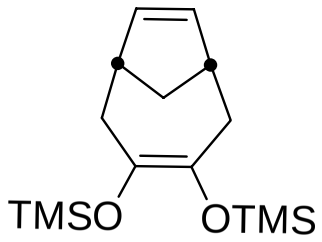

O
O

82

5.719
2.970
2.965
2.959
2.951
2.946
2.938
2.932
2.925
2.919
2.501
2.483
2.454
2.435
2.323
2.318
2.315
2.310
2.295
2.267
2.262
2.249
2.246
2.223
2.196
1.504
1.458
9
8
7
6
5
4
3
2
1
0
ppm
19.63
19.81
19.76
31.49
9.32

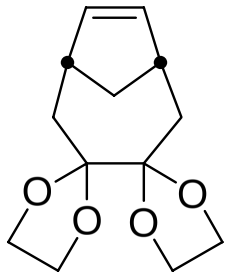

5.612
5.598
5.229
3.585
3.050
3.024
3.000
2.975
2.953
2.405
2.387
2.378
2.362
2.351
2.335
2.313
2.309
2.264
2.238
2.213
2.187
1.012
0.987
0.968
0.961
0.943
0.918
MeOOC
COOMe
9
8
7
6
5
4
3
2
1
0
ppm
12.22
37.22
12.94
31.36
6.25

83


TMSO
OTMS

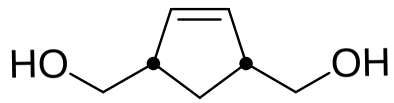
84

5.682
2.763
2.752
2.742
2.737
2.731
2.726
2.716
2.507
2.494
2.478
2.441
2.427
2.415
2.140
2.134
2.131
2.090
2.084
2.080
2.054
2.046
2.028
2.016
2.002
1.989
1.461
1.422
0.298
0.273
0.258
0.238
0.230
0.223
0.217
0.211
0.203
0.199
0.173
0.168
0.164
0.154
0.147
0.143
0.140
0.124
0.121
0.114
0.103
0.091
0.069
0.055
0.051
0.038
0.017
0.006
-0.005
-0.018
-0.031
-0.041
-0.078
-0.084
-0.097
9
8
7
6
5
4
3
2
1
0
ppm
6.33
6.54
6.96
7.18
4.34
3.34
65.31


O
O
O
O

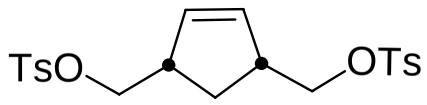
85

5.616
3.824
3.750
3.731
3.716
2.509
2.486
2.463
2.198
2.159
1.773
1.746
1.625
1.600
1.586
1.575
1.561
1.536
1.490
9
8
7
6
5
4
3
2
1
0
ppm
11.27
42.87
11.22
5.74
11.51
17.40

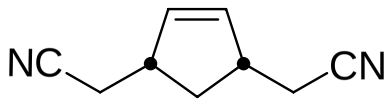

HO
OH

86

5.658
5.637
5.615
5.233
3.939
3.501
3.485
2.869
2.853
2.835
2.821
2.805
2.788
2.179
2.148
2.135
2.118
2.103
2.072
1.361
1.343
1.324
1.316
1.297
1.279
9
8
7
6
5
4
3
2
1
0 ppm
16.63
16.73
33.33
16.87
8.28
8.16

