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# DEVELOPMENT OF TRIAZATRUXENE SYNTHESIS USING *N*-BROMOSUCCINIMIDE

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A Thesis Submitted in Partial Fulfillment of the Requirements

for the Degree of Master of Science Program in Chemistry

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อนุพันธ์ของไตรเอซาทรุกซีนกำลังได้รับความสนใจเป็นอย่างมากในการพัฒนาวัสดุไฟฟ้าอินทรีย์เชิงแสง เนื่องจากไตรเอซาทรุกซีนมีสมบัติทางแสงที่น่าสนใจ และมีเสถียรภาพทางความร้อนสูง ซึ่งในงานวิจัยที่ผ่านมามักจะสังเคราะห์ไตรเอซาทรุกซีนด้วยปฏิกิริยาไซโคลคอนเดนเซชันของออกซินโดลหรืออินโดล โดยต้องใช้ฟอสฟอรัสออกซีคลอไรด์หรือโบรมีนเหลวเป็นรีเอเจนต์ ซึ่งจัดเป็นสารเคมีที่อันตรายมาก มีความว่องไวในการเกิดปฏิกิริยาสูง และเป็นของเหลวซึ่งไม่สะดวกต่อการจัดเก็บและการใช้งานในปริมาณมาก งานวิจัยนี้จึงได้ศึกษาและพัฒนากระบวนการใหม่สำหรับการสังเคราะห์ไตรเอซาทรุกซีนจากอินโดลโดยใช้*เอ็น*-โบรโมซักซินิไมด์ซึ่งเป็นรีเอเจนต์ของแข็ง เพื่อเพิ่มความสะดวกต่อการใช้งาน อีกทั้งยังเป็นอันตรายน้อยกว่า และมีราคาถูกกว่าฟอสฟอรัสออกซีคลอไรด์และโบรมีน โดยจะศึกษาหาภาวะที่เหมาะสมที่สุดในการเกิดปฏิกิริยา เช่น ตัวทำละลาย ปริมาณรีเอเจนต์ ความเข้มข้นของสารตั้งต้น อุณหภูมิ ระยะเวลาในการทำปฏิกิริยาและวิธีการเติมรีเอเจนต์ รวมถึงการทดลองเพื่อทำนายหรือสนับสนุนกลไกการเกิดปฏิกิริยา จากนั้นจะนำภาวะที่ดีที่สุดมาขยายขนาดการสังเคราะห์ และศึกษาขอบเขตของปฏิกิริยาโดยใช้อินโดลที่มีหมู่แทนที่ต่างๆ เป็นสารตั้งต้น



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NATTHAWUT TOWORAKAJOHNKUN: DEVELOPMENT OF TRIAZATRUXENE SYNTHESIS USING *N*-BROMOSUCCINIMIDE. ADVISOR: ASSOC. PROF. PAITOON RASHATASAKHON, Ph.D., CO-ADVISOR: PROF. MONGKOL SUKWATTANASINITT, Ph.D., 74 pp.

Derivatives of triazatruxene (TAT) recently gain much attention for the development of organic optoelectronic materials due to their interesting photophysical properties and high thermal stability. Previous reports on the synthesis of triazatruxene usually rely on cyclocondensation reaction of oxindole or indole, using phosphorus oxychloride or liquid bromine as the reagent. These reagents are highly hazardous, extremely reactive, and exist in liquid form which is inconvenient for storage or uses in large quantities. This research aims to develop a new process for the synthesis of TAT from indole using solid *N*-bromosuccinimide as the reagent, which should be more users friendly, less hazardous, and more cost-effective than phosphorus oxychloride and bromine. The optimal conditions for this reaction which include solvent, the amount of reagent, reactant concentration, temperature, reaction times and addition method are investigated. Additional experiments are also conducted in order to gain access toward the reaction mechanism. The optimized condition is then used on a larger scale to demonstrate the reproducibility of the process. The scope of the reaction is examined using variously substituted indoles as starting materials.



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# LIST OF ABBREVIATION

| | |
|---|---|
| BHT | Butylated hydroxytoluene |
| $Br_2$ | Bromine |
| $^{o}C$ | Degree celsius |
| $cm^2$ | Square centimeter |
| d | Doublet |
| dd | Doublet of doublet |
| DMF | Dimethyl formamide |
| DMSO | Dimethyl sulfoxide |
| [$d_6$]-acetone | Deuterated acetone |
| [$d_6$]-DMSO | Deuterated dimethyl sulfoxide |
| EtOAc | Ethyl acetate |
| g | Gram (s) |
| h | Hour |
| HRMS | High resolution mass spectroscopy |
| HTMs | Hole-transporting materials |
| Hz | Hertz |
| *J* | Coupling constant |
| LED | Light-emitting diode |
| m | Multiplet |
| M | Molar |
| MeCN | Acetonitrile |
| MeOH | Methyl alcohol |

| | |
|---|---|
| mg | Milligram (s) |
| min | Minute (s) |
| mL | Milliliter (s) |
| mM | Millimolar |
| mmol | Millimole |
| MS | Mass spectroscopy |
| m.p. | Melting point |
| NBS | *N*-Bromosuccinimide |
| $NEt_3$ | Triethylamine |
| nm | Nanometer (s) |
| NMR | Nuclear magnetic resonance |
| OLED | Organic light-emitting diode |
| OSCs | Organic solar cells |
| Pd/C | Palladium on carbon |
| ppm | Parts per million |
| PL | Photoluminescent |
| s | Singlet |
| SD | Standard deviation |
| t | Triplet |
| TAT | Triazatruxene |
| TFA | Trifluoroacetic acid |
| THF | Tetrahydrofuran |
| TLC | Thin layer chromatography |
| $\delta$ | Chemical shift |

# CHAPTER I

# INTRODUCTION

## 1.1 Triazatruxene

Triazatruxene (**TAT**) is often considered as a C3 symmetric cycletrimer of indoles, of which the extended $\pi$-conjugation system cause an excellent thermal stability and photophysical properties [1]. Moreover, the three indolic NH groups, which are 5-, 10-, 15-positions (**Figure 1**), serve as facile points for the attachment of side chains. For these reason, **TAT** derivatives have been widely used as materials in optoelectronic devices [2] such as organic light-emitting diodes (OLEDs) [3], organic solar cells (OSCs) [4], batteries and capacitors [5].

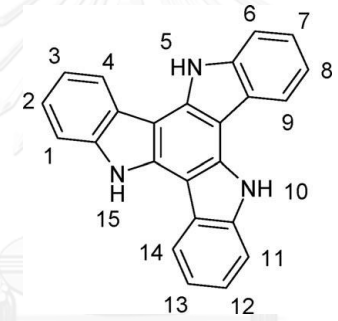


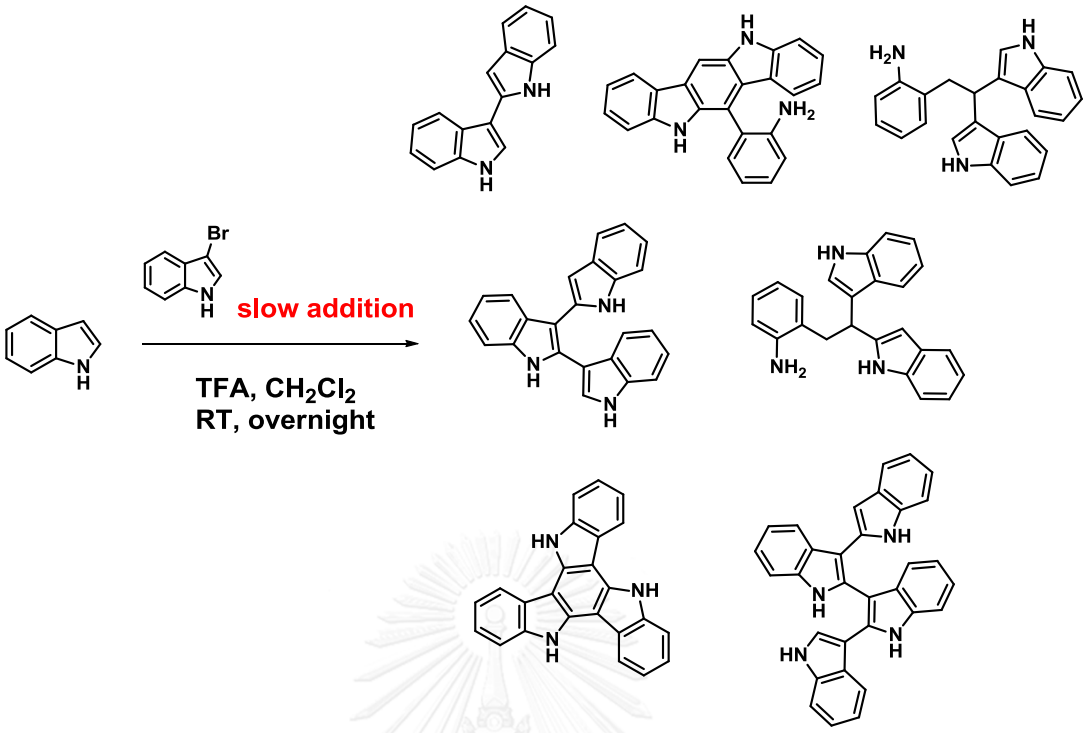

**Figure 1** Structure and numbering system of triazatruxene.



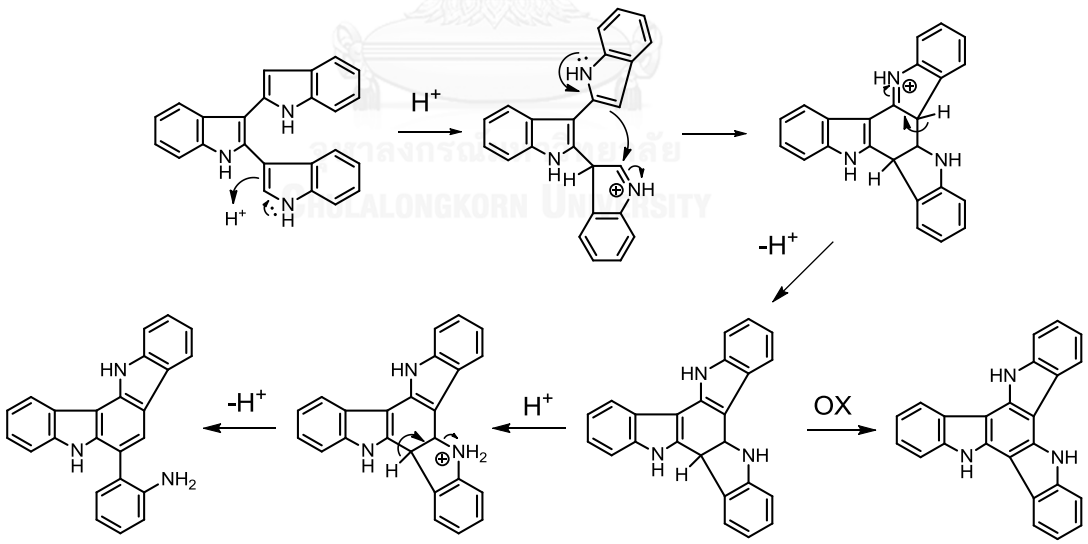
## 1.2 Literature reviews

### 1.2.1 Synthetic pathway.

In 1986, Bocchi and Palla [6] studied the reaction between indoles and 3-bromoindoles under acidic condition using trifluoroacetic acid (TFA) which gave many products such as dimer, trimers and tetramers of indole,. They isolated and characterized the unusual open trimers along with cyclic trimer which was **TAT** as one of those products (**Scheme 1**). Moreover, they proposed the mechanism of product formations to involve protonation/deprotonation process (**Scheme 2**).



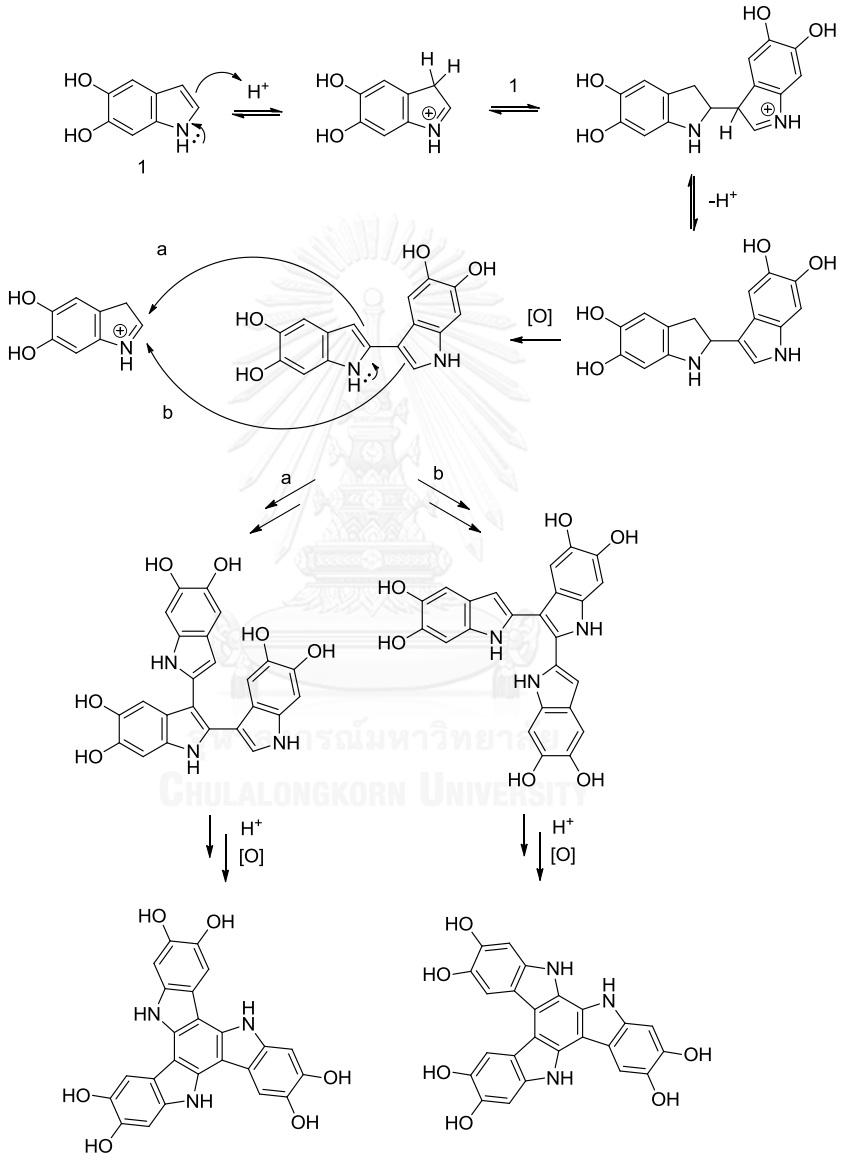

**Scheme 1** The reaction between indoles and 3-bromoindoles using trifluoroacetic acid.




**Scheme 2** Proposed mechanism of open and cyclic trimers.

In 1998, Manini and co-workers [7] studied the cyclotrimerization reaction of electron-rich indoles by various oxidizing systems in acidic media and proposed the mechanism of symmetrical and asymmetrical cyclotrimerizations (**Scheme 3**). The

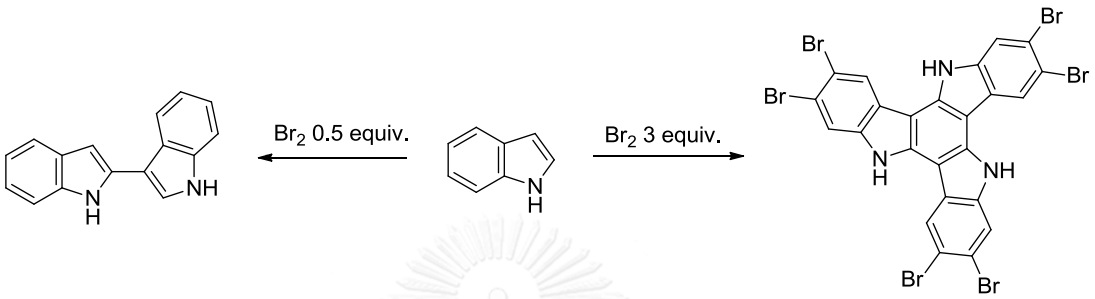
reaction started when an indole was protonated at the 3-position to form an indolium cation. Then, another molecule of nucleophilic indole attacked the indolium cation to generate 2,3'-biindolyl precursor. After that, there were two possibilities for the 2,3'-biindole to attack the indolium cation to produce different products, which were symmetrical and asymmetrical triazatruxene.



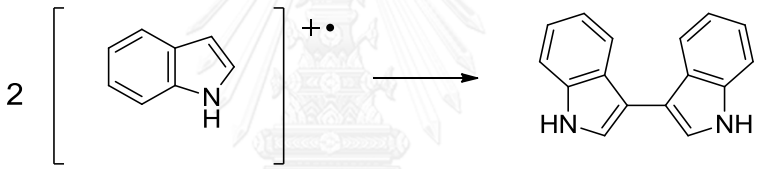
**Scheme 3** The acid-promoted oxidation of 5,6-dihydroxyindole.

In 2000, Robertson and co-workers [8] studied the bromination reaction between indoles and bromine in acetonitrile. They found that the ratio of bromine to indole affect the reaction. The asymmetric indole dimer and

hexabromotriazatruxene were prepared as major products when using 0.5 and 3 mole equivalent of bromine, respectively (**Scheme 4**). In addition, they reported an evidence from a cyclic voltammetry experiment that the coupling of two indole radical cations can lead to symmetrical indole dimer, and subsequent asymmetrical triazatruxene (**Scheme 5**).

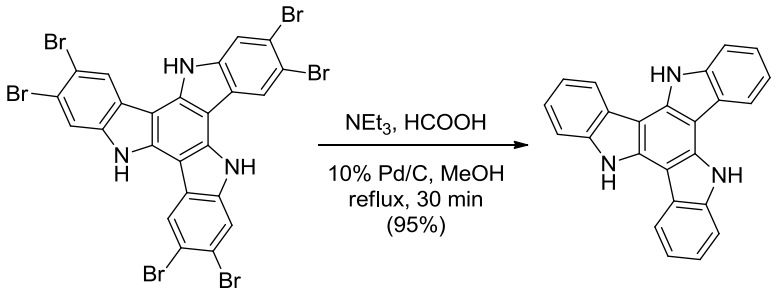



**Scheme 4** Reactions of indole with $Br_2$ in $CH_3CN$



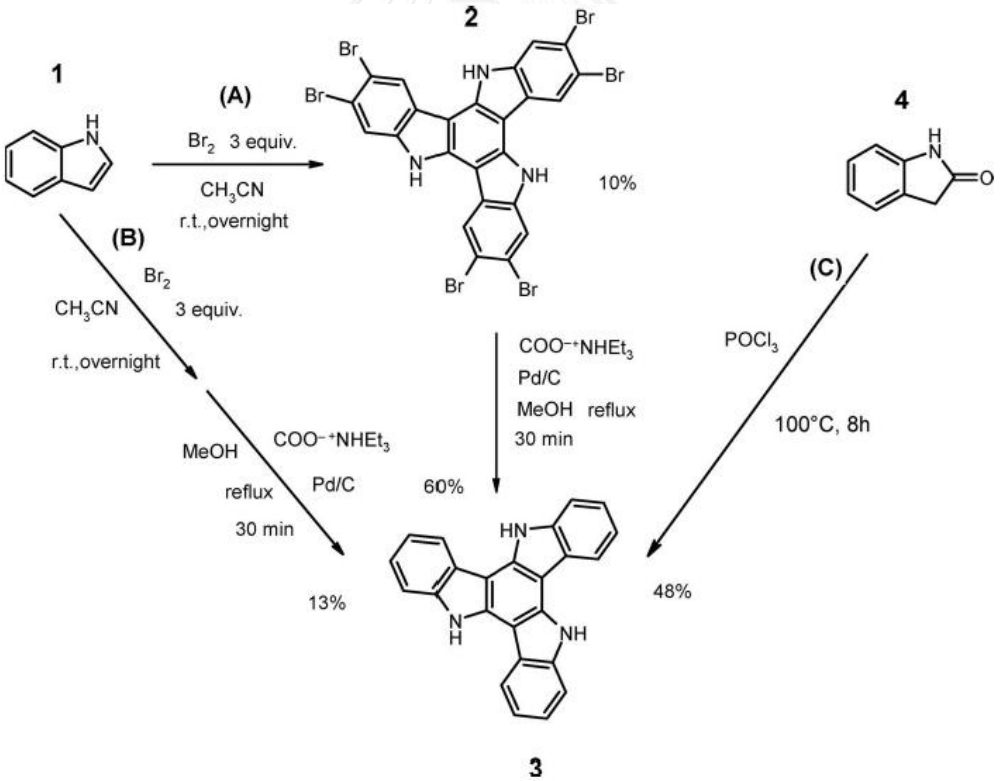

**Scheme 5** Proposed the electrochemical formation of symmetric dimer via coupling of two radical cation of indoles.

In 2004, Gómez-Lor and Echavarren [9] studied alkylation and intramolecular palladium-catalyzed arylation for triaza analogue of crushed-fullerene. They used triazatruxene as a core structure, which was prepared from debromination of hexabromotriazatruxene by triethylamine, formic acid, and 10% palladium on activated carbon to give a product in 95% yield (**Scheme 6**).



**Scheme 6** Dehalogenation reaction of hexabromotriazatruxene

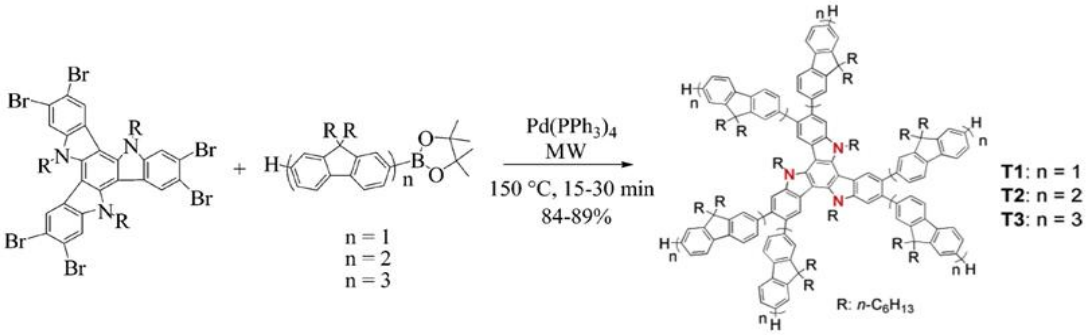
In 2010, Franceschin et al. [10] reported a comparative studies among three synthetic methods for the preparation of triazatruxene (**Scheme 7**). Pathway A and B involve reactions between indole and liquid bromine ($Br_2$), which suggested that the trimerization was a troublesome step. Attempt to by-pass the purification of hexabromotriazatruxene could slightly improve the overall yield to 13%. However, the debromination step was very efficient. On the other hand, the reaction between oxindole and phosphorus oxychloride proved to be a more prominent method as it could produce triazatruxene in 48% yield. Nevertheless, the higher cost of oxindole compared to indole and the hazardous nature of phosphorus oxychloride and bromine (see section 1.3) make us interest in the development of a new synthetic method.




**Scheme 7** Comparison of different synthetic routes for the preparation of triazatruxene.

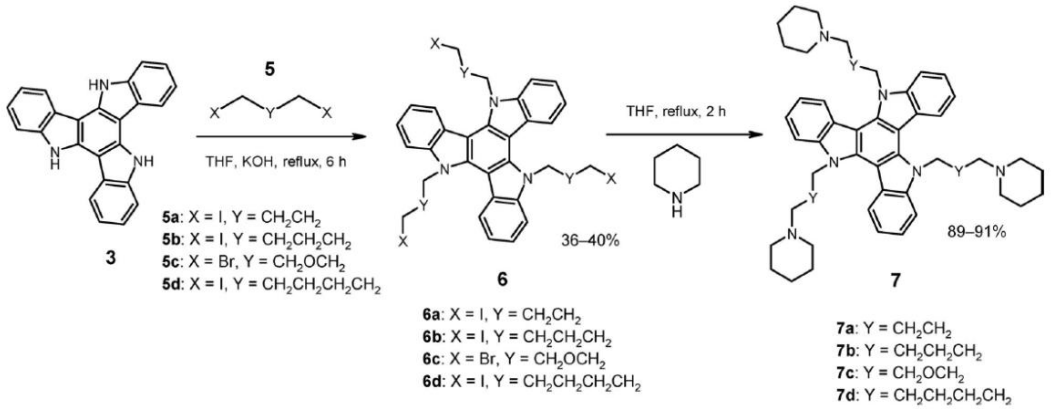
1.2.2 Application of triazatruxene.

In 2006, Lai and co-workers [11] used triazatruxene derivative as a core structure to study the optical properties. In order to synthesize target compounds, they started with hexabromotriazatruxene, which was reported by Robertson et al. [8] Then, three compounds, which were **T1**, **T2**, and **T3**, were synthesized by Suzuki coupling *via* microwave (**Scheme 8**). Those compounds showed emission in the blue light region at 429 nm for **T1** and 440 nm for **T2-3**. The largest **T3** compound was chosen in OLED device and the measurement of electroluminescent found that the light emission was at 442 nm.



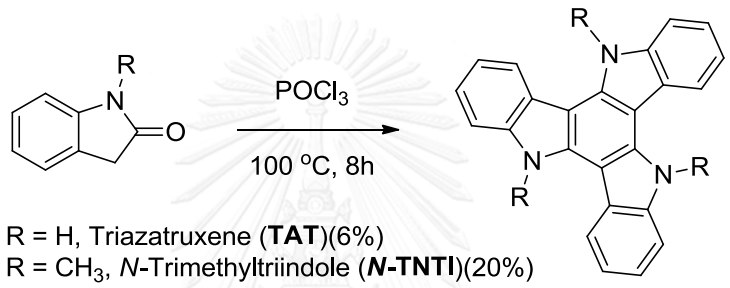

**Scheme 8** Chemical structures and synthesis of T1, T2 and T3

In 2010, Franceschin et al. [10] not only compared three synthetic methods for the preparation of triazatruxene but also synthesized four hydrophilic triazatruxene derivatives with different side chains in terms of length and basicity (**Scheme 9**) which showed a good fluorescence in both DMSO and water at a voltage of 500 V.



**Scheme 9** Structures and synthesis of **7a-d**

In 2012, Shelton and co-workers [12] synthesized triazatruxene (**TAT**) and *N*-trimethyltriindole (**N-TMTI**) (**Scheme 10**). They used those compounds as hole selective materials in organic solar cells. To synthesize **TAT** and ***N*-TMTI**, they used oxindole and its derivative to react with the phosphorus oxychloride as reported by Franceschin et al. [10]. **TAT** and ***N*-TMTI** increased the power conversion efficiency from 0.16 to 0.71% for TAT and 0.87% for TMTI, respectively, in planar heterojunction photovoltaic devices.




**Scheme 10** Chemical structures and synthesis of **TAT** and ***N*-TMTI**

### 1.3 Reagent selection

According to the literature surveys, only two synthetic methods have been reported for the preparation of **TAT**, which involved the reaction between indole and liquid bromine ($Br_2$) and the treatment of oxindole with phosphorus oxychloride ($POCl_3$). Both $Br_2$ and $POCl_3$ had high toxicity.

The phosphorus oxychloride ($POCl_3$) [13] displays level-4 health hazards in the material safety data sheet (MSDS), which means it is life-threatening and major or permanent damage may result from single or repeated overexposures. This chemical is, however, not flammable as its flammable levels is zero. The reactivity is at level 2, which indicates its low stability and may undergo violent chemical changes. In addition, $POCl_3$ is corrosive, acute toxic and carcinogen. According to MSDS of liquid bromine ($Br_2$) [14], the health hazards level is slightly lower than that of $POCl_3$. Nevertheless, its level 3 health hazards means it could cause major injury unless

prompt action is taken and medical treatment is given. Like $POCl_3$, the $Br_2$ was also not flammable, but its reactivity is at level zero which denotes a relatively stable nature. However, the $Br_2$ was corrosive, acute toxic and hazardous to the aquatic environment. As for the *N*-bromosuccinimide (NBS) [15], the information on MSDS suggests a relatively lower health hazard and reactivity than $POCl_3$ and $Br_2$. The slightly higher flammability for NBS (level-1) may result from the carbon atoms available in the structure, which should not post significant concerns because our reactions will be performed mostly at ambient temperature (**Figure 2**).

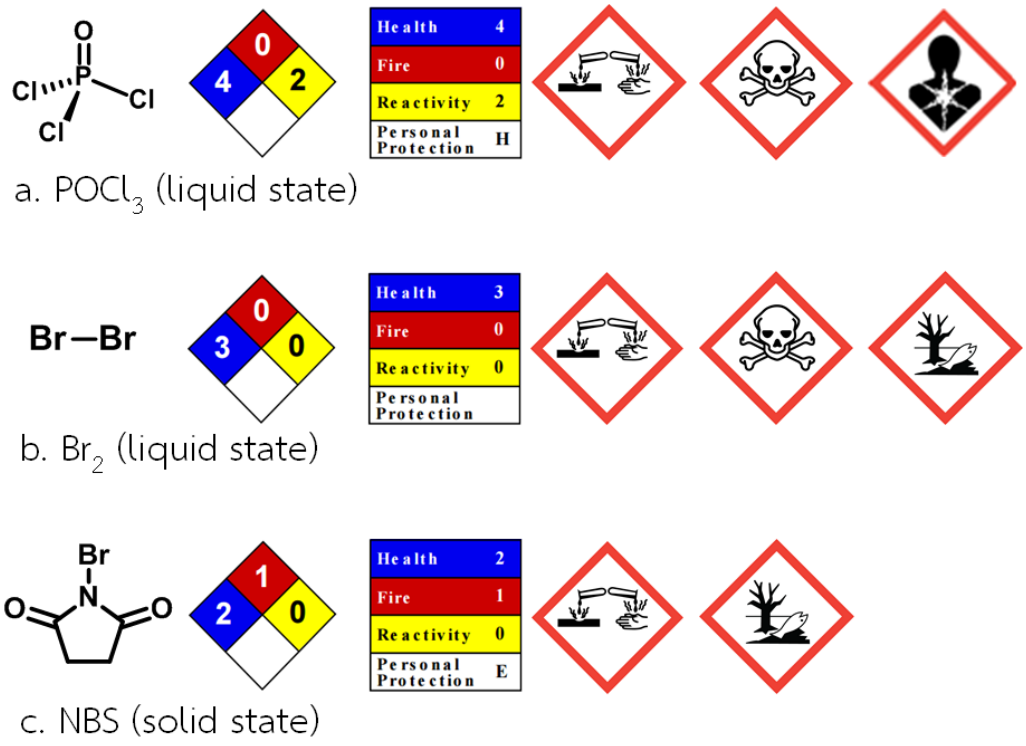



**Figure 2** Safty information of $POCl_3$, $Br_2$ and NBS.

From the Franceschin's report [10], the trimerization of indole using $Br_2$ usually afford **TAT** in low yields ranging from 6 to 13%. Due to the toxicity of $POCl_3$ and $Br_2$, and the inconvenient handling of this reactive liquid reagent, we opted to use *N*-bromisuccinimide (NBS) as an alternative reagent for the cyclotrimerization of indole.

The objectives of this work were reaction optimization which the standard **TAT** and its asymmetric analog are prepared as the references for reaction efficiency determination by HPLC. The effects of solvent, amount of NBS, reactant concentration, temperature, reaction time, reagent addition rate and method of addition are thoroughly investigated on the reaction at 0.1 g scale. Then, the optimal condition will be scaled up to 1 and 10 g and studied substrate scope with varies substituted indoles.

