1	Supplementary Material
2	New Lanostane-Type Triterpenes with Anti-Inflammatory Activity from the
3	Epidermis of Wolfporia cocos
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11	ABSTRACT
12	A chemical study on the epidermis of cultivated edible mushroom Wolfiporia cocos resulted in the
13	isolation and identification of 46 lanostane triterpenoids, containing 17 new compounds (1-17). An
14	experimental determination of their anti-inflammatory activity showed that poricoic acid GM (39) most
15	strongly inhibited NO production in LPS-induced RAW264.7 murine macrophages with an $IC_{50}$ value
16	at 9.73 $\mu$ M. Furthermore, poricoic acid GM induced HO-1 protein expression and inhibited iNOS and
17	COX2 protein expression as well as the release of PGE <sub>2</sub> , IL-1 $\beta$ , IL-6, TNF- $\alpha$ and reactive oxygen
18	species (ROS) in LPS-induced RAW264.7 cells. Mechanistically, poricoic acid GM suppressed the
19	phosphorylation of the IkBa protein, which prevented NF-kB from entering the nucleus to lose
20	transcriptional activity and inhibited the dissociation of Keap1 from Nrf2, thereby activating Nrf2 into
21	the nucleus to regulate antioxidant genes. Furthermore, the MAPK signaling pathway may play a
22	significant role in poricoic acid GM-induced elimination of inflammation. This work further confirms
23	that lanostane triterpenoids are key ingredients responsible for the anti-inflammatory properties of the
24	edible medicinal mushroom W. cocos.
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- 26 *Keywords*: Wolfiporia cocos; triterpene acid; anti-inflammatory activity; NF-κB signaling pathway;
- 27 Keap1-Nrf2 signaling pathway; MAPK signaling pathway