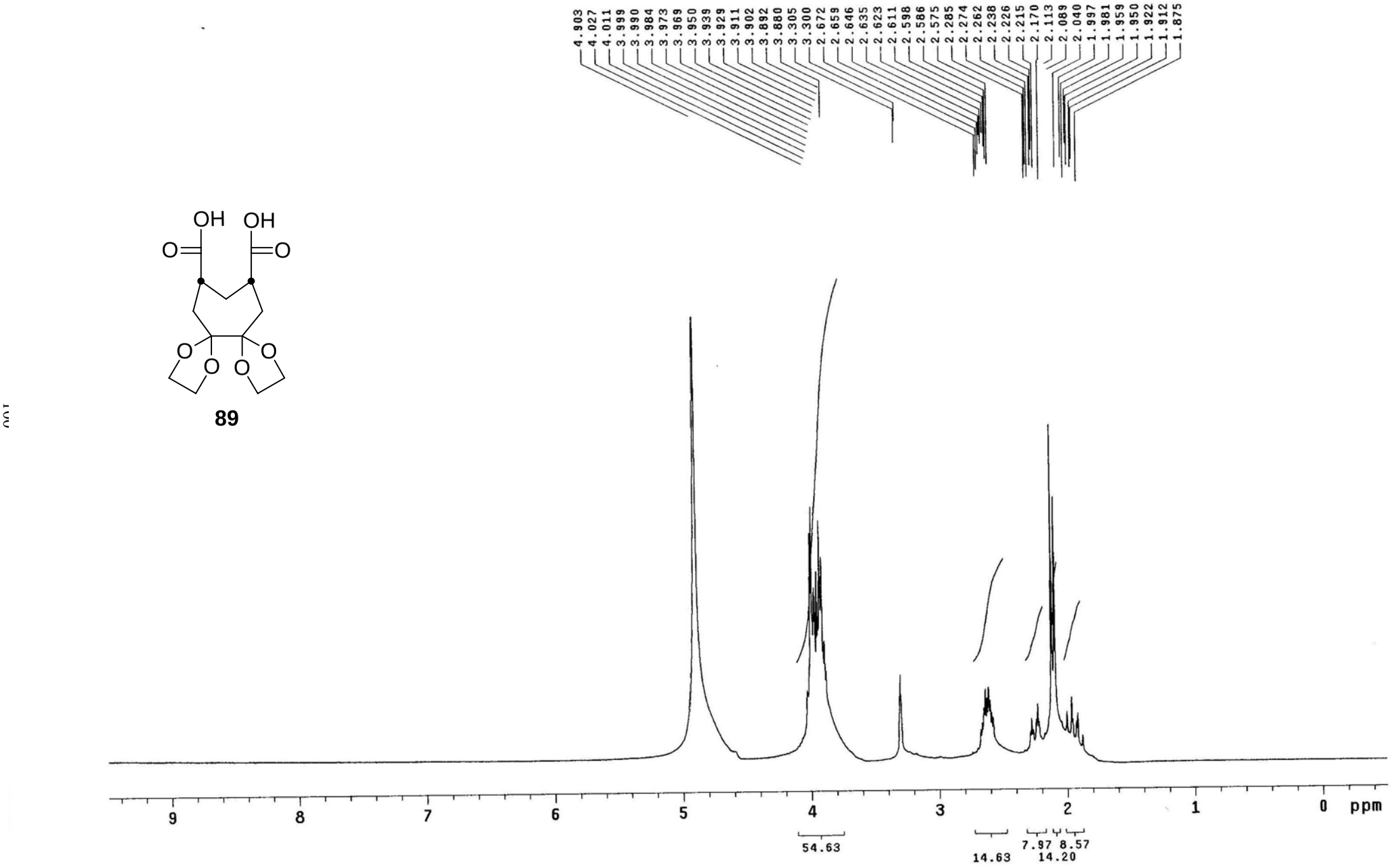


87


NC
CN

88

5.729
5.715
3.086
3.066
3.041
3.018
2.996
2.546
2.518
2.501
2.490
2.472
2.444
2.433
2.411
2.376
2.367
1.236
1.210
1.188
1.165
1.142
9
8
7
6
5
4
3
2
1
0
ppm
18.61
18.56
52.74
10.09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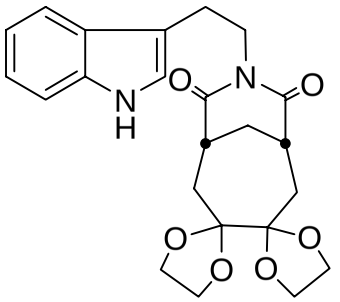
4.027
4.011
3.999
3.990
3.984
3.973
3.969
3.950
3.939
3.929
3.911
3.902
3.892
3.880
3.305
3.300
2.672
2.659
2.646
2.635
2.623
2.611
2.598
2.586
2.575
2.285
2.274
2.262
2.238
2.226
2.215
2.170
2.113
2.089
2.040
1.997
1.981
1.959
1.950
1.922
1.912
1.875
OH
OH
O
O
O
O
O
O
9
8
7
6
5
4
3
2
1
0
ppm
54.63
14.63
7.97
8.57
14.20

89



90

8.026
7.877
7.854
7.343
7.316
7.240
7.235
7.193
7.169
7.149
7.143
7.120
7.096
7.061
4.017
4.000
3.986
3.963
3.949
3.942
3.934
3.924
3.916
3.909
3.903
3.892
3.877
3.864
3.851
3.833
3.801
2.988
2.962
2.933
2.911
2.895
2.301
2.284
2.262
2.212
2.143
2.121
2.096
2.073
2.052
2.026
1.666
1.262
1.234
1.215
9
8
7
6
5
4
3
2
1
0
ppm
3.28
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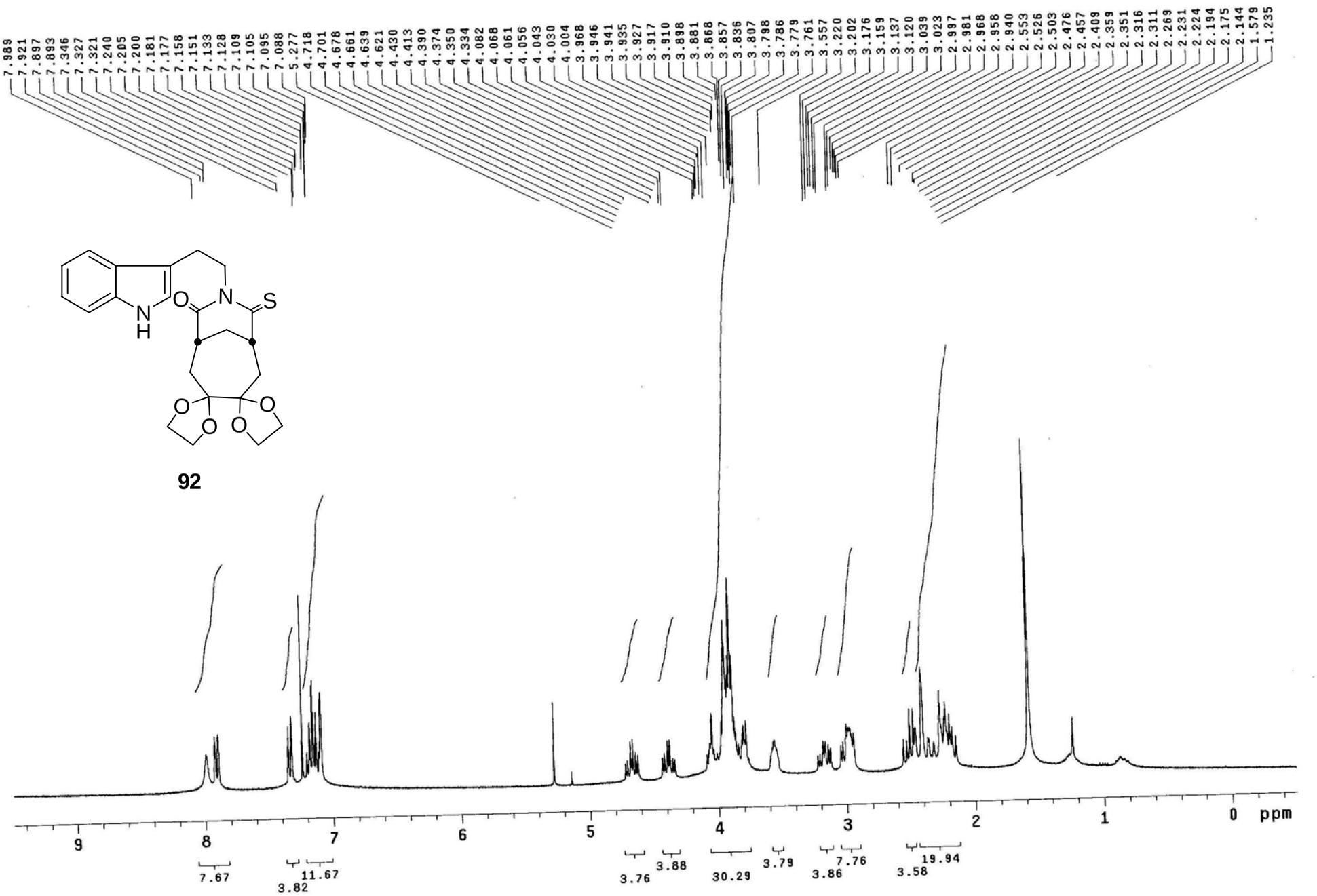
3.85
7.60
37.06
14.98
7.54
18.34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7.321
7.240
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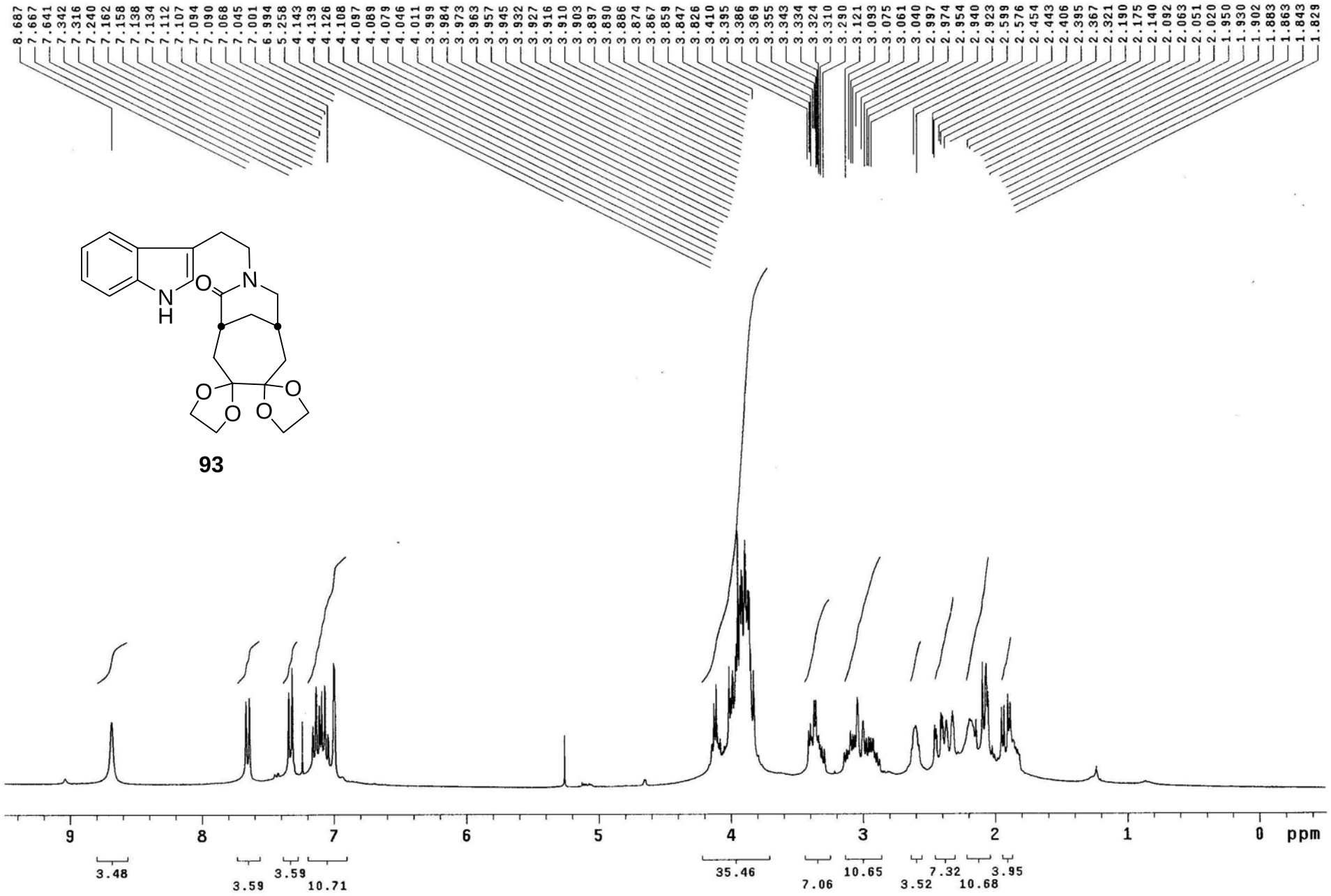
7.200
7.181
7.177
7.158
7.151
7.133
7.128
7.109
7.105
7.095
7.088
5.277
4.718
4.701
4.678
4.661
4.639
4.621
4.430
4.413
4.390
4.374
4.350
4.334
4.082
4.068
4.061
4.056
4.043
4.030
4.004
3.968
3.946
3.941
3.935
3.927
3.917
3.910
3.898
3.881
3.868
3.857
3.836
3.807
3.798
3.786
3.779
3.761
3.557
3.220
3.202
3.176
3.159
3.137
3.120
3.039
3.023
2.997
2.981
2.968
2.958
2.940
2.553
2.526
2.503
2.476
2.457
2.409
2.359
2.351
2.316
2.311
2.269
2.231
2.224
2.194
2.175
2.144
1.579
1.235
O
N
S
N
H
O
O
O
O
O
9
8
7
6
5
4
3
2
1
0
ppm
7.67
3.82
11.67
3.76
3.88
30.29
3.79
3.86
7.76
3.58
19.94

92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7.134
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7.094
7.090
7.068
7.045
7.001
6.994
5.258
4.143
4.139
4.126
4.108
4.097
4.089
4.079
4.046
4.011
3.999
3.984
3.973
3.963
3.957
3.945
3.932
3.927
3.916
3.910
3.903
3.897
3.890
3.886
3.874
3.867
3.859
3.847
3.826
3.410
3.395
3.386
3.369
3.355
3.343
3.334
3.324
3.310
3.290
3.121
3.093
3.075
3.061
3.040
2.997
2.974
2.954
2.940
2.923
2.599
2.576
2.454
2.443
2.406
2.395
2.367
2.321
2.190
2.175
2.140
2.092
2.063
2.051
2.020
1.950
1.930
1.902
1.883
1.863
1.843
1.829
N
H
O
N
O
O
O
O
O
9
8
7
6
5
4
3
2
1
0
ppm
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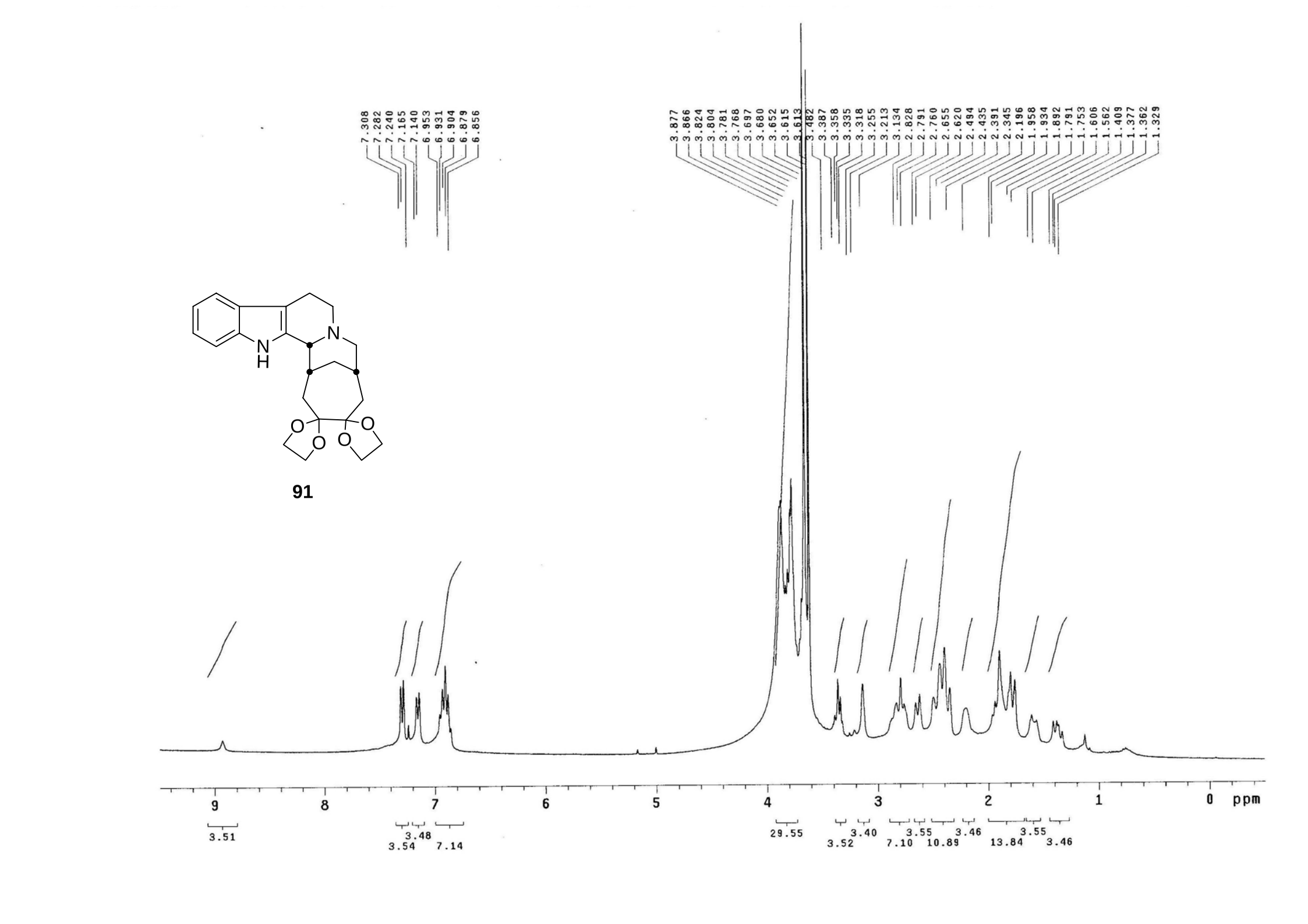
3.59
3.59
10.71
35.46
7.06
10.65
3.52
7.32
10.68
3.95

93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7.165
7.140
6.953
6.931
6.904
6.879
6.856
3.877
3.866
3.824
3.804
3.781
3.768
3.697
3.680
3.652
3.615
3.613
3.482
3.387
3.358
3.335
3.318
3.255
3.213
3.134
2.828
2.791
2.760
2.655
2.620
2.494
2.435
2.391
2.345
2.196
1.958
1.934
1.892
1.791
1.753
1.606
1.562
1.409
1.377
1.362
1.329
N
H
N
O
O
O
O
9
8
7
6
5
4
3
2
1
0
ppm
3.51
3.54
3.48
7.14
29.55
3.52
3.40
7.10
3.55
10.89
3.46
13.84
3.55
3.46

91

自　　傳

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