# CHAPTER II

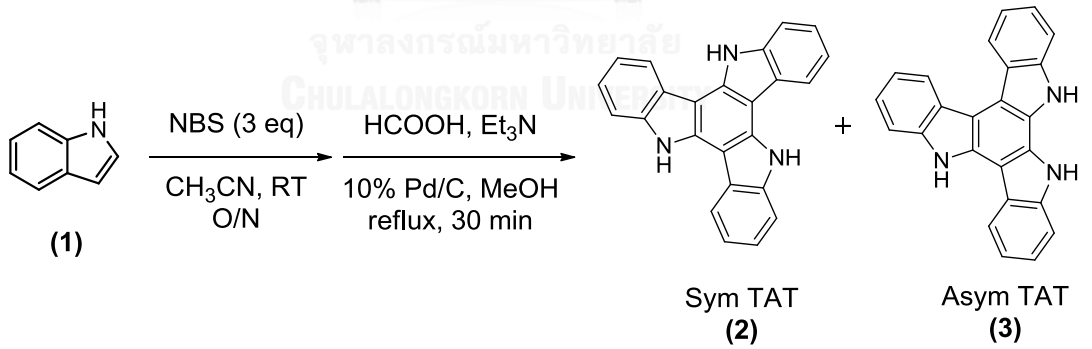
# EXPERIMENTAL

## 2.1 Materials and instruments

All reagents were purchased from Merck® (Germany), Fluka® (Switzerland) or Sigma-Aldrich and used without further purification. Thin-layer chromatography (TLC) was performed on Kieselgel F-254 pre-coated plastic TLC plates from EM Science. Column chromatography was carried out with silica gel (60, 230-400 mesh) from ICN Silitech. The $^{1}$H and $^{13}$C NMR spectra were obtained on a Varian Mercury NMR spectrometer, which operated at 400 MHz for $^{1}$H and 100 MHz for $^{13}$C nuclei (Varian Company, CA, USA). Mass spectra were recorded on a Microflex MALDI-TOF mass spectrometer (Bruker Daltonics) using doubly recrystallized **α**-cyano-4-hydroxy cinnamic acid (CCA) and dithranol as a matrix.

## 2.2 Synthetic procedures

2.2.1 Preparation of 10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2**) and 6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3**) as standard material.




**Scheme 11** Synthesis of triazatruxenes (**TAT**) using *N*-bromosuccinimide (NBS) under unoptimized conditions.

Indole (1 g, 8.5 mmol) was dissolved in MeCN (20 mL), and NBS (4.54 g, 25.5 mmol) was slowly added over a period of about 5 min. The mixture was stirred overnight (12 h) at room temperature, and the solid was filtered and washed with MeCN (200 mL). Without purification, the solid crude product (1.78 g) was mixed with

$NEt_3$ (4.2 mL, 30.2 mmol), HCOOH (1.2 mL, 30.2 mmol) and 10% Pd/C (200 mg, 0.18 mmol) in MeOH (30 mL), and the mixture was heated for 30 min under reflux. After that, the mixture was filtered through a pad of Celite, diluted with dichloromethane and washed by aqueous 10% HCl and brine. The organic solvent was evaporated and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 15:85) to give pale-gray solid of symmetrical **TAT** (**2**), $R_f$ = 0.25 (34 mg, 3%) and dark-gray solid of asymmetrical **TAT** (**3**), $R_f$ = 0.125 (45 mg, 4%). For symmetrical **TAT** (**2**), $^1$H NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 11.13 (s, 3H, N-H), 8.56 (d, *J* = 7.6 Hz, 3H, aromatic H), 7.73 (d, *J* = 7.6 Hz, 3H, aromatic H), 7.35 (dt, *J* = 22.9, 7.6 Hz, 6H, aromatic H) ppm, $^{13}$C NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 139.9, 135.4, 123.8, 123.5, 120.5, 120.4, 111.9, 111.8 ppm and MALDI-TOF MS (*m/z*): calc.: (344.119 [$C_{24}H_{15}N_3$]); found: (344.296 [$M^-$]). For asymmetrical **TAT** (**3**), $^1$H NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 11.07 (s, 1H, N-H), 10.80 (s, 1H, N-H), 10.69 (s, 1H, N-H), 8.95 (d, *J* = 7.8 Hz, 1H, aromatic H), 8.88 (dd, *J* = 5.9, 2.7 Hz, 1H, aromatic H), 8.66 (d, *J* = 7.8 Hz, 1H, aromatic H), 7.77 (dd, *J* = 5.9, 2.7 Hz, 1H, aromatic H), 7.72 (d, *J* = 8.1 Hz, 2H, aromatic H), 7.49 – 7.31 (m, 6H, aromatic H) ppm, $^{13}$C NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 140.4, 140.2, 140.0, 131.0, 127.1, 125.0, 124.9, 124.8, 123.8, 123.6, 123.4, 123.0, 122.6, 121.5, 120.5, 119.8, 119.7, 116.2, 112.3, 112.2, 112.14, 112.07, 112.0, 110.4 ppm and MALDI-TOF MS (*m/z*): calc.: (344.119 [$C_{24}H_{15}N_3$]); found: (344.358 [$M^-$]).



**2.3 HPLC instruments.**

Waters HPLC equipped with a binary pump and UV/Visible detector was used for quantitative experiments. The HPLC instruments are as follows:

- Degasser: Waters 2 Channel
- Pump: Waters 1525, binary bump
- Autosampler: Water 2707
- Injection loop size: 20 µL
- Column: Sunfire, symmetry C18, 4.6 x 150 mm, 5 µm

- Mobile phase: MeCN (HPLC grade) and milli-Q
- Diode array detector (DAD): Waters 2489 UV/Vis Detector
- Software: Breeze 2

**2.4 Reaction optimization.**

The key parameters for the reaction optimization are listed below along with their selections and values.

- Types of solvent ($CHCl_3$, EtOAc, Acetone, MeCN and MeOH)
- Amounts of NBS (1-5 eq.)
- Reactant concentration (0.11, 0.21, 0.43 and 0.85 M)
- Reaction temperature (0, 25 and 50°C)
- Reaction time (1, 2, 3, 6 and 12 h)
- Reagent addition rate and method of addition (NBS to indole in 10, 90 mins and Indole to NBS in 10 min)
- Prove of radical pathway (0.2 and 1 eq of BHT)

For simplicity, a one-parameter-at-a-time method will be used for this optimization studies. The effect of each parameter will be evaluated base on the resulted HPLC yields.

**2.5 Large-scale demonstration of the optimized conditions (100X).**

In order to demonstrate the practicality and reproducibility of the optimal condition, the reaction will be scaled up to 1 and 10 g.

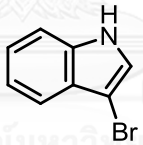
## 2.6 Reactants for the study of reaction scope.

The following compounds were purchased from commercial sources: 5-methyl-1*H*-indole (**1a**), 5-methoxy-1*H*-indole (**1b**), 5,6-dimethoxy-1*H*-indole (**1c**), 1-methyl-1*H*-indole (**1i**), 1*H*-indol-5-ol (**1m**), 1*H*-indol-5-amine (**1p**), 5-nitro-1*H*-indole (**1d**), methyl 1*H*-indole-5-carboxylate (**1e**), 5-chloro-1*H*-indole (**1f**) and 1*H*-benzo[g]indole (**1g**).

The following compounds were prepared according to literature procedures: 3-bromo-1*H*-indole (**1h**), 1-ethyl-1*H*-indole (**1j**), 1-benzyl-1*H*-indole (**1k**), 1-(1*H*-indol-1-yl)ethanone (**1l**), 1*H*-indol-5-yl acetate (**1n**), 5-((*tert*-butyldimethylsilyl)oxy)-1*H*-indole (**1o**), *N*-(1*H*-indol-5-yl)acetamide (**1q**), *tert*-butyl 1*H*-indol-5-ylcarbamate (**1r**), 2-(1*H*-indol-5-yl)-1*H*-benzo[d,e]isoquinoline-1,3(2*H*)-dione (**1s**) and 2-(1*H*-indol-5-yl)isoindoline-1,3-dione (**1t**).

### 2.6.1 Synthesis of substituted indole.

#### 2.6.1.1 3-bromo-1*H*-indole (**1h**) [16]



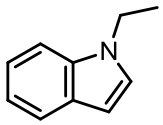

**1h**



Indole (1.17 g, 10.0 mmol) was dissolved in MeCN (5 mL) and the solution of NBS (1.96 g, 11.0 mmol) in MeCN (7.5 mL) was added dropwise to an ice-cooled reaction. The mixture was allowed to warm to room temperature and stirred for 2 h. Then, this mixture was poured into 150 mL of ice water and resulting precipitate was filtrated and washed with water and dried under vacuum. The crude was dissolved in EtOAc and purified by column chromatography on silica gel (EtOAc/*n*-hexane, 10:90) to give white solid of **1h**, $R_f$ = 0.4 (845 mg, 43%). In solid state, this compound can decompose readily under room temperature. In order to avoid the decomposition, it was stored as wet solid mixed with volatile solvents. $^1$H NMR ([$d_6$]-DMSO, 400 MHz): $\delta$ = 11.48 (s, 1H, $N_{arom}$-H), 7.54 (s, 1H, aromatic H), 7.43 (t, *J* = 8.7 Hz, 2H, aromatic H),

7.17 (dd, *J* = 11.1, 4.0 Hz, 1H, aromatic H), 7.11 (dd, *J* = 7.8, 7.1 Hz, 1H, aromatic H) ppm.

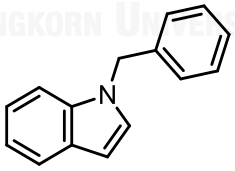
2.6.1.2 1-ethyl-1*H*-indole (**1j**) [17]



**1j**

Ethyl bromine (1.27 mL, 17.1 mmol) was added to a solution of indole (1 g, 8.5 mmol) and KOH (1.44 g, 25.6 mmol) in DMF (8 mL). The mixture was stirred at room temperature for 3 h. Then, the mixture was extracted by EtOAc and water. The mixture was washed with 100 mL of water for 3 times, brine and dry over anhydrous $Na_2SO_4$. The organic solvent was evaporated and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 10:90) to give yellow liquid of **1j**, $R_f$ = 0.5 (928 mg, 75%), $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 7.78 (d, *J* = 7.9 Hz, 1H, aromatic H), 7.47 (d, *J* = 8.2 Hz, 1H, aromatic H), 7.34 (t, *J* = 7.6 Hz, 1H, aromatic H), 7.25 (d, *J* = 7.8 Hz, 1H, aromatic H), 7.22 (d, *J* = 3.1 Hz, 1H, aromatic H), 6.63 (d, *J* = 3.0 Hz, 1H, aromatic H), 4.26 (q, *J* = 7.3 Hz, 2H, $CH_2$), 1.56 (t, *J* = 7.3 Hz, 3H, $CH_3$) ppm.

2.6.1.3 1-Benzyl-1*H*-indole (**1k**) [18]

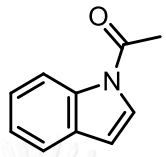


**1k**

A solution of indole (1.17 g, 10.0 mmol) in DMF (10 mL) was added dropwise to a stirred suspension of NaH (60% dispersion in mineral oil; 480 mg, 12.0 mmol) in DMF (10 ml) at 0 °C. The reaction mixture was stirred for 30 min and then, benzyl bromine (1.79 mL, 15.0 mmol) was added dropwise to the reaction mixture and stirred at room temperature overnight. Then, the reaction mixture was extracted by EtOAc and water. The solution was washed with 150 mL of water for 3 times, brine and dry over anhydrous $Na_2SO_4$. The organic solvent was evaporated and the residue

was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 10:90) to give yellow oil of **1k**, $R_f$ = 0.5 (1.79 g, 86%), $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ = 7.81 (d, *J* = 7.5 Hz, 1H, aromatic H), 7.43 – 7.36 (m, 4H, aromatic H), 7.32 (dd, *J* = 7.0, 0.9 Hz, 1H, aromatic H), 7.28 (dd, *J* = 5.5, 1.2 Hz, 1H, aromatic H), 7.25 – 7.20 (m, 3H, aromatic H), 6.70 (d, *J* = 3.1 Hz, 1H, aromatic H), 5.39 (s, 2H, $CH_2$) ppm.

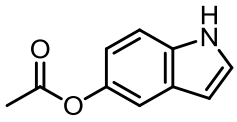
2.6.1.4 1-(1*H*-indol-1-yl)ethanone (**1l**) [19]



**1l**

Indole (575 mg, 5.0 mmol), acetic anhydride (970 mg, 9.5 mmol), triethylamine (0.75 g, 7.5 mmol) and *N,N*-dimethyl-4-aminopyridine (116 mg, 0.95 mmol) were dissolved in 1,2-dichloroethane (23 mL). The reaction mixture was stirred at 80 ºC overnight. After that, EtOAc and water were added to the reaction mixture and washed with water, brine and dry over anhydrous $Na_2SO_4$. The organic solvent was evaporated and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 10:90) to give pale yellow oil of **1l**, $R_f$ = 0.4 (668 mg, 84%), $^1$H NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 8.44 (d, *J* = 8.2 Hz, 1H, aromatic H), 7.70 (d, *J* = 3.8 Hz, 1H, aromatic H), 7.60 (d, *J* = 7.7 Hz, 1H, aromatic H), 7.35 – 7.30 (m, 1H, aromatic H), 7.26 (td, *J* = 7.6, 1.0 Hz, 1H, aromatic H), 6.68 (d, *J* = 3.7 Hz, 1H, aromatic H), 2.65 (s, 3H, $CH_3$) ppm.

2.6.1.5 1*H*-indol-5-yl acetate (**1n**) [20]

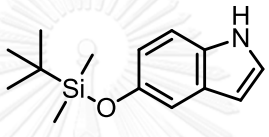


**1n**

A solution of 5-hydroxy-indole (600 mg, 4.51 mmol) in pyridine (15 mL) was added acetic anhydride (0.47 mL, 4.96 mmol) and dimethylaminopyridine (5 mg, cat). The reaction mixture was stirred for 3 h at room temperature. After that, pyridine was

evaporated and partitioned between water and EtOAc. The aqueous layer was washed with water, brine and dry over anhydrous $Na_2SO_4$. The organic solvent was evaporated and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 20:80) to give off-white solid of **1n**, $R_f$ = 0.5 (590 mg, 75%), $^1$H NMR ($CDCl_3$, 400 MHz): **δ** = 8.19 (s, 1H, $N_{arom}$-H), 7.35 (d, *J* = 8.7 Hz, 1H, aromatic H), 7.33 (d, *J* = 1.9 Hz, 1H, aromatic H), 7.26 (s, 1H, aromatic H), 7.23 (t, *J* = 2.7 Hz, 1H, aromatic H), 6.91 (dd, *J* = 8.7, 2.2 Hz, 1H, aromatic H), 6.53 (s, 1H, aromatic H), 2.32 (s, 3H, $CH_3$). ppm.

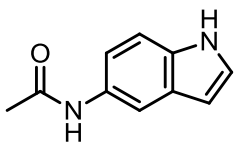
2.6.1.6 5-((*tert*-butyldimethylsilyl)oxy)-1*H*-indole (**1o**) [21]



**1o**

A solution of 5-hydroxy-indole (500 mg, 3.76 mmol), tert-butyldimethylsilyl cholide (623 mg, 4.14 mmol) and imidazole (537 mg, 7.89 mmol) in DMF (5 mL) was stirred for 20 h at room temperature. Diethyl ether was added and the mixture was washed with 1 M HCl, water, brine and dry over anhydrous $Na_2SO_4$. The organic solvent was evaporated and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 20:80) to give yellow solid of **1o**, $R_f$ = 0.5 (735 mg, 79%), $^1$H NMR ($CDCl_3$, 400 MHz): **δ** = 8.01 (s, 1H, $N_{arom}$-H), 7.23 (d, *J* = 8.7 Hz, 1H, aromatic H), 7.17 (t, *J* = 2.7 Hz, 1H, aromatic H), 7.07 (d, *J* = 2.0 Hz, 1H, aromatic H), 6.76 (dd, *J* = 8.7, 2.2 Hz, 1H, aromatic H), 6.44 (s, 1H, aromatic H), 1.01 (s, 9H, $CH_3$), 0.20 (s, 6H, $CH_3$) ppm.

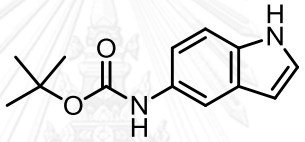
2.6.1.7 *N*-(1*H*-indol-5-yl)acetamide (**1q**) [22]



**1q**

Acetic anhydride (456 µL, 4.8 mmol) was added dropwise to a solution of 1*H*-indol-5-amine (528 mg, 4.0 mmol) in pyridine (20 mL). The reaction mixture was stirred at room temperature for 2 h. After that, the reaction mixture was extracted by EtOAc and water. The organic phase was washed with 1 M HCl solution, brine and dry over anhydrous $Na_2SO_4$. The organic solvent was evaporated and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60) to give brown liquid of **1q**, $R_f$ = 0.25 (265 mg, 38%), $^1$H NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 10.35 (s, 1H, NH), 9.35 (s, 1H, $N_{arom}$-H), 8.06 (s, 1H, aromatic H), 7.40 (d, *J* = 8.7 Hz, 1H, aromatic H), 7.36 (dd, *J* = 8.7, 1.6 Hz, 1H, aromatic H), 7.32 (t, *J* = 2.6 Hz, 1H, aromatic H), 6.47 (s, 1H, aromatic H), 2.19 (s, 3H, $CH_3$) ppm.

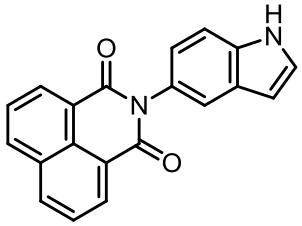
2.6.1.8 *tert*-butyl 1*H*-indol-5-ylcarbamate (**1r**) [23]



**1r**

A solution of 1*H*-indol-5-amine (500 mg, 3.8 mmol) in EtOAc (50 mL) was added di-*tert*-butyldicarbonate (2.05 g, 9.5 mmol). The reaction mixture was stirred at room temperature for 24 h. After that, the reaction mixture was quenched with water 20 mL. The aqueous layer was extracted with EtOAc for 3 times and dry over anhydrous $Na_2SO_4$. The organic solvent was evaporated and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 20:80) to give dark green oil of **1r**, $R_f$ = 0.5 (909 mg, quantitative yield) , $^1$H NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 10.09 (s, 1H, NH), 8.09 (s, 1H, $N_{arom}$-H), 7.81 (s, 1H, aromatic H), 7.31 (d, *J* = 8.7 Hz, 1H, aromatic H), 7.27 (t, *J* = 2.7 Hz, 1H, aromatic H), 7.23 (d, *J* = 8.7 Hz, 1H, aromatic H), 6.40 (s, 1H, aromatic H), 1.49 (s, 9H, $CH_3$) ppm.

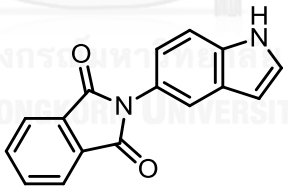
2.6.1.9 2-(1*H*-indol-5-yl)-1*H*-benzo[d,e]isoquinoline-1,3(2*H*)-dione (**1s**)



**1s**

A solution of 1*H*-indol-5-amine (200 mg, 1.52 mmol) in acetic acid (7.5 mL) was added naphthalic anhydride (300 mg, 1.52 mmol). The reaction mixture was stirred under reflux for 2 h. After that, the crude solid was precipitated in water 200 mL and filtrated under vacuum. The crude solid was washed with water 400 mL and was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 20:80) to give green solid of **1s**, $R_f$ = 0.4 (379 mg, 80%), $^1$H NMR ([$d_6$]-DMSO, 400 MHz): $\delta$ = 11.27 (s, 1H, $N_{arom}$-H), 8.51 (d, *J* = 7.8 Hz, 4H, aromatic H), 7.91 (t, *J* = 7.8 Hz, 2H, aromatic H), 7.53 – 7.41 (m, 3H, aromatic H), 7.04 (d, *J* = 8.5 Hz, 1H, aromatic H), 6.49 (s, 1H, aromatic H) ppm.

2.6.1.10 2-(1*H*-indol-5-yl)isoindoline-1,3-dione (**1t**)

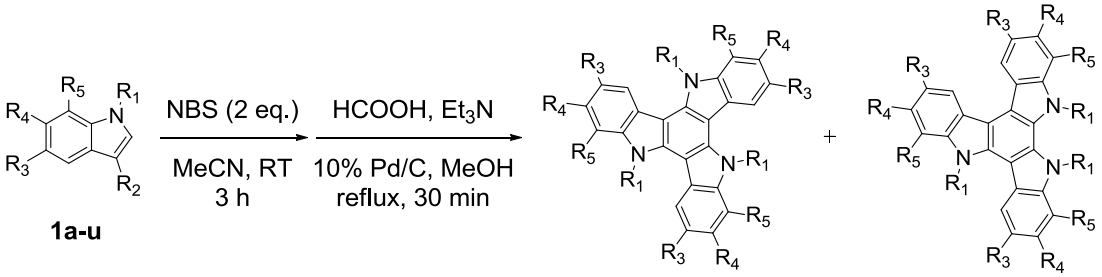


**1t**

A solution of 1*H*-indol-5-amine (200 mg, 1.52 mmol) in acetic acid (7.5 mL) was added phthalic anhydride (225 mg, 1.52 mmol). The reaction mixture was stirred under reflux for 2 h. After that, the crude solid was precipitated in water 200 mL and filtrated under vacuum. The crude solid was washed with water 400 mL and was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 20:80) to give green solid of **1s**, $R_f$ = 0.5 (312 mg, 78%), $^1$H NMR ([$d_6$]-DMSO, 400 MHz): $\delta$ = 11.32 (s, 1H, $N_{arom}$-H), 7.96 (dd, *J* = 5.2, 3.2 Hz, 2H, aromatic H), 7.90 (dd, *J* = 5.5, 3.0 Hz, 2H,

aromatic H), 7.57 (s, 1H, aromatic H), 7.50 (d, *J* = 8.5 Hz, 1H, aromatic H), 7.45 (s, 1H, aromatic H), 7.10 (d, *J* = 8.6 Hz, 1H, aromatic H), 6.51 (s, 1H, aromatic H). ppm.

2.6.2 Substrate scope studies.



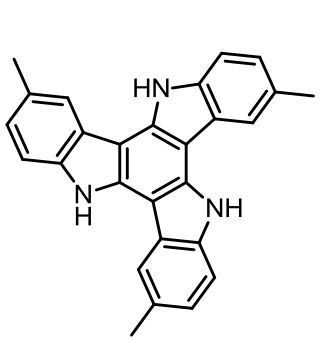

**a**: $R_1$=H, $R_2$=H, $R_3$=$CH_3$, $R_4$=H, $R_5$=H
**b**: $R_1$=H, $R_2$=H, $R_3$=$OCH_3$, $R_4$=H, $R_5$=H
**c**: $R_1$=H, $R_2$=H, $R_3$=$OCH_3$, $R_4$=$OCH_3$, $R_5$=H
**d**: $R_1$=H, $R_2$=H, $R_3$=$NO_2$, $R_4$=H, $R_5$=H
**e**: $R_1$=H, $R_2$=H, $R_3$=$COOCH_3$, $R_4$=H, $R_5$=H
**f**: $R_1$=H, $R_2$=H, $R_3$=Cl, $R_4$=H, $R_5$=H
**g**: $R_1$=H, $R_2$=H, $R_3$=H, $R_4$=$R_5$=butadiene
**h**: $R_1$=H, $R_2$=Br, $R_3$=H, $R_4$=H, $R_5$=H
**i**: $R_1$=$CH_3$, $R_2$=H, $R_3$=H, $R_4$=H, $R_5$=H
**j**: $R_1$=$C_2H_5$, $R_2$=H, $R_3$=H, $R_4$=H, $R_5$=H
**k**: $R_1$=benzyl, $R_2$=H, $R_3$=H, $R_4$=H, $R_5$=H
**l**: $R_1$=acetyl, $R_2$=H, $R_3$=H, $R_4$=H, $R_5$=H
**m**: $R_1$=H, $R_2$=H, $R_3$=OH, $R_4$=H, $R_5$=H
**n**: $R_1$=H, $R_2$=H, $R_3$=acetate, $R_4$=H, $R_5$=H
**o**: $R_1$=H, $R_2$=H, $R_3$=OTBDMS, $R_4$=H, $R_5$=H
**p**: $R_1$=H, $R_2$=H, $R_3$=$NH_2$, $R_4$=H, $R_5$=H
**q**: $R_1$=H, $R_2$=H, $R_3$=NHCOCH3, $R_4$=H, $R_5$=H
**r**: $R_1$=H, $R_2$=H, $R_3$=NHBoc, $R_4$=H, $R_5$=H
**s**: $R_1$=H, $R_2$=H, $R_3$=naphthalimide, $R_4$=H, $R_5$=H
**t**: $R_1$=H, $R_2$=H, $R_3$=phthalimide, $R_4$=H, $R_5$=H



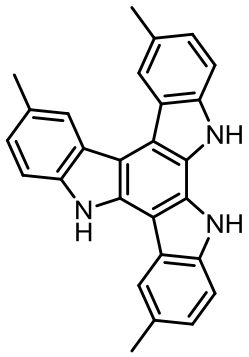
General procedure for the synthesis of substituted triaxatruxene.

Substituted indole (1 eq.) was dissolved in acetonitrile (ca 0.43 M) and *N*-bromosuccinimide (2 eq.) was slowly added portionwise (about 10 min). The mixture was stirred for 3 h, and then solid crude was filtered and washed with acetonitrile. The solid crude product was mixed with triethylamine (13 eq) formic acid (13 eq) and 10% palladium on carbon (0.1 eq) in methanol (ca 0.2 M), and the mixture was heated for 30 min under reflux. After that, the mixture was filtered through Celite, diluted with dichloromethane and washed by aqueous hydrochloric acid (10%) and brine (sat. NaCl). The organic solvent was evaporated and purified by column chromatography.

2.6.2.1 3,8,13-trimethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2a**) and 2,9,14-trimethyl-6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3a**).



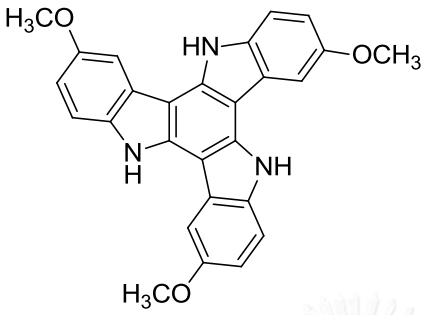

**2a**



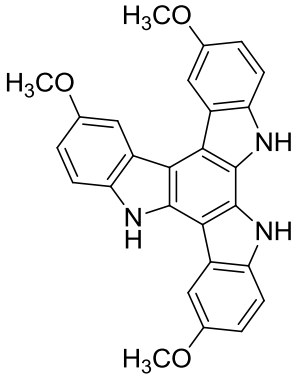

**3a**

Compounds **2a** and **3a** were prepared from 5-methylindole. The crude product was purified by column chromatography (ethyl acetate/*n*-hexane, 20:80) to give pale-gray solid of symmetrical product (**2a**), $R_f$ = 0.25 (31 mg, 16%) and dark-gray solid of asymmetrical product (**3a**), $R_f$ = 0.125 (23 mg, 12%). For **2a**, $^1$H NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 10.95 (s, 1H, $N_{arom}$-H), 8.32 (s, 1H, aromatic H), 7.58 (d, *J* = 8.2 Hz, 1H, aromatic H), 7.18 (d, *J* = 7.3 Hz, 1H, aromatic H), 2.57 (s, 3H, CH3) ppm, $^{13}$C NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 138.1, 135.6, 129.3, 124.6, 124.1, 120.4, 111.4, 101.9, 21.8 ppm and MALDI-TOF MS (*m/z*): calc.: (=386.166 [$C_{27}H_{21}N_3$]); found: (386.484 [$M^-$]). For **3a**, $^1$H NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 10.89 (s, 1H, $N_{arom}$-H), 10.60 (s, 1H, $N_{arom}$-H), 10.49 (s, 1H, $N_{arom}$-H), 8.73 (s, 1H, aromatic H), 8.66 (s, 1H, aromatic H), 8.42 (s, 1H, aromatic H), 7.63 (d, *J* = 8.1 Hz, 1H, aromatic H), 7.58 (dd, *J* = 8.1, 3.9 Hz, 2H, aromatic H), 7.30 – 7.19 (m, 3H, aromatic H), 2.68 (s, 6H, CH3), 2.58 (s, 3H, CH3) ppm, $^{13}$C NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 138.5, 131.3, 131.30, 131.28, 129.5, 128.5, 128.3, 127.4, 126.10, 126.08, 125.3, 124.6, 124.2, 123.5, 123.3, 122.58, 122.57, 121.4, 115.87, 115.85, 115.83, 111.9, 111.72, 111.70, 22.2, 22.1, 21.7 ppm and MALDI-TOF MS (*m/z*): calc.: (386.166 [$C_{27}H_{21}N_3$]); found: (386.513 [$M^-$]).

2.6.2.2 3,8,13-trimethoxy-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2b**) and 2,9,14-trimethoxy-6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3b**).



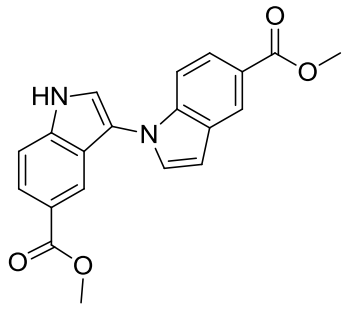

**2b**




**3b**

Compounds **2b** and **3b** were prepared from 5-methoxyindole. The crude product was purified by column chromatography (ethyl acetate/*n*-hexane, 30:70) to give gray solid of symmetrical product (**2b**), $R_f$ = 0.25 (36 mg, 18%) and dark-green solid of asymmetrical product (**3b**), $R_f$ = 0.175 (21 mg, 11%). For **2b**, $^1$H NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 10.96 (s, 1H, $N_{arom}$-H), 8.05 (d, *J* = 2.1 Hz, 1H, aromatic H), 7.54 (d, J = 8.7 Hz, 1H, aromatic H), 6.98 (dd, *J* = 8.7, 2.4 Hz, 1H, aromatic H), 3.95 (s, 3H, CH3) ppm, $^{13}$C NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 155.5, 136.2, 134.6, 124.4, 112.2, 112.0, 104.1, 102.2, 56.4 ppm and MALDI-TOF MS (*m/z*): calc.: (=434.150 [$C_{27}H_{21}N_3O_3$]); found: (434.578 [$M^-$]). For **3b**, $^1$H NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 10.91 (s, 1H, $N_{arom}$-H), 10.60 (s, 1H, $N_{arom}$-H), 10.48 (s, 1H, $N_{arom}$-H), 8.38 (s, 1H, aromatic H), 8.33 (s, 1H, aromatic H), 8.14 (s, 1H, aromatic H), 7.60 (dd, *J* = 8.7, 4.1 Hz, 3H, aromatic H), 7.11 – 7.00 (m, 3H, aromatic H), 4.07 (s, 6H, CH3), 3.96 (s, 3H, $CH_3$) ppm, $^{13}$C NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 155.5, 154.6, 154.5, 135.4, 135.0, 134.8, 131.7, 128.1, 125.2, 124.3, 123.9, 123.7, 116.0, 114.3, 114.0, 112.9, 112.7, 112.5, 112.4, 110.0, 107.6, 105.8, 105.2, 104.6, 56.5, 56.4, 56.1 ppm and MALDI-TOF MS (*m/z*): calc.: (434.150 [$C_{27}H_{21}N_3O_3$]); found: (434.632 [$M^-$]).

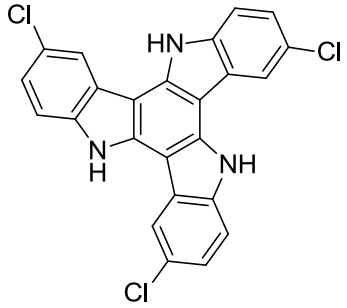
2.6.2.3 dimethyl 1'*H*-[1,3'-biindole]-5,5'-dicarboxylate (**2e**).



**2e**

Compound **2e** was prepared from methyl 1*H*-indole-5-carboxylate. The crude product was purified by column chromatography (ethyl acetate/*n*-hexane, 20:80) to give pale-pink solid of dimer product (**2e**), $R_f$ = 0.125 (43 mg, 22%), $^1$H NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 11.37 (s, 1H, $N_{arom}$-H), 8.42 (s, 1H, aromatic H), 8.39 (s, 1H, aromatic H), 7.96 (dd, *J* = 8.7, 1.4 Hz, 1H, aromatic H), 7.89 (dd, *J* = 8.6, 1.5 Hz, 1H, aromatic H), 7.82 (d, *J* = 8.7 Hz, 1H, aromatic H), 7.79 (d, *J* = 3.4 Hz, 1H, aromatic H), 7.56 (d, *J* = 8.5 Hz, 1H, aromatic H), 6.93 (d, *J* = 3.3 Hz, 1H, aromatic H), 6.84 (s, 1H, aromatic H), 3.90 (d, *J* = 0.8 Hz, 6H, CH3) ppm, $^{13}$C NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 168.1, 167.8, 139.4, 137.9, 130.4, 129.9, 129.6, 128.4, 124.9, 124.5, 124.2, 124.0, 123.7, 123.4, 112.0, 111.7, 106.5, 95.6, 52.1, 52.0 ppm and MALDI-TOF MS (*m/z*): calc.: (347.103 [$C_{20}H_{16}N_2O_4$]); found: (347.319 [$M^-$]).

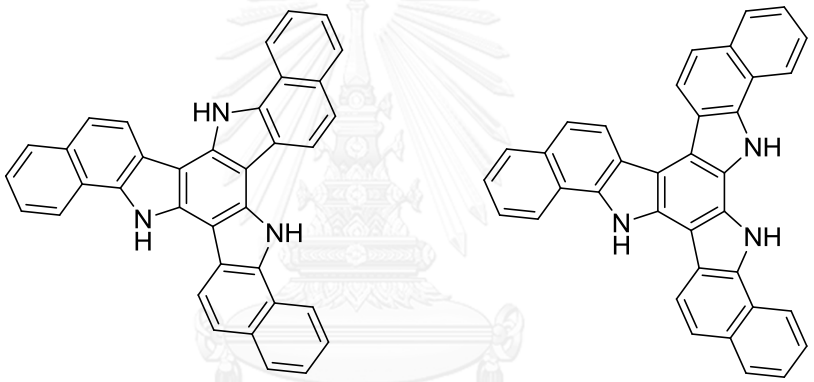
2.6.2.4 3,8,13-trichloro-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2f**).



**2f**

Compound **2f** was prepared from 5-chloroindole The crude product was purified by column chromatography (ethyl acetate/*n*-hexane, 15:85) to give white solid of symmetrical product (**2f**), $R_f$ = 0.34 (24 mg, 12%), $^1$H NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 11.38 (s, 1H, $N_{arom}$-H), 8.51 (s, 1H, aromatic H), 7.71 (d, *J* = 8.5 Hz, 1H, aromatic H), 7.37 (d, *J* = 8.5, 1.9 Hz, 1H, aromatic H) ppm, $^{13}$C NMR ([$d_6$]-acetone, 400 MHz): $\delta$ = 138.3, 136.2, 125.8, 124.6, 123.6, 119.8, 113.1, 101.7 ppm and MALDI-TOF MS (*m/z*): calc.: (446.002 [$C_{24}H_{12}Cl_3N_3$]); found: (446.483 [$M^-$]).

2.6.2.5 12,19-dihydro-5*H*-benzo[i]benzo[6,7]indolo[3,2-a]benzo[6,7]indolo[3,2-c]carbazole (**2g**) and 6,13-dihydro-5*H*-benzo[i]benzo[6,7]indolo[2,3-a]benzo[6,7]indolo[2,3-c]carbazole (**3g**).



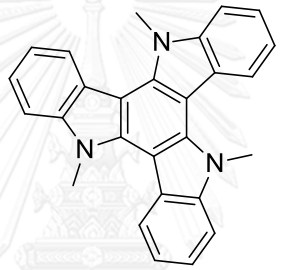

**2g** **3g**



Compounds **2g** and **3g** were prepared from 1*H*-benzo[g]indole The crude product was purified by column chromatography (ethyl acetate/*n*-hexane, 20:80) to give dark-green solid of symmetrical product (**2g**), $R_f$ = 0.45 (34 mg, 17%) and green solid of asymmetrical product (**3g**), $R_f$ = 0.25 (24 mg, 12%). For **2g**, $^1$H NMR ([$d_6$]-DMSO, 400 MHz): $\delta$ = 12.26 (s, 1H, $N_{arom}$-H), 9.28 (d, *J* = 8.6 Hz, 1H, aromatic H), 9.17 (d, *J* = 8.4 Hz, 1H, aromatic H), 8.14 (d, *J* = 8.1 Hz, 1H, aromatic H), 7.91 (d, *J* = 8.6 Hz, 1H, aromatic H), 7.73 (t, *J* = 7.5 Hz, 1H, aromatic H), 7.58 (t, *J* = 7.4 Hz, 1H, aromatic H) ppm, $^{13}$C NMR ([$d_6$]-DMSO, 400 MHz): $\delta$ = 133.0, 131.8, 130.4, 128.4, 125.1, 124.1, 122.4, 121.6, 120.9, 119.7, 117.7, 103.6 ppm and MALDI-TOF MS (*m/z*): calc.: (494.166 [$C_{36}H_{21}N_3$]); found: (494.731 [$M^-$]). For **3g**, $^1$H NMR ([$d_6$]-DMSO, 400 MHz): $\delta$ = 12.39 (s, 1H, $N_{arom}$-H), 12.34 (s, 1H, $N_{arom}$-H), 12.22 (s, 1H, $N_{arom}$-H), 9.31 (d, *J* = 8.7 Hz, 1H,

aromatic H), 9.18 (d, *J* = 8.2 Hz, 1H, aromatic H), 9.01 (dd, *J* = 8.8, 4.6 Hz, 2H, aromatic H), 8.53 (t, *J* = 7.7 Hz, 2H, aromatic H), 8.20 – 8.11 (m, 3H, aromatic H), 7.90 (dd, *J* = 14.0, 8.7 Hz, 3H, aromatic H), 7.76 (dt, *J* = 15.0, 7.3 Hz, 3H, aromatic H), 7.60 (dt, *J* = 21.8, 7.2 Hz, 3H, aromatic H) ppm and $^{13}$C NMR ([$d_6$]-DMSO, 400 MHz): $\delta$ = 133.6, 133.2, 133.1, 130.8, 130.6, 130.4, 130.1, 128.7, 128.5, 128.5, 128.2, 125.8, 125.0, 124.9, 124.82, 124.76, 124.1, 122.4, 122.1, 121.9, 121.8, 121.6, 121.42, 121.39, 121.2, 120.8, 119.59, 119.57, 119.4, 118.6, 118.5, 117.7, 113.9, 110.2, 107.0, 103.6 ppm and MALDI-TOF MS (*m/z*): calc.: (494.166 [$C_{36}H_{21}N_3$]); found: (494.620 [$M^-$]).

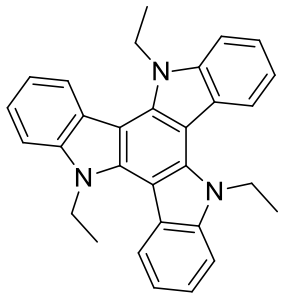
2.6.2.6 5,10,15-trimethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2i**).




**2i**

Compound **2i** was prepared from 1-methylindole The crude product was purified by column chromatography (dichloromethane/*n*-hexane, 20:80) to give pale-brown solid of symmetrical product (**2i**), $R_f$ = 0.25 (47 mg, 24%), $^1$H NMR ([$d_6$]-DMSO, 400 MHz): $\delta$ = 8.52 (d, *J* = 8.0 Hz, 1H, aromatic H), 7.74 (d, *J* = 8.1 Hz, 1H, aromatic H), 7.47 (t, *J* = 7.2 Hz, 1H, aromatic H), 7.34 (t, *J* = 7.2 Hz, 1H, aromatic H), 4.44 (s, 3H, $CH_3$) ppm., $^{13}$C NMR ([$d_6$]-DMSO, 400 MHz): $\delta$ = 141.4, 138.3, 123.1, 121.9, 121.7, 119.9, 110.2, 101.9, 35.8 ppm and MALDI-TOF MS (*m/z*): calc.: (386.166 [$C_{27}H_{21}N_3$]); found: (386.608 [$M^-$]).

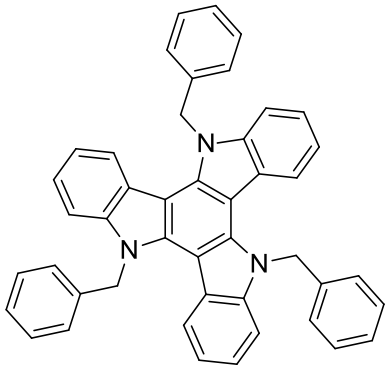
2.6.2.7 5,10,15-triethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2j**).



**2j**

Compound **2j** was prepared from 1-ethyl-1*H*-indole. The crude product was purified by column chromatography (dichloromethane/*n*-hexane, 20:80) to give pale-brown solid of symmetrical product (**2j**), $R_f$ = 0.25 (49 mg, 25%), $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ = 8.36 (d, *J* = 7.9 Hz, 1H, aromatic H), 7.67 (d, *J* = 8.1 Hz, 1H, aromatic H), 7.47 (t, 1H, aromatic H), 7.36 (t, *J* = 7.5 Hz, 1H, aromatic H), 5.04 (q, *J* = 7.0 Hz, 2H, $CH_2$), 1.62 (t, *J* = 7.1 Hz, 3H, $CH_3$) ppm, $^{13}$C NMR ($CDCl_3$, 400 MHz): $\delta$ = 140.9, 138.6, 123.6, 122.9, 121.5, 119.8, 110.3, 103.3, 41.7, 15.4 ppm and MALDI-TOF MS (*m/z*): calc.: (428.213 [$C_{30}H_{27}N_3$]); found: (428.589 [$M^-$]).

2.6.2.8 5,10,15-tribenzyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2k**).

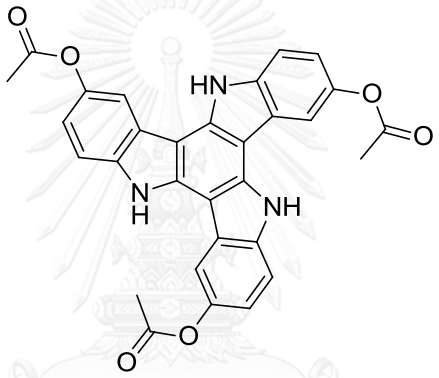


**2k**

Compound **2k** was prepared from 1-benzyl-1H-indole. The crude product was purified by column chromatography (dichloromethane/*n*-hexane, 20:80) to give white

solid of symmetrical product (**2k**), $R_f$ = 0.25 (41 mg, 21%), $^1$H NMR ($CDCl_3$, 400 MHz): **δ** = 7.91 (d, *J* = 8.1 Hz, 1H, aromatic H), 7.43 (d, *J* = 7.4 Hz, 2H, aromatic H), 7.35 (t, *J* = 7.5 Hz, 2H, aromatic H), 7.28 (q, *J* = 7.2 Hz, 1H, aromatic H), 7.20 – 7.12 (m, 2H, aromatic H), 6.93 (t, *J* = 7.4 Hz, 1H. aromatic H), 6.00 (s, 2H, $CH_2$) ppm, $^{13}$C NMR ($CDCl_3$, 400 MHz): **δ** = 141.8, 139.7, 138.2, 129.1, 127.5, 126.6, 123.2, 121.6, 120.3, 110.9, 103.4, 51.5 ppm and MALDI-TOF MS (*m/z*): calc.: (615.267 [$C_{45}H_{33}N_3$]); found: (615.055 [$M^-$]).

2.6.2.9 10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole-3,8,13-triyl triacetate (**2n**).




**2n**

Compound **2n** was prepared from 1*H*-indol-5-yl acetate (**1n**). The crude product was purified by column chromatography (ethyl acetate/*n*-hexane, 30:70) to give dark green solid of symmetrical product (**2n**), $R_f$ = 0.25 (19 mg, 10%), $^1$H NMR ([$d_6$]-acetone, 400 MHz): **δ** = 11.25 (s, 1H, $N_{arom}$-H), 8.23 (s, 1H, aromatic H), 7.68 (d, *J* = 8.6 Hz, 1H, aromatic H), 7.13 (d, *J* = 8.5 Hz, 1H, aromatic H), 2.34 (s, 3H, $CH_3$) ppm, $^{13}$C NMR ([$d_6$]-acetone, 400 MHz): **δ** = 170.4, 145.8, 137.5, 136.3, 123.8, 117.6, 113.1, 111.9, 111.9, 21.1 ppm and MALDI-TOF MS (*m/z*): calc.: (519.143 [$C_{30}H_{21}N_3O_6$]); found: (518.935 [$M^-$]).

# CHAPTER III

# RESULTS AND DISCUSSION

## 3.1 The preparation of HPLC standards.

For the purpose of reaction monitoring and product quantification, a reliable analytical method is highly essential. Since the synthetic process can generate two isomeric compounds, a symmetrical triazatruxene (**2**) and asymmetrical triazatruxene (**3**), HPLC was thus selected as the analytical method because it is capable of separating and quantifying both compounds. The standard compounds for HPLC analysis were prepared using an un-optimized procedure reported in previous literature [10], but the liquid $Br_2$ was replaced by *N*-bromosuccinimide (NBS). This reaction gave two isomeric compounds which are symmetrical and asymmetrical **TAT** in low isolated yields (**Table 1**). The crude reaction mixture could be separated by column chromatography to afford adequate amount and purity of the reference compounds to be used as standards in HPLC analysis.

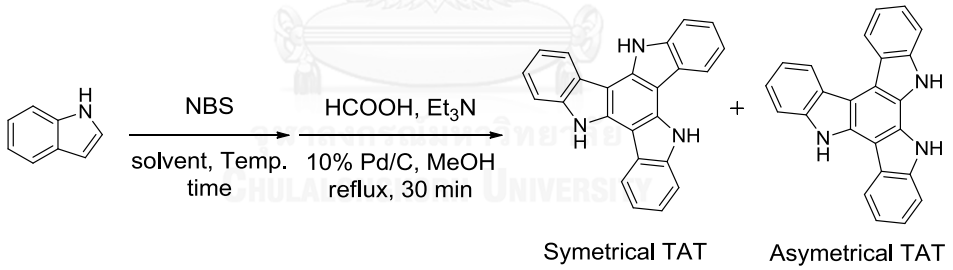



**Table 1** Preparation of Triazatruxenes (**TAT**) using un-optimized conditions.[a]

| Entry | Scale (g) | NBS (eq.) | [indole] (M) | Temp (°C) | Time (h) | % isolated yield | |
|---|---|---|---|---|---|---|---|
| | | | | | | Sym | Asym |
| 1 | 1 | 3 | 0.43 | 28 | 12 | 3 | 4 |
| 2 | 1 | 5 | 0.43 | 28 | 12 | 6 | 8 |

[a]Reaction conditions: Indole (8.5 mmol), HCOOH (30.2 mmol), $Et_3N$ (30.2 mmol), 10% Pd/C (0.18 mmol), in $CH_3OH$ (30 mL)

### 3.2 HPLC Analytical Method

With the two standards isomeric **TAT** in hands, HPLC conditions were studied to achieve as fast and efficient analysis of the reaction mixture containing both isomers. The optimized HPLC conditions were as follows: Symmetrical C18 column, 4.6 x 150 mm, 5 µm, 70% MeCN:$H_2O$ isocratic mobile phase and 25 °C with the injection volume of 25 µl. The symmetrical and asymmetrical isomers were detected at 3.9 and 4.5 min, respectively, by a diode array UV/Vis absorption detector (235 nm).

Solutions with various concentration of both 2 and 3 in $CH_3CN$ were prepared (0.1-0.5 mM) for the construction of calibration curves for quantification of both isomers (**Table 2 and 3**), which were plotted between concentration (x-axis) and integrated peak areas (y-axis) for each compounds (**Figure 3 and 4**). The analysis sample was dissolved in a known amount of solvent ($CH_3CN$). The amounts of products were calculated from the concentration obtained from the calibration curve and dilution factor.

**Table 2** Peak areas and concentrations of symmetrical **TAT**.

| [Sym **TAT**] (mmol/L) | Run 1 | Run 2 | Run 3 | Average peak area | %SD |
|---|---|---|---|---|---|
| 0.1 | 2,398,456 | 2,245,888 | 2,355,703 | 2,333,349 | 3.3729 |
| 0.2 | 4,394,788 | 4,510,882 | 4,392,750 | 4,432,807 | 1.5255 |
| 0.3 | 6,690,585 | 6,466,981 | 6,669,575 | 6,609,047 | 1.86835 |
| 0.4 | 8,678,398 | 8,672,413 | 8,672,426 | 8,674,412 | 0.03979 |
| 0.5 | 10,697,620 | 10,643,054 | 10,871,314 | 10,737,329 | 1.11013 |

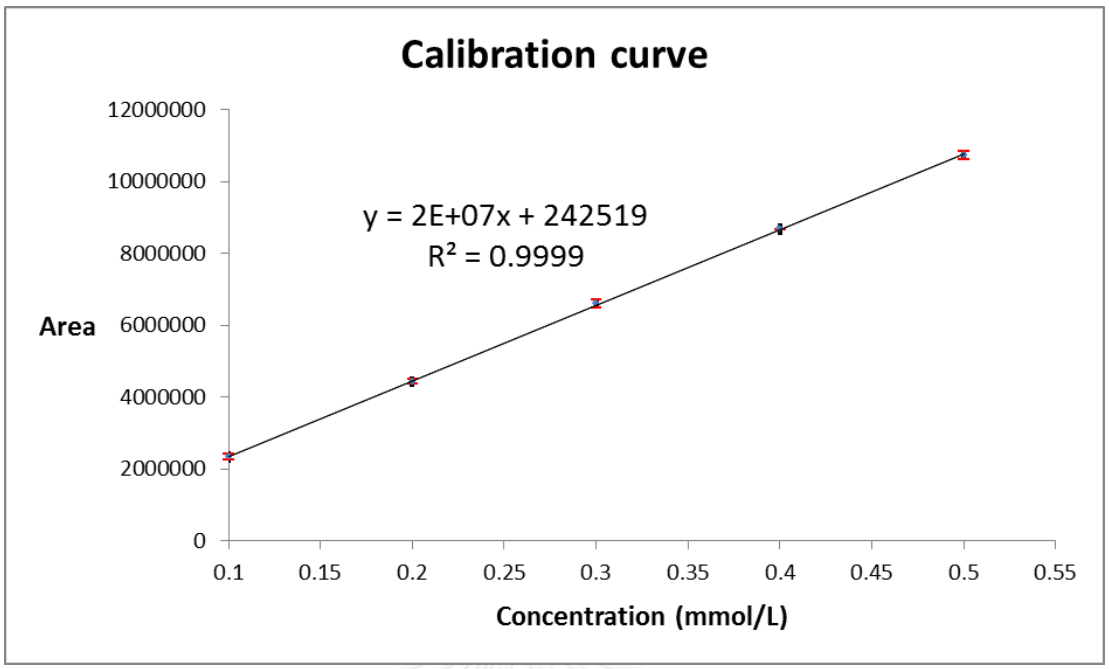



**Figure 3** Calibration curve of symmetrical **TAT**

**Table 3** Peak areas and concentrations of asymmetrical **TAT**.

| [Asym **TAT**] (mmol/L) | Run 1 | Run 2 | Run 3 | Average peak area | %SD |
|---|---|---|---|---|---|
| 0.1 | 5,060,318 | 5,014,994 | 4,965,559 | 5,013,624 | 0.94531 |
| 0.2 | 10,563,370 | 10,112,841 | 10,591,091 | 10,422,434 | 2.57592 |
| 0.3 | 15,622,214 | 16,055,362 | 15,650,922 | 15,776,166 | 1.53533 |
| 0.4 | 21,007,801 | 20,228,886 | 21,407,079 | 20,881,255 | 2.86958 |
| 0.5 | 23,951,807 | 25,245,343 | 24,366,438 | 24,521,196 | 2.69362 |

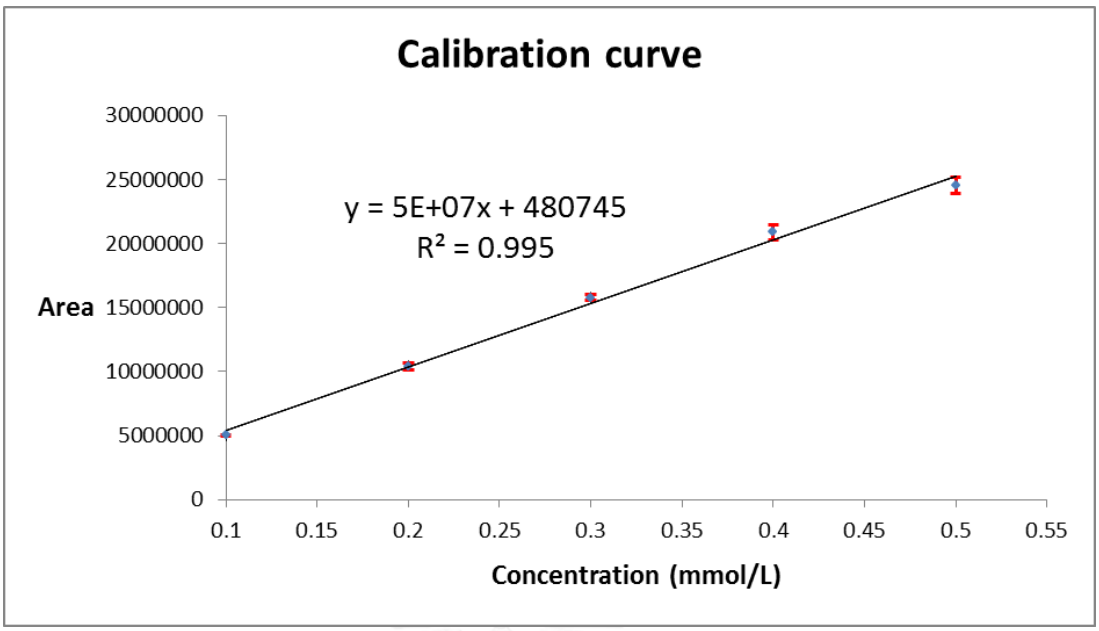



**Figure 4** Calibration curve of asymmetrical **TAT**

### 3.3 Optimization studies

The reaction optimization was studied at 0.1 g of indole. We began with the examination of solvent by using non-polar solvent ($CHCl_3$), polar aprotic solvents (EtOAc, acetone, MeCN) and polar protic solvent (MeOH) (**Table 4, entry 1-5**). Probably due to the insolubility of *N*-bromosuccinimide (NBS) in $CHCl_3$ and EtOAc, reactions in those solvents were very slow. In addition, acetone and MeOH caused a number of unexpected products on HPLC chromatograms. MeCN was then chosen as the best solvent for further experiments. Next, we screened the amount of NBS from 1 to 5 eq (**Table 4, entry 4 and 6-9**). When increase eq of NBS, the ratio between symmetrical and asymmetrical was decrease. The results suggest that the amount of NBS can affect this product ratio and also mechanism to produce both symmetrical and asymmetrical products. Then, we screened reactant concentration (**Table 4, entry 7 and 10-12**) because this kind of reaction involves combination of 3 molecules, it is very possible that the reactant concentration can affect the product yield. Next, we screened temperature between 0 and 50°C (**Table 4, entry 7, 13 and14**). The results suggested that the reaction were performed at ambient temperature (28°C) and 50°C are not significantly different in term of yield and product ratio. Therefore, we select 28°C as the optimal condition because it is more

convenient. Then, we screened the reaction time from 1 to 6 h and also overnight for about 12 h (**Table 4, entry 7 and 15-18**). From the table, the reaction yield reach an optimal point of about 40 %yield after 3 hours. Prolong stirring of the reaction mixture does not increase the product yield. The optimal conditions, which involved the treatment of indole with 2 equivalents of NBS in acetonitrile at room temperature for 3 h (**Table 4, entry 17**), followed by reductive debromination, could provide **TAT** and asymmetric **TAT** in a total yield of 39% (2-steps HPLC yield).

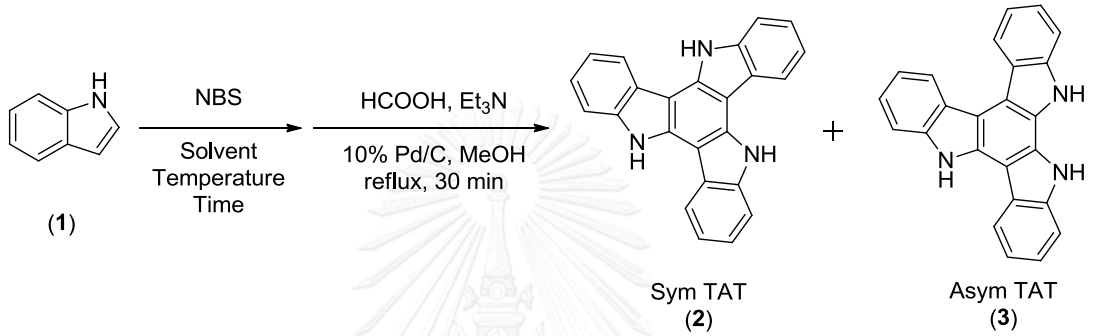



**Table 4** Optimization studies on the cyclotrimerization reaction.[a]

| Entry | Solvent | Eq. of NBS | Concentration (M) | Temperature (°C) | Time (h) | Yield [%][b] (**2**) | (**3**) |
|---|---|---|---|---|---|---|---|
| 1 | $CHCl_3$ | 3 | 0.43 | 28 | O/N | 2 | 12 |
| 2 | EtOAc | 3 | 0.43 | 28 | O/N | 1 | 1 |
| 3 | Acetone | 3 | 0.43 | 28 | O/N | - | - |
| 4 | MeCN | 3 | 0.43 | 28 | O/N | 15 | 18 |
| 5 | MeOH | 3 | 0.43 | 28 | O/N | - | - |
| 6 | MeCN | 1 | 0.43 | 28 | O/N | 10 | 1 |
| 7 | MeCN | 2 | 0.43 | 28 | O/N | 23 | 12 |
| 8 | MeCN | 4 | 0.43 | 28 | O/N | 13 | 24 |
| 9 | MeCN | 5 | 0.43 | 28 | O/N | 9 | 18 |
| 10 | MeCN | 2 | 0.11 | 28 | O/N | 8 | 6 |
| 11 | MeCN | 2 | 0.21 | 28 | O/N | 21 | 11 |
| 12 | MeCN | 2 | 0.85 | 28 | O/N | 21 | 12 |
| 13 | MeCN | 2 | 0.43 | 0 | O/N | 5 | 4 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 14 | MeCN | 2 | 0.43 | 50 | O/N | 21 | 8 |
| 15 | MeCN | 2 | 0.43 | 28 | 1 | 15 | 16 |
| 16 | MeCN | 2 | 0.43 | 28 | 2 | 16 | 15 |
| 17 | MeCN | 2 | 0.43 | 28 | 3 | 23 | 16 |
| 18 | MeCN | 2 | 0.43 | 28 | 6 | 23 | 17 |

[a]Reaction conditions: Indole (0.85 mmol), HCOOH (3.02 mmol), $Et_3N$ (3.02 mmol), 10% Pd/C (0.018 mmol), in MeOH (3 mL); [b]HPLC yields estimated from the calibration curves.

During the addition of NBS into a solution of indole, we usually observed exothermic reaction or generation of heat. The fast addition of NBS can cause the volatile solvent to evaporate. Therefore we next study the effect of addition rate and method of addition which are solid NBS was added in small portions for a period of 10 and 90 min and the solution of indole was slowly added in to a solution of NBS in MeCN (**Table 5**). The results suggest that addition rate of 10 min can afford highest yield of both product. When the solution of indole was slowly added in to a solution of NBS in MeCN, the reaction was poorly yielded. The overall results suggested that the addition rate and method of addition greatly influenced the reaction efficiency. It is possible that during the course of this reaction, 3-bromoindole and unbrominated indole are involve in the reaction mechanism. Addition rates that are too fast or too slow may result in the improper amount of 3-bromoindole and unbrominated indole. One evidence for this hypothesis was that the reaction using pure 3-bromoindole under the same condition fails to give the expected **TAT** (**Table 8, entry 8**).

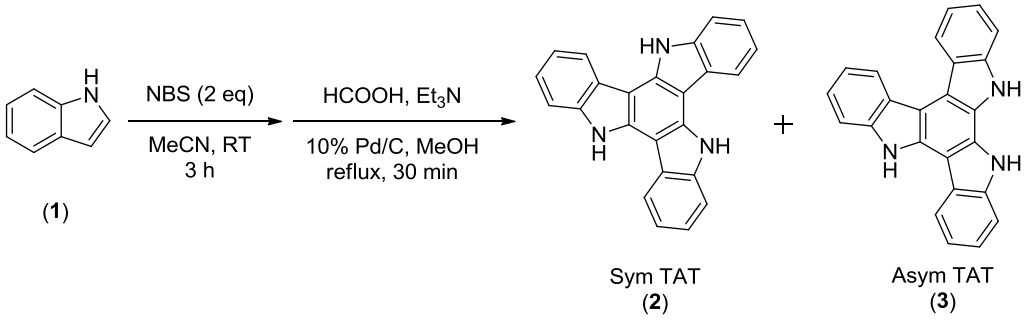



**Table 5** Reagent addition rate and method of addition studies.[a]

| Entry | Reagent addition rate and method of addition | Yield [%][b] | |
|---|---|---|---|
| | | (**2**) | (**3**) |
| 1 | NBS to indole in 10 min | 23 | 16 |
| 2 | NBS to indole in 90 min | 14 | 12 |
| 3 | Indole to NBS in 10 min | 6 | 2 |

[a]Reaction conditions: Indole (0.85 mmol), NBS (1.70 mmol), in MeCN (2 mL), HCOOH (3.02 mmol), $Et_3N$ (3.02 mmol), 10% Pd/C (0.018 mmol), in MeOH (3 mL); [b]HPLC yields estimated from the calibration curves.

Finally, we study the possibility of whether or not this reaction involves free radical pathway. For this purpose, a series of reactions was performed, one without BHT and the other two with BHT **(Table 6**), which is a well-known radical scavenger [24]. The results showed that the addition of BHT can slightly decrease the product yields, but the expected products still dominated regardless of the amount of BHT. We then conclude that this reaction should not involve radical species, but the slightly lower yield may cause by side reaction between NBS and BHT; for example, benzylic bromination. [25, 26]

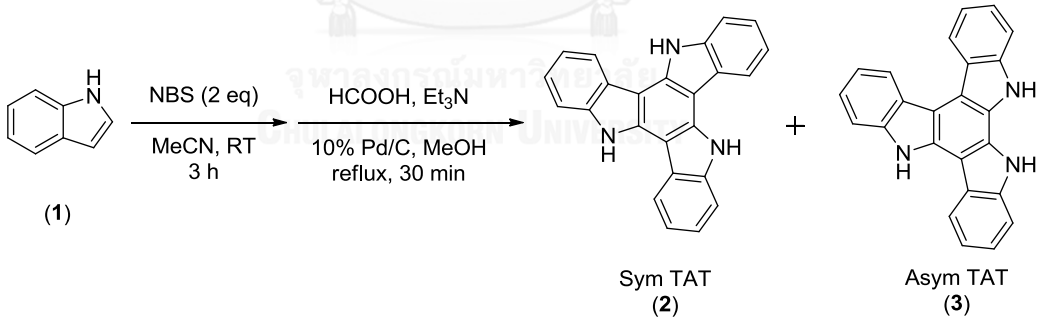



**Table 6** Prove of radical pathway by BHT.[a]

| Entry | Additive reagent | Yield [%][b] | |
|---|---|---|---|
| | | (**2**) | (**3**) |
| 1 | None | 23 | 16 |
| 2 | BHT (0.2 eq of indole) | 19 | 11 |
| 3 | BHT (1 eq of indole) | 18 | 12 |

[a]Reaction conditions: Indole (0.85 mmol), NBS (1.70 mmol), in MeCN (2 mL), HCOOH (3.02 mmol), $Et_3N$ (3.02 mmol), 10% Pd/C (0.018 mmol), in MeOH (3 mL); [b]HPLC yields estimated from the calibration curves.

### 3.4 Application of the optimal conditions on large-scale.

With the optimal reaction conditions in hands, we expanded scales of reaction to 1 and 10 g in order to test the scalability of reaction (**Table 7**). From our experiment, the expected products were obtained in a relatively similar yield of 25 and 30% after column chromatography, respectively.

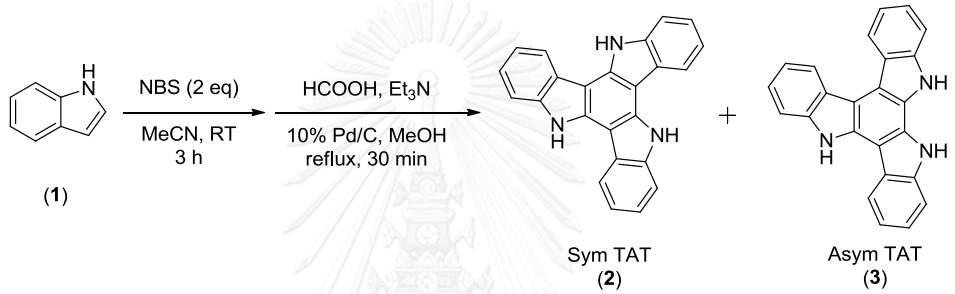



**Table 7** Reaction scaling-up studies.

| Entry | Scale (g) | Yield [%][a] | |
|---|---|---|---|
| | | (**2**) | (**3**) |
| 1 | 1.0 | 15±2 | 10±1 |
| 2 | 10.0 | 19±3 | 11±1 |

[a]Isolated yield after chromatographic purification.

### 3.5 Substrate scope studies.

In order to expand the scope and understand the limitation of this reaction, a series of substituted indoles were used as starting materials (**Table 8**).

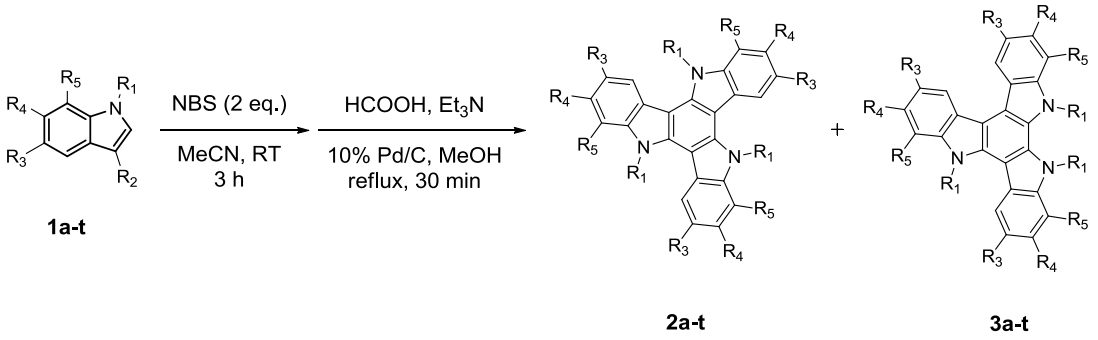
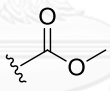
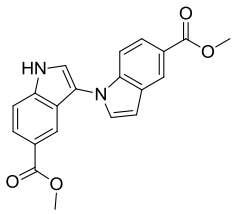
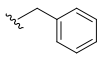
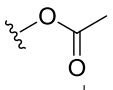
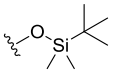
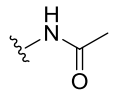
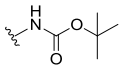
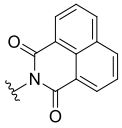
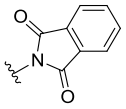



**Table 8** Substrate scope with varies substituted indoles studies.

| Entry | Substrate (**1**) | Substituted indole | | | | | % isolated yield | |
|---|---|---|---|---|---|---|---|---|
| | | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | (**2**) | (**3**) |
| 1 | a | H | H | $-CH_3$ | H | H | 16 | 12 |
| 2 | b | H | H | $-OCH_3$ | H | H | 18 | 11 |
| 3 | c | H | H | $-OCH_3$ | $-OCH_3$ | H | Complex mixture | |
| 4 | d | H | H | $-NO_2$ | H | H | Complex mixture | |
| 5 | e | H | H |  | H | H |  (Unexpected dimer, 22%) | |
| 6 | f | H | H | -Cl | H | H | 12 | - |
| 7 | g | H | H | H |  | | 17 | 12 |
| 8 | h | H | Br | H | H | H | No reaction | |
| 9 | i | $-CH_3$ | H | H | H | H | 24 | - |
| 10 | j | $-C_2H_5$ | H | H | H | H | 25 | - |
| 11 | k |  | H | H | H | H | 21 | - |
| 12 | l |  | H | H | H | H | No reaction | |
| 13 | m | H | H | -OH | H | H | Complex mixture | |
| 14 | n | H | H |  | H | H | 10 | - |
| 15 | o | H | H |  | H | H | Complex mixture | |

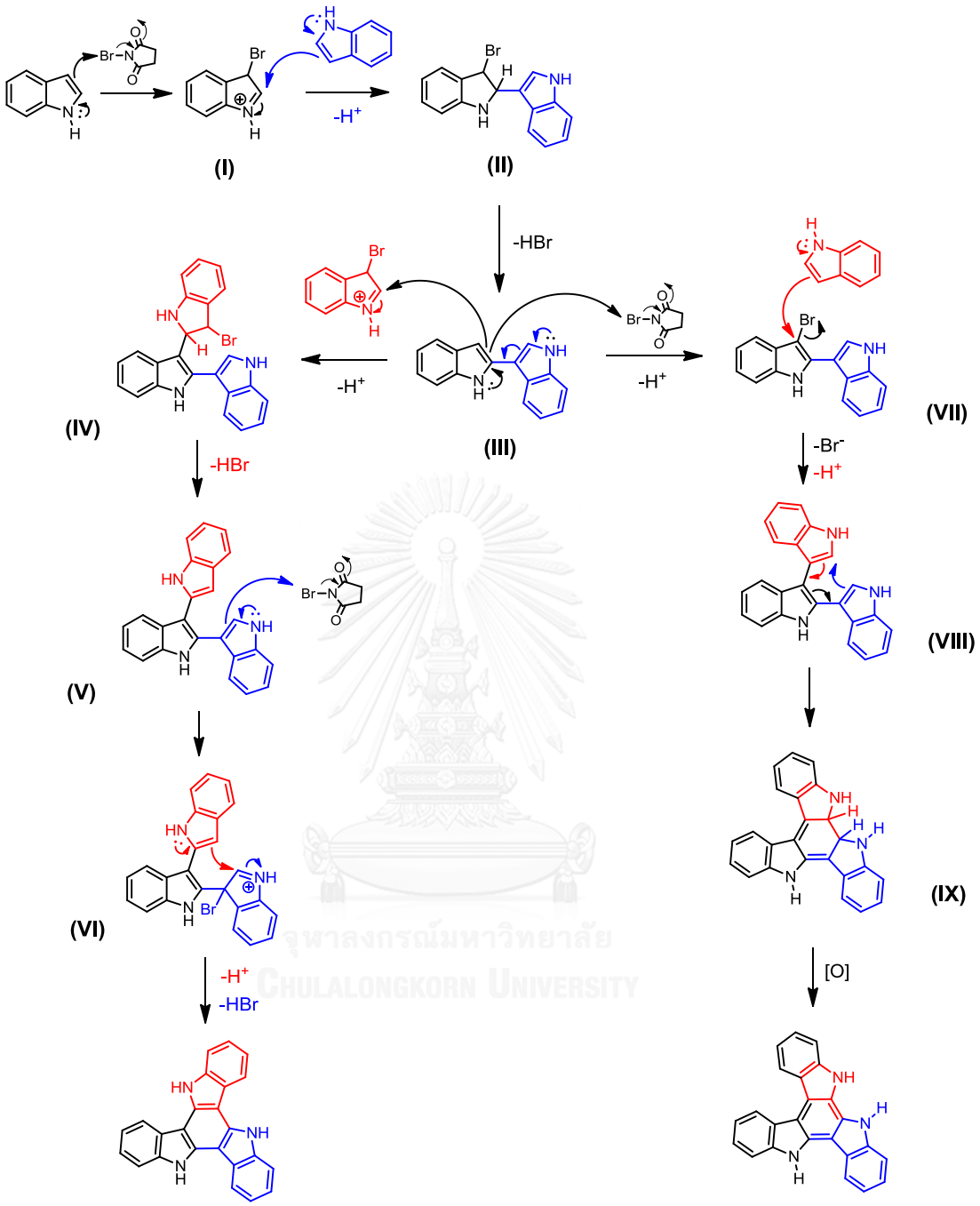
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 16 | p | H | H | $-NH_2$ | H | H | Complex mixture |
| 17 | q | H | H |  | H | H | Complex mixture |
| 18 | r | H | H |  | H | H | Complex mixture |
| 19 | s | H | H |  | H | H | No reaction |
| 20 | t | H | H |  | H | H | No reaction |

The data from entry 1-6 indicated that this reaction can be influenced by both electron-donating (EDG) and withdrawing groups (EWG). With the methyl or methoxy groups at the 5-position (**Table 8, entry 1 and 2**), the reaction provided similar amount of two products as compared to the un-substituted indole. Interestingly, 5-chloroindole reacted under this condition to produce only the symmetical **TAT** (**Table 8, entry 6**). These results may relate to the ability of Cl to function as both EDG (via resonance) and EWG (via inductive effect). When two methoxy group or an EWG are present, the reaction did not provide the expected **TAT**. In both cases, some competitive reactions may occur which lead to the complex mixture (**Table 8, entry 3-4**) or the reaction will halt at the dimer state (**Table 8, entry 5**). When free hydroxy group or free amino group was at the 5-position, the reaction became uncontrollable as several products were formed (**Table 8, entry 13 and 16**). These could be a result from undesired reaction between NBS and those reactive functional groups. Attempts to protect the -OH group as an ester could lead to the substrate that yield only symmetrical **TAT** product (**Table 8, entry 14**). Silicon protecting group was found to be unstable under the reaction conditions (**Table 8, entry 15**). Compounds with amide or carbamate protected amino group (**Table 8, entry 17-18**) also did not yield the expected **TAT**, whereas the substrates with imide protected amino group (**Table 8, entry 19-20**) were unreactive towards the reaction condition. These results imply that the –NH group may be able to react with NBS (for instance; Hoffman

rearrangement) and lead to the formation of complex mixture. Furthermore, benzo (**Table 8, entry 7**) can form both symmetrical and asymmetrical products as well in a comparable yield of 29%.

To our delight, indole substrates with an alkyl substituent on the nitrogen could provide symmetrical **TAT** as sole products in good yields (**Table 8, entry 9-11**). These may result from the higher steric hindrance in the asymmetrical structures that prevent the formation of asymmetrical **TAT**. However, the use of *N*-acetyl indole in this reaction resulted in a complete recovery of starting material (**Table 8, entry 12**). In addition, 3-bromoindole was also found to be inactive under the reaction condition (**Table 8, entry 8**). It is obvious that the electronic property of the nitrogen could control the overall reaction and 3-bromoindole should be one of many reaction intermediates. With all of the above information, a plausible mechanism for this transformation is proposed in **scheme 12**.

The reaction mechanism (**Scheme 12**) should involve electrophilic bromination of indole to produce intermediate **I** followed by nucleophilic attack, deprotonation, and dehydrohalogenation to form 2,3-dimer **III**. In order to generate symmetrical **TAT**, dimer **III** will react with another mole of intermediate **I** by nucleophilic attack between C-3 of the dimer **III** and C-2 of the intermediate **I**. A sequence of deprotonation, cyclization, and dehydrohalogenation then finally produce the symmetrical **TAT**. For the conversion of dimer **III** to asymmetrical **TAT**, the electrophilic bromination occur at the dimer **III**, followed by a nucleophilic attack of indole and C-3 of the intermediate (**VII**). A sequence of dehydrohalogenation, electrocyclic ring-closing, and oxidation then finally produce the asymmetrical **TAT**.




**Scheme 12** Proposed mechanism of symmetrical and asymmetrical **TAT**

# CHAPTER IV

## CONCLUSION

We have demonstrated that *N*-bromosuccinimide (NBS) can be a safe and practical reagent for cyclotrimerization of indole to triazatruxenes under mild conditions. The optimization studies by variation of indole concentration, reaction time and temperature, and amount of NBS were evaluated based on HPLC yields of symmetrical and asymmetrical triazatruxenes (**TAT**). From the data, the best solvent for the reaction was MeCN and the amount of NBS was optimized to 2 eq. The concentration of indole at 0.43 M and the ambient reaction temperature could result in the best yield of **TAT**s. The reaction yield could reach its threshold after 3 h of reaction when the addition rate for NBS was at 10 mins. These conditions provided the overall HPLC yield of 39% after two consecutive steps. The reaction exhibited some robustness and reproducibility as the synthesis on 1 and 10-g scale could afford the expected products in slightly lower yield of 25-30% after purification by column chromatography. The reaction displayed a compatibility with 5-alkyl, 5-alkoxy, and *N*-alkyl indoles. Substrates with strong electron-donating and withdrawing groups tended to give complex mixture of products, while benzoindole could provide the corresponding product in decent yield. The reaction mechanism was proposed to undergo via electrophilic bromination of indole and nucleophilic attack at the bromoindolium ion.

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# APPENDIX

# APPENDIX

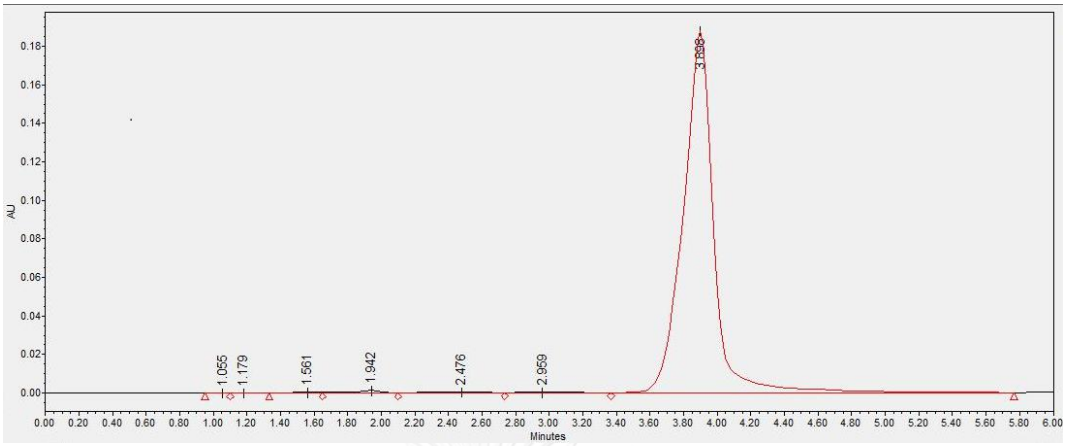


**Figure A. 1** HPLC chromatogram of 0.1 mM of symmetrical **TAT** in MeCN.

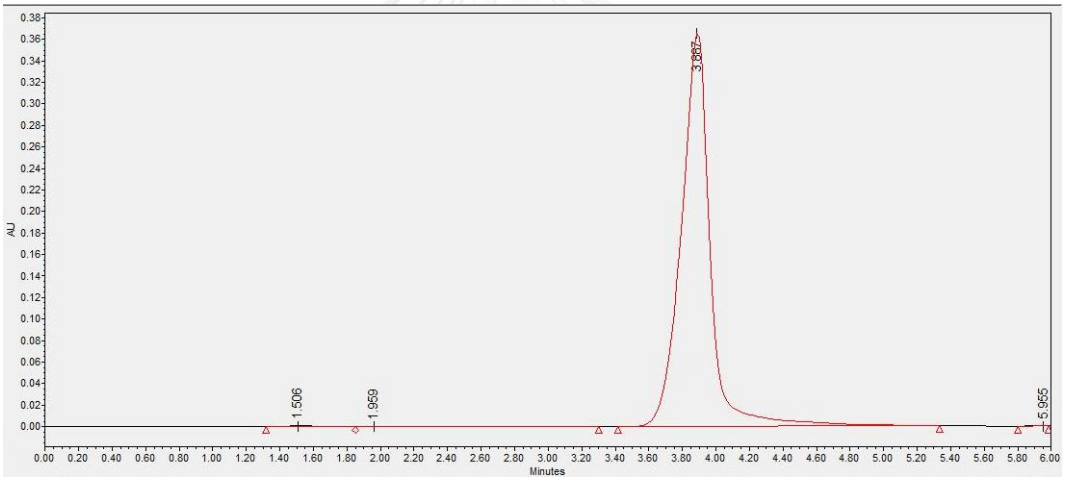


**Figure A. 2** HPLC chromatogram of 0.2 mM of symmetrical **TAT** in MeCN.

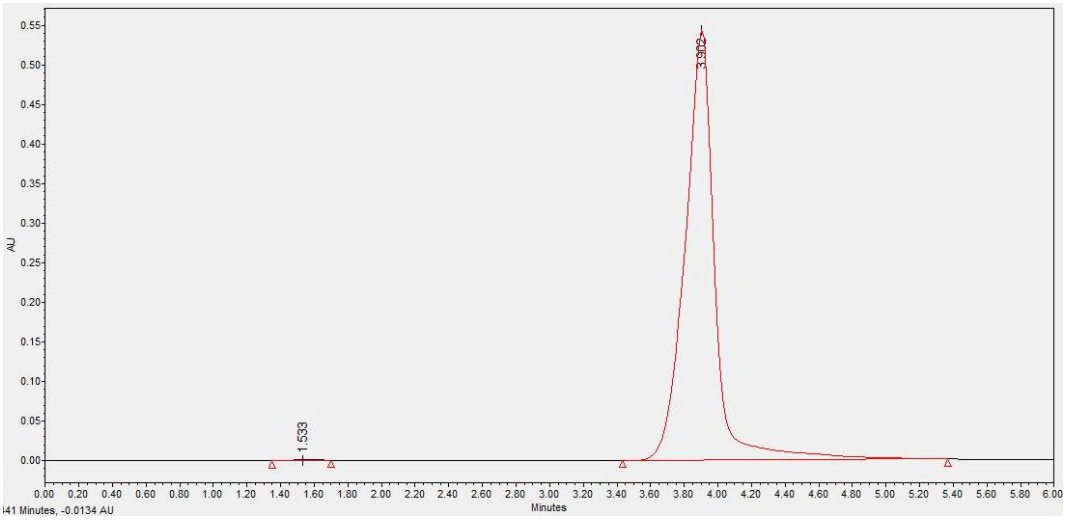


**Figure A. 3** HPLC chromatogram of 0.3 mM of symmetrical **TAT** in MeCN.

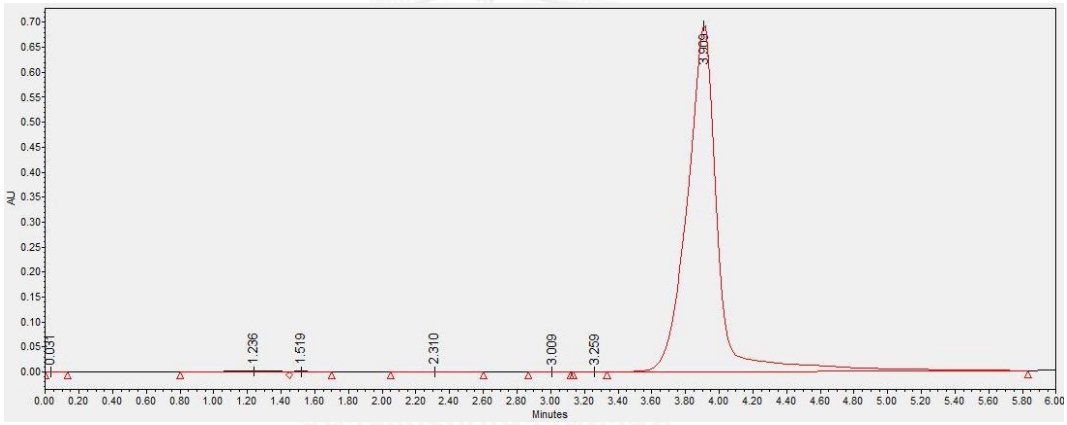


**Figure A. 4** HPLC chromatogram of 0.4 mM of symmetrical **TAT** in MeCN.

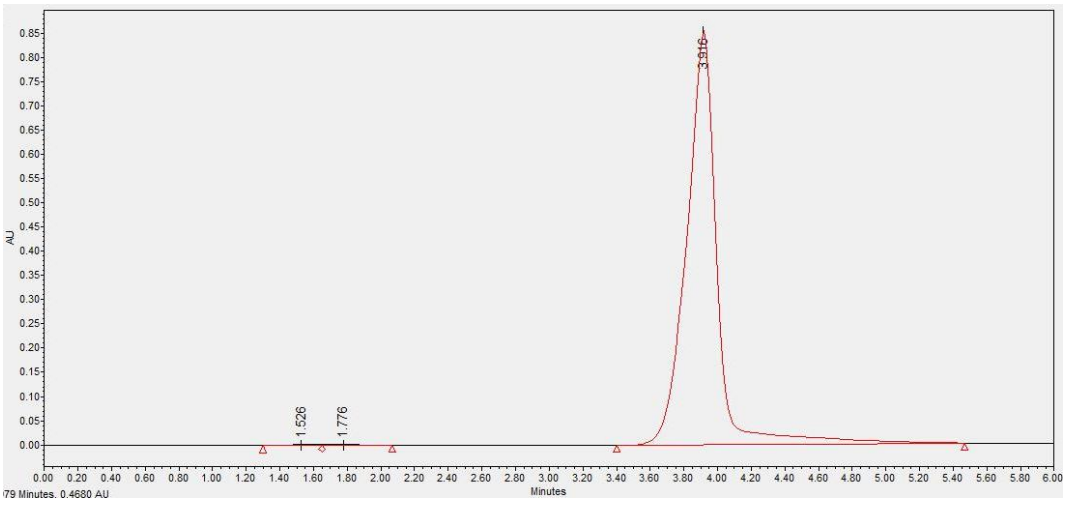


**Figure A. 5** HPLC chromatogram of 0.5 mM of symmetrical **TAT** in MeCN.

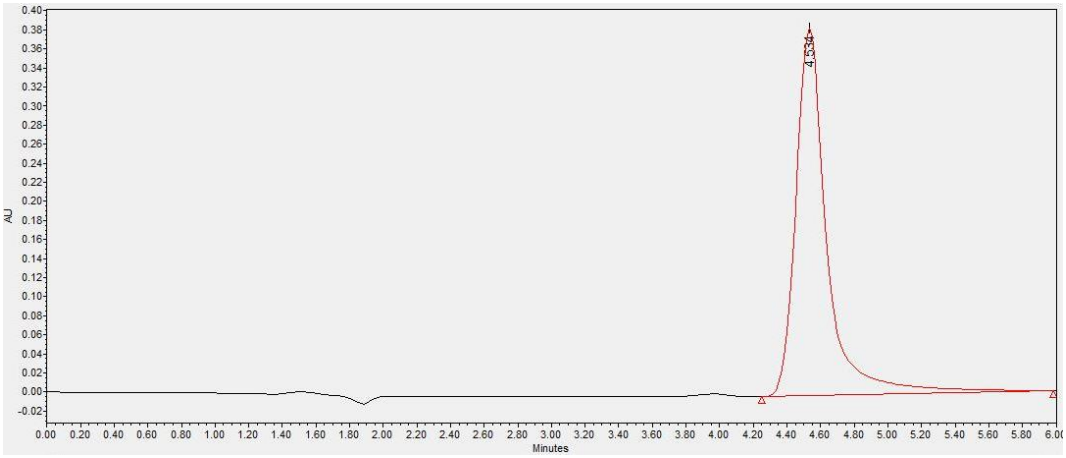


**Figure A. 6** HPLC chromatogram of 0.1 mM of asymmetrical **TAT** in MeCN.

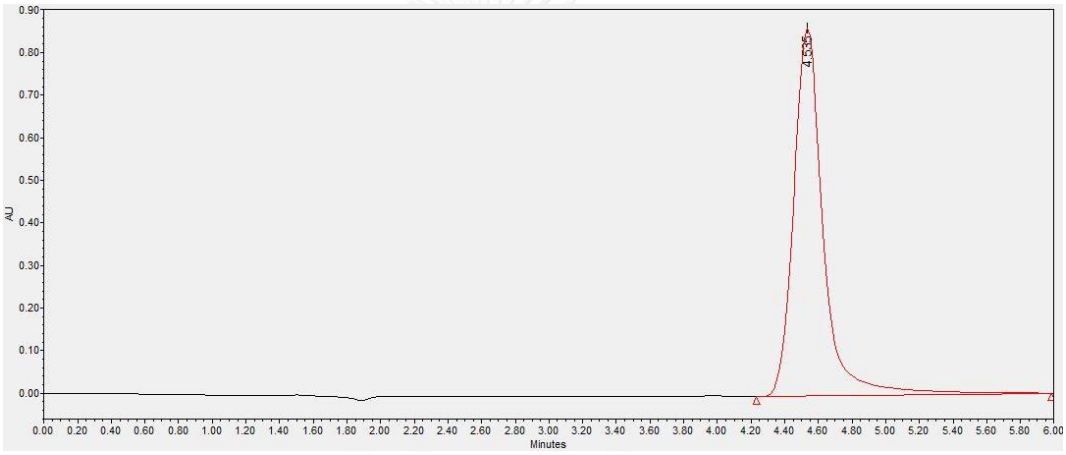


**Figure A. 7** HPLC chromatogram of 0.2 mM of asymmetrical **TAT** in MeCN.

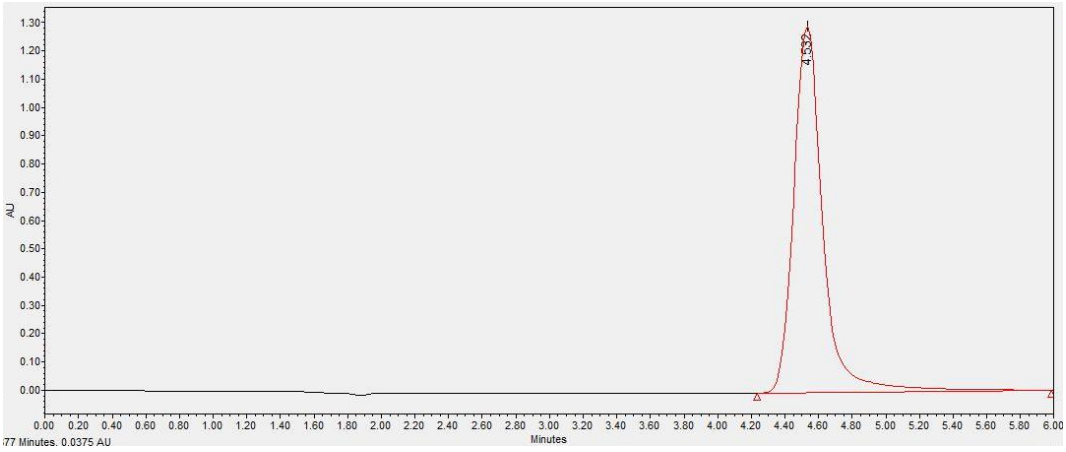


**Figure A. 8** HPLC chromatogram of 0.3 mM of asymmetrical **TAT** in MeCN.

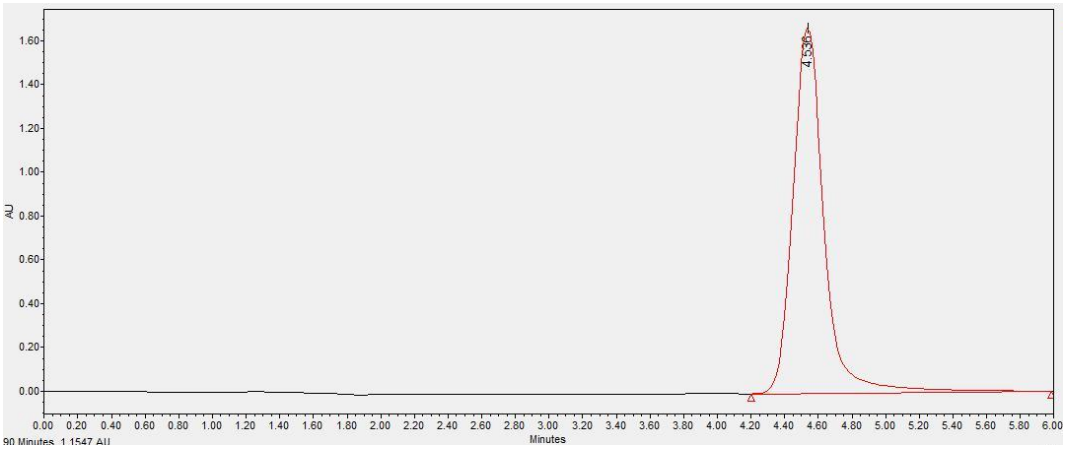


**Figure A. 9** HPLC chromatogram of 0.4 mM of asymmetrical **TAT** in MeCN.

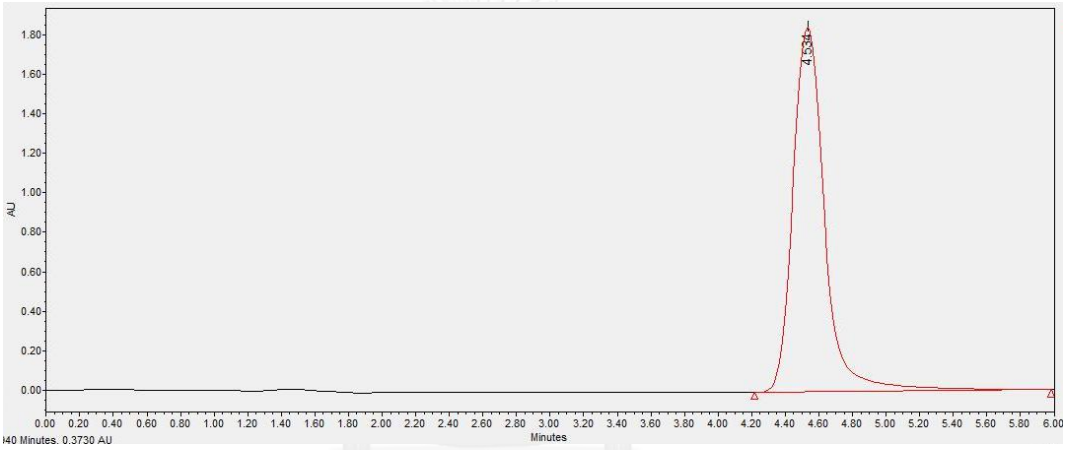


**Figure A. 10** HPLC chromatogram of 0.5 mM of asymmetrical **TAT** in MeCN.

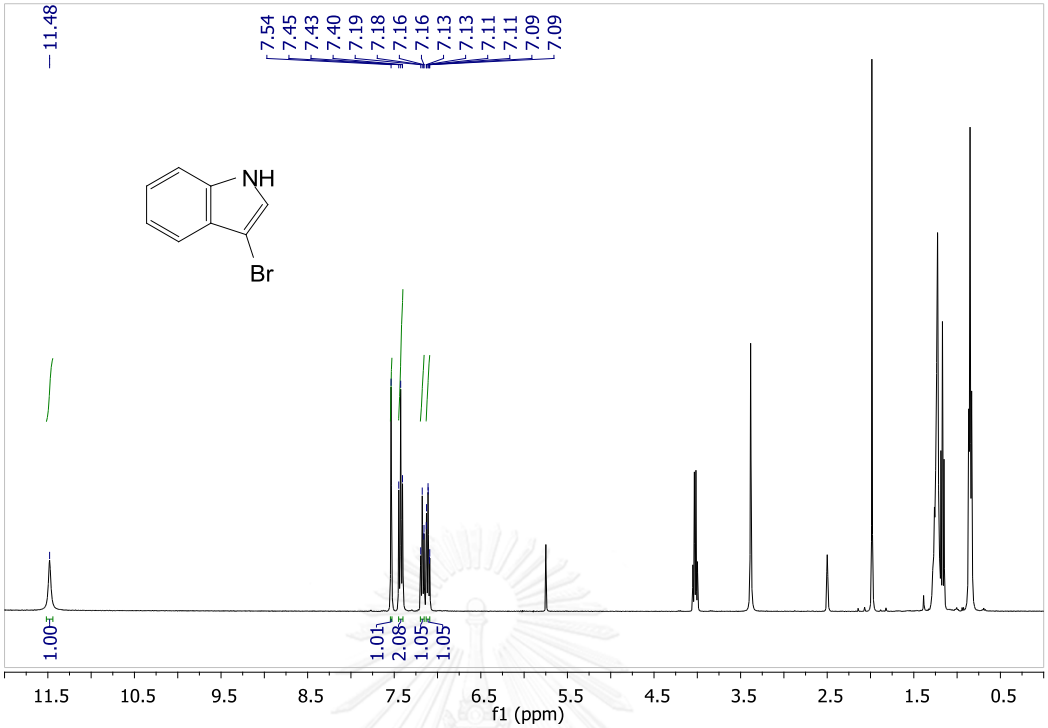


**Figure A. 11** $^{1}$H-NMR of 3-bromo-1*H*-indole (**1h**) in [$d_6$]-acetone.

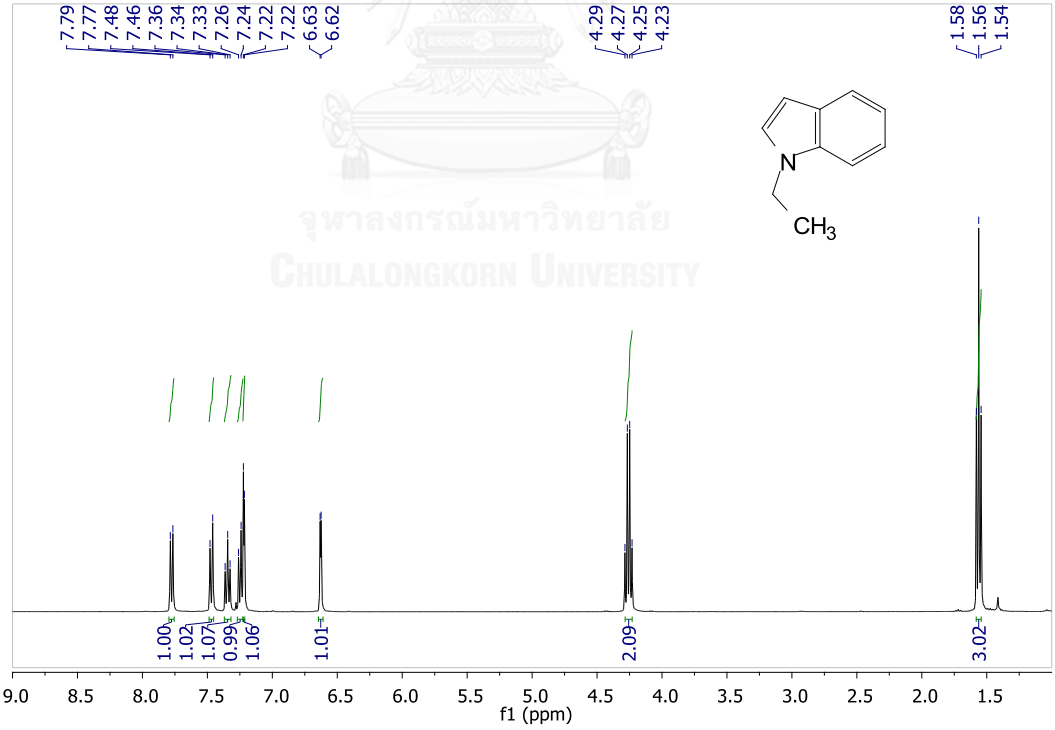


**Figure A. 12** $^{1}$H-NMR of 1-ethyl-1*H*-indole (**1j**) in $CDCl_3$.

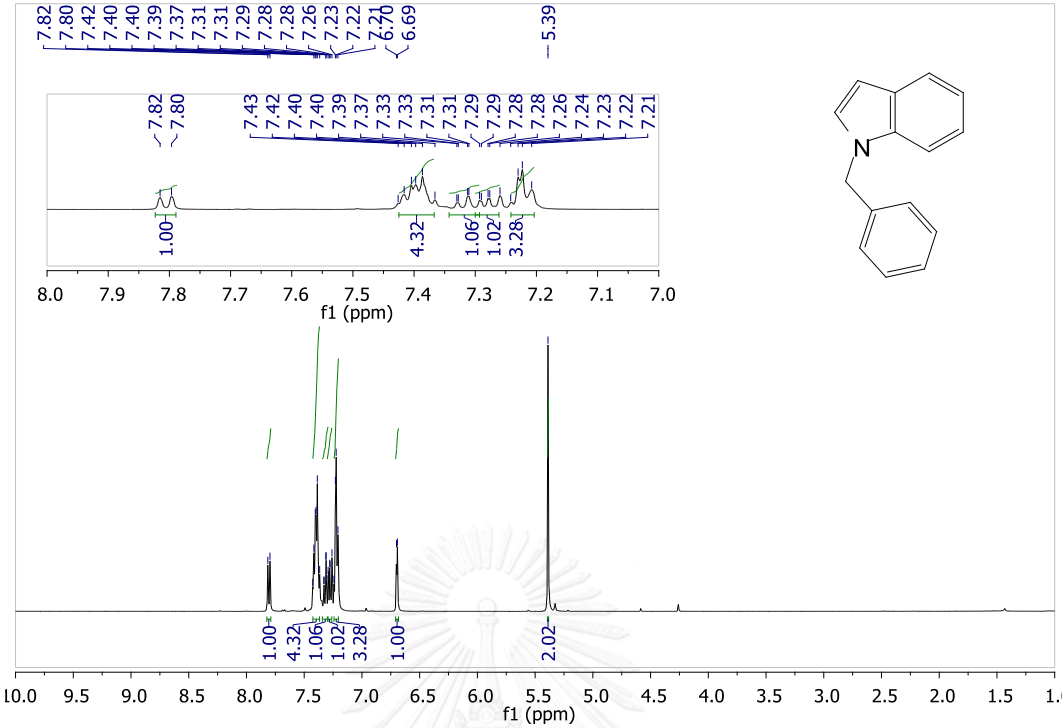


**Figure A. 13** $^{1}$H-NMR of 1-benzyl-1*H*-indole (**1k**) in $CDCl_3$.

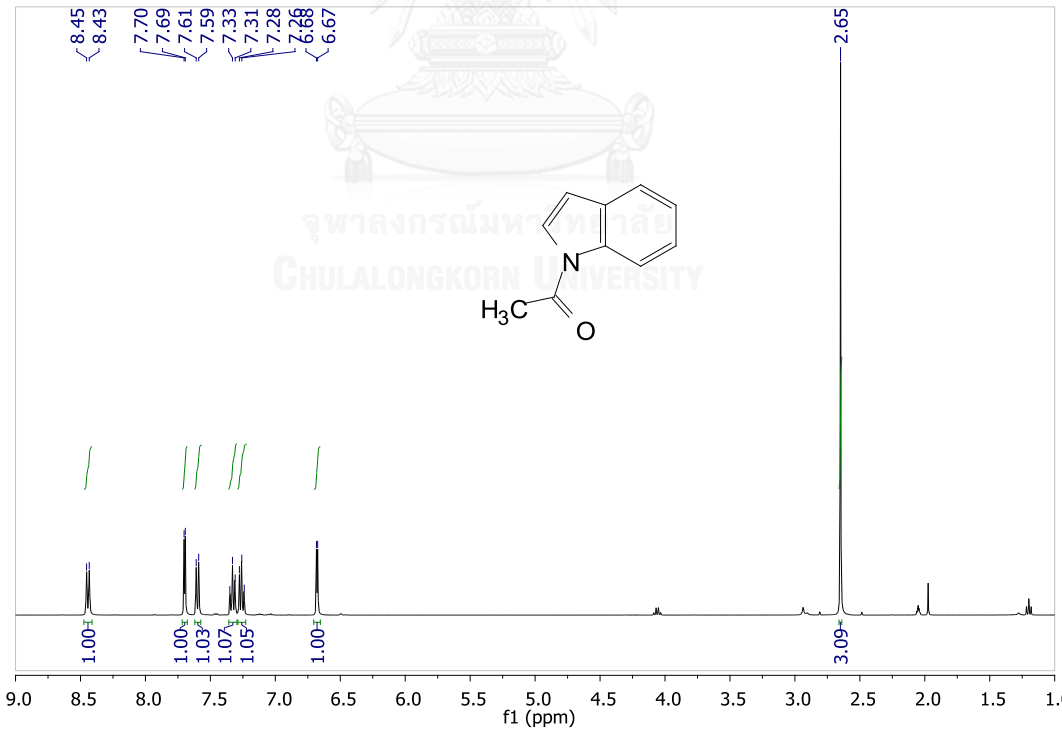


**Figure A. 14** $^{1}$H-NMR of 1-(1*H*-indol-1-yl)ethanone (**1l**) in [$d_6$]-acetone.

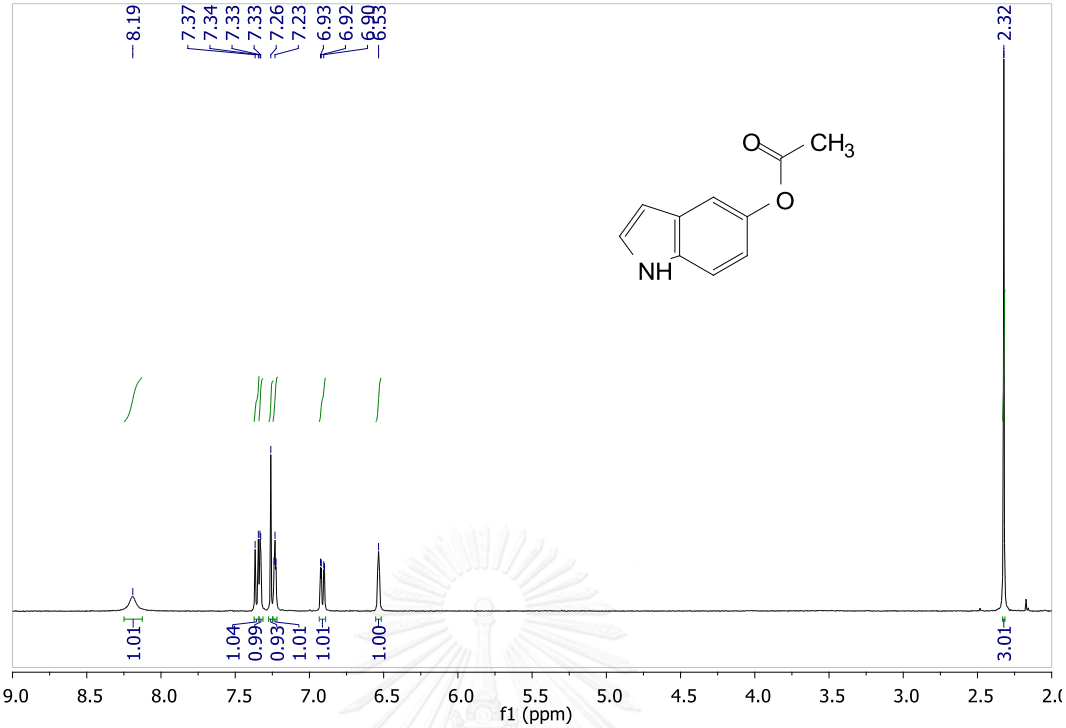


**Figure A. 15** $^{1}$H-NMR of 1*H*-indol-5-yl acetate (**1n**) in $CDCl_3$.

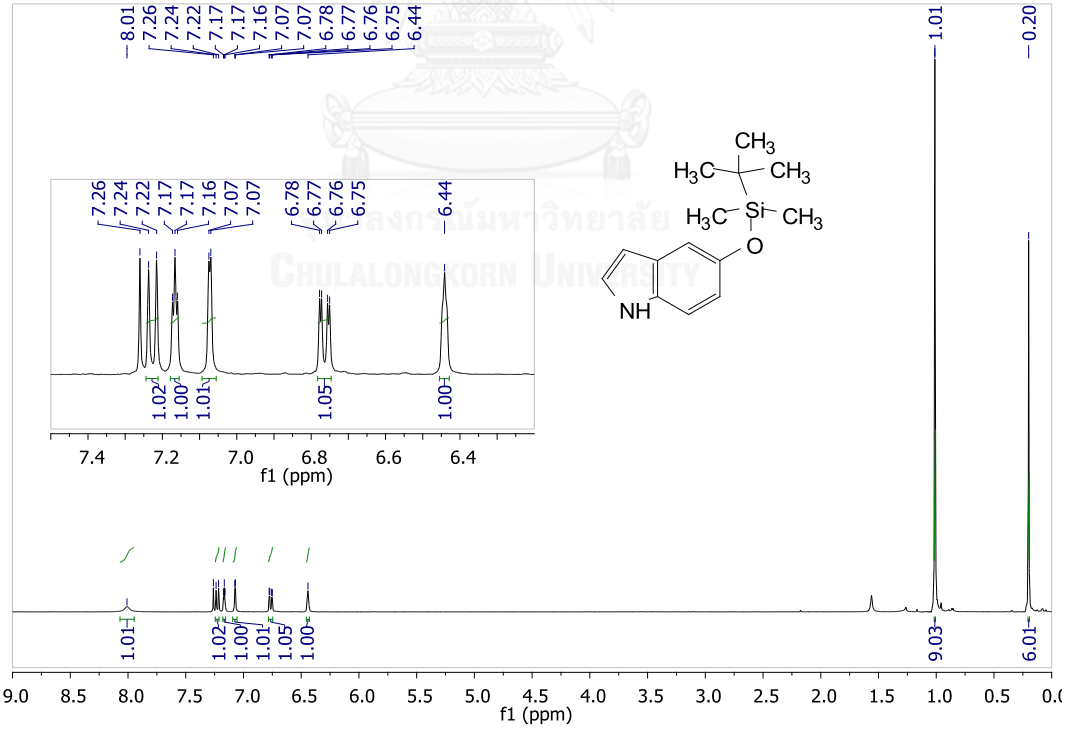


**Figure A. 16** $^{1}$H-NMR of 5-((*tert*-butyldimethylsilyl)oxy)-1*H*-indole (**1o**) in $CDCl_3$.

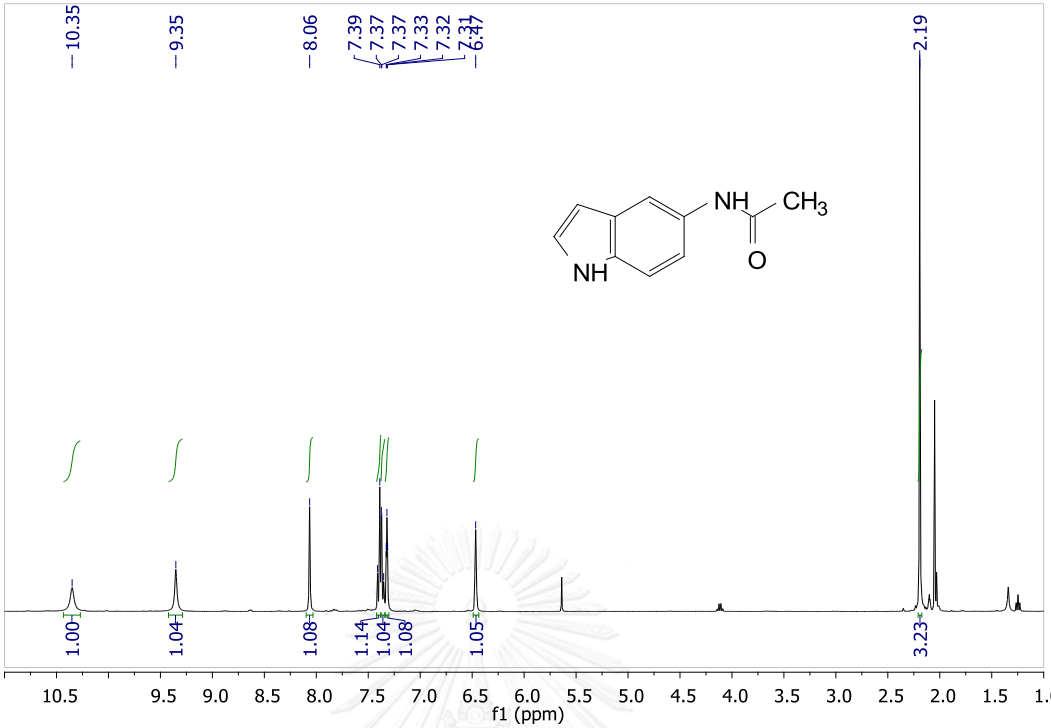


**Figure A. 17** $^{1}$H-NMR of N-(1*H*-indol-5-yl)acetamide (**1q**) in [$d_6$]-acetone.

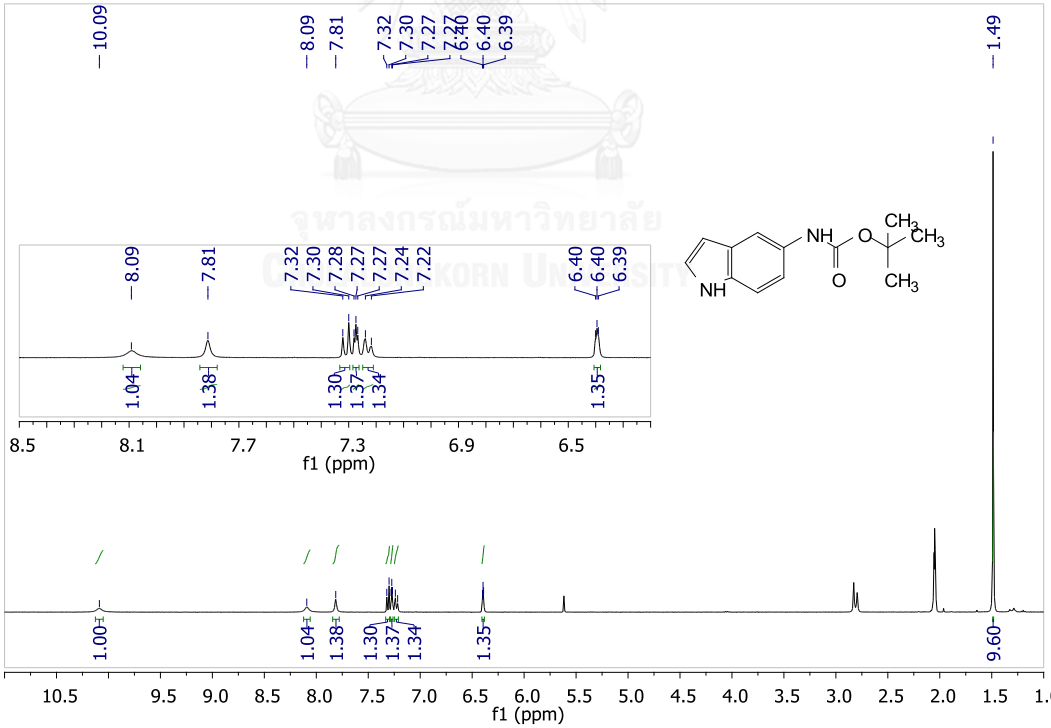


**Figure A. 18** $^{1}$H-NMR of *tert*-butyl 1*H*-indol-5-ylcarbamate (**1r**) in [$d_6$]-acetone.

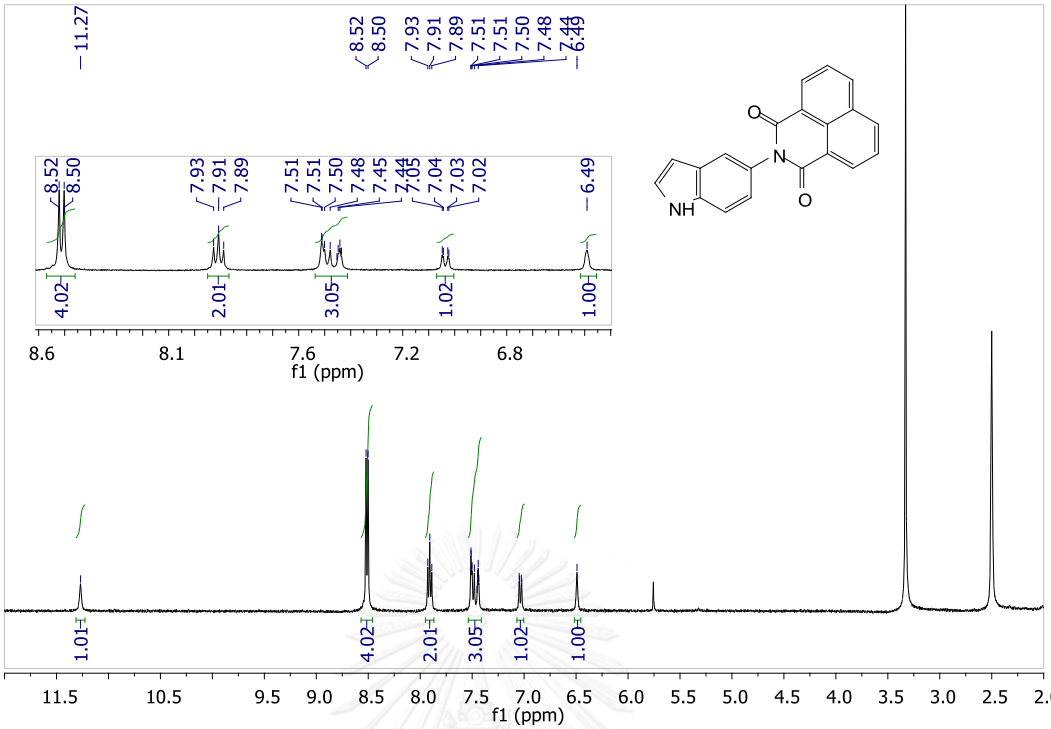


**Figure A. 19** $^{1}$H-NMR of 2-(1*H*-indol-5-yl)-1*H*-benzo[d,e]isoquinoline-1,3(2*H*)-dione (**1s**) in [$d_6$]-DMSO.

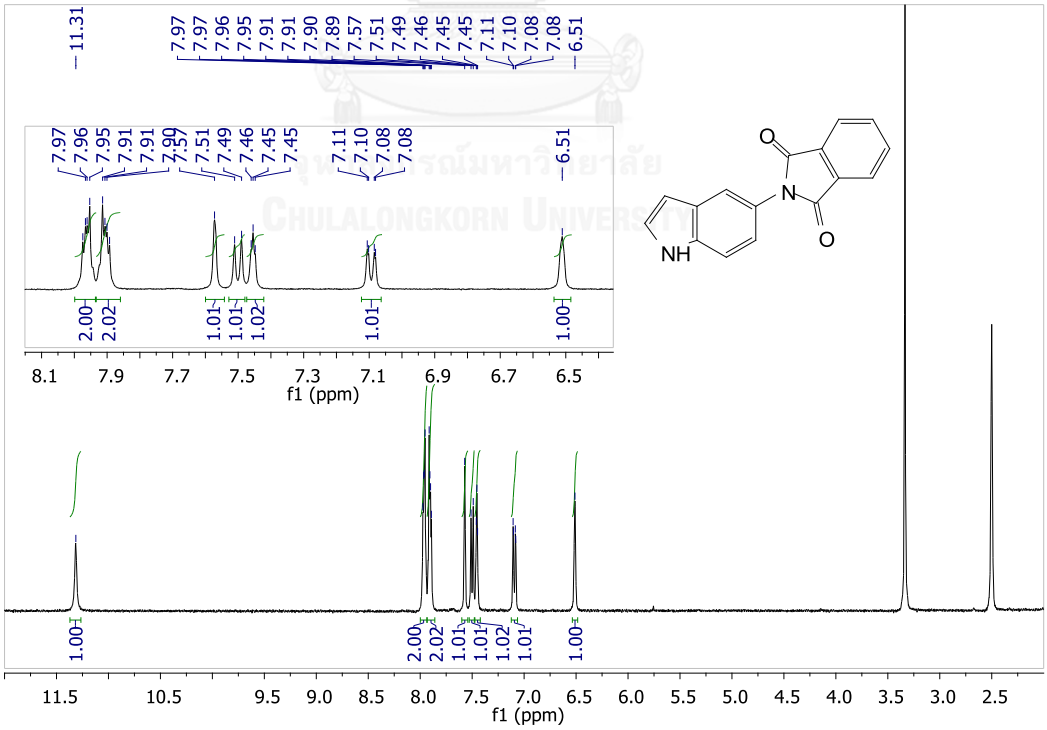


**Figure A. 20** $^{1}$H-NMR of 2-(1*H*-indol-5-yl)isoindoline-1,3-dione (**1t**) in [$d_6$]-DMSO.

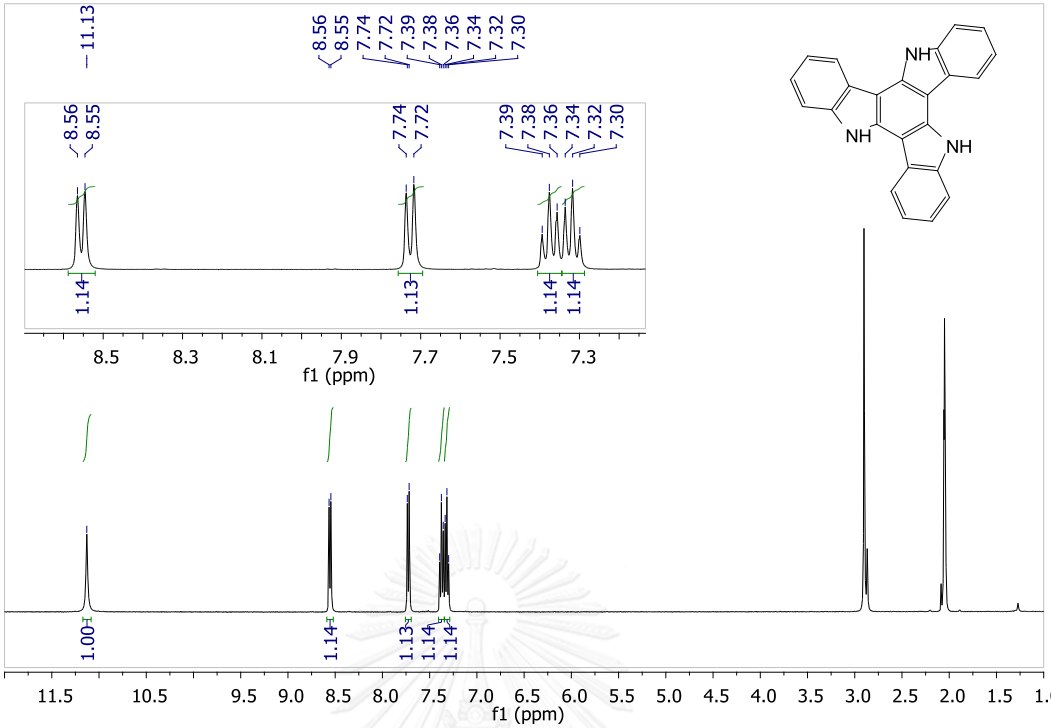


**Figure A. 21** $^{1}$H-NMR of 10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2**) in [$d_6$]-acetone.

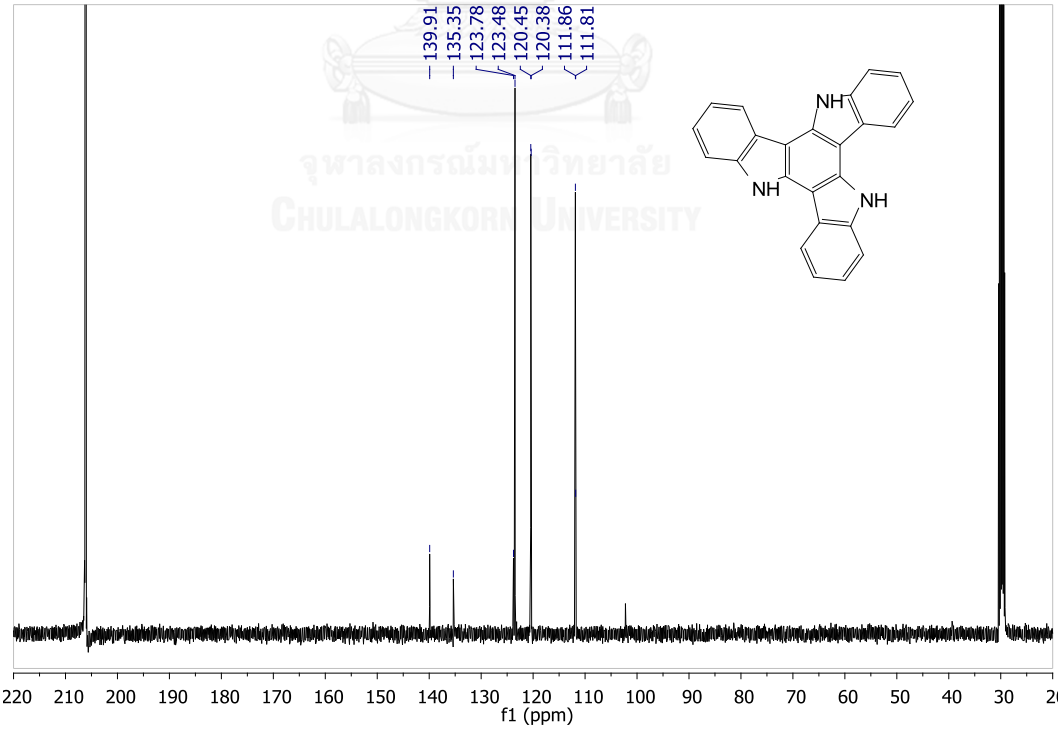


**Figure A. 22** $^{13}$C-NMR of 10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2**) in [$d_6$]-acetone.

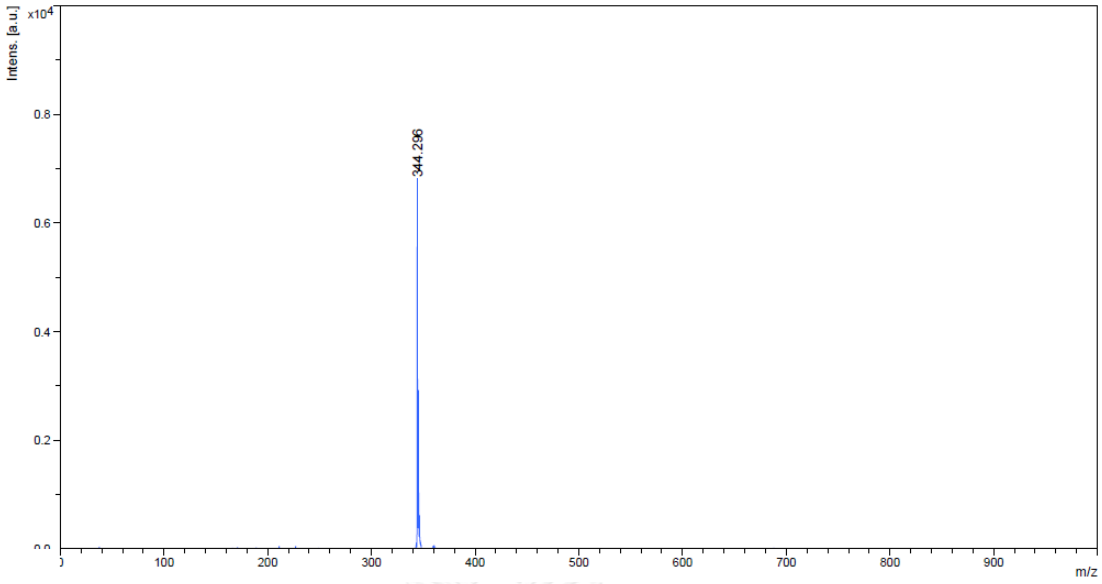


**Figure A. 23** MALDI-TOF mass spectrum of 10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2**).

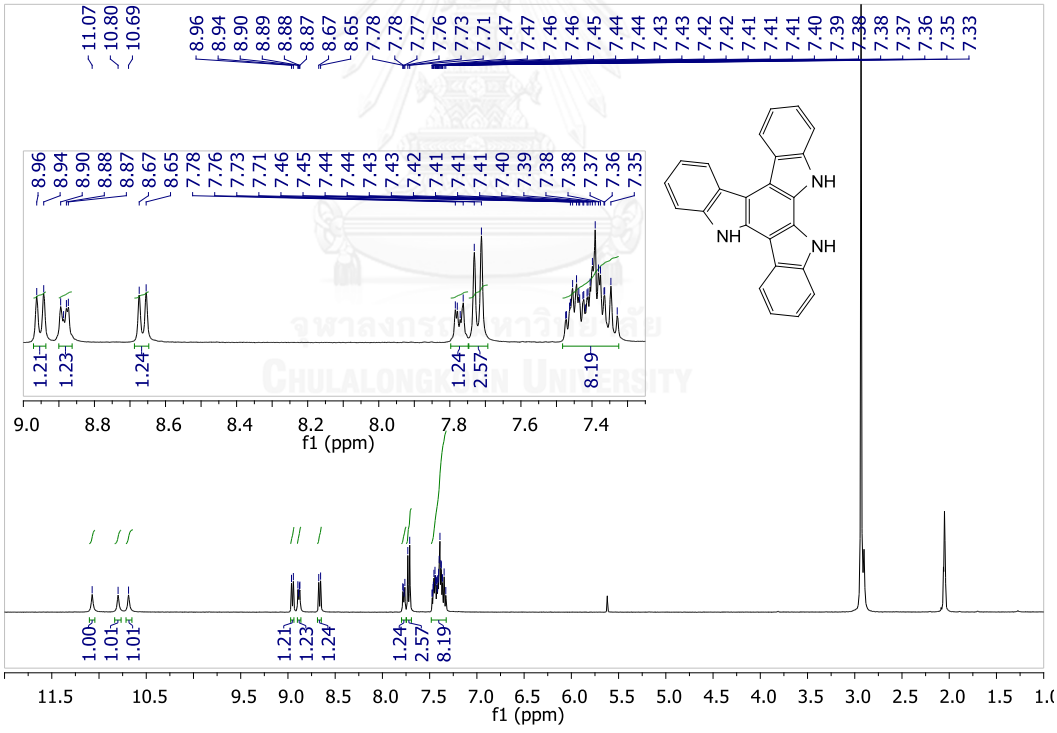


**Figure A. 24** $^{1}$H-NMR of 6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3**) in [$d_6$]-acetone.

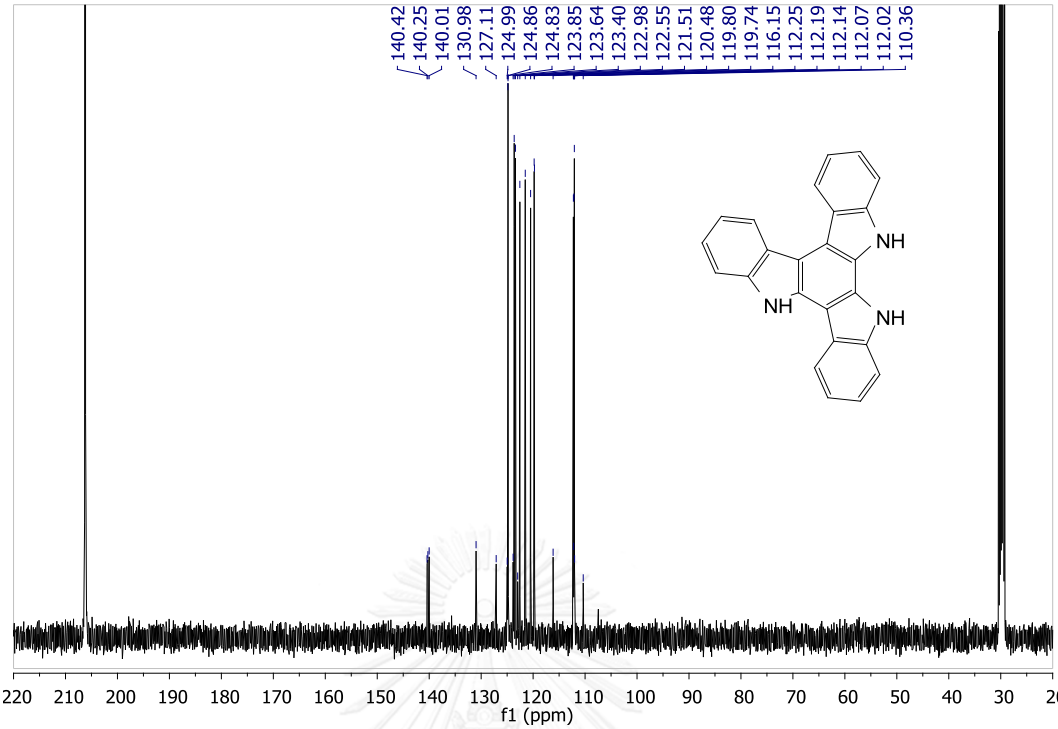


**Figure A. 25** $^{13}$C-NMR of 6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3**) in [$d_6$]-acetone.

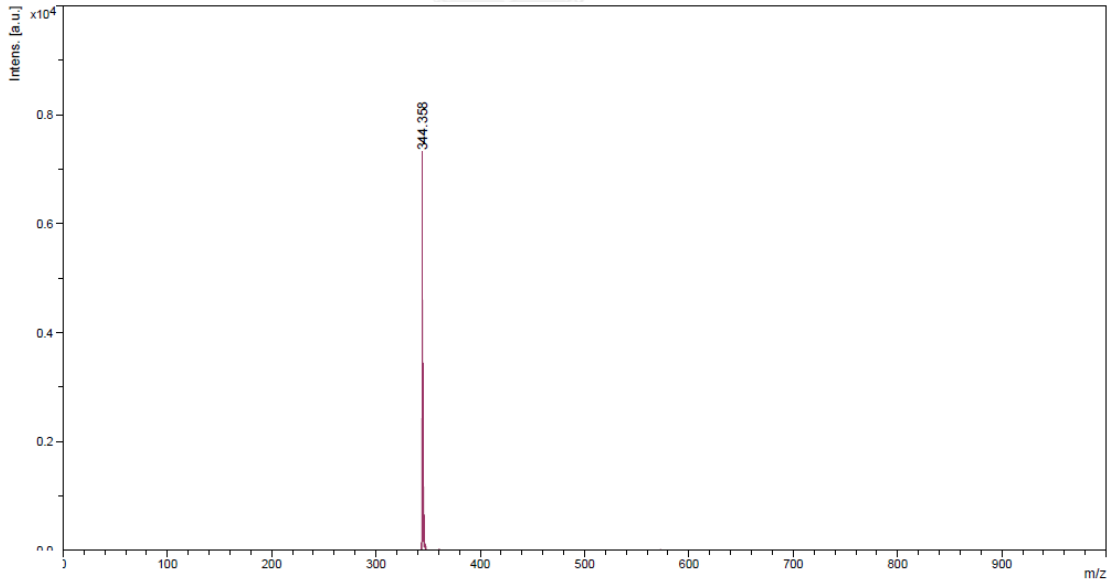


**Figure A. 26** MALDI-TOF mass spectrum of 6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3**).

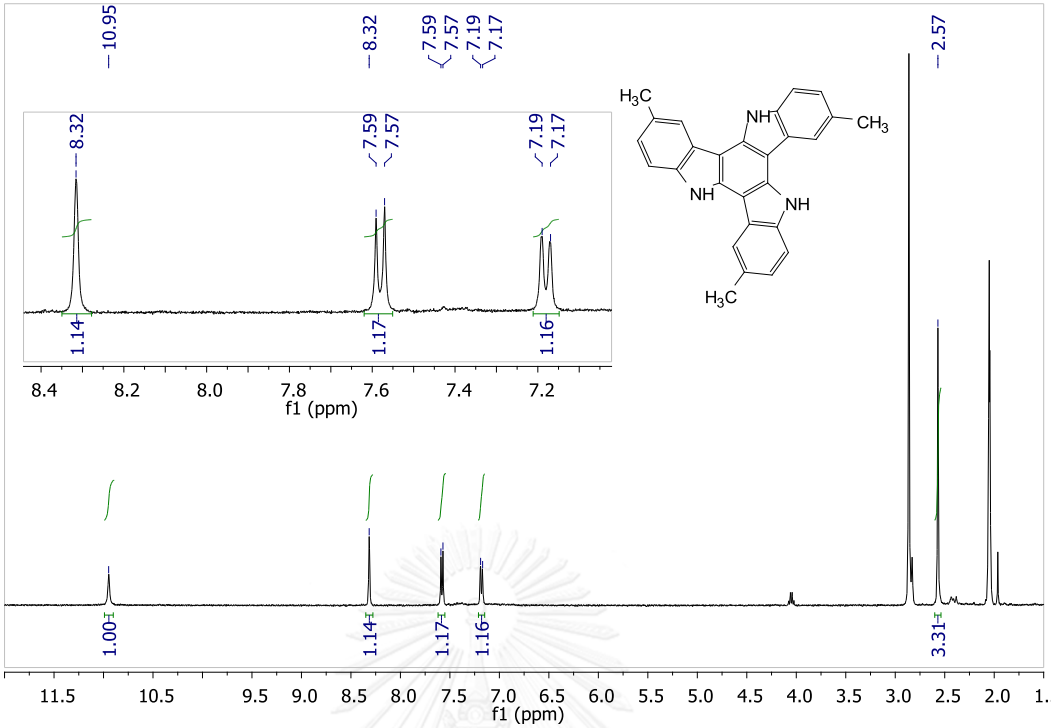


**Figure A. 27** $^{1}$H-NMR of 3,8,13-trimethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2a**) in [$d_6$]-acetone.

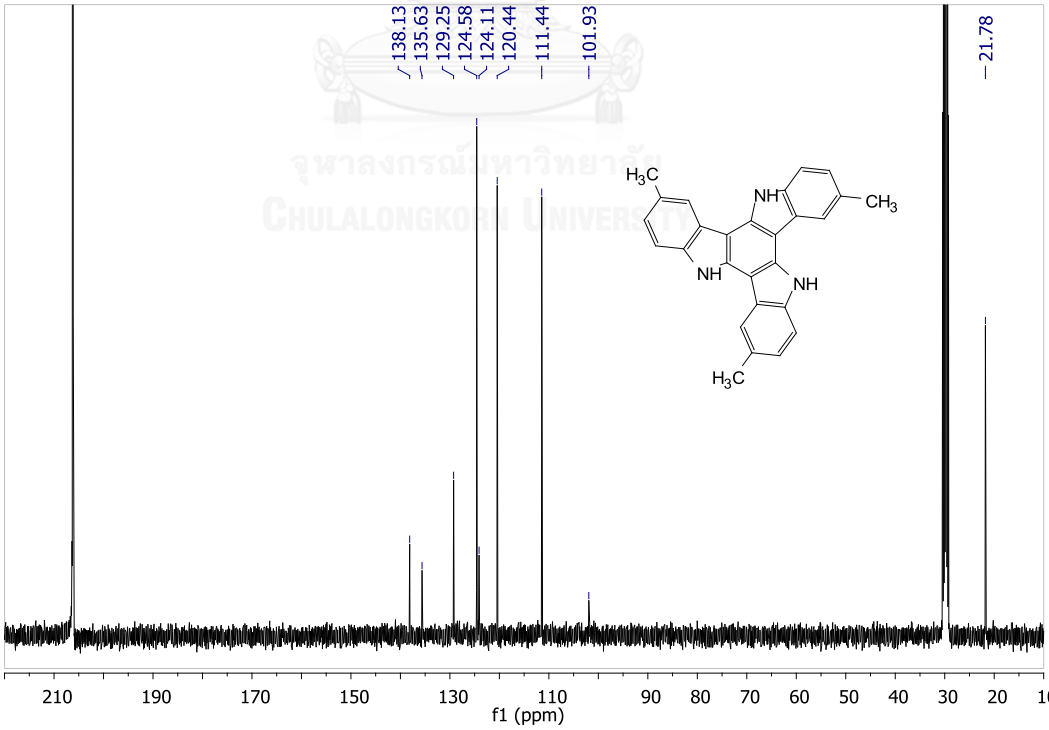


**Figure A. 28** $^{13}$C-NMR of 3,8,13-trimethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2a**) in [$d_6$]-acetone.

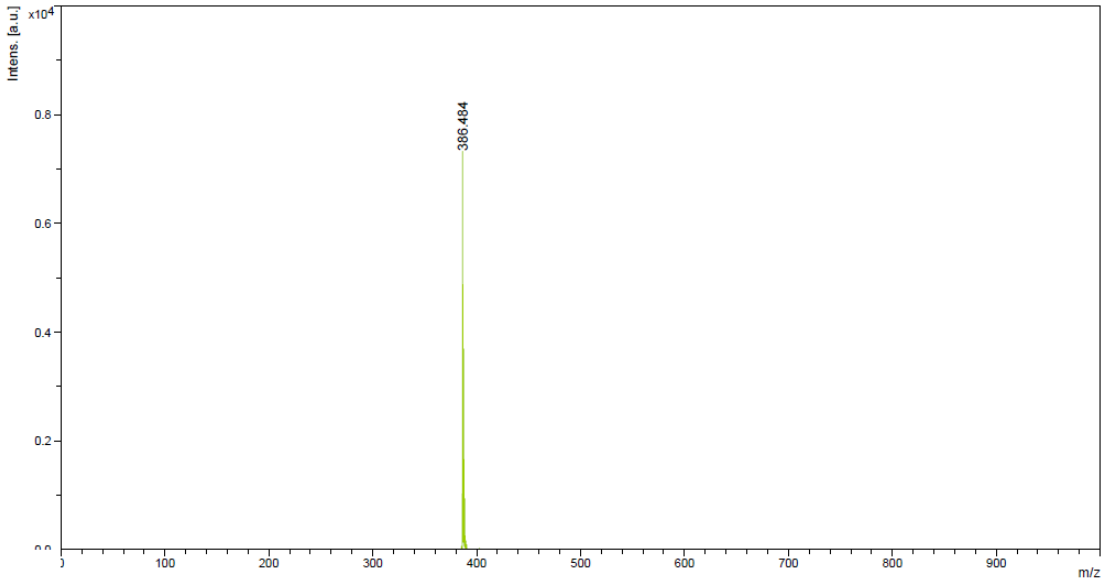


**Figure A. 29** MALDI-TOF mass spectrum of 3,8,13-trimethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2a**).

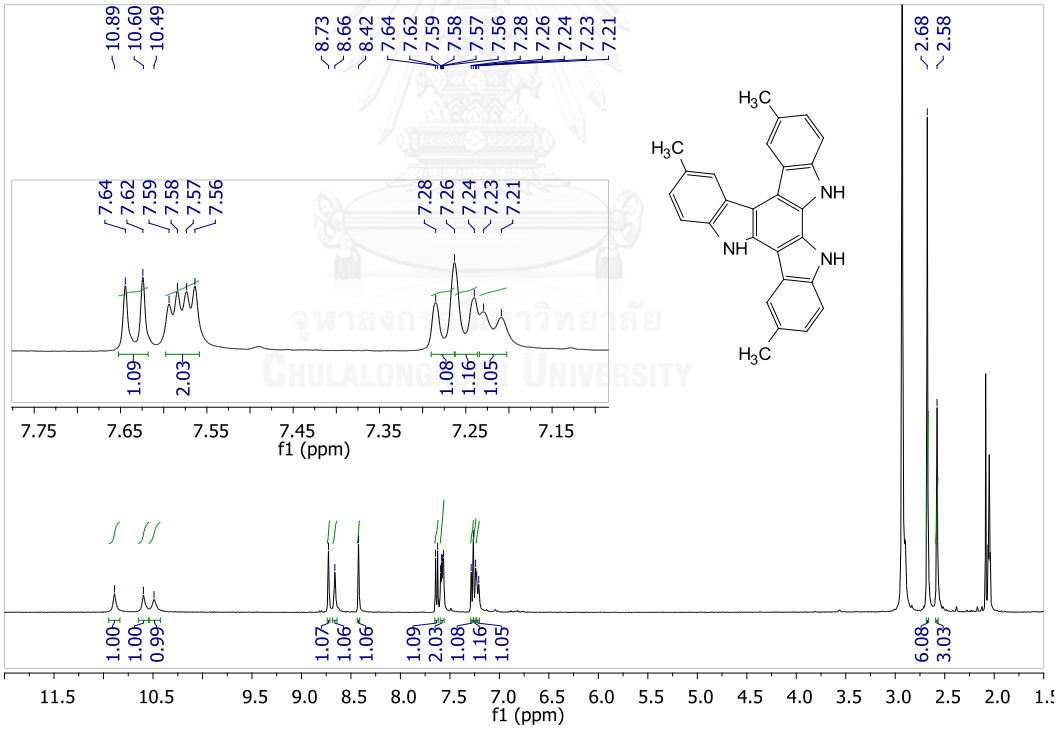


**Figure A. 30** $^{1}$H-NMR of 2,9,14-trimethyl-6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3a**) in [$d_6$]-acetone.

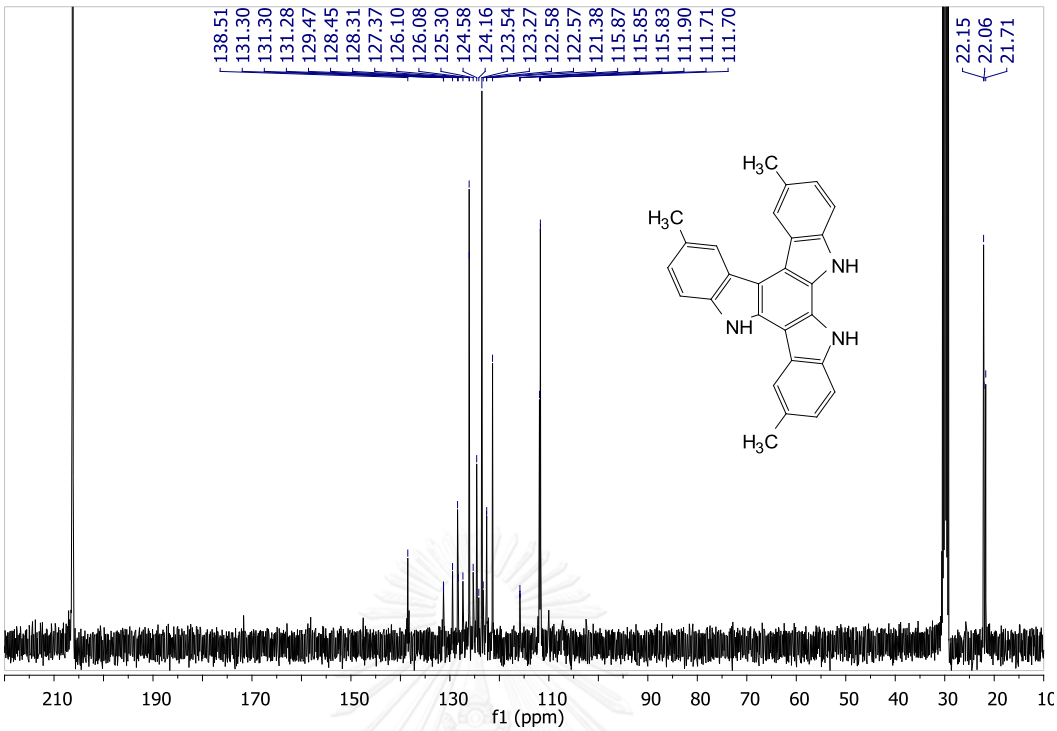


**Figure A. 31** $^{13}$C-NMR of 2,9,14-trimethyl-6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3a**) in [$d_6$]-acetone.

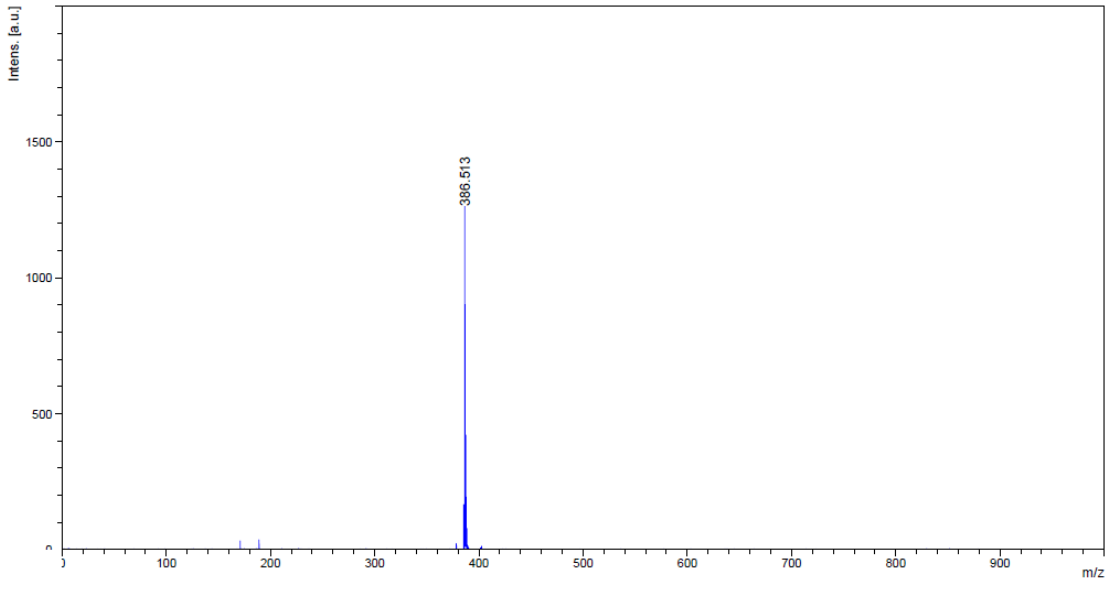


**Figure A. 32** MALDI-TOF mass spectrum of 2,9,14-trimethyl-6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3a**).

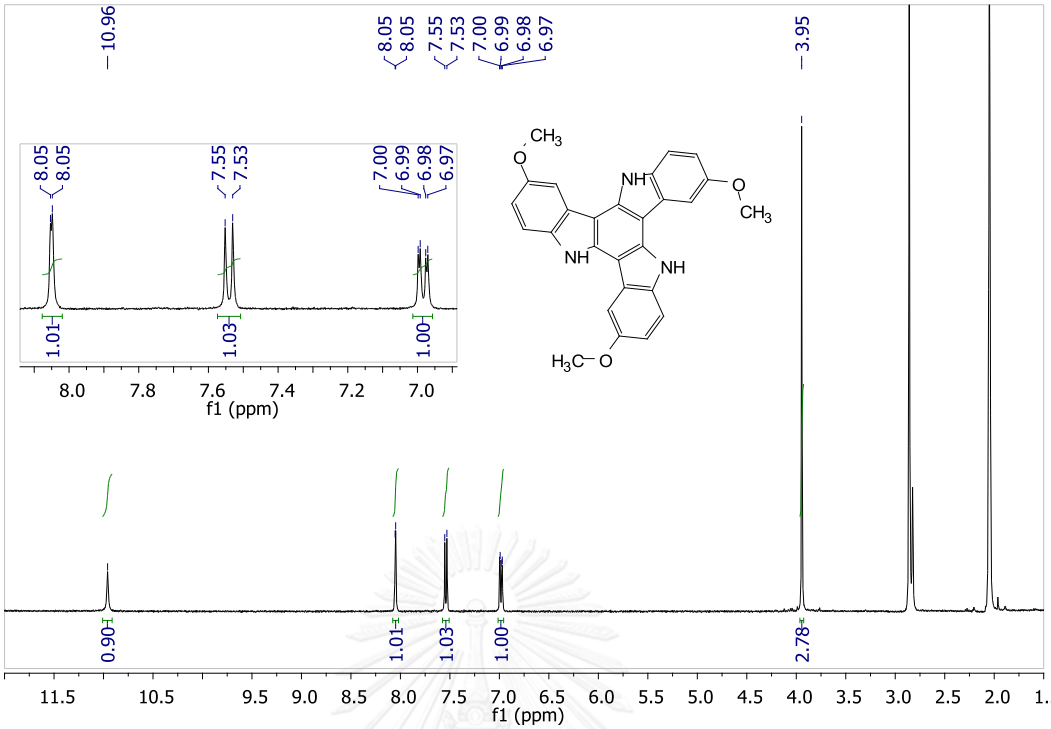


**Figure A. 33** $^{1}$H-NMR of 3,8,13-trimethoxy-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2b**) in [$d_6$]-acetone.

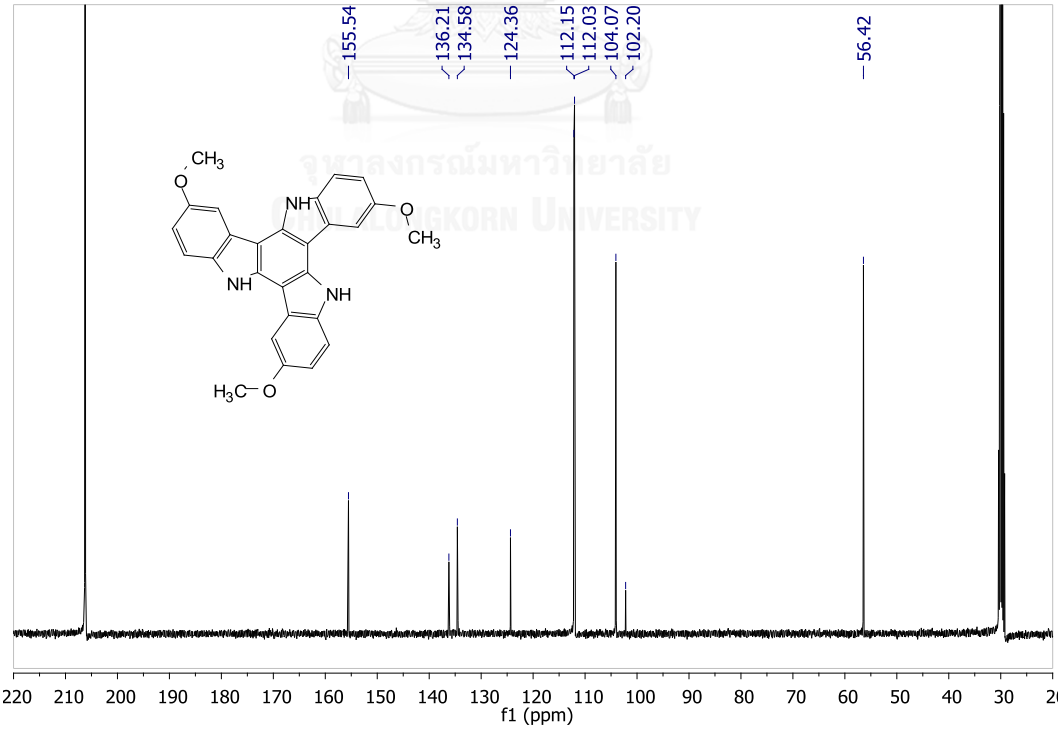


**Figure A. 34** $^{13}$C-NMR of 3,8,13-trimethoxy-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2b**) in [$d_6$]-acetone.

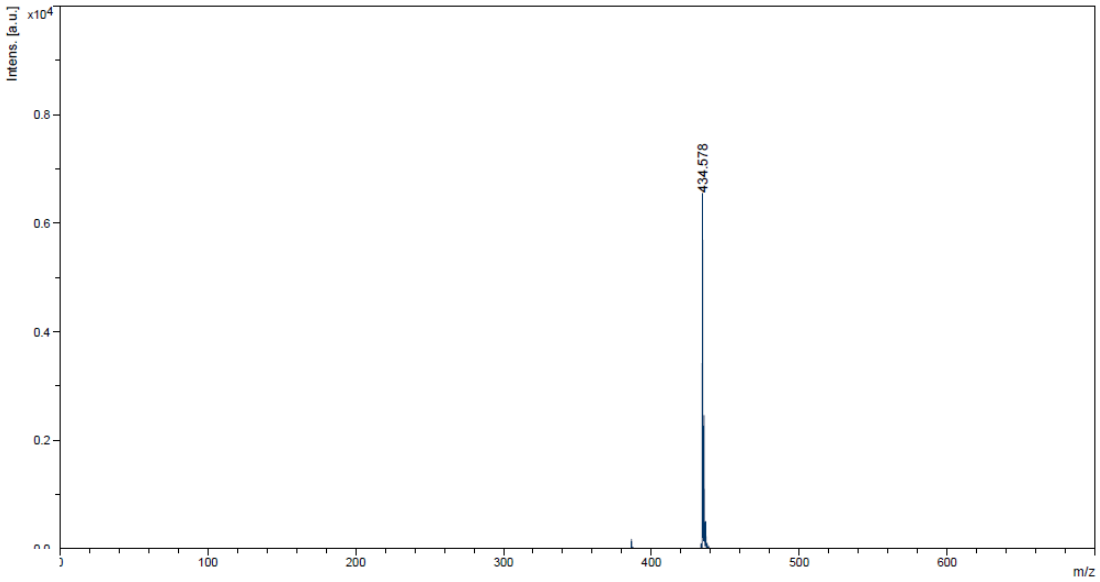


**Figure A. 35** MALDI-TOF mass spectrum of 3,8,13-trimethoxy-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2b**).

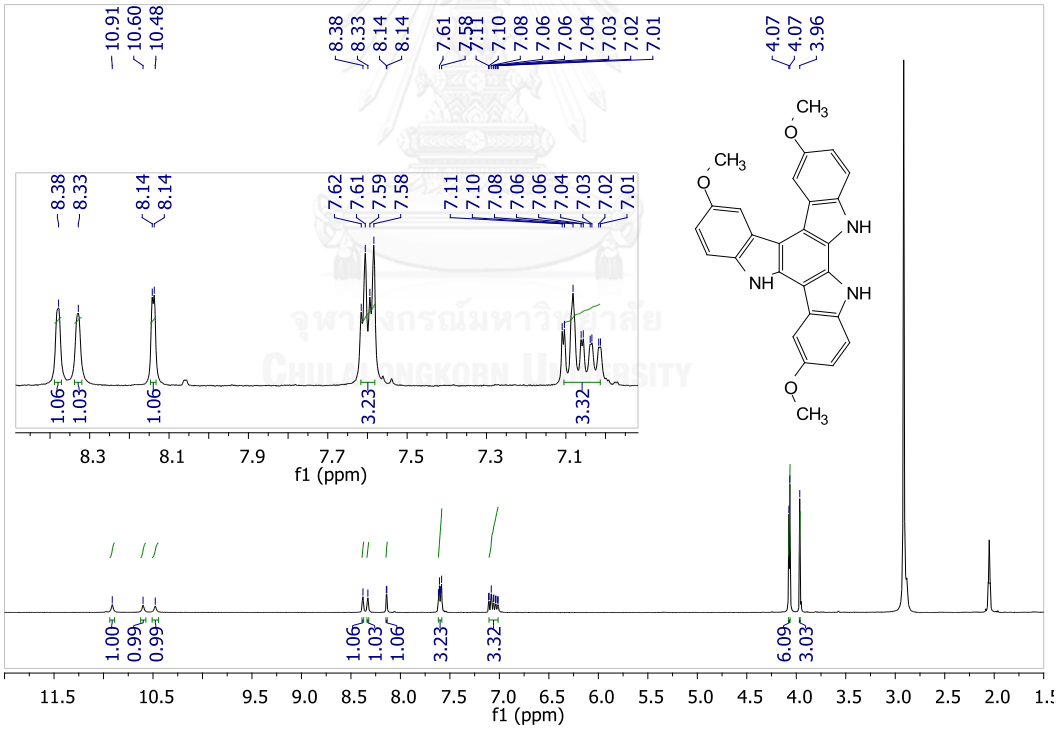


**Figure A. 36** $^{1}$H-NMR of 2,9,14-trimethoxy-6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3b**) in [$d_6$]-acetone.

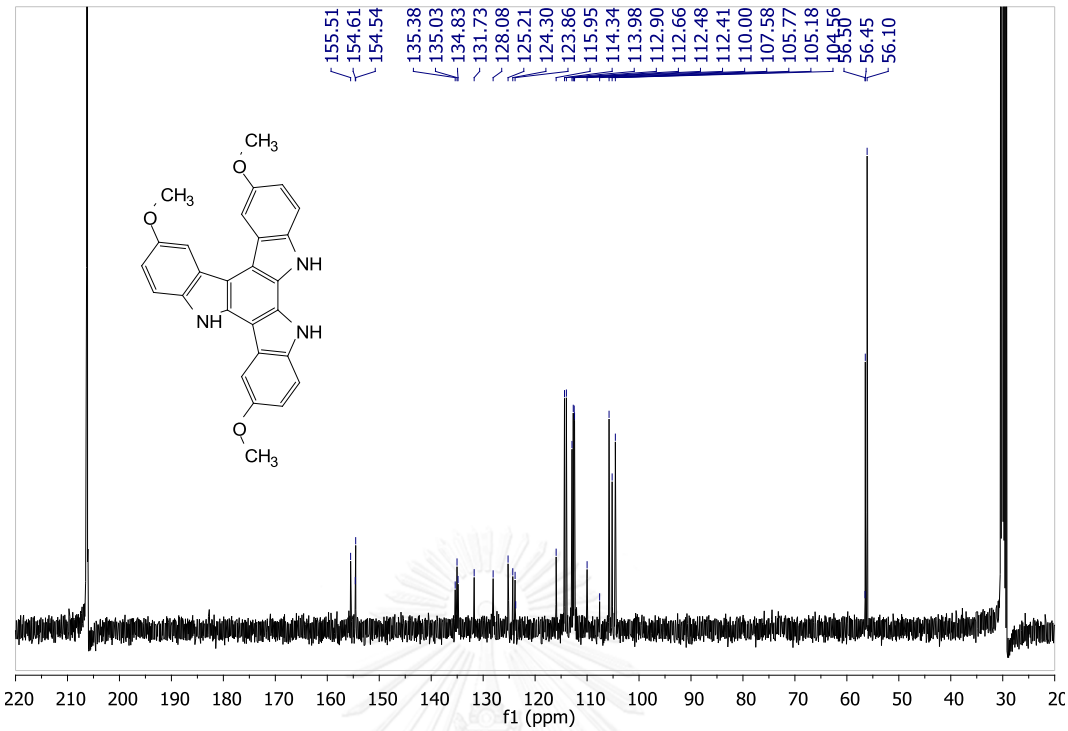


**Figure A. 37** $^{13}$C-NMR of 2,9,14-trimethoxy-6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3b**) in [$d_6$]-acetone.

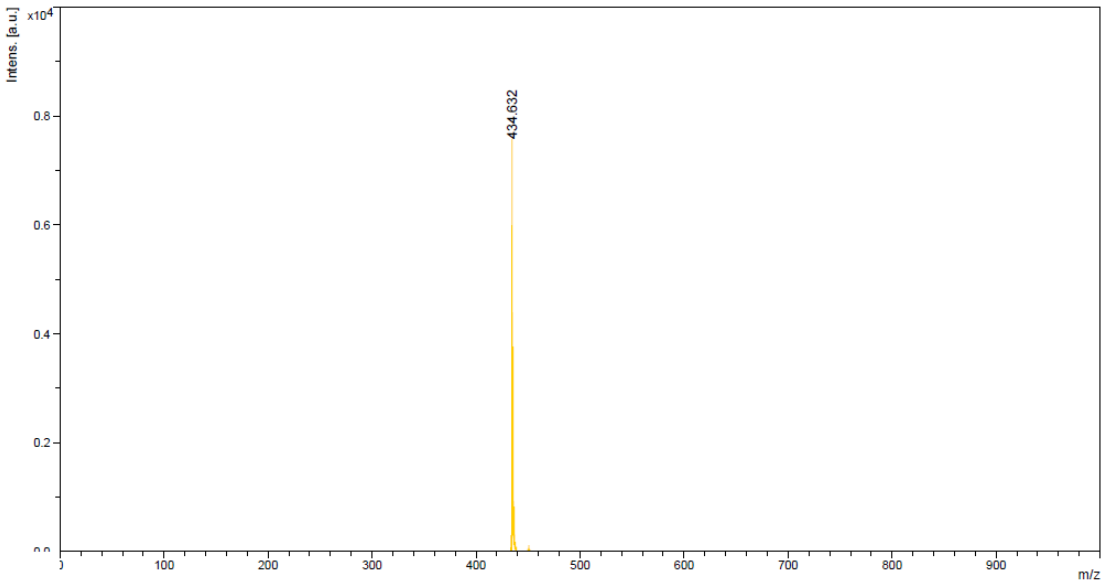


**Figure A. 38** MALDI-TOF mass spectrum of 2,9,14-trimethoxy-6,11-dihydro-5*H*-diindolo[2,3-a:2',3'-c]carbazole (**3b**).

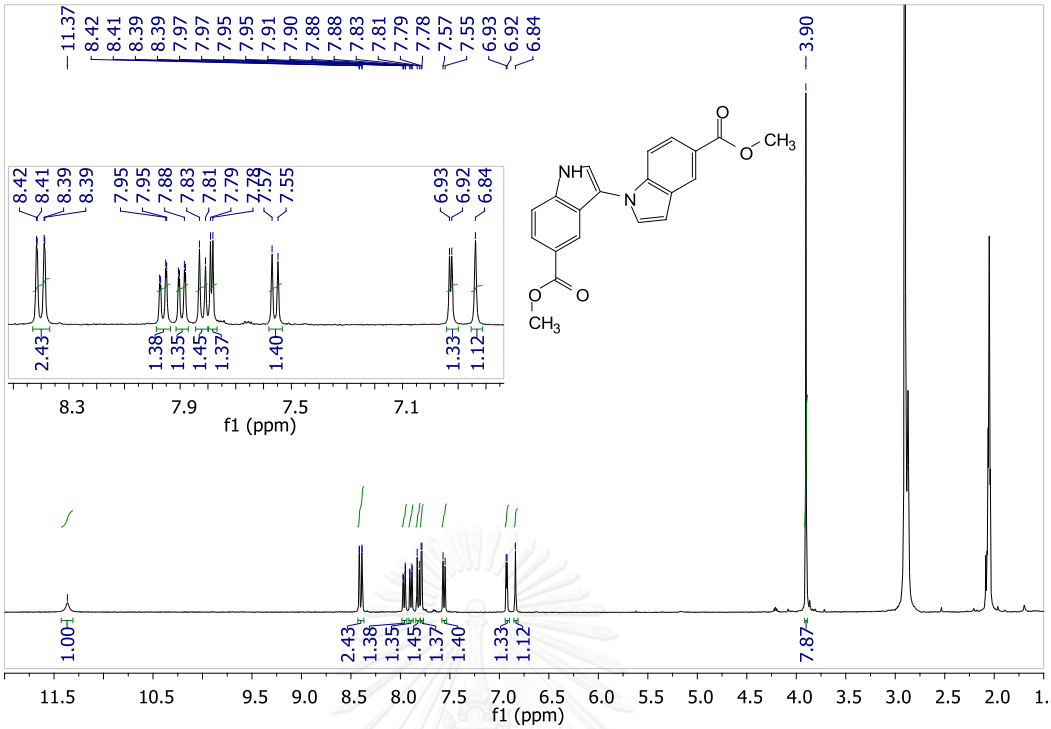


**Figure A. 39** [1]H-NMR of dimethyl 1'*H*-[1,3'-biindole]-5,5'-dicarboxylate (**2e**) in [$d_6$]-acetone.

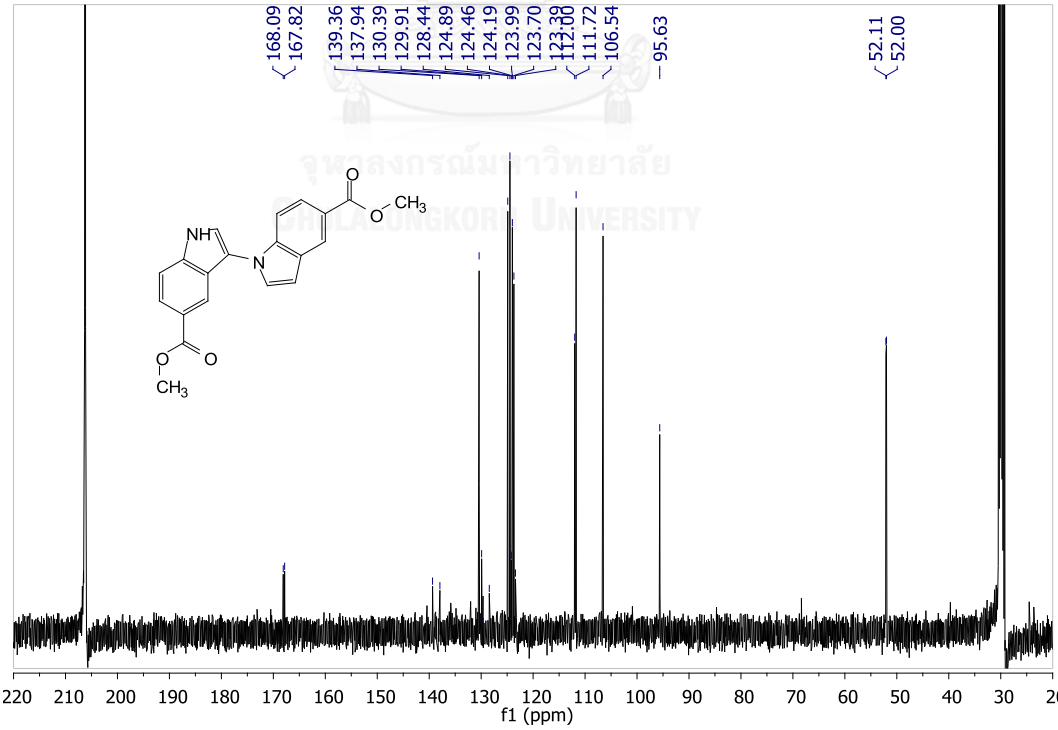


**Figure A. 40** [13]C-NMR of dimethyl 1'*H*-[1,3'-biindole]-5,5'-dicarboxylate (**2e**) in [$d_6$]-acetone.

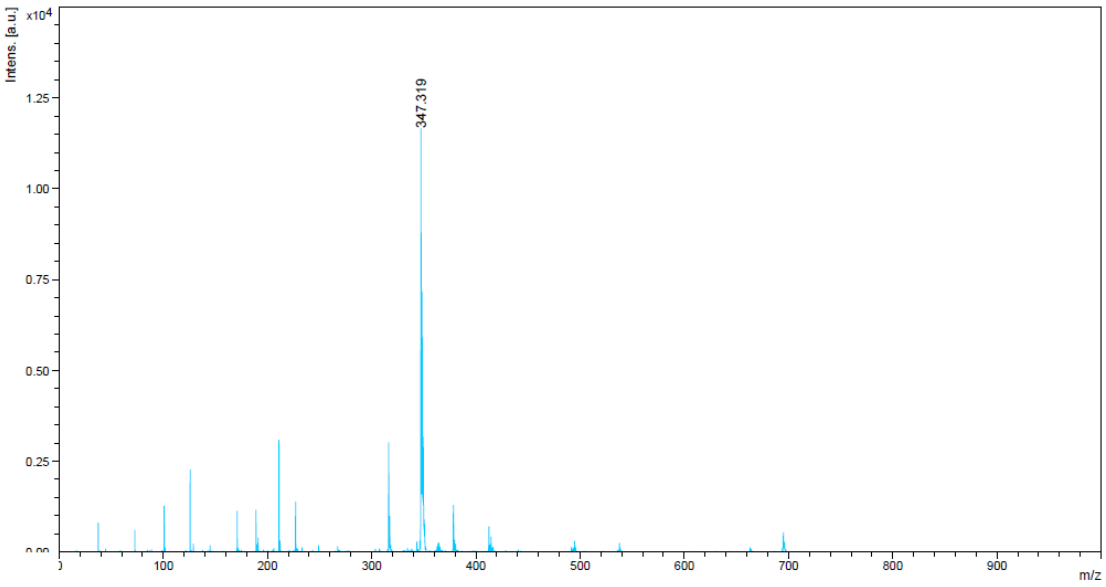


**Figure A. 41** MALDI-TOF mass spectrum of dimethyl 1'*H*-[1,3'-biindole]-5,5'-dicarboxylate (**2e**).

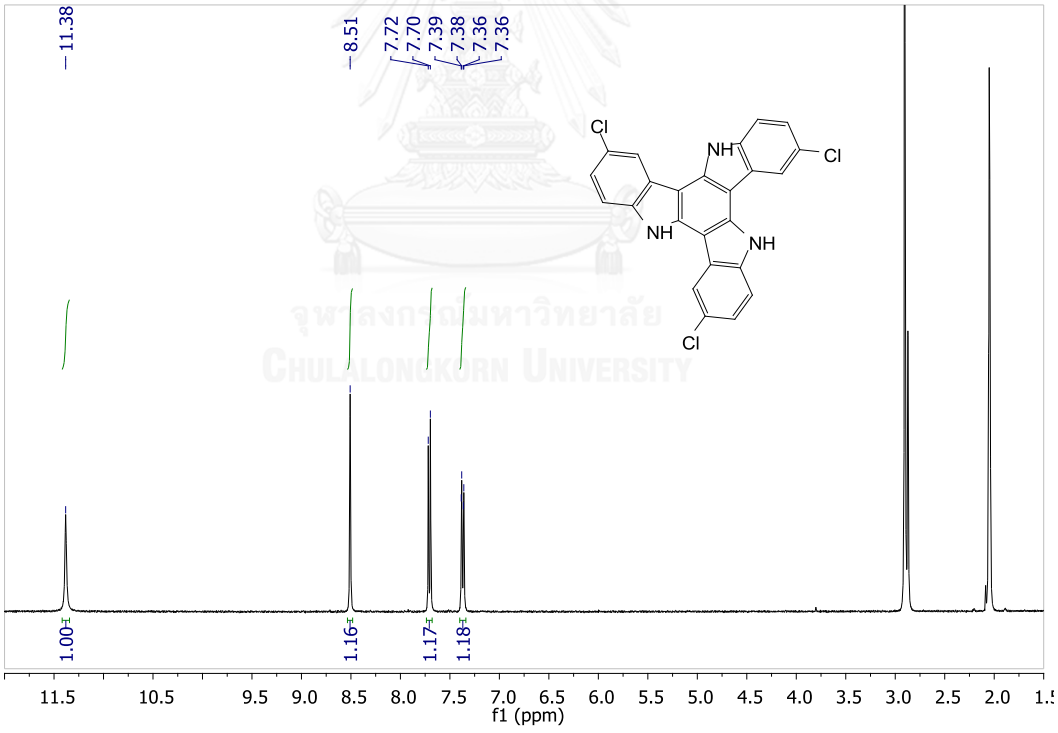


**Figure A. 42** $^{1}$H-NMR of 3,8,13-trichloro-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2f**) in [$d_6$]-acetone.

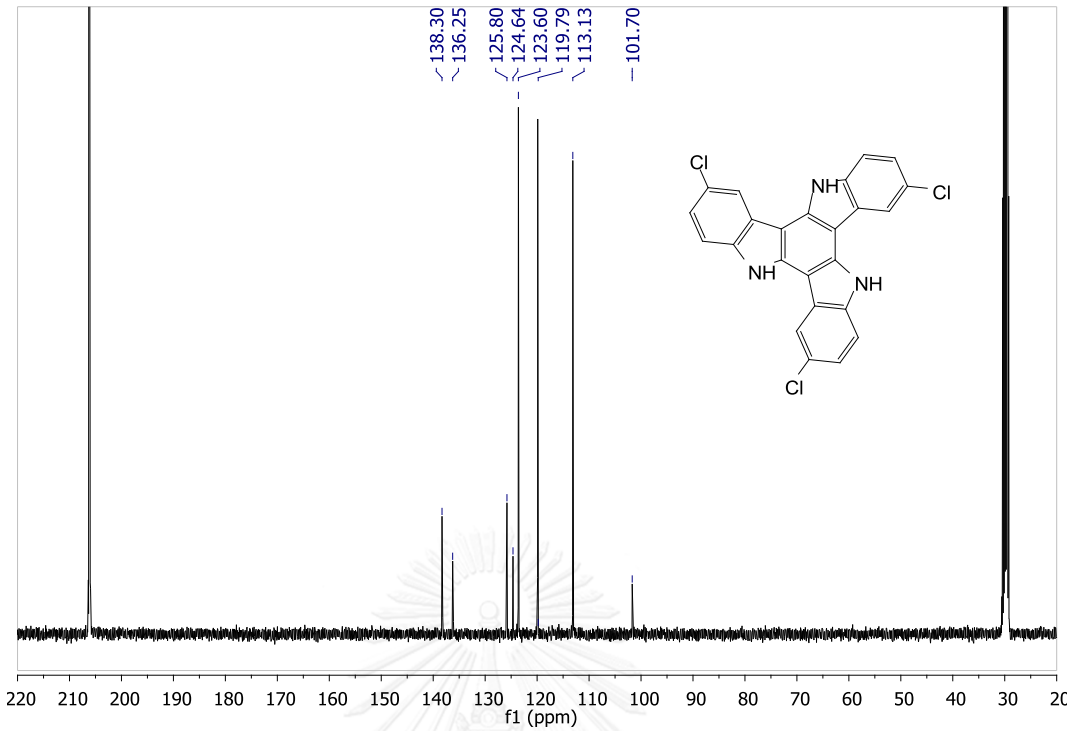


**Figure A. 43** $^{13}$C-NMR of 3,8,13-trichloro-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2f**) in [$d_6$]-acetone.

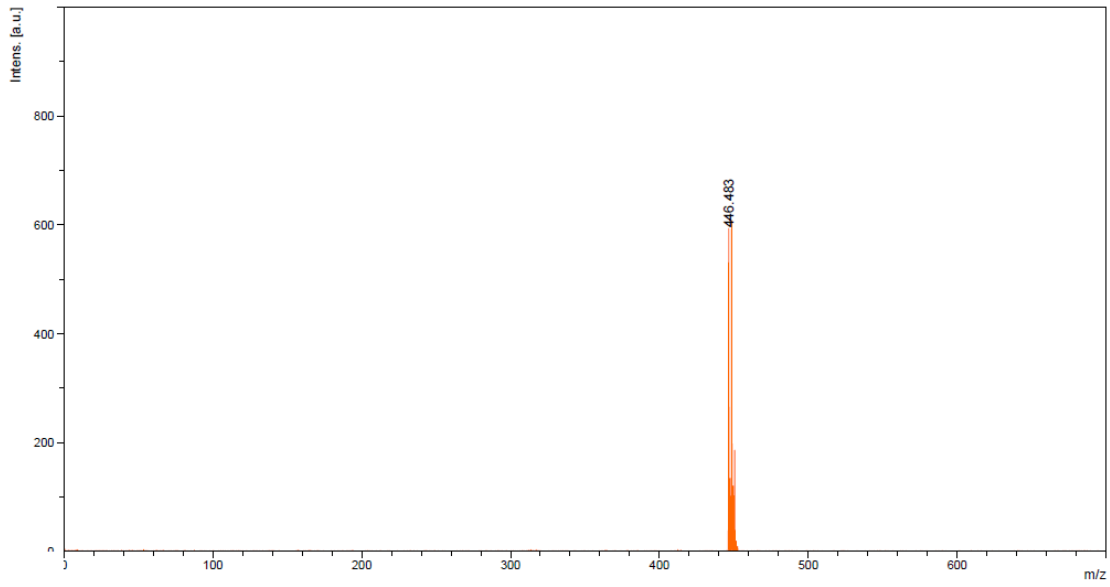


**Figure A. 44** MALDI-TOF mass spectrum of 3,8,13-trichloro-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2f**).

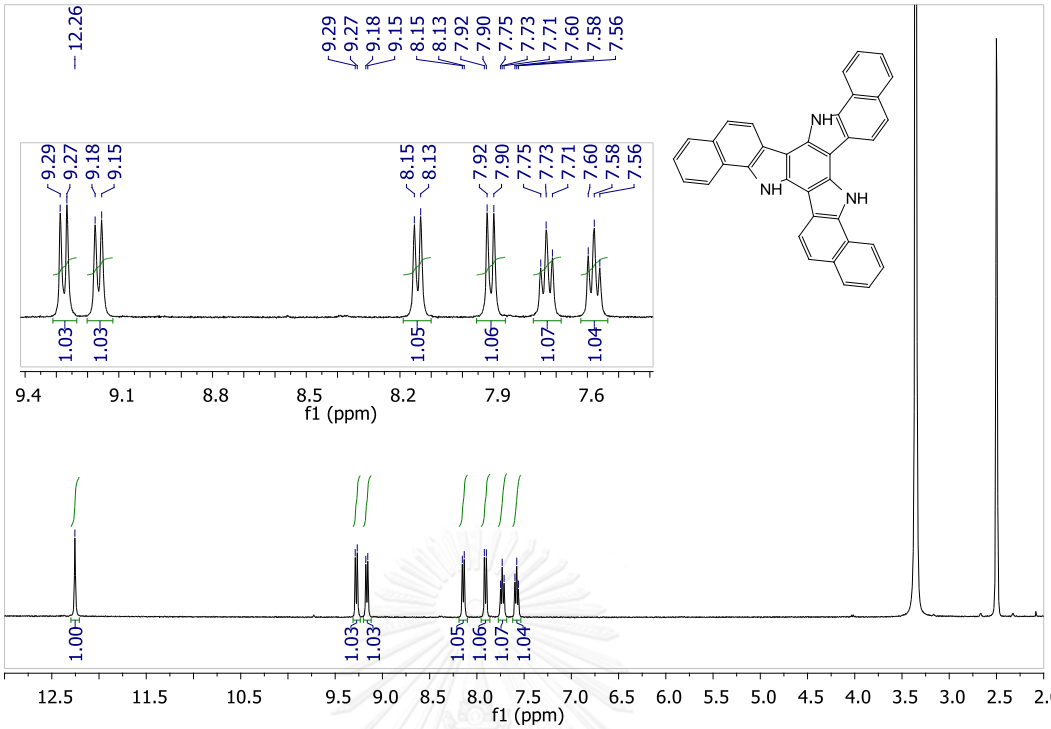


**Figure A. 45** $^{1}$H-NMR of 12,19-dihydro-5*H*-benzo[i]benzo[6,7]indolo[3,2-a]benzo[6,7]indolo[3,2-c]carbazole (**2g**) in [$d_6$]-DMSO

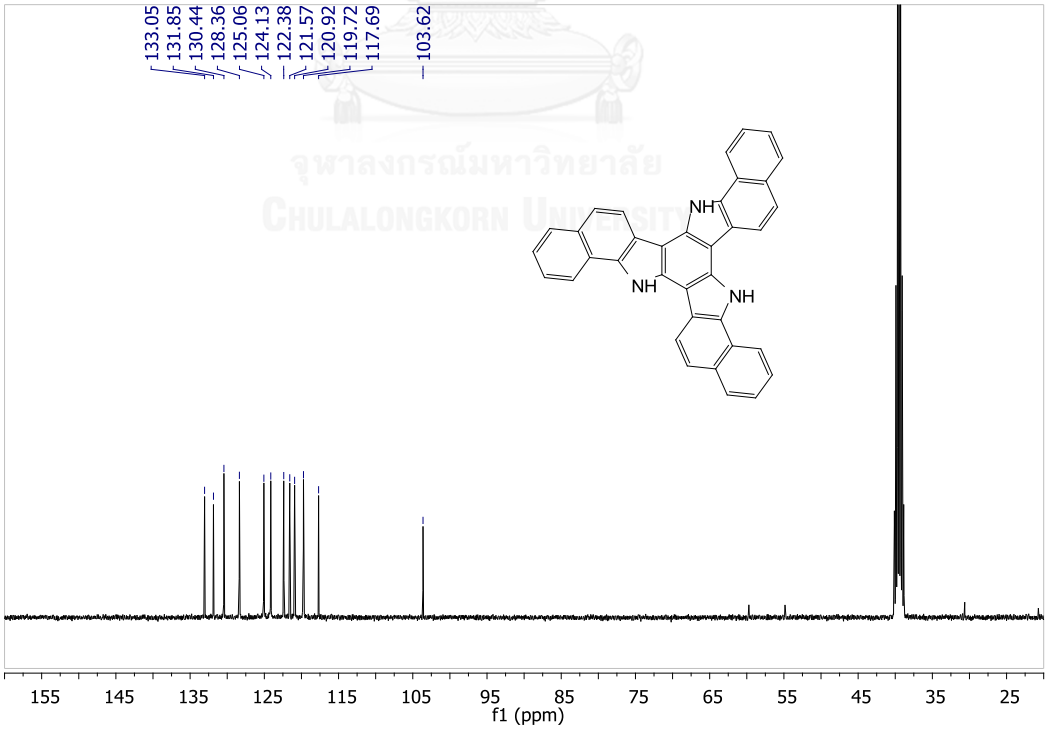


**Figure A. 46** $^{13}$C-NMR of 12,19-dihydro-5*H*-benzo[i]benzo[6,7]indolo[3,2-a]benzo[6,7]indolo[3,2-c]carbazole (**2g**) in [$d_6$]-DMSO

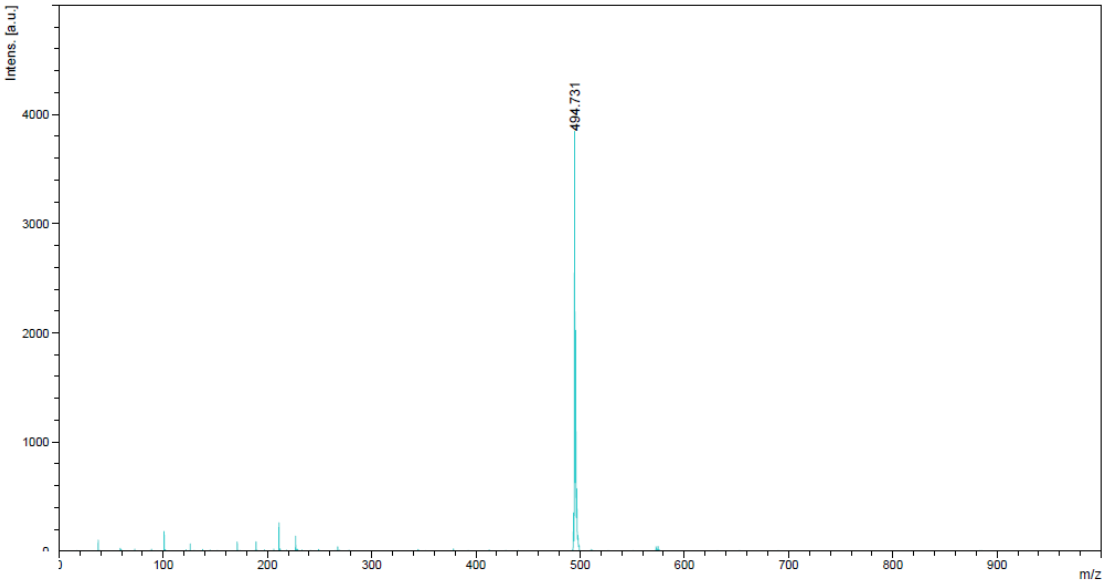


**Figure A. 47** MALDI-TOF mass spectrum of 12,19-dihydro-5*H*-benzo[i]benzo[6,7]indolo[3,2-a]benzo[6,7]indolo[3,2-c]carbazole (**2g**).

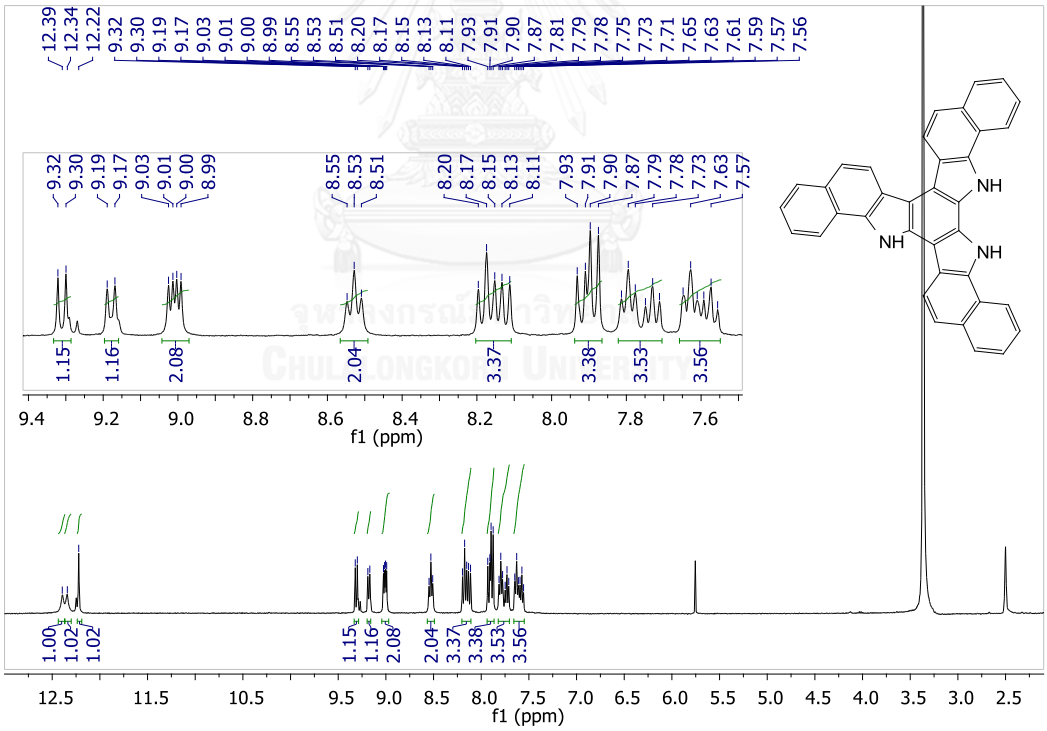


**Figure A. 48** $^{1}$H-NMR of 6,13-dihydro-5*H*-benzo[i]benzo[6,7]indolo[2,3-a]benzo[6,7]indolo[2,3-c]carbazole (**3g**) in [$d_6$]-DMSO.

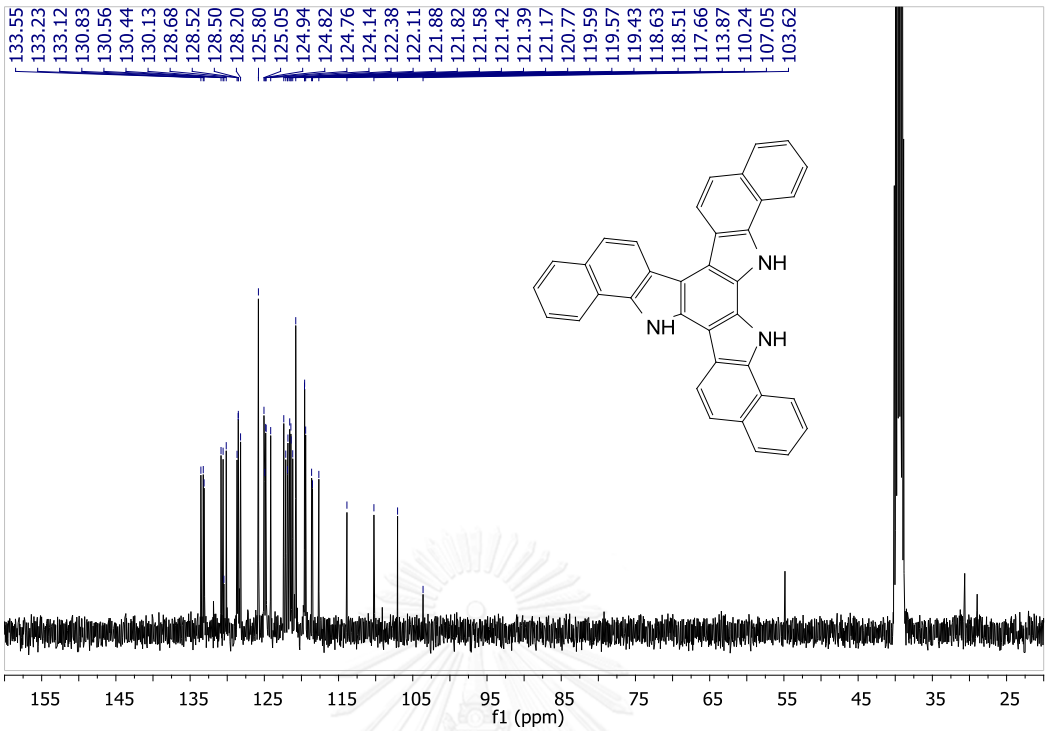


**Figure A. 49** $^{13}$C-NMR of 6,13-dihydro-5*H*-benzo[i]benzo[6,7]indolo[2,3-a]benzo[6,7]indolo[2,3-c]carbazole (**3g**) in [$d_6$]-DMSO.

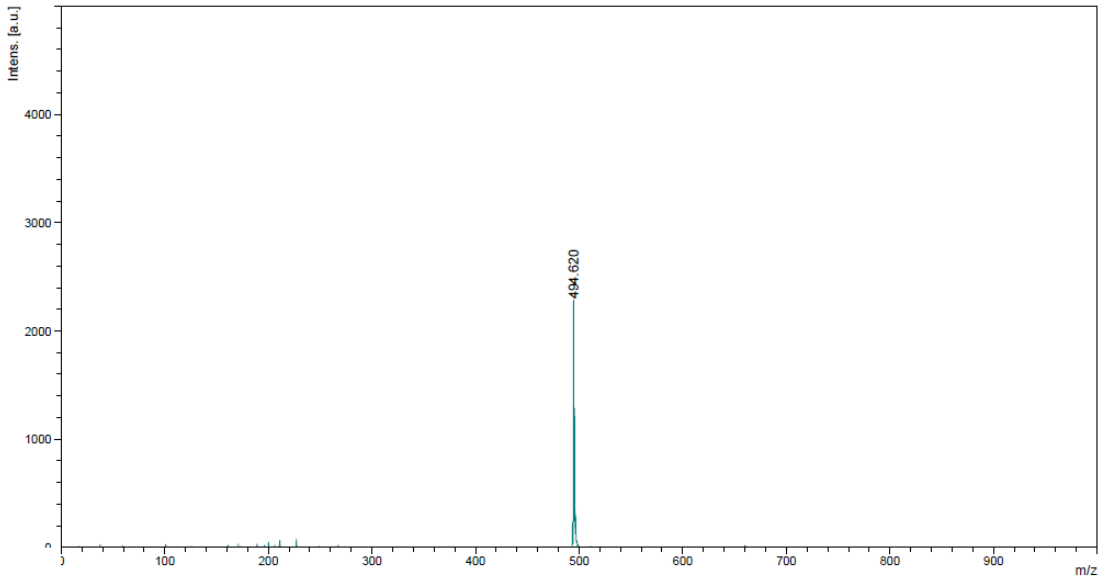


**Figure A. 50** MALDI-TOF mass spectrum of 6,13-dihydro-5*H*-benzo[i]benzo[6,7]indolo[2,3-a]benzo[6,7]indolo[2,3-c]carbazole (**3g**).

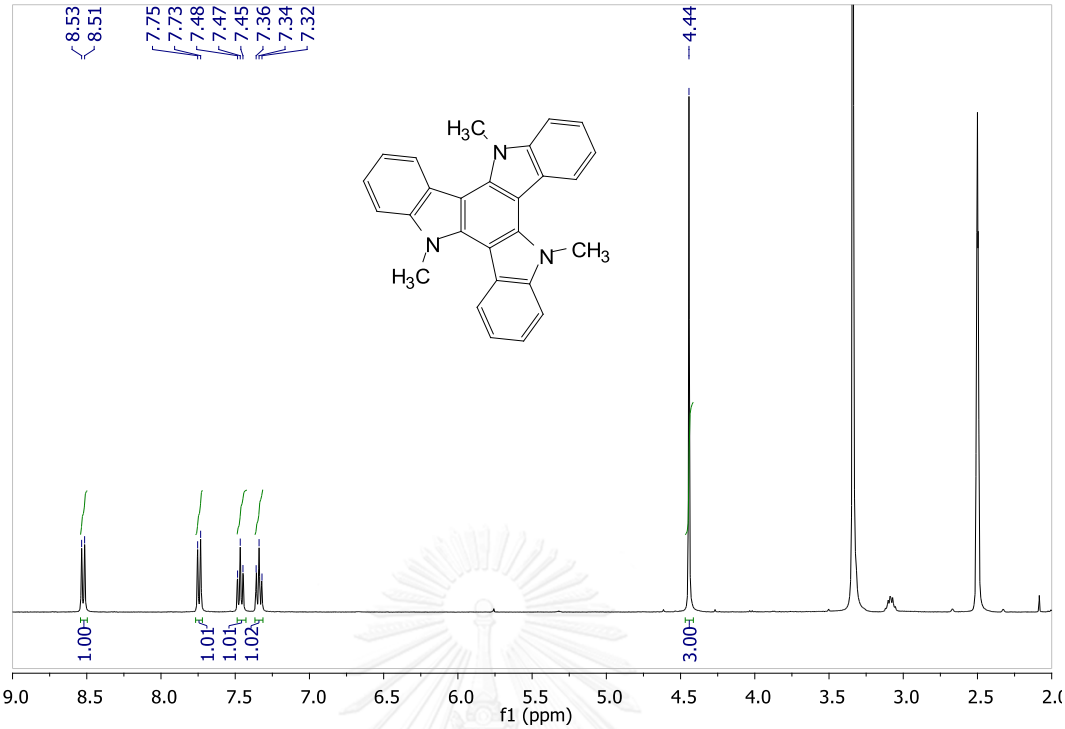


**Figure A. 51** $^{1}$H-NMR of 5,10,15-trimethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2i**) in [$d_6$]-DMSO.

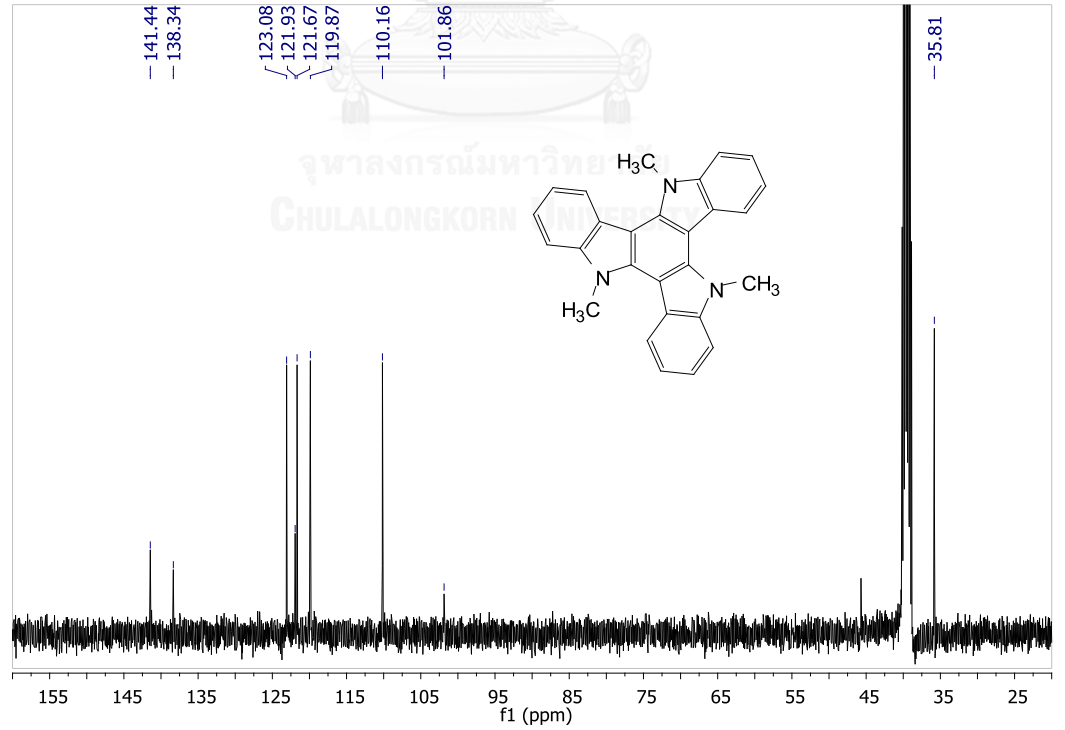


**Figure A. 52** $^{13}$C-NMR of $^{1}$H-NMR of 5,10,15-trimethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2i**) in [$d_6$]-DMSO.

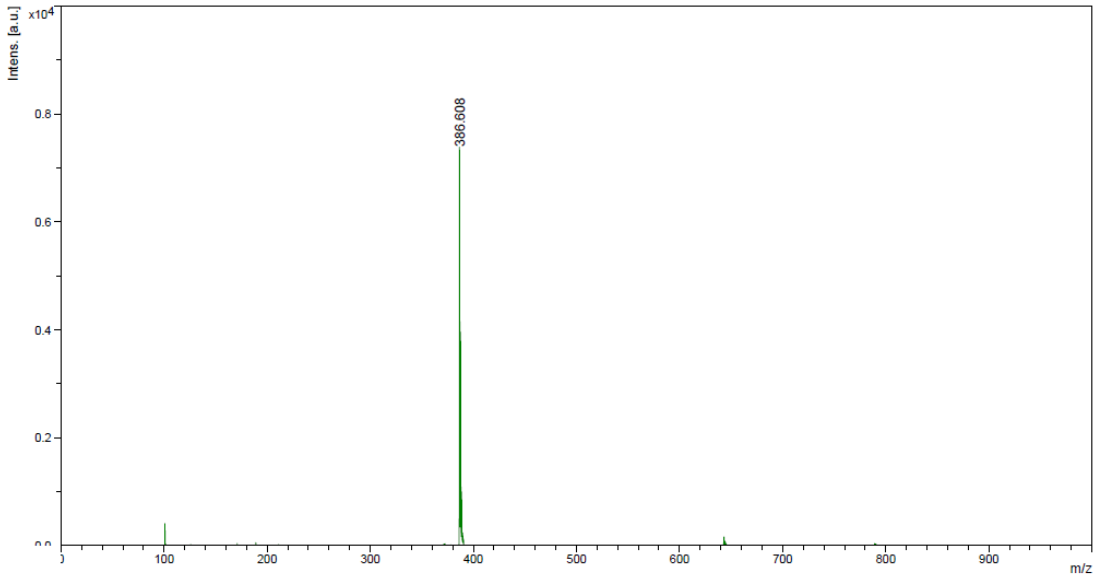


**Figure A. 53** MALDI-TOF mass spectrum of $^{1}$H-NMR of 5,10,15-trimethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2i**).

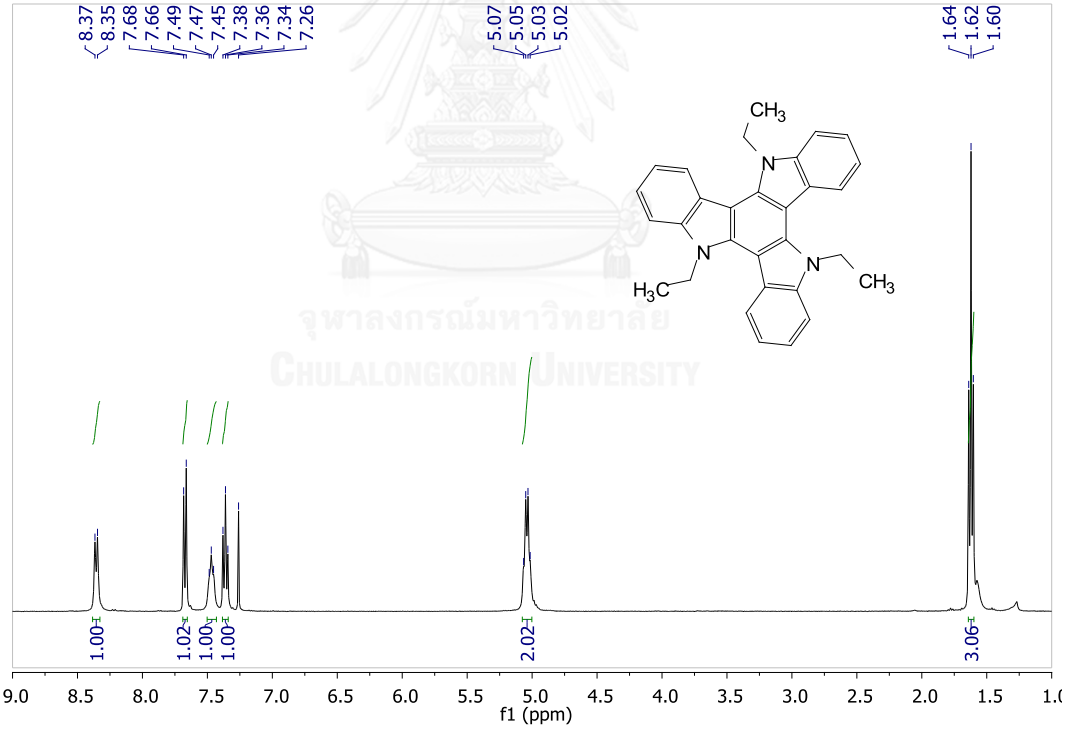


**Figure A. 54** $^{1}$H-NMR of 5,10,15-triethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2j**) in $CDCl_3$.

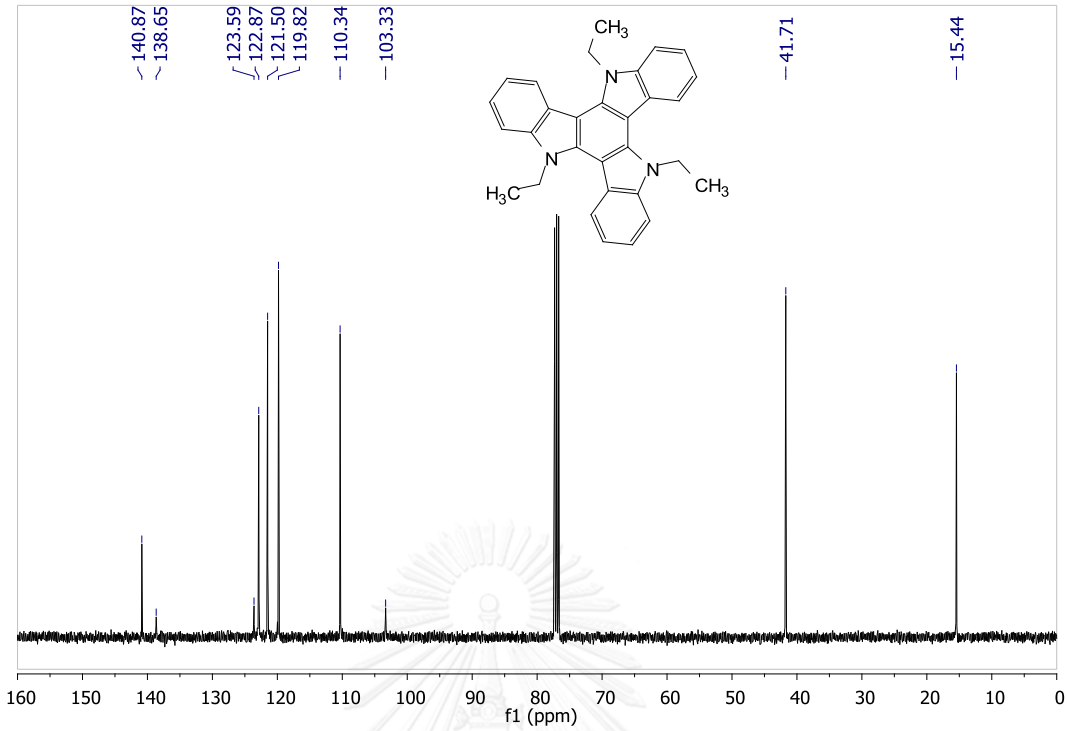


**Figure A. 55** $^{13}$C-NMR of 5,10,15-triethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2j**) in $CDCl_3$.

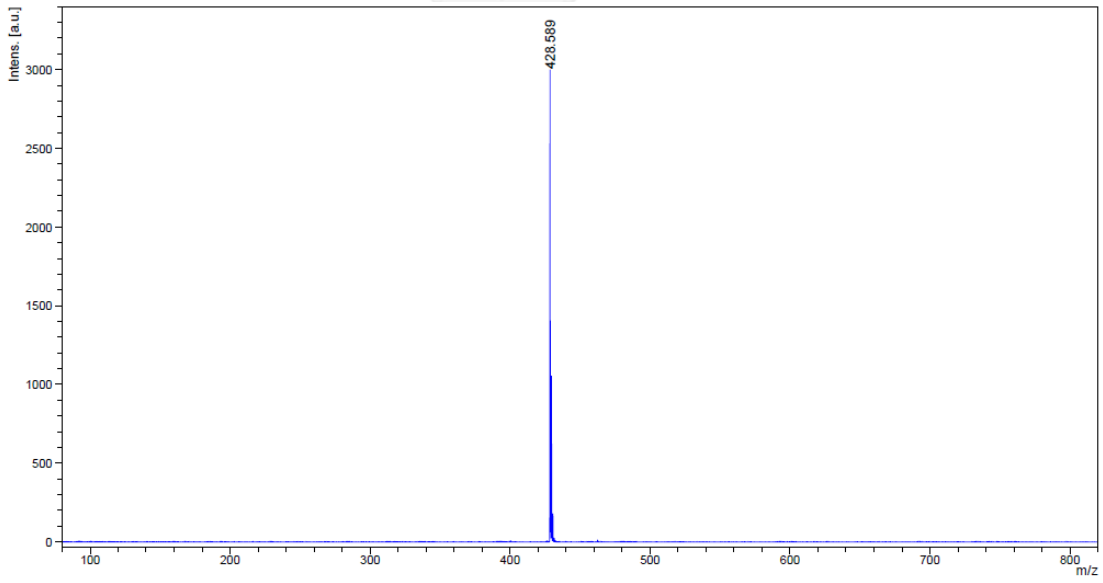


**Figure A. 56** MALDI-TOF mass spectrum of 5,10,15-triethyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2j**).

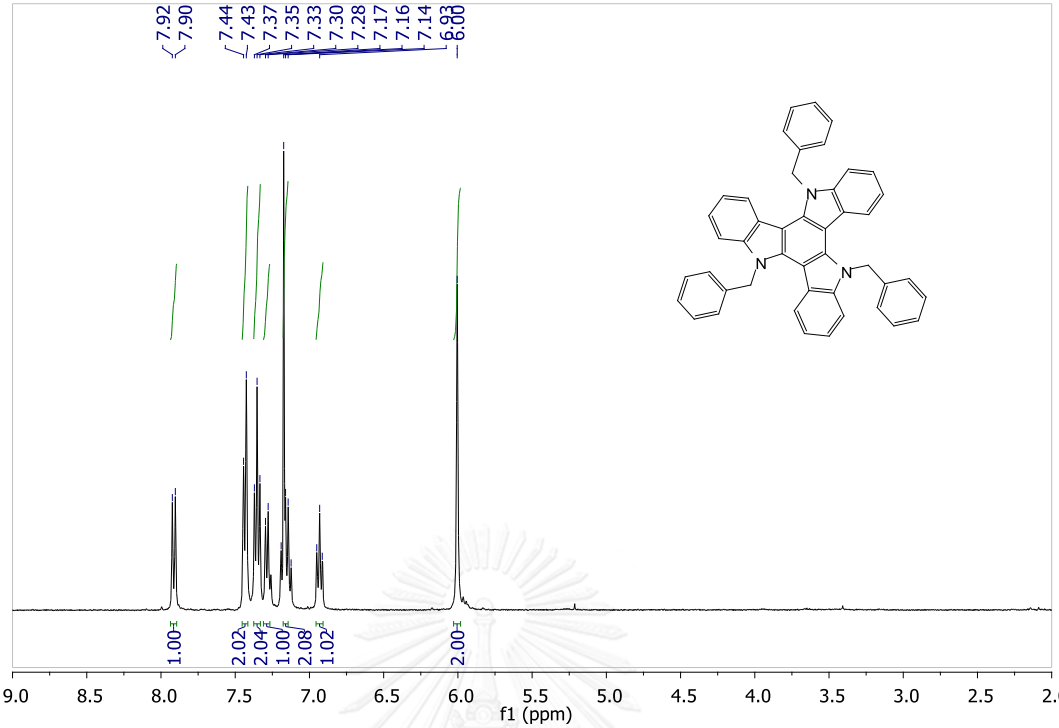


**Figure A. 57** $^{1}$H-NMR of 5,10,15-tribenzyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2k**) in $CDCl_3$.

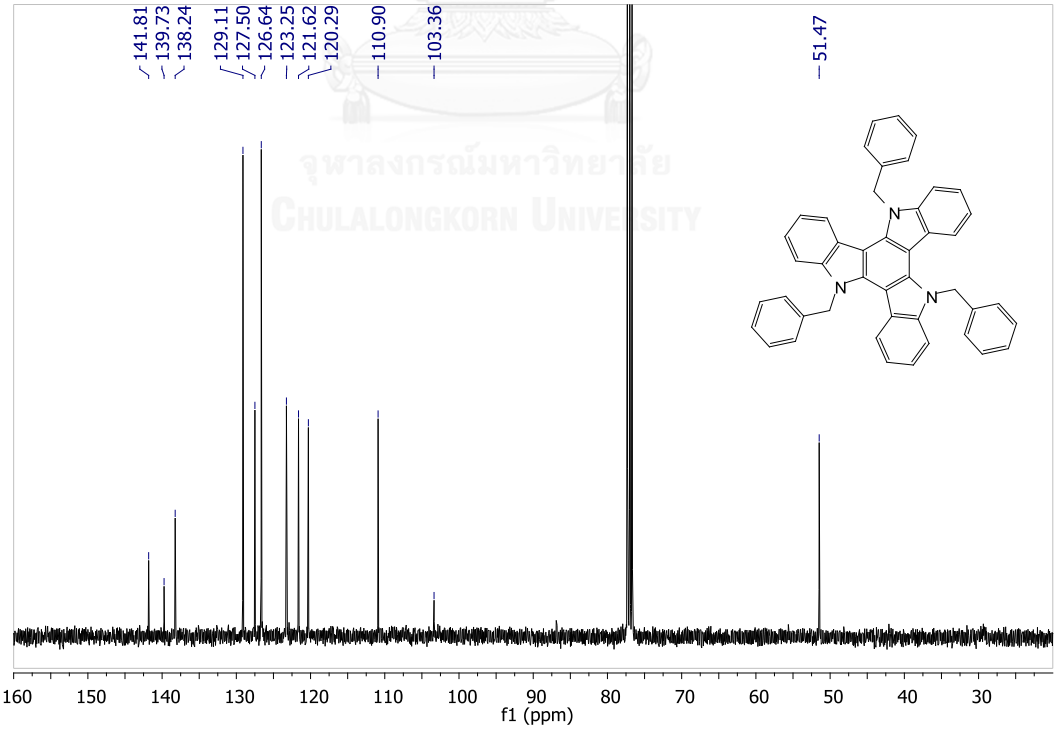


**Figure A. 58** $^{13}$C-NMR of 5,10,15-tribenzyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2k**) in $CDCl_3$.

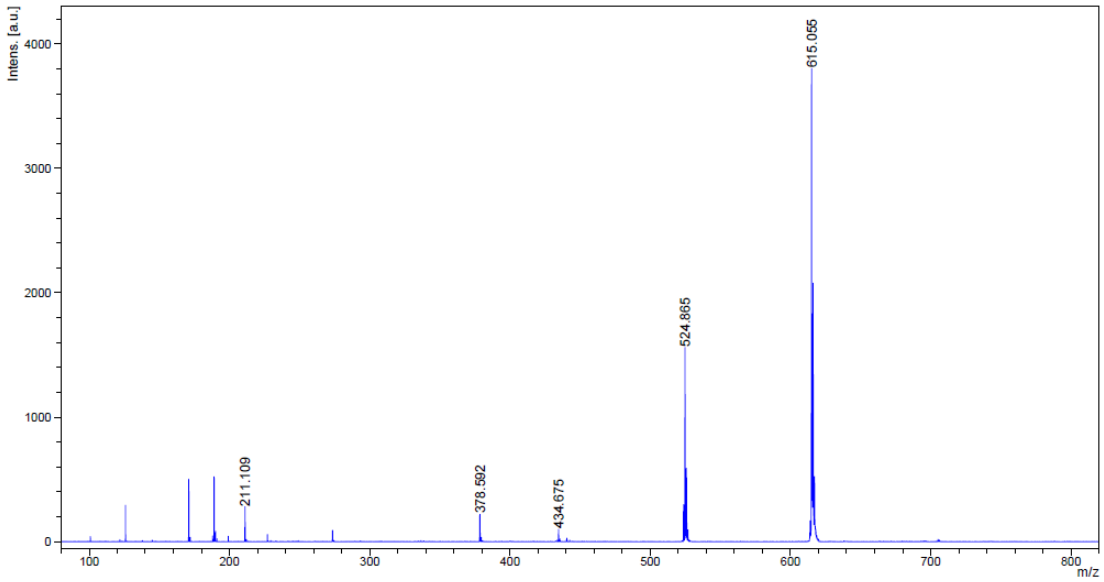


**Figure A. 59** MALDI-TOF mass spectrum of 5,10,15-tribenzyl-10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole (**2k**).

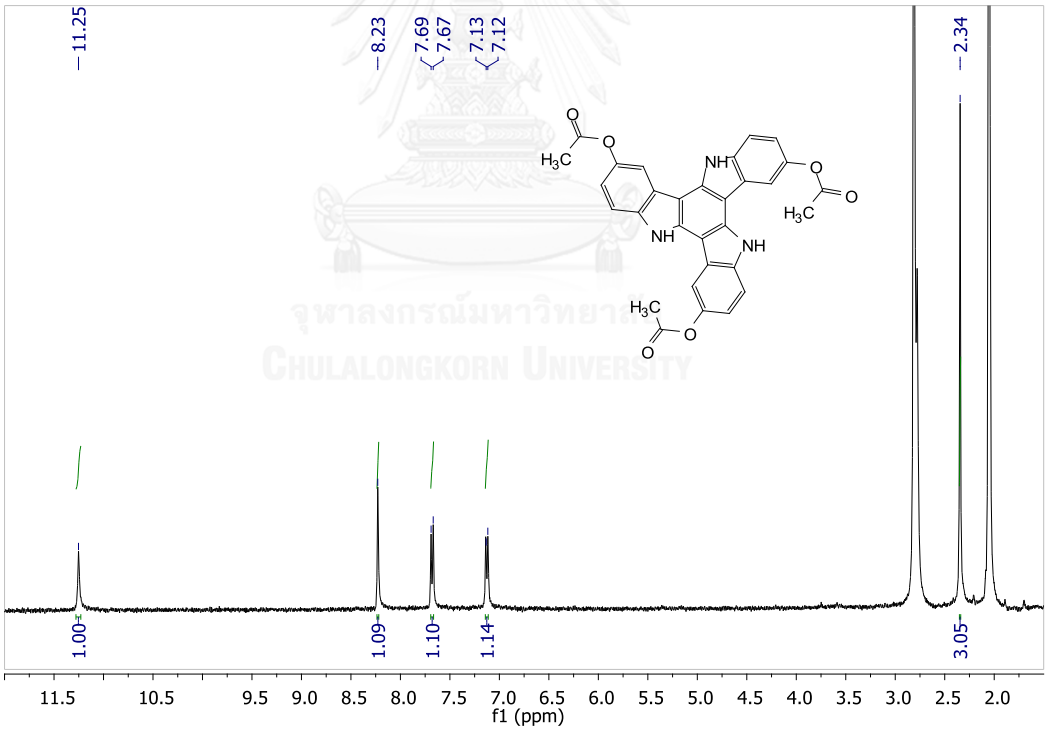


**Figure A. 60** $^{1}$H-NMR of 10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole-3,8,13-triyl triacetate (**2n**) in [$d_6$]-acetone.

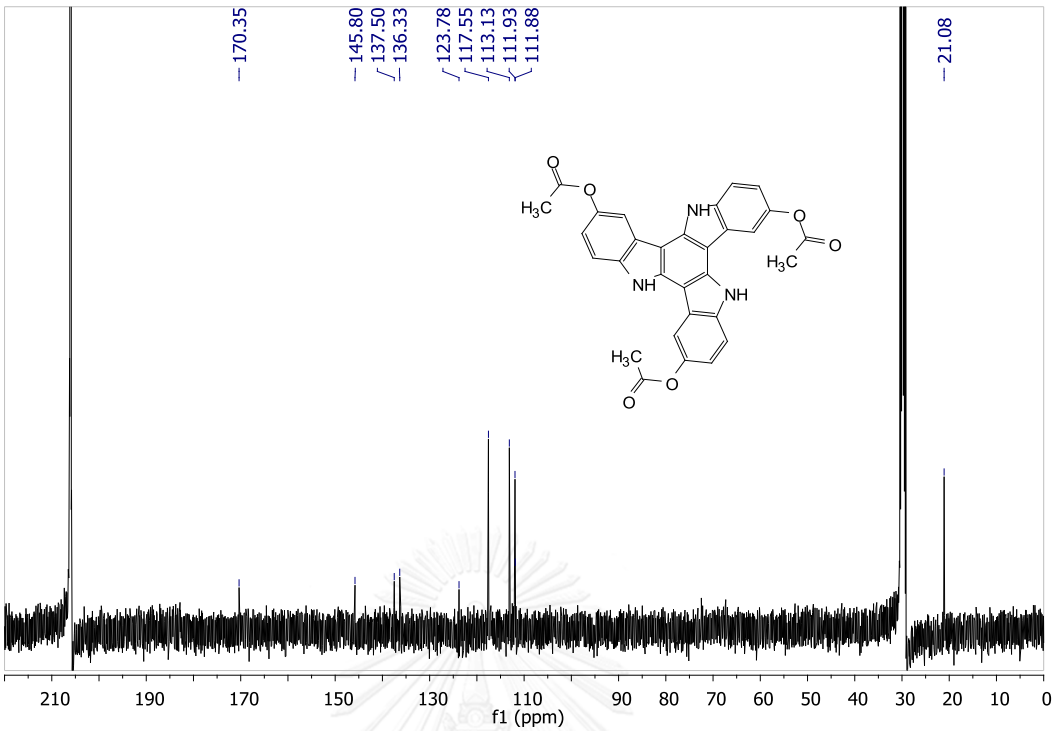


**Figure A. 61** $^{13}$C-NMR of 10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole-3,8,13-triyl triacetate (**2n**) in [$d_6$]-acetone.

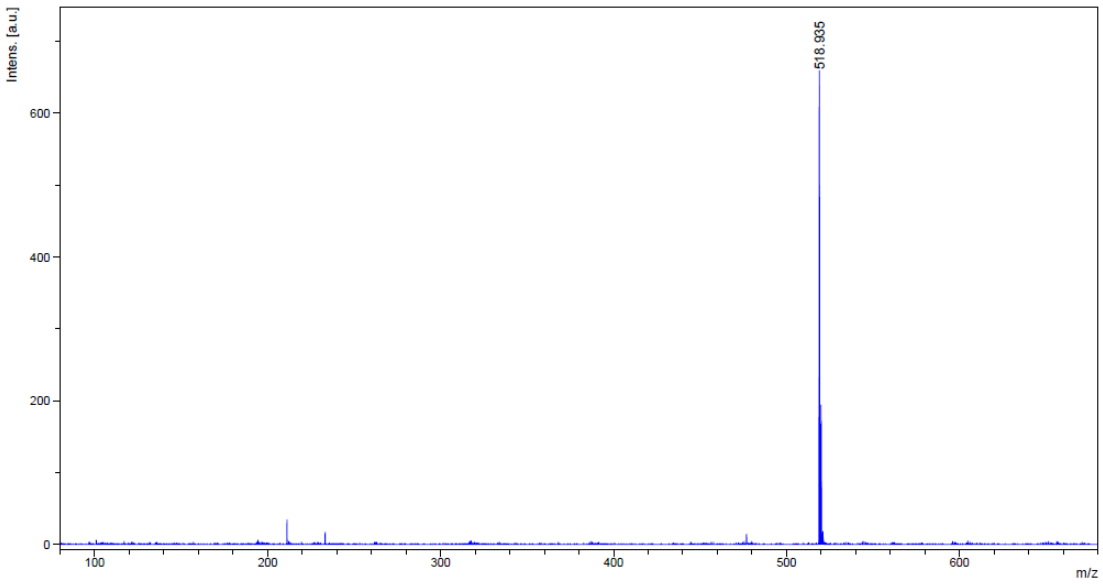


**Figure A. 62** MALDI-TOF mass spectrum of 10,15-dihydro-5*H*-diindolo[3,2-a:3',2'-c]carbazole-3,8,13-triyl triacetate (**2n**).

# VITA

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