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19       Figure S71. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 9       45         20       Figure S72. HRESIMS spectrum of compound 10       45         21       Figure S73. <sup>1</sup> H NMR spectrum (150 MHz, $C_5D_5N$ ) of compound 10       46         22       Figure S74. <sup>13</sup> C NMR spectrum (150 MHz, $C_5D_5N$ ) of compound 10       46         23       Figure S75. HSQC spectrum (600 MHz, $C_5D_5N$ ) of compound 10       47         24       Figure S76. HMBC spectrum (600 MHz, $C_5D_5N$ ) of compound 10       47         25       Figure S77. <sup>1</sup> H- <sup>1</sup> H COSY spectrum (600 MHz, $C_5D_5N$ ) of compound 10       48         26       Figure S78. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 10       48         27       Figure S79. HRESIMS spectrum of compound 11       49         28       Figure S80. <sup>1</sup> H NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 11       49         29       Figure S81. <sup>13</sup> C NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 11       50         30       Figure S84. <sup>1</sup> H- <sup>1</sup> H COSY spectrum (600 MHz, $C_5D_5N$ ) of compound 11       50         31       Figure S84. <sup>1</sup> H- <sup>1</sup> H COSY spectrum (600 MHz, $C_5D_5N$ ) of compound 11       51         32       Figure S84. <sup>1</sup> H- <sup>1</sup> H COSY spectrum (600 MHz, $C_5D_5N$ ) of compound 11       51         33       Figure S84. <sup>1</sup> H COSY spectrum (600 MHz, $C_5D_5N$ ) of compound 11       52         34 <td>17</td> <td></td> <td></td>	17							
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26       Figure S78. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 10       48         27       Figure S79. HRESIMS spectrum of compound 11       49         28       Figure S80. <sup>1</sup> H NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 11       49         29       Figure S81. <sup>13</sup> C NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 11       50         30       Figure S82. HSQC spectrum (600 MHz, $C_5D_5N$ ) of compound 11       50         31       Figure S83. HMBC spectrum (600 MHz, $C_5D_5N$ ) of compound 11       51         32       Figure S84. <sup>1</sup> H- <sup>1</sup> H COSY spectrum (600 MHz, $C_5D_5N$ ) of compound 11       51         33       Figure S85. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 11       52         34       Figure S86. HRESIMS spectrum (600 MHz, $C_5D_5N$ ) of compound 12       52         35       Figure S87. <sup>1</sup> H NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 12       53         36       Figure S88. <sup>13</sup> C NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 12       53         37       Figure S89. HSQC spectrum (600 MHz, $C_5D_5N$ ) of compound 12       54         38       Figure S90. HMBC spectrum (600 MHz, $C_5D_5N$ ) of compound 12       54         39       Figure S91. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 12       54         39       Figure S92. HRESIMS spectrum (600 MHz, $C_5D_5N$ ) of compound 13       55         40       <								
27       Figure S79. HRESIMS spectrum of compound 11       49         28       Figure S80. <sup>1</sup> H NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 11       49         29       Figure S81. <sup>13</sup> C NMR spectrum (150 MHz, $C_5D_5N$ ) of compound 11       50         30       Figure S82. HSQC spectrum (600 MHz, $C_5D_5N$ ) of compound 11       50         31       Figure S83. HMBC spectrum (600 MHz, $C_5D_5N$ ) of compound 11       51         32       Figure S84. <sup>1</sup> H- <sup>1</sup> H COSY spectrum (600 MHz, $C_5D_5N$ ) of compound 11       51         33       Figure S85. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 11       52         34       Figure S86. HRESIMS spectrum of compound 12       52         35       Figure S86. HRESIMS spectrum (600 MHz, $C_5D_5N$ ) of compound 12       53         36       Figure S88. <sup>13</sup> C NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 12       53         37       Figure S88. <sup>13</sup> C NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 12       53         37       Figure S89. HSQC spectrum (600 MHz, $C_5D_5N$ ) of compound 12       54         38       Figure S90. HMBC spectrum (600 MHz, $C_5D_5N$ ) of compound 12       54         39       Figure S91. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 12       54         39       Figure S93. <sup>1</sup> H NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 13       55         40       Figure S93. <sup>1</sup>								
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30       Figure S82. HSQC spectrum (600 MHz, $C_5D_5N$ ) of compound 11       50         31       Figure S83. HMBC spectrum (600 MHz, $C_5D_5N$ ) of compound 11       51         32       Figure S84. <sup>1</sup> H- <sup>1</sup> H COSY spectrum (600 MHz, $C_5D_5N$ ) of compound 11       51         33       Figure S85. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 11       52         34       Figure S86. HRESIMS spectrum of compound 12       52         35       Figure S87. <sup>1</sup> H NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 12       53         36       Figure S88. <sup>13</sup> C NMR spectrum (150 MHz, $C_5D_5N$ ) of compound 12       53         37       Figure S89. HSQC spectrum (600 MHz, $C_5D_5N$ ) of compound 12       54         38       Figure S90. HMBC spectrum (600 MHz, $C_5D_5N$ ) of compound 12       54         39       Figure S91. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 12       55         40       Figure S91. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 12       55         41       Figure S93. <sup>1</sup> H NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 13       56         42       Figure S93. <sup>1</sup> H NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 13       56         43       Figure S94. <sup>13</sup> C NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 13       56         43       Figure S95. HSQC spectrum (600 MHz, $C_5D_5N$ ) of compound 13       56         43 <td< td=""><td></td><td></td><td></td></td<>								
31       Figure S83. HMBC spectrum (600 MHz, $C_5D_5N$ ) of compound 11.       51         32       Figure S84. <sup>1</sup> H- <sup>1</sup> H COSY spectrum (600 MHz, $C_5D_5N$ ) of compound 11.       51         33       Figure S85. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 11.       52         34       Figure S86. HRESIMS spectrum of compound 12.       52         35       Figure S87. <sup>1</sup> H NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 12.       53         36       Figure S88. <sup>13</sup> C NMR spectrum (150 MHz, $C_5D_5N$ ) of compound 12.       53         37       Figure S89. HSQC spectrum (600 MHz, $C_5D_5N$ ) of compound 12.       54         38       Figure S90. HMBC spectrum (600 MHz, $C_5D_5N$ ) of compound 12.       54         39       Figure S91. NOESY spectrum (600 MHz, $C_5D_5N$ ) of compound 12.       55         40       Figure S92. HRESIMS spectrum of compound 13.       55         41       Figure S93. <sup>1</sup> H NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 13.       56         42       Figure S93. <sup>1</sup> H NMR spectrum (600 MHz, $C_5D_5N$ ) of compound 13.       56         43       Figure S94. <sup>13</sup> C NMR spectrum (150 MHz, $C_5D_5N$ ) of compound 13.       56         43       Figure S95. HSQC spectrum (600 MHz, $C_5D_5N$ ) of compound 13.       56         43       Figure S95. HSQC spectrum (600 MHz, $C_5D_5N$ ) of compound 13.       57								
32       Figure S84. ${}^{1}$ H- ${}^{1}$ H COSY spectrum (600 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 11.       51         33       Figure S85. NOESY spectrum (600 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 11.       52         34       Figure S86. HRESIMS spectrum of compound 12.       52         35       Figure S87. ${}^{1}$ H NMR spectrum (600 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 12.       53         36       Figure S88. ${}^{13}$ C NMR spectrum (150 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 12.       53         37       Figure S89. HSQC spectrum (600 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 12.       54         38       Figure S90. HMBC spectrum (600 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 12.       54         39       Figure S91. NOESY spectrum (600 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 12.       55         40       Figure S92. HRESIMS spectrum of compound 13.       55         41       Figure S93. ${}^{1}$ H NMR spectrum (600 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 13.       56         42       Figure S94. ${}^{13}$ C NMR spectrum (600 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 13.       56         43       Figure S95. HSQC spectrum (600 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 13.       56         43       Figure S95. HSQC spectrum (600 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 13.       56         43       Figure S95. HSQC spectrum (600 MHz, C <sub>5</sub> D <sub>5</sub> N) of compound 13.       57								
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# 1. Materials and methods

# 1.1. General experimental procedures

UV spectra were recorded on a JASCO V-650 UV spectrophotometer. Optical rotations were measured on a JASCO P2000 automatic polarimeter. 1D- and 2D-NMR spectra were recorded on a Bruker Avance 600 spectrometer with solvent peaks as references. HRESIMS data were obtained with an Agilent 1290 Infinity liquid chromatography system and an Agilent 6540 UHD Accurate-Mass Q-TOF mass spectrometer. High-performance liquid chromatography (HPLC) data were recorded on an Agilent 1260 instrument equipped with a photo-diode array (PDA) and a YMC C<sub>18</sub> column ( $250 \times 4.6$  mm, 5  $\mu$ M). Preparative HPLC was performed on Sanotac instrument China with a UV detector and a YMC C<sub>18</sub> column ( $250 \times 20$  mm, 5  $\mu$ M). Column chromatographic separations were carried out with silica gel (200-300 mesh, Qingdao Marine Chemical Group Corporation, Qingdao, China), ODS ( $50 \mu$ M, YMC, Kyoto, Japan). TLC was conducted with glass precoated with silica gel GF254 (Yantai Chemical Industrial Institute, Yantai, China). Chromatographic grade methanol and acetonitrile were purchased from Fisher. All other solvents were of chemical grade (Da Mao Chemical Co. Ltd, Tianjin, China).

## 1.2. Extraction and isolation

## *1.2.1. Tuckahoacid A* (*1*)

White amorphous powder (MeOH);  $[\alpha]_{20}^{20}$ -22.00 (c 0.1, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 205 (0.70), 250 (1.12) nm; CD (c  $1.1 \times 10^{-3}$  M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 255 (3.46), 280 (-0.71) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see **Table 2**; HRESIMS m/z 519.3083 [M + Na]<sup>+</sup> (calcd for C<sub>31</sub>H<sub>44</sub>O<sub>5</sub>Na, 519.3086).

#### 1.2.2. Tuckahoacid B (2)

White amorphous powder (MeOH);  $[\alpha]_{D}^{20}$  +2.91 (c 0.3, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 222 (2.52), 270 (0.58) nm; CD (*c* 1.1 × 10<sup>-3</sup> M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 263 (2.27) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see **Table 2**; HRESIMS m/z 513.3229 [M - H]<sup>-</sup> (calcd for C<sub>31</sub>H<sub>45</sub>O<sub>6</sub>, 513.3216).

#### *1.2.3. Tuckahoacid C*(**3**)

White amorphous powder (MeOH);  $[\alpha]_{D}^{20}$  -11.20 (c 0.1, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 228 (2.75), 268 (0.58) nm; CD (c  $1.1 \times 10^{-3}$  M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 272 (6.87) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see **Table 2**; HRESIMS m/z 513.3230 [M - H]<sup>-</sup> (calcd for C<sub>31</sub>H<sub>45</sub>O<sub>6</sub>, 513.3216).

### 1.2.4. Tuckahoacid D (4)

White amorphous powder (MeOH);  $[\alpha]_{D}^{20}$  -11.33 (c 0.2, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 211 (1.49), 252 (2.03) nm; CD (*c* 1.1 × 10<sup>-3</sup> M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 201 (20.93), 253 (-20.61) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see **Table 2**; HRESIMS *m*/*z* 515.3385 [M - H]<sup>-</sup> (calcd for C<sub>31</sub>H<sub>47</sub>O<sub>6</sub>, 515.3373).

## 1.2.5. Tuckahoacid E (5)

White amorphous powder (MeOH);  $[\alpha]_{D}^{20}$  -2.67 (c 0.2, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 197 (0.07), 251 (0.28) nm; CD (*c* 1.1 × 10<sup>-3</sup> M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 198 (8.06), 251 (-10.40) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see  $\delta_{C}$  21.4 (3-CH<sub>3</sub>CO), 170.8 (3-CH<sub>3</sub>CO) and **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see  $\delta_{H}$  2.04 (3H, s, 3-CH<sub>3</sub>CO) and **Table 2**; HRESIMS *m*/*z* 581.3451 [M + Na]<sup>+</sup> (calcd for C<sub>33</sub>H<sub>50</sub>O<sub>7</sub>Na, 581.3454).

#### 1.2.6. Tuckahoacid F (6)

White amorphous powder (MeOH);  $[\alpha]_{D}^{20}$  +1.5 (c 0.2, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 218 (2.66), 270 (2.00) nm; CD (*c* 1.1 × 10<sup>-3</sup> M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 269 (1.55) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see **Table 2**; HRESIMS *m/z* 499.3072 [M - H]<sup>-</sup> (calcd for C<sub>30</sub>H<sub>43</sub>O<sub>6</sub>, 499.3060).

## *1.2.7. Tuckahoacid G* (7)

White amorphous powder (MeOH);  $[\alpha]_{D}^{20}$  -10.29 (c 0.2, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 197 (0.08), 245 (0.40) nm; CD (*c* 1.1 × 10<sup>-3</sup> M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 202 (11.87), 245 (-4.34) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see  $\delta_{C}$  55.7 (12-OCH<sub>3</sub>) and **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see  $\delta_{H}$  3.49 (3H, s, 12-OCH<sub>3</sub>) and **Table 2**; HRESIMS m/z 515.3384 [M - H]<sup>-</sup> (calcd for C<sub>31</sub>H<sub>47</sub>O<sub>6</sub>, 515.3373).

## 1.2.8. Tuckahoacid H (8)

White amorphous powder (MeOH);  $[\alpha]_{D}^{20}$  -10.7 (c 0.2, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 211 (0.86), 245 (1.23) nm; CD (*c* 1.1 × 10<sup>-3</sup> M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 202 (11.07), 246 (-8.13) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see  $\delta_{C}$  55.7 (12-OCH<sub>3</sub>) and **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see  $\delta_{H}$  3.54 (3H, s, 12-OCH<sub>3</sub>) and **Table 2**; HRESIMS *m*/*z* 517.3544 [M - H] (calcd for C<sub>31</sub>H<sub>49</sub>O<sub>6</sub>, 517.3529).

## 1.2.9. Tuckahoacid I (9)

White amorphous powder (MeOH);  $[\alpha]_{2^0}^{2^0}$  -11.00 (c 0.1, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 198 (0.22), 244 (2.68) nm; CD (*c* 1.1 × 10<sup>-3</sup> M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 202 (15.29), 240 (-8.94) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see  $\delta_C$  55.7 (12-OCH<sub>3</sub>) and **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see  $\delta_H$  3.51 (3H, s, 12-OCH<sub>3</sub>) and **Table 2**; HRESIMS m/z 517.3540 [M - H]<sup>-</sup> (calcd for C<sub>31</sub>H<sub>49</sub>O<sub>6</sub>, 517.3529).

# 1.2.10. Tuckahoacid J (10)

White amorphous powder (MeOH);  $[\alpha]_D^{20} + 11.00$  (c 0.2, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 216 (2.22), 240 (0.37) nm; CD (c  $1.1 \times 10^{-3}$  M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 240 (7.48) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see  $\delta_C$  51.7 (3-COOCH<sub>3</sub>), 50.5 (25-OCH<sub>3</sub>) and **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see  $\delta_H$  3.62 (3H, s, 3-COOCH<sub>3</sub>),  $\delta_H$  3.04 (3H, s, 25-OCH<sub>3</sub>) and **Table 3**; HRESIMS m/z 565.3508 [M + Na]<sup>+</sup> (calcd for C<sub>33</sub>H<sub>50</sub>O<sub>6</sub>Na, 565.3505).

### 1.2.11. Tuckahoacid K (11)

White amorphous powder (MeOH);  $[\alpha]_{D}^{20}$  +6.29 (c 0.2, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 196 (0.08), 242 (0.26) nm; CD (c  $1.1 \times 10^{-3}$  M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 240 (4.51) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see  $\delta_{C}$  51.8 (3-COOCH<sub>3</sub>) and **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see  $\delta_{H}$  3.63 (3H, s, 3-COOCH<sub>3</sub>) and **Table 3**; HRESIMS *m*/*z* 511.3434 [M - H]<sup>-</sup> (calcd for C<sub>32</sub>H<sub>47</sub>O<sub>5</sub>, 511.3423).

## 1.2.12. Tuckahoacid L (12)

White amorphous powder (MeOH);  $[\alpha]_D^{20}$  -33.00 (c 0.1, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 202 (0.25), 242 (0.72) nm; CD (c  $1.1 \times 10^{-3}$  M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 241 (4.08) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see  $\delta_C$  51.8 (3-COOCH<sub>3</sub>) and **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see  $\delta_H$  3.62 (3H, s, 3-COOCH<sub>3</sub>) and **Table 3**; HRESIMS m/z 543.3337 [M - H]<sup>-</sup> (calcd for C<sub>32</sub>H<sub>47</sub>O<sub>7</sub>, 543.3322).

#### 1.2.13. Tuckahoacid M (13)

White amorphous powder (MeOH);  $[\alpha]_{D}^{20}$  -28.00 (c 0.1, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 205 (0.51), 242 (1.13) nm; CD (c  $1.1 \times 10^{-3}$  M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 241 (9.68) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see  $\delta_{C}$  51.7 (3-COOCH<sub>3</sub>) and **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data,

see  $\delta_{\rm H}$  3.62 (3H, s, 3-COOCH<sub>3</sub>) and **Table 3**; HRESIMS *m*/*z* 543.3334 [M - H]<sup>-</sup> (calcd for C<sub>32</sub>H<sub>47</sub>O<sub>7</sub>, 543.3322).

#### 1.2.14. Tuckahoacid N (14)

White amorphous powder (MeOH);  $[\alpha]_{2^0}^{2^0} +10.00$  (c 0.1, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 242 (1.44), 288 (0.87) nm; CD (c  $1.1 \times 10^{-3}$  M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 222 (4.21), 250 (-0.54), 290 (6.70) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see  $\delta_C$  51.8 (3-COOCH<sub>3</sub>) and **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see  $\delta_H$  3.62 (3H, s, 3-COOCH<sub>3</sub>) and **Table 3**; HRESIMS *m*/*z* 545.3487 [M - H]<sup>-</sup> (calcd for C<sub>32</sub>H<sub>49</sub>O<sub>7</sub>, 545.3478).

#### 1.2.15. Tuckahoacid O (15)

White amorphous powder (MeOH);  $[\alpha]_{D}^{20}$  +9.6 (c 0.1, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 242 (0.47), 289 (0.30) nm; CD (*c* 1.1 × 10<sup>-3</sup> M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 220 (3.98), 243 (-2.03), 292 (6.50) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see  $\delta_{C}$  51.8 (3-COOCH<sub>3</sub>) and **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see  $\delta_{H}$  3.63 (3H, s, 3-COOCH<sub>3</sub>) and **Table 3**; HRESIMS *m*/*z* 561.3438 [M - H]<sup>-</sup> (calcd for C<sub>32</sub>H<sub>49</sub>O<sub>8</sub>, 561.3427).

### 1.2.16. Tuckahoacid P (16)

White amorphous powder (MeOH);  $[\alpha]_{20}^{20}$  +2.67 (c 0.1, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 242 (0.63), 290 (0.39) nm; CD (c 1.1 × 10<sup>-3</sup> M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 221 (5.00), 251 (-0.60), 289 (6.48) nm; <sup>13</sup>C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see  $\delta_C$  51.8 (3-COOCH<sub>3</sub>) and **Table 1**; <sup>1</sup>H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see  $\delta_H$  3.63 (3H, s, 3-COOCH<sub>3</sub>) and **Table 3**; HRESIMS m/z 585.3396 [M + Na]<sup>+</sup> (calcd for C<sub>32</sub>H<sub>50</sub>O<sub>8</sub>Na, 585.3403).

## 1.2.17. Tuckahoacid Q (17)

White amorphous powder (MeOH);  $[\alpha]_{D}^{20}$  +4.67 (c 0.2, MeOH); UV (MeOH)  $\lambda_{max}$  (log  $\varepsilon$ ) = 214 (2.17), 267 (0.19) nm; CD (*c* 1.1 × 10<sup>-3</sup> M, MeOH)  $\lambda_{max}$  ( $\Delta \varepsilon$ ) = 200 (-5.08), 207 (0.98), 214 (-4.17), 227 (2.09) nm; {}^{13}C NMR (C<sub>5</sub>D<sub>5</sub>N, 150 MHz) data, see **Table 1**; {}^{1}H NMR (C<sub>5</sub>D<sub>5</sub>N, 600 MHz) data, see **Table 3**; HRESIMS m/z 497.3278 [M - H]<sup>-</sup> (calcd for C<sub>31</sub>H<sub>45</sub>O<sub>5</sub>, 497.3267).

# 1.3. Cell culture

RAW264.7 murine macrophages were obtained from the Chinese Academy of Sciences (Shanghai, China) and cultured in Dulbecco's Modified Eagle Medium (DMEM, Gibco, USA) with 4.5 g/L glucose, 10% fetal bovine serum (FBS, Gibco, USA), and 1% penicillin/streptomycin (Gibco, USA) in a cell incubator (37 °C and 5% CO<sub>2</sub>).

## 1.4. Cell viability assay

Briefly, RAW264.7 cells (10000 cells/well) were seeded into a 96-well plate and incubated overnight at 37 °C. The tested compounds were added to the cells, dimethyl sulfoxide (DMSO) was used as the vehicle control. Following incubation for 24 h, 20  $\mu$ L of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT, Sigma-Aldrich, USA) agent was added to cells, and then incubated for 4 h at 37 °C. Next, the absorbance at 570 nm was recorded using a microplate reader (Thermo Fisher, Waltham, USA).

# 1.5. Detection of NO, PGE<sub>2</sub>

In brief, RAW264.7 cells were seeded into a 96-well plate at a density of 10000 cells/well, and then incubated overnight. Next, cells were pre-treated with the tested compounds at the

indicated concentrations for 1 h and followed by stimulation of LPS (200 ng/mL, isolated from *Escherichia coli* 055: B5, Sigma, Shanghai, China) for another 24 h. Subsequently, the culture medium was collected, and centrifuged for 5 min at 4 °C (1,000 rpm). The supernatants were used to measure the NO levels using Griess reagent (Beyotime, Shanghai, China). On the other hand, the level of PGE<sub>2</sub> in the supernatants was then assessed using ELISA kits according to the manufacturer's protocols (R&D Systems, Minneapolis, MN, USA).

# 1.6. Immunofluorescent

RAW264.7 cells were seeded into a 24-well plate at a density of  $2.5 \times 10^5$  cells/well, and incubated overnight. Then, cells were pre-treated with the tested compounds for 1 h and followed stimulation of LPS (200 ng/mL) for another 1 h. Cells were washed with PBS, fixed with 4% paraformaldehyde (PFA) for 10 min, and permeabilized with 0.5% Triton X-100 for 20 min at RT. Next, cells were blocked with 1% bovine serum albumin (BSA) for 30 min at RT and incubated with primary antibody (1:100) overnight at 4°C. After washing with PBS thrice, cells were incubated with FITC fluorescent secondary antibody (1:1000) for 1 h in the darkroom at RT. The nucleuses were then stained with Hoechst 33258 (DAPI, 0.5 μg/mL, Beyotime, Shanghai, China) for 15 min in the darkroom at RT. Finally, the subcellular localizations of NF-κB and Nrf2 were observed using the Fluorescent inverted microscope (Olympus, Japan).

# 1.7. qRT-PCR

In brief, RAW264.7 cells were seeded into a 24-well plate at a density of  $2.5 \times 10^5$  cells/mL and then incubated overnight. Next, cells were pre-treated with the tested compounds at the indicated concentrations for 1 h and followed by stimulation of LPS (200 ng/mL) for another 4 h. Total RNA was extracted with TRIzol kit (Invitrogen, USA). According to the instructions, 2  $\mu$ g RNA as template was added into HiScript II Q RT Supermix (Nanjing Nuowizan Biological Technology, China) for qPCR reverse transcription to obtain cDNA. The cDNA samples were amplified by Transstart Top Green qPCR Supermix (Beijing Quansi Gold Biotechnology, China) at a final volume of 20  $\mu$ L. qRT-PCR was performed using Thermo Scientific Pikoreal (Thermo Fisher Scientific, MA, USA). Real-time PCR primers were designed and synthesized by Shanghai Sangon Co., Ltd. The sequences of the primers were listed in Table S3.

# 1.8. Western blotting

Following treatment with the tested compounds, RAW264.7 cells were washed with phosphate buffered solution (PBS) and then lysed with pre-cold radio-immunoprecipitation assay (RIPA) buffer containing 1% protease and phosphatase inhibitors (ApexBio, USA). After centrifuging for 5 min at 4 °C (12,000 rpm), the supernatants were collected, mixed with loading buffer, and then boiled at 100 °C for 5 min. Next, the cell lysates were subjected to sodium dodecyl sulfate polyacrylamide gel (SDS-PAGE) electrophoresis. The proteins were then transferred to the polyvinylidene difluoride (PVDF) membranes (Millipore, Bedford, USA). The membranes were blocked with tris-buffered saline with tween 20 (TBST) buffer containing 5% non-fat milk powder and incubated with specific primary antibodies (1:1000) overnight at 4 °C. After washing with TBST buffer 3 times, the membranes were incubated with horseradish peroxidase (HRP)-labeled secondary antibody for 1 h at room temperature (RT). Next, the membranes were washed with TBST buffer thrice, and the immunoblot signals were detected in the Gel DOC<sup>TM</sup> XR+system using a chemiluminescence agent (Beyotime, Shanghai, China). The antibodies used in this experiment were as follows: Primary antibody against iNOS was purchased from Abcam (USA), Primary antibody against COX2, JNK, and LaminB were from ProteinTech Group (USA), the remaining antibodies were purchased from Santa Cruz (Shanghai, China).

## **1.9.** Statistical analysis

All results were representative of three independent experiments. Data were expressed as mean values  $\pm$  standard deviation (SD). Statistical analyses were performed with GraphPad Prism 5.0 software (La Jolla, CA, USA), and compared by One-way ANOVA. The differences were considered statistically significant when p < 0.05.

## 1.10. ECD calculation

In general, conformational analyses were carried out via random searching in the Sybyl-X 2.0 using the MMFF94S force field with an energy cutoff of 5 kcal/mol.<sup>1</sup> The results showed five lowest energy conformers for both compounds. Subsequently, geometry optimizations and frequency analyses were implemented at the B3LYP-D3(BJ)/6-31G\* level in PCM methanol using ORCA4.2.1<sup>2,3</sup> All conformers used for property calculations in this work were characterized to be a stable point on potential energy surface (PES) with no imaginary frequencies. The excitation energies, oscillator strengths, and rotational strengths (velocity) of the first 60 excited states were calculated using the TD-DFT methodology at the PBE0/def2-TZVP level in methanol. The ECD spectra were simulated by the overlapping Gaussian function (half the bandwidth at 1/e peak height, sigma = 0.30 for all).<sup>4</sup> Gibbs free energies for conformers were determined by using thermal correction at B3LYP-D3(BJ)/6-31G\* level and electronic energies evaluated at the wB97M-V/def2-TZVP level in PCM methanol using ORCA4.2.1<sup>2,3</sup> To get the final spectra, the simulated spectra of the conformers were averaged according to the boltzmann distribution theory and their relative Gibbs free energy ( $\Delta G$ ). By comparing the experimental spectra with the calculated model molecules, the absolute configuration of the only chiral center was determined to be.

## References

(1) Sybyl Software, version X 2.0; Tripos Associates Inc.: St. Louis, MO, 2013.

(2) Neese, F. The ORCA program system, Wiley Interdiscip. Rev.: *Comput. Mol. Sci.*, **2012**, *2*, 73-78.

(3) Neese, F. Software update: the ORCA program system, version 4.0, Wiley Interdiscip. Rev.: *Comput. Mol. Sci.* **2017**, *8*, e1327.

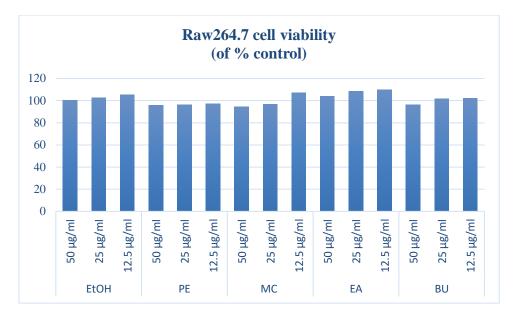
(4) Stephens, P. J.; Harada, N. ECD cotton effect approximated by the Gaussian curve and other methods. *Chirality* **2010**, *22*, 229–233.

## 1.11. The crystallization condition

5 mg of compound and 500  $\mu$ L of MeOH were added into the vitric autosampler bottle and dissolved completely. The saturation of the compound was beneficial, sometimes we could add some drops of water. Parafilm was used to seal the bottle. We poked two eyelets at the parafilm with the needle. The vitric autosampler bottle should be put in low temperature environment and the solvent should volatilize slowly.

Samples	Concentration	RAW264.7 cell viability
Samples	$(\mu g/mL)$	(of % control)
	50	100.5
EtOH extract	25	102.5
	12.5	105.4
	50	95.7
PE	25	96.1
	12.5	97.1
	50	94.4
MC	25	96.5
	12.5	107.0
	50	103.9
EA	25	108.5
	12.5	109.9
	50	96.1
BuOH	25	101.6
	12.5	102.2

**Table S1.** Cell viability of the EtOH extract and solvent-partitioned fractions in RAW264.7 macrophages.



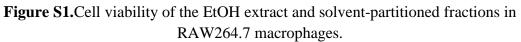
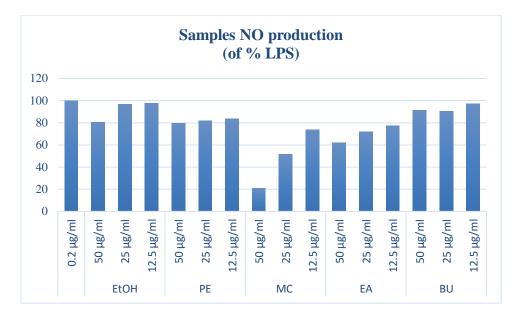
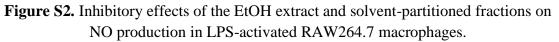


Table S2. Inhibitory effects of the EtOH extract and solvent-partitioned fractions on
NO production in LPS-activated RAW264.7 macrophages.

	Concentration	NO production	
Samples	(µg/mL)	(of % LPS)	
LPS	0.2	100	
	50	80.3	
EtOH extract	25	96.5	
	12.5	97.8	
	50	79.6	
PE	25	81.7	
	12.5	83.6	
	50	21.1	
MC	25	51.8	
	12.5	73.9	
	50	61.8	
EA	25	71.9	
	12.5	77.2	
	50	91.3	
BuOH	25	90.4	
	12.5	97.2	





Gene	Sequence (5' to 3')
:NOC	F: AGCCAAGCCCTCACCTACTT
iNOS	R: GCCTCCAATCTCTGCCTATC
COX-2	F: CCAGCACTTCACCCATCAGT
COX-2	R: GGGATACACCTCTCCACCAA
TNF-α	F: CAGACCCTCACACTCAGATCATCTT
Imr-a	R: CAGAGCAATGACTCCAAAGTAGACCT
IL-6	F: CACGGCCTTCCCTACTTCAC
IL-0	R: TGCAAGTGCATCATCGTTGT
II 10	F: GTTGACGGACCCCAAAAGAT
IL-1β	R: CCTCATCCTGGAAGGTCCAC
β-actin	F: ATGTGGATCAGCAAGCAGGA
p-actin	R: AAGGGTGTAAAACGCAGCTCA
Nrf2	F: TCAGCGACAGAAGGACTATGAG
INI12	R: AGGCATCTTGTTTGGGAATG
Keap1	F: TCTCCAAGGGTCTCCTGAAT
Keapi	R: CAACACCACCAACATTTACA
HO-1	F: GCCAGCCACAGCACTAT
110-1	R: GGCGGTCTTAGCCTCTTCTG
NOO1	F: AGTGGCATCCTGCGTTTCT
ngui	R: TCTCCTCCCAGACGGTTTC

Table S3.	Thog	oguonoog	of the	nrimara
Table 55.	THE S	equences	or the	primers.

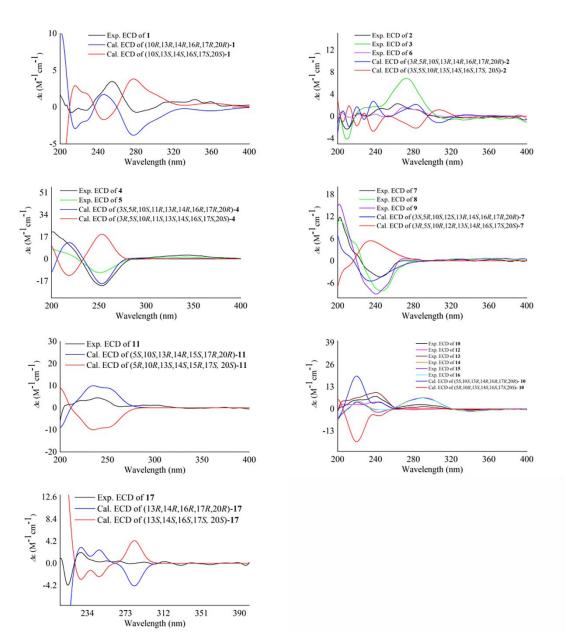


Figure S3. Experimental ECD and calculated ECD spectra of new compounds.

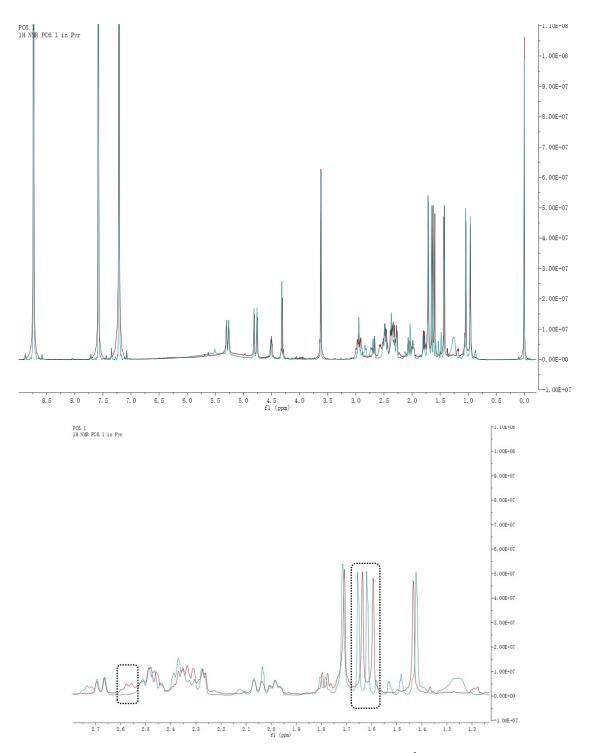
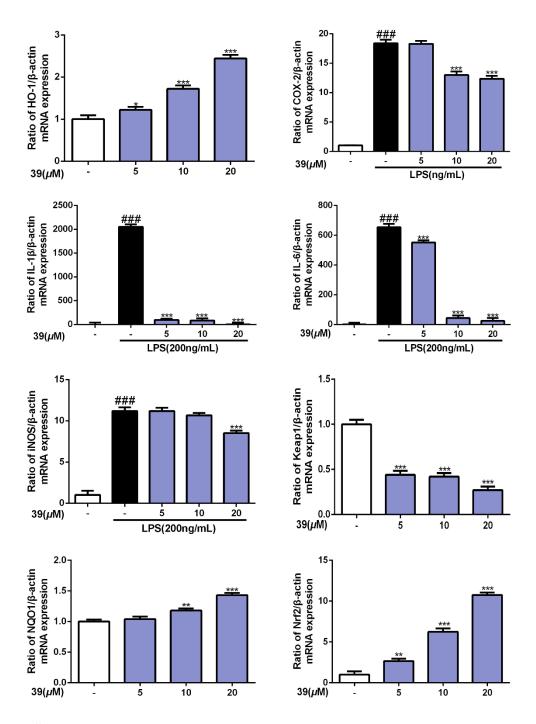
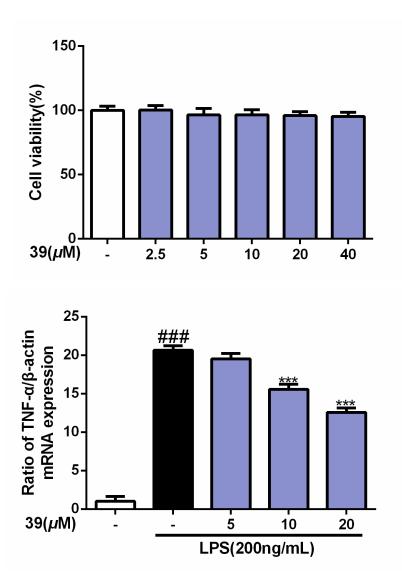


Figure S4. The stack graph of compounds 15 and 16 <sup>1</sup>H NMR spectra.



**Figure S5**. RAW264.7 cells were treated with poricoic acid GM (**39**) from 5 to 20  $\mu$ M at the indicated dose with stimulated by LPS (200 ng/mL) for 4 h. The mRNA of iNOS, COX-2, TNF- $\alpha$ , IL-1 $\beta$  and IL-6 and  $\beta$ -actin was detected by RT-PCR with specific primers. The amplified DNA fragment was analyzed by 1% agarose gel and visualized by ethidium bromide staining. Effects of poricoic acid GM (**39**) on Nrf2, HO-1, Keap1 and NQO1 gene expressions in RAW264.7 cells. The cells were treated with poricoic acid GM (**39**) (5, 10 and 20  $\mu$ M) for 4 h. Data shown are the means ± SD from three independent experiments, \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001 vs LPS-treated group and ###p < 0.001 vs control group.



**Figure S6**. RAW264.7 cells were seeded on 96 well plates and treated with different concentrations of poricoic acid GM (**39**) (2.5, 5, 10, 20, 40  $\mu$ M) for 24 h. MTT was added to detect the cell survival rate. RAW264.7 cells were treated with poricoic acid GM (**39**) from 5 to 20  $\mu$ M at the indicated dose with stimulated by LPS (200 ng/mL) for 4 h. The mRNA of TNF- $\alpha$  and  $\beta$ -actin was detected by RT-PCR with specific primers. The amplified DNA fