Malaysian Journal of Chemistry, 2020, Vol. 22(3), 1-16
(Special Issue: *International Conference in Organic Synthesis* - ICOS 2019, Universiti Teknologi MARA)

A Facile One-Step Synthesis of New N^2, N^9-Benzylated Quaternary β-Carbolin-3-ium Bromides via Krapcho Decarboxylation

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A simple and efficient synthetic methodology has been developed via Krapcho decarboxylation to construct four new N^2,N^9-benzylated quaternary β-carbolin-3-ium bromide salts (**5a-d**) by treating ethyl-β-carboline-3-carboxylate (**4**) with various substituted benzyl bromides in the presence of NaH in DMF under refluxing conditions with very good to excellent yields (81-95%).

Key words: β-carboline; N^2,N^9-benzylated quaternary β-carbolin-3-ium bromide; ethyl-β-carboline-3-carboxylate; Krapcho decarboxylation.

Received: December 2019 ; Accepted: May 2020

The aromatic β-carboline skeleton is one of the most intriguing indole-based heterocycles; its basic ring system is found in many natural products and pharmaceutical drugs [1]. According to previous investigations, β-carbolines exhibited a broad spectrum of pharmacological effects, including antitumor [2], antiparasitic [3], antibacterial [4], and antiviral [5]. Recent interests in these alkaloids have been stimulated by their potential antitumor activities acting through multiple mechanisms, such as DNA intercalation [6], topoisomerase-I & -II inhibition [7,8], cyclin-dependent kinases [9], kinesin-like protein Eg5 [10], and mitogen-activated protein kinase-2 [11]. As a result, their significant potential as therapeutics has triggered interest in the development of more efficient and rapid synthesis of new β-carboline derivatives. Knowing the significance of β-carboline and its derivatives, Pictet-Spengler proposed a simple route for the synthesis of β-carboline skeleton [12], and this method has been extensively used for the synthesis of alkaloid scaffolds, such as 1,2,3,4-tetrahydro-β-carboline-3-carboxylate, which are key intermediates for thousands of naturally occurring indole alkaloids.

Krapcho decarboxylation of aromatic esters by KCN or LiCl in polar solvents, e.g., DMF, DMSO, has been extensively investigated since the 1960s by A. P. Krapcho [13]. Esters are derived from carboxylic acids. Carboxylic acids have many advantages as surrogates of organometallic nucleophiles. They are stable, easy to make and store, and readily available. Besides, they generate carbon dioxide as a by-product in the decarboxylation process instead of producing metal waste. A variety of decarboxylative coupling reactions of carboxylic acids have been developed over the past few decades [14].

In our continuing search for a novel and effective method for the preparation of various organic molecules, we were prompted to seek a mild and efficient condition-for the decarboxylation of ethyl-β-carboline-3-carboxylate to produce N^2,N^9-benzylated quaternary β-carbolin-3-ium bromide. In order to improve the existing methodologies and increase the yields of the product, we herein describe a simple, efficient, and inexpensive procedure for the Krapcho decarboxylation using NaH in DMF under refluxing conditions with good to excellent yields.

EXPERIMENTAL SECTION

1. Materials and Chemicals

All chemicals were analytical reagent grade and purchased from Aldrich Co. Ltd., which were used directly without further purification. The reaction progress was monitored using thin-layer chromatography (TLC). TLC analysis was carried out on glass-backed TLC silica plates (silica gel 60 F_{254},

†Paper presented at the International Conference in Organic Synthesis (ICOS 2019), 9-10 December 2019, Universiti Teknologi MARA.

0.25 mm) impregnated with fluorescence indicator (Merck art. 1.05554). The detection of UV-active substances was visualized using ultraviolet light (λ_{max} = 254 nm).

2. Instrumentation

NMR spectra were recorded in deuterated chloroform ($CDCl_3$) and dimethyl sulfoxide (DMSO) using Bruker AV 500 MHz spectrometer. The chemical shifts are reported in ppm downfield to TMS (δ = 0) for ^{1}H-NMR and relative to the central $CDCl_3$ and DMSO resonance for ^{13}C-NMR. Spin multiplicities are expressed as s (singlet), d (doublet), t (triplet), and m (multiplet), while coupling constants (*J*) are given in hertz. FT-IR spectra were recorded on Nicolet 6700 FT-IR spectrometer (Thermo Scientific, MA, USA) in the mid-IR region (400-4000 cm^{-1}) using Attenuated Total Reflection (ATR) technique. The melting point was determined with an uncorrected in open capillary tubes with Stuart SMP 20 Melting Point B-545 apparatus. The electrospray ionization mass spectrometry (ESI-MS) was determined on LC-MS THERMO QUEST Finnigan LCQ DUO system. Elemental analysis (CHN) was carried out by using Thermo Finnigan Flash EA 1112 elemental analyzer.

3. Synthesis

3.1. Synthesis of 2,3,4,9-tetrahydro-1H-pyrido[3, 4-b]indole-3-carboxylic acid (2)

A mixture of L-tryptophan (**1**, 10.0 g, 49.02 mmol) and 2.5 M NaOH (2.0 g, 49.02 mmol) was first dissolved in H_2O (40 mL) and stirred until it became clear before the addition of formaldehyde (37%, 4.88 mL, 49.02 mmol). The mixture was stirred at room temperature for 3h and subsequently refluxed for another 3h. TLC was used to monitor the reaction progress. Upon completion, the mixture was neutralized (~pH5) with glacial acetic acid, cooled, and the precipitate formed was filtered, washed with H_2O, and dried under vacuum to give the desired compound **2**. Compound **2** was used directly in the next step without further purification.

3.2. Synthesis of ethyl 1,2,3,4-tetrahydro-β-carboline-3-carboxylate (3)

A mixture of 1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid (**2**, 5.0 g, 50.0 mmol), anhydrous ethanol (250 mL), and thionyl chloride (10 mL) was refluxed for 2h and then evaporated under reduced pressure. The resulting mixture was poured into 100 mL of cold H_2O, and the mixture was adjusted to ~pH9 with saturated sodium hydrogen carbonate. The mixture was extracted with ethyl acetate (3 × 100 mL). The organic layers were combined, washed with H_2O, and brined, dried over anhydrous sodium sulfate, filtered, and concentrated under vacuum. The filtrate was crystallized with ethyl acetate to yield the desired compound **3**. M.p: 150ºC, white needle crystals, yield: 92%, ESI-MS *m/z*=244 $[M+H]^+$, FT-IR (ATR, cm^{-1}): 3277, 3051, 2979, 2903, 2829, 1712, 1448, 1368, 1327, 1210, 1119, 1034, 742, ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 10.72 (1H, s), 7.38 (1H, d, *J* = 7.5 Hz), 7.27 (1H, d, *J* = 7.5 Hz), 7.03-7.00 (1H, m), 6.96-6.93 (1H, m), 4.26 (2H, q, *J* = 7.0 Hz), 4.07 (s, 2H), 3.77 (1H, dd, J_1 = 5.0 Hz, J_2 = 9.5 Hz), 3.13 (1H, dd, J_1 = 4.5 Hz, J_2 = 15.5 Hz), 2.88 (1H, dd, J_1 = 9.5 Hz, J_2 = 15.00 Hz), 2.45 (1H, s), 1.33 (3H, t, *J* = 8.0 Hz) ppm, ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 173.1, 135.7, 133.7, 133.5, 128.6, 127.0, 123.7, 122.2, 120.8, 120.4, 120.2, 118.2, 117.1, 112.4, 110.8, 105.5, 60.1, 55.3, 41.4, 30.7, 25.0, 14.3.

3.3. Synthesis of ethyl β-carboline-3-carboxylate (4)

A suspension of compound **3** (5.0 g, 50.0 mmol) and sulfur (3.28 g, 150 mmol) in anhydrous xylene (200 mL) was refluxed for 12h and then cooled to room temperature. The mixture was stored at 4°C overnight to yield light yellow crystals. After filtration, the precipitate was washed with cold xylene and petroleum ether. The solid was dried and recrystallized from ethyl acetate to afford compound **4**. M.p: 231-232ºC, white solid, yield: 99%, ESI-MS *m/z*=241 $[M+H]^+$, FT-IR (ATR, cm^{-1}): 3238, 1712, 1693, 1628, 1594, 1500, 1366, 1338, 1295, 1251, 1227, 1121, 1098, 1021, ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 10.70 (1H, br), 8.97 (1H, s), 8.90 (1H, s), 8.38 (1H, d, *J* = 7.8 Hz), 7.68-7.57 (2H, m), 7.37-7.24 (1H, m), 4.37 (2H, q, *J* = 7.0 Hz), 1.36 (2H, t, *J* = 7.0 Hz) ppm, ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 165.6, 141.0, 137.5, 136.8, 133.7, 128.7, 127.5, 122.2, 120.9, 120.3, 117.5, 112.4, 60.6, 14.4 ppm.

3.4. General procedure for the synthesis of compounds 5a-d

A mixture of ethyl β-carboline-3-carboxylate (**4**, 0.5 g, 2.08 mmol) and anhydrous DMF (12.5 mL) was stirred at room temperature for 10 minutes, then 60% NaH dispersed in mineral oil (0.166 g, 4.16 mmol) and benzyl/substituted benzyl bromide (8.29 mmol) were added. The mixture was stirred and refluxed for 3h. After completion of the reaction, as indicated by TLC, the solution was poured into cold water (150 mL) and extracted with ethyl acetate (3 ×100 mL). The combined organic phase was washed with H_2O, and brined, dried over anhydrous sodium sulfate, filtered, and evaporated in vacuo. The obtained solid was recrystallized from ethyl acetate to yield the desired compounds **5a-d**.

2,9-Dibenzyl-β-carbolin-2-ium bromide (5a)

M.p: >270ºC, light yellow solid, yield: 95%, ESI-MS *m/z*=349 $[M-Br]^+$, FT-IR (ATR, cm^{-1}): 3364, 2980, 1644, 1512, 1497, 1465, 1450, 1336, 1272, 1211, 1137, ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 11.09 (1H, s), 8.36

(1H, d, *J* = 6.5 Hz), 8.32 (1H, d, *J* = 6.5 Hz), 8.25 (1H, d, *J* = 8.0 Hz), 7.82 (1H, t, *J* = 7.5 Hz), 7.71 (1H, d, *J* = 8.5 Hz), 7.63-7.61 (2H, m), 7.48 (1H, t, *J* = 7.5 Hz), 7.44-7.42 (3H, m), 7.39-7.37 (3H, m), 7.30-7.26 (2H, m), 6.22 (2H, s), 6.08 (2H, s) ppm, ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 144.9, 136.1, 135.2, 133.7, 132.7, 132.6, 131.0, 129.7, 129.5, 129.4, 129.0, 128.3, 127.5, 123.3, 122.5, 119.6, 117.2, 111.4, 64.3, 48.4 ppm, Anal. Calc. for $C_{25}H_{21}BrN_2$: C, 69.94; H, 4.93; N, 6.52, Found: C, 69.84; H, 5.13; N, 6.46.

2,9-Bis(2-fluorobenzyl)-*β*- carbolin-2-ium bromate (5b)

M.p: >270ºC, yellow crystal, yield: 91%, ESI-MS *m/z*=385 $[M\text{-}Br]^+$, FT-IR (ATR, cm^{-1}): 3398, 2996, 2778, 1636, 1612, 1584, 1492, 1455, 1336, 1270, 1229, 1208, 1178, 1170, 1137, 1103, ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 11.02 (1H, s), 8.50 (1H, d, *J* = 5.5 Hz), 8.36 (1H, d, *J* = 5.5 Hz), 8.31 (1H, t, *J* = 7.0 Hz), 8.22 (1H, d, *J* = 8.0 Hz), 7.82 (1H, t, *J* = 7.0 Hz), 7.79 (1H, d, *J* = 7.5 Hz), 7.74 (1H, d, *J* = 8.5 Hz), 7.45 (1H, t, *J* = 7.5 Hz), 7.39 (1H, q, *J* = 7.5 Hz), 7.27-7.23 (2H, m), 7.19-7.17 (1H, m), 7.10 (1H, t, *J* = 7.0 Hz), 7.06 (1H, d, *J* = 9.5 Hz), 6.96 (1H, t, *J* = 10.0 Hz), 6.35 (2H, s), 6.04 (2H, s) ppm, ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 162.1, 162.0, 160.1, 160.0, 144.7, 136.0, 132.9, 132.7, 132.1, 132.0, 131.6, 131.2, 130.5, 130.4, 129.0, 128.2, 125.6, 125.3, 124.8, 124.7, 123.2, 122.5, 122.1, 122.0, 121.5, 121.3, 119.5, 117.2, 115.9, 115.8, 115.7, 115.6, 111.6, 57.9, 43.2 ppm, Anal. Calc. for $C_{25}H_{19}BrF_2N_2$: C, 64.53; H, 4.12; N, 6.02; Found: C, 64.23; H, 3.64; N, 5.75.

2,9-Bis(4-fluorobenzyl)-*β*-carbolin-2-ium bromate (5c)

M.p: >270ºC, light yellow crystal, yield: 83%, ESI-MS *m/z*=385 $[M\text{-}Br]^+$, FT-IR (ATR, cm^{-1}): 3428, 2928, 1639, 1599, 1505, 1463, 1451, 1329, 1267, 1217, 1160, 1134, ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 9.94 (1H, s), 8.42 (1H, d, *J* = 6.5 Hz), 8.38 (1H, d, *J* = 6.5 Hz), 8.22 (1H, d, *J* = 8.0 Hz), 7.74 (1H, td, J_1 = 1.0 Hz, J_2 = 8.0 Hz), 7.60 (1H, d, *J* = 8.5 Hz), 7.49-7.46 (2H, m), 7.10 (1H, t, *J* = 8.0 Hz), 7.20-7.18 (2H, m), 6.97 (2H, t, *J* = 8.5 Hz), 6.86 (2H, t, *J* = 8.5 Hz), 6.01 (2H, s), 5.89 (2H, s) ppm, ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 162.3, 161.4, 144.9, 136.0, 133.5, 133.1, 132.1, 131.0, 130.9, 130.6, 129.6, 128.8, 128.7, 127.9, 123.5, 122.7, 119.4, 117.8, 116.4, 116.2, 115.9, 115.7, 111.0, 60.0, 47.0 ppm, Anal. Calc. for $C_{25}H_{19}BrF_2N_2$: C, 64.53; H, 4.12; N, 6.02; Found: C, 56.21; H, 3.07; N, 5.21.

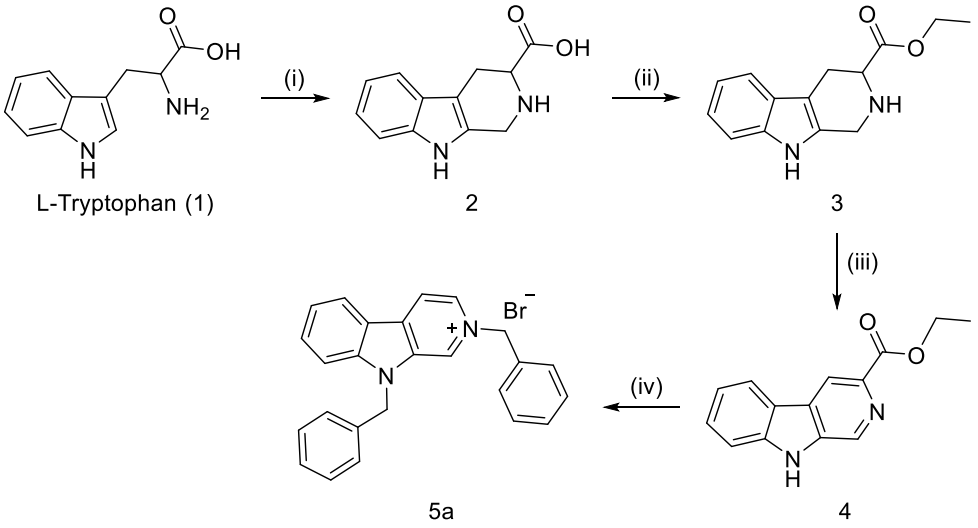
2,9-Bis(2,3-difluorobenzyl)-*β*- carbolin-2-ium bromate (5d)

M.p: >270ºC, yellow crystal, yield: 81%, ESI-MS *m/z*=421 $[M\text{-}Br]^+$, FT-IR (ATR, cm^{-1}): 3452, 3005, 2939, 1642, 1630, 1612, 1489, 1467, 1396, 1374, 1356, 1336, 1287, 1277, 1254, 1224, 1201, 1153, ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 10.77 (1H, s), 8.48 (1H, d, *J* = 6.0 Hz), 8.39 (1H, d, *J* = 6.0 Hz), 8.25 (1H, d, *J* = 8.0 Hz), 8.03-8.00 (1H, m), 7.83 (1H, t, *J* = 8.5 Hz), 7.74 (1H, d, *J* = 8.5 Hz), 7.54 (1H, t, *J* = 7.5 Hz), 7.49 (1H, t, *J* = 7.5 Hz), 7.26-7.22 (2H, m), 7.12-7.05 (3H, m), 6.32 (2H, s), 6.06 (2H, s) ppm, ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 144.7, 136.1, 133.3, 133.1, 131.8, 130.1, 129.4, 127.1, 125.7, 125.2, 124.9, 124.8, 124.4, 124.3, 123.5, 123.4, 123.3, 122.8, 119.5, 119.4, 119.3, 117.9, 117.8, 117.5, 111.5, 57.6, 42.9 ppm, Anal. Calc. for $C_{25}H_{17}BrF_4N_2$: C, 59.90; H, 3.42; N, 5.59; Found: C, 59.21; H, 3.07; N, 5.90.

RESULTS AND DISCUSSION

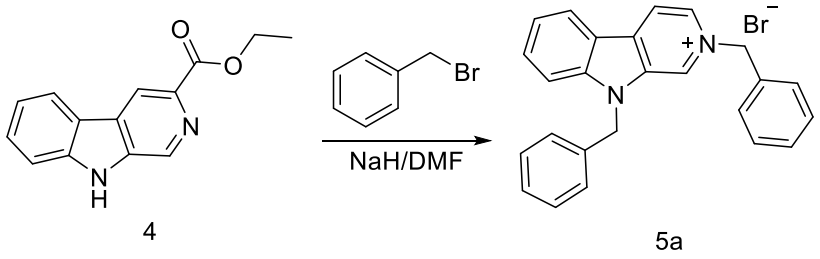
As shown in Scheme 1, compound **2** was synthesized from L-tryptophan (**1**) via Pictet-Spengler reaction in the presence of NaOH and formaldehyde (HCHO) at room temperature to reflux for 3 to 6 hours and obtained a quantitative yield. Without further purification, compound **2** was used for the next step. Esterification of compound **2** in the presence of thionyl chloride ($SOCl_2$) in ethanol at refluxing temperature gave compound **3** as white needle crystals with 92% yield. In the next step, compound **4** was synthesized from compound **3** using dehydrogenation reaction in the presence of sulfur in xylene under refluxing conditions. In the final step, compound **5a** was synthesized from compound **4** via Krapcho decarboxylation reaction as outlined in Scheme 1. Here, NaH in DMF was used at refluxing temperature and stirring for 2 hours, and we obtained **5a** at an excellent yield (90%).

To obtain excellent yields, we have optimized the reaction conditions by varying temperature, NaH equivalents, and reaction time. The results for the reaction of 2,9-dibenzyl-*β*-carbolin-2-ium bromide (**5a**) and ethyl-*β*-carboline-3-carboxylate (**4**) at various temperatures, NaH equivalents, and reaction times are summarized in Table 1. The results revealed various decarboxylation efficiencies, and the displacement of an ester group increased at a higher temperature (reflux). The best result was obtained with 2 eqv. of NaH under refluxing conditions for 3h (Table 1, entry 6) with an excellent yield of 95%.



Scheme 1. Synthesis of 2,9-dibenzyl-β-carbolin-2-ium bromide (**5a**). **Reagents and conditions**: (i) NaOH, H-CHO, rt-ref, 3-6h; (ii) $SOCl_2$, EtOH, reflux, 2h; (iii) Sulfur, xylene, reflux, 12h; (iv) Benzyl-Br, NaH, DMF, rt, 3h (optimized).

Table 1. Optimization of Reaction Conditions



4 5a

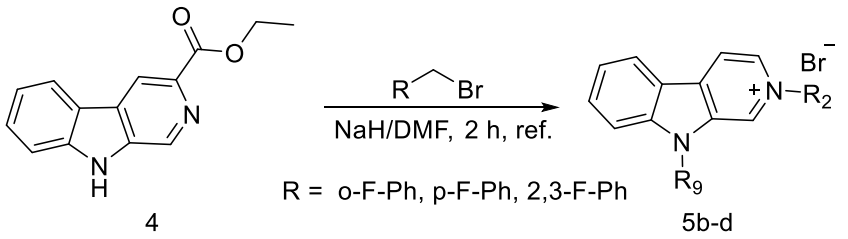
Entry	NaH (eq)	Time (h)	Conditions	Yield (%)[a]
1	1	0.5-2	rt	<10
2	1.5	4	rt	<10
3	2	5	50-60ºC	69
4	2	24	50-60ºC	75
5	1.5	3	Reflux	90
6	2	3	Reflux	95

[a]Isolated yields

Based Table 1, entry 6 proved that the transformation of the starting material **4** gave final product **5a** with no ester group, thereby confirming the decarboxylation process. The reactions were efficient and offered some advantages over previously described decarboxylation on these substrates, particularly concerning reaction time and temperature. Although progress has been made to the synthesis, however the mechanism of the transformation in the presence of NaH and anhydrous DMF has not been fully defined. The chemical structures of the synthesized compounds were confirmed by ESI-MS, ^{1}H and ^{13}C-NMR spectra, and elemental analysis data. After having optimized the reaction conditions, we synthesized a series of N^2,N^9-benzylated quaternary β-carbolin-3-ium bromide salts (**5b-d**) to explore the scope and generality of the reaction. This involved employing different aromatic alkyl halides (Scheme 2).

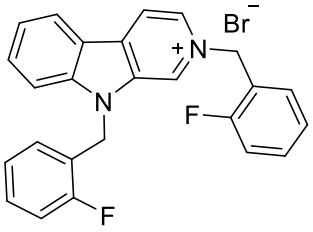
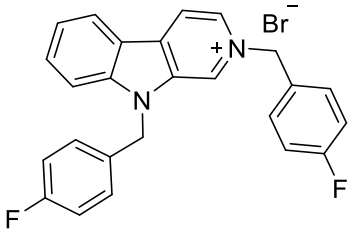
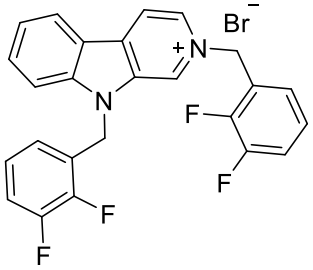
The corresponding structures and yields of the final products (**5b-d**) are presented in Table 2. To the best of our knowledge, all substituted N^2,N^9-benzylated

quaternary β-carbolin-3-ium bromide salts (**5b-d**) are new and were confirmed by ESI-MS, $^1H/^{13}C$-NMR, and elemental analysis data as well as single-crystal X-ray analyses (Figures 1-3) [15,16,17].



Scheme 2. Synthesis of N^2,N^9-benzylated quaternary β-carbolin-3-ium bromide salts (**5b-d**)

Table 2. Chemical structures with yields of compounds **5b-d**

Entry	Product	Yield (%)[a]
5b		**92**
5c		**88**
5d		**81**

[a]Isolated yield

The crystal structures of compounds **5b-d** are given in Figures 1 to 3.

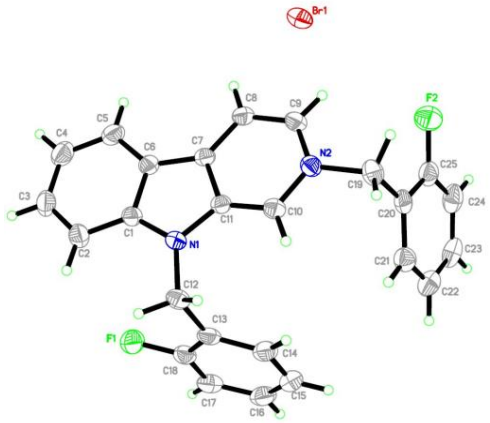


Figure 1. ORTEP diagram of 2,9-bis(2-fluorobenzyl)-β-carbolin-3-ium bromide (**5b**)

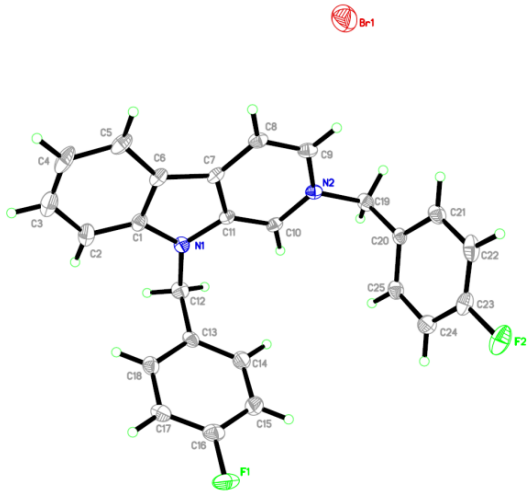


Figure 2. ORTEP diagram of 2,9-bis(4-fluorobenzyl)-β-carbolin-3-ium bromide (**5c**)

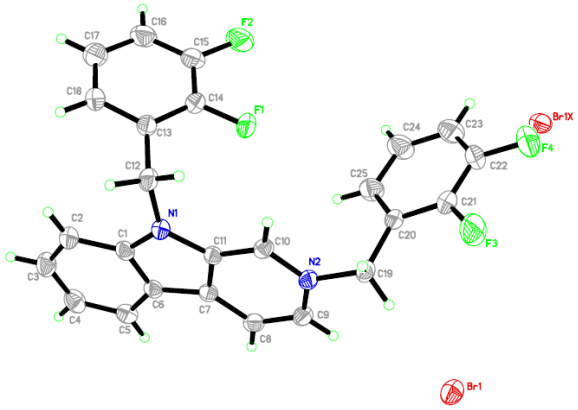
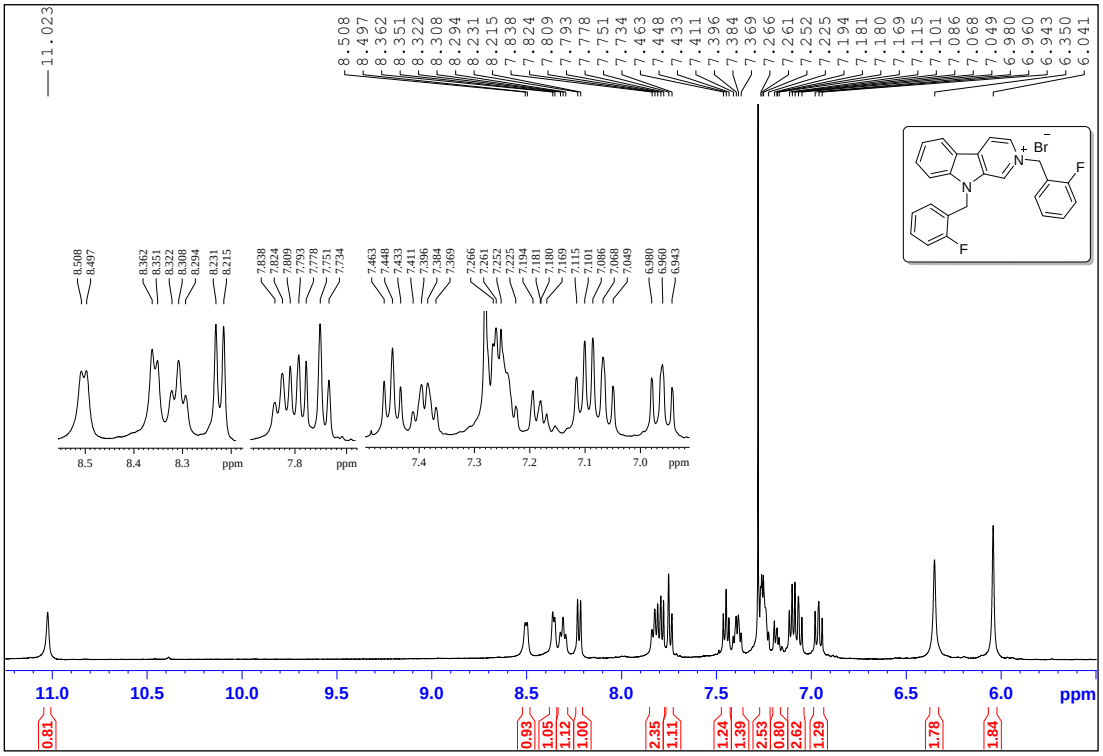
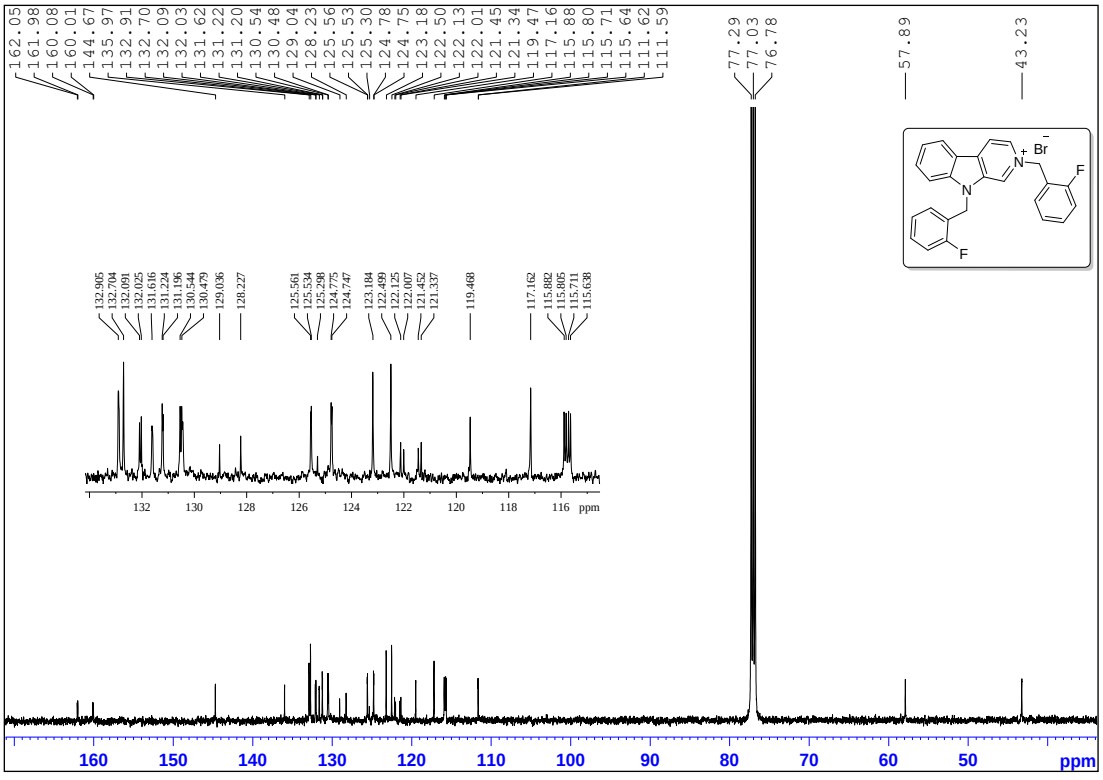


Figure 3. ORTEP diagram of 2,9-bis(2,3-difluorobenzyl)-β-carbolin-3-ium bromide (**5d**)

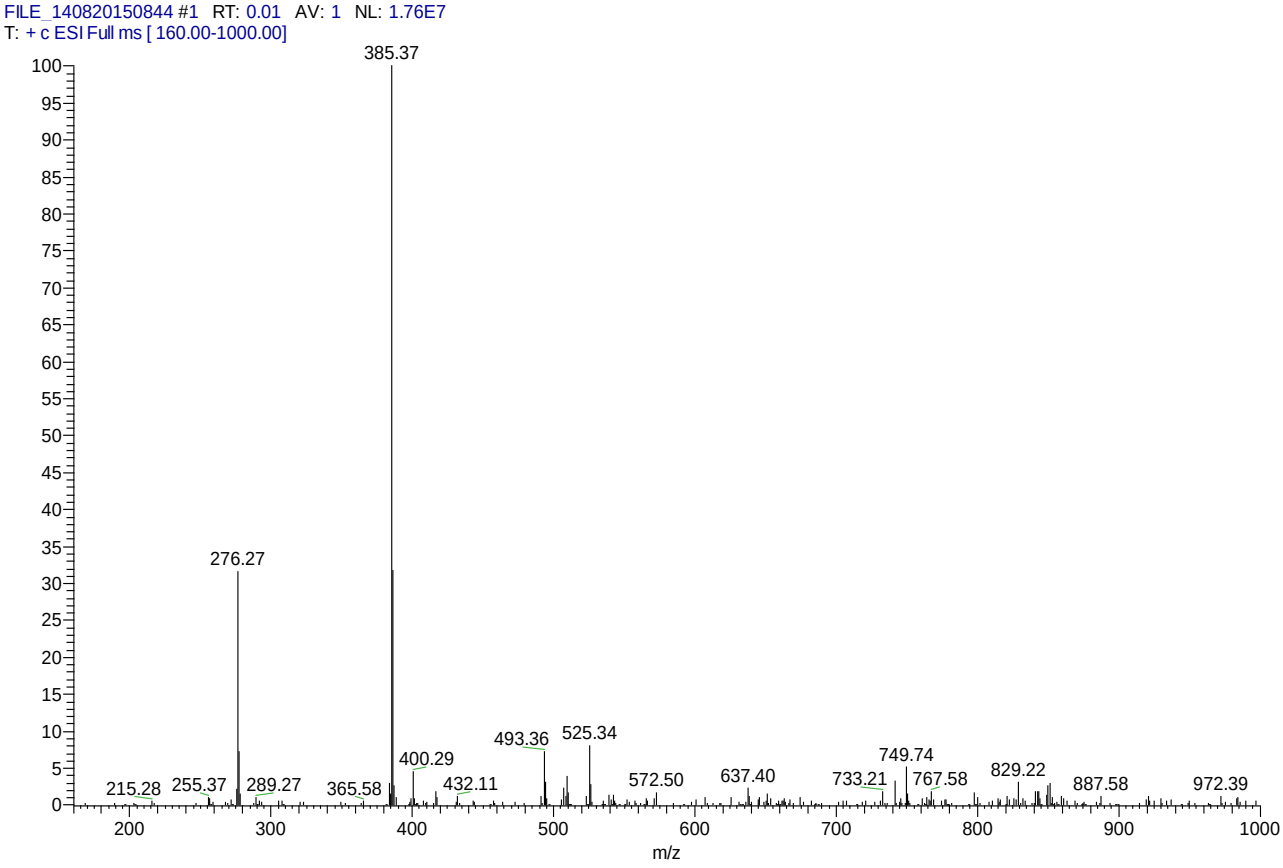
Appendix 1a. ^{1}H-NMR of compound **5b**



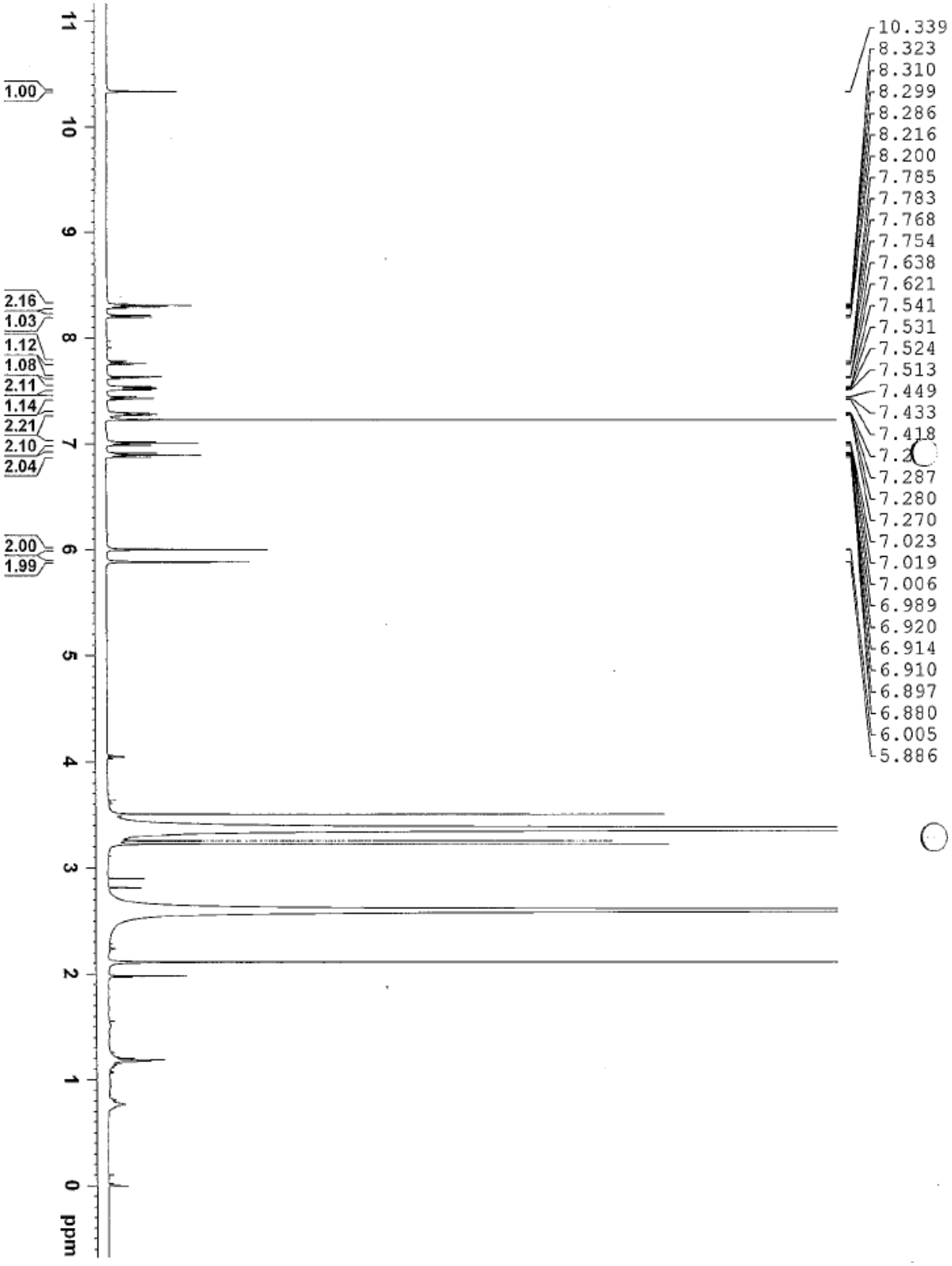
Appendix 1b. ^{13}C-NMR of compound **5b**



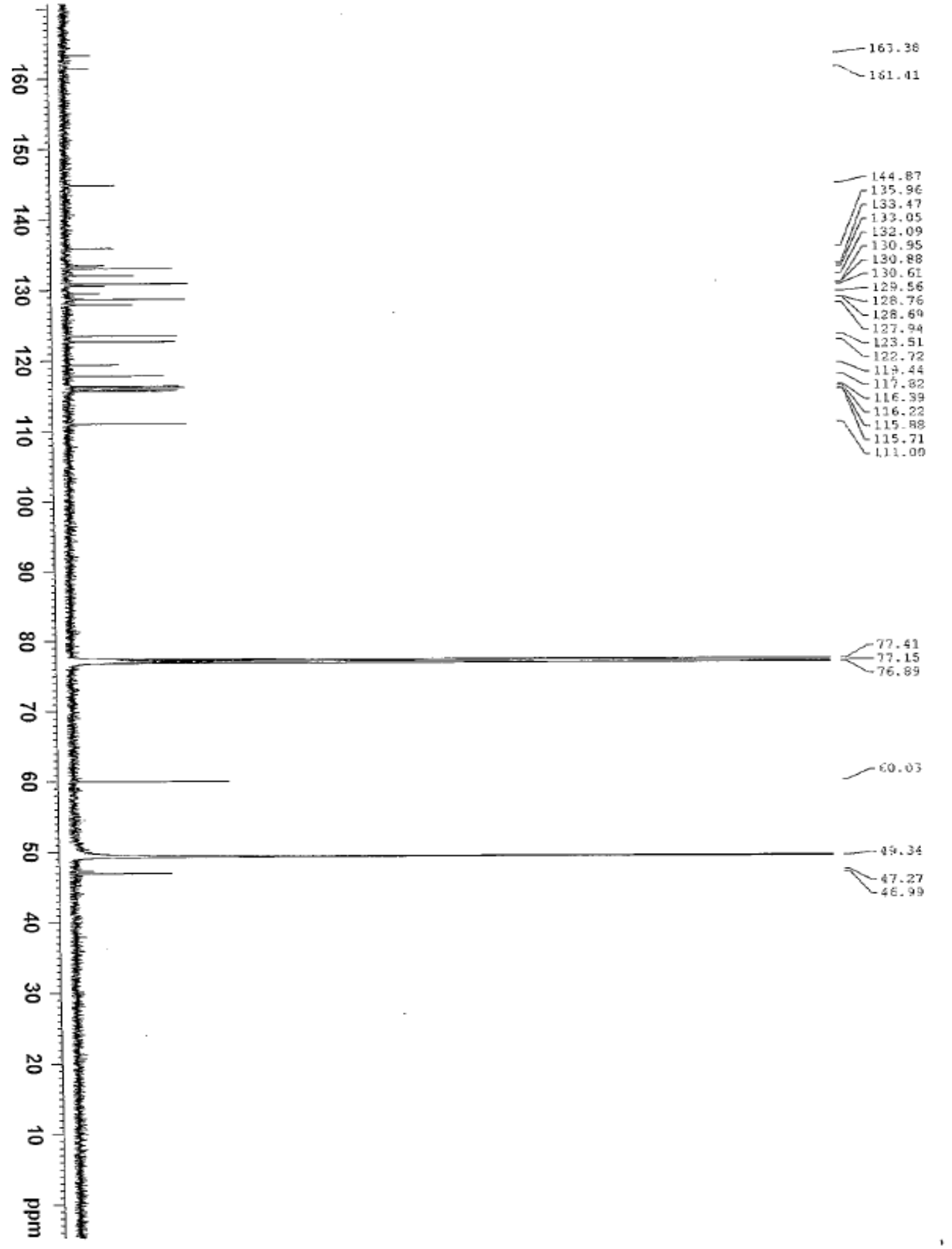
Appendix 1c. ESI-MS of compound **5b**



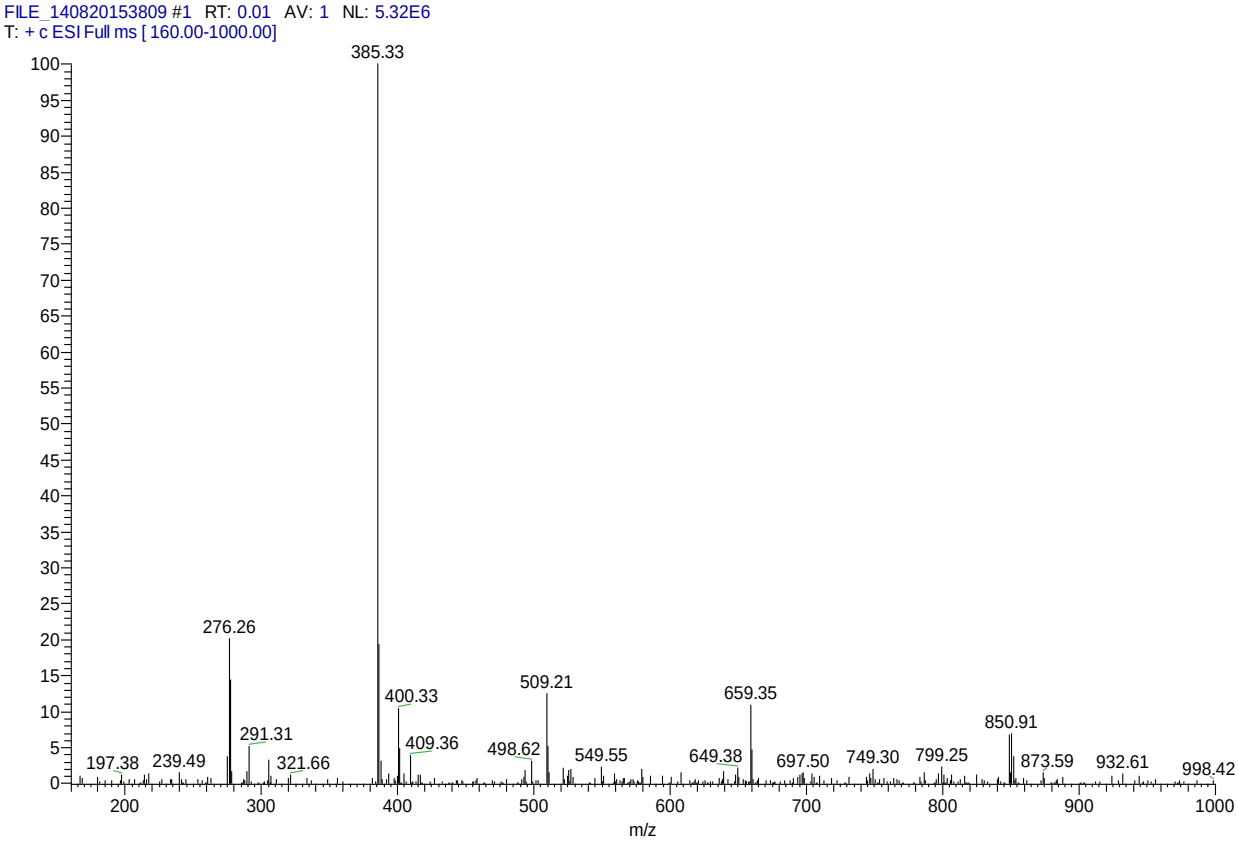
Appendix 2a. ^{1}H-NMR of compound **5c**



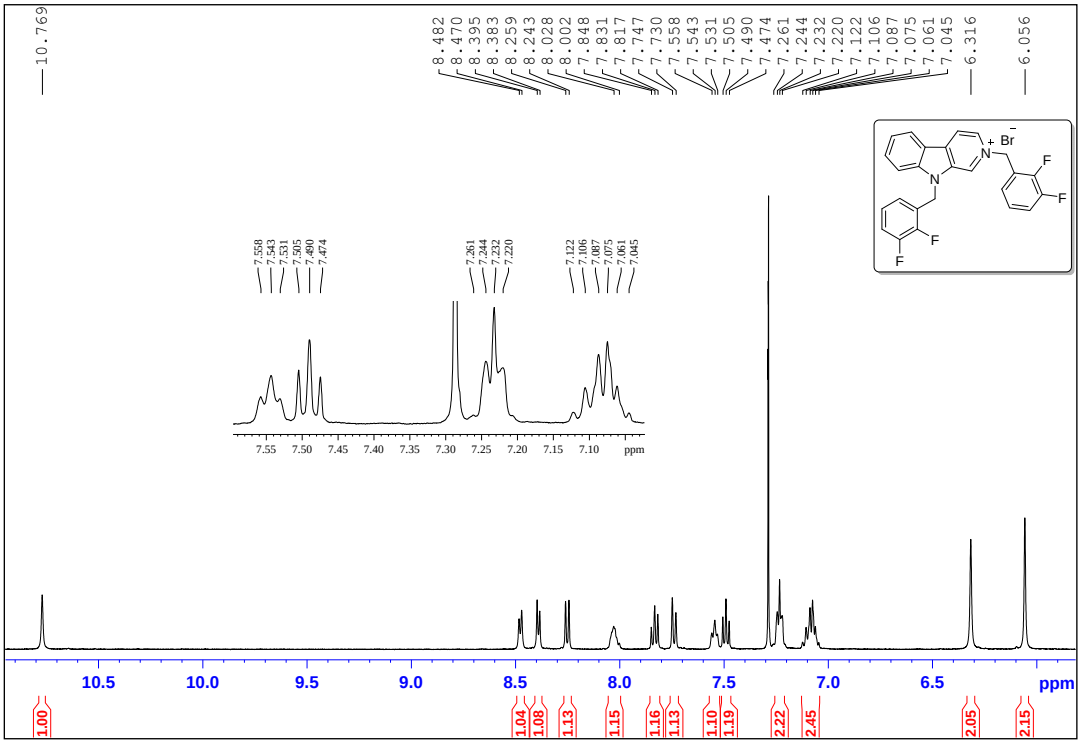
Appendix 2b. ^{13}C-NMR of compound **5c**



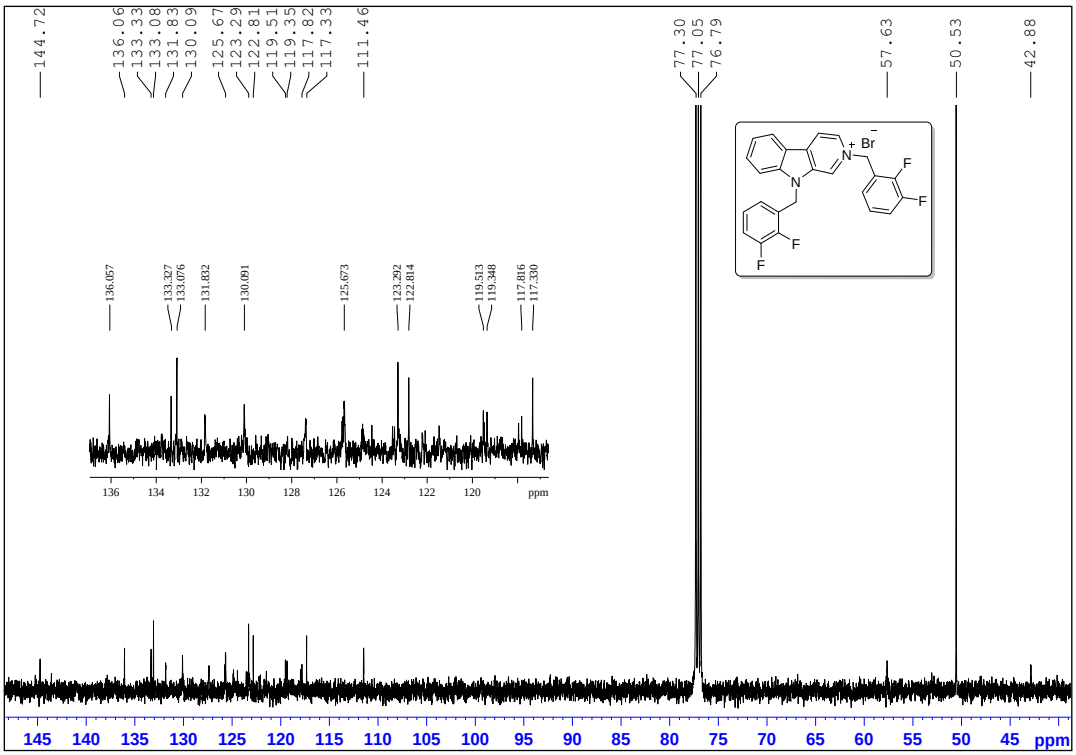
Appendix 2c. ESI-MS of compound **5c**



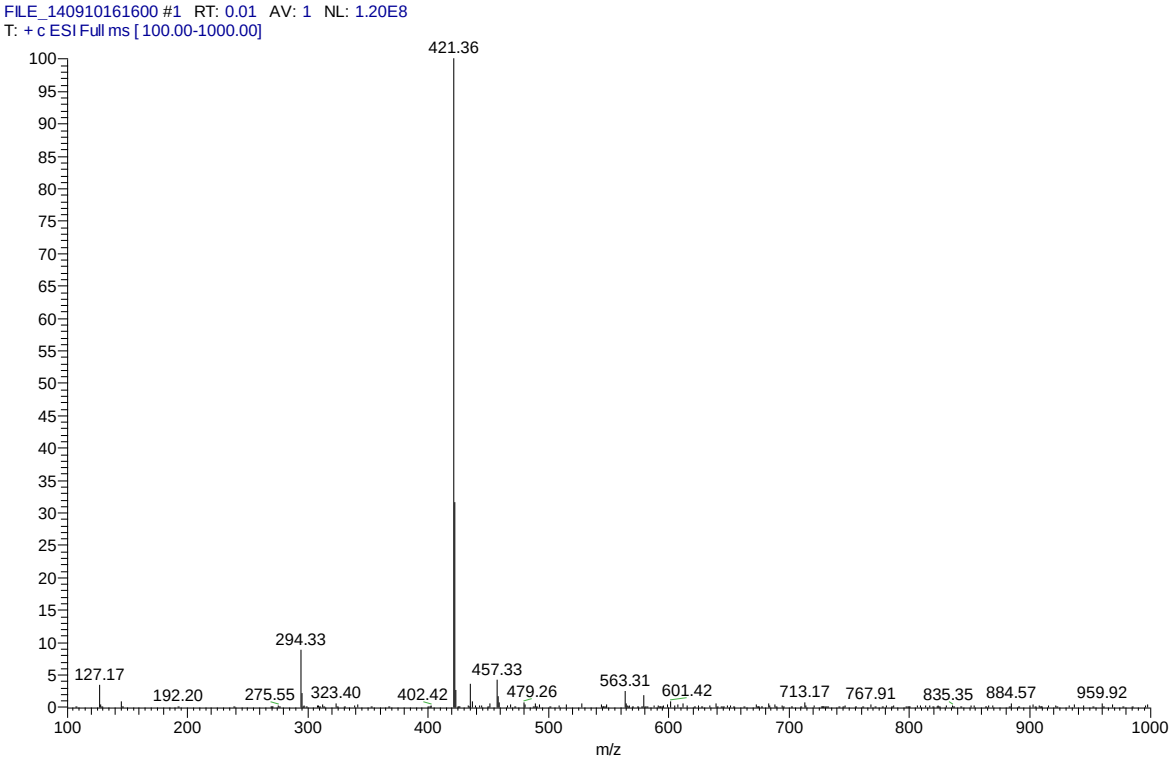
Appendix 3a. ^{1}H-NMR of compound **5d**



Appendix 3b. ^{13}C-NMR of compound **5d**



Appendix 3c. ESI-MS of compound **5d**



Appendix 4. Crystal structure and refinement data for compound **5b**

CCDC	1017043
Formula	$C_{25}H_{19}BrF_2N_2$
Formula Weight (gm·mole^{-1})	465.32
Temperature (K)	294
Wavelength (Å)	0.71073
Crystal System	Orthorhombic
Space group	$P2_12_12_1$
Unit cell (Å)	a = 7.4788 (13), b = 15.548 (3), c = 17.386 (3)
Volume (Å^3)	2021.7 (6)
Z	4
Calculated density (g·cm^{-3})	1.529
Absorption coefficient (mm^{-1})	2.066
***F*(000)**	944
Crystal size (mm)	0.10 × 0.11 × 0.38
Theta min – max (°)	1.8 – 30.3
Dataset	$-10 \leq h \leq 10$; $-21 \leq k \leq 21$; $-24 \leq l \leq 24$
Total/unique data/ R(int)	23396, 5984, 0.082
Observed data [I>2.0σ(I)]	4006
Data/parameters	5984, 271
R/wR2/Goodness-of-fit	0.0483, 0.1285, 1.01
Flack x	0.021 (9)
Largest diff. peak and hole e·Å^{-3}	-0.60, 0.91

Appendix 5. Crystal structure and refinement data of compound **5c**

CCDC	**XXXXXX**
Formula	$C_{25}H_{19}BrF_2N_2$
Formula Weight (gm·mole^{-1})	465.33
Temperature (K)	297
Wavelength (Å)	0.71073
Crystal System	Monoclinic
Space group	$P2_1/c$
Unit cell (Å), β (°)	a = 7.0818 (7), b = 16.3554 (16), c = 17.5419 (17), β = 100.466 (2)
Volume (Å^3)	1998.0 (3)
Z	4
Calculated density (g·cm^{-3})	1.547
Absorption coefficient (mm^{-1})	2.09
***F*(000)**	944
Crystal size (mm)	0.51 × 0.19 × 0.10
Theta min – max (°)	1.7 – 27.6
Dataset	$-9 \leq h \leq 9$; $-20 \leq k \leq 21$; $-22 \leq l \leq 22$
Total/unique data/ R(int)	17031, 4585, 0.036
Observed data [I>2.0σ(I)]	3062
Data/parameters	4585, 271
R/wR2/Goodness-of-fit	0.121, 0.344, 2.30
Largest diff. peak and hole e·Å^{-3}	-1.73, 1.50

Appendix 6. Crystal structure and refinement data of compound **5d**

CCDC	**XXXXXX**
Formula	$C_{25}H_{17}BrF_4N_2$
Formula Weight (gm·mole^{-1})	501.31
Temperature (K)	294
Wavelength (Å)	0.71073
Crystal System	Monoclinic
Space group	$C2/c$
Unit cell (Å), β (°)	a = 21.0117 (17), b = 15.4135 (12), c = 13.0639 (11), β = 95.4101 (19)
Volume (Å^3)	4212.1 (6)
Z	8
Calculated density (g·cm^{-3})	1.581
Absorption coefficient (mm^{-1})	2.00
***F*(000)**	2016
Crystal size (mm)	0.44 × 0.31 × 0.23
Theta min – max (°)	1.6 – 27.6
Dataset	$-27 \leq h \leq 27$; $-20 \leq k \leq 20$; $-16 \leq l \leq 15$
Total/unique data/ R(int)	18782, 4833, 0.030
Observed data [I>2.0σ(I)]	3394
Data/parameters	4833, 291
R/wR2/Goodness-of-fit	0.052, 0.159, 1.02
Largest diff. peak and hole e·Å^{-3}	-0.39, 0.79

CONCLUSION

A series of new N^2,N^9-benzylated quaternary β-carbolin-3-ium salt derivatives (**5a-d**) were successfully synthesized from ethyl-β-carboline-3-carboxylate (**4**) via Krapcho decarboxylation under refluxing conditions with good to excellent yields (81 – 95%). Further mechanism study shall be carried out to reveal the mechanism of the transformation in the presence of NaH and anhydrous DMF in the reaction.

ACKNOWLEDGMENT

The authors gratefully acknowledge the Research University Grant Scheme of Universiti Sains Malaysia (RUT-USM) for financial support. Mazlin Mohideen is thankful to the Ministry of Education Malaysia (KPM), for the provision of research scholarship (MyPhD).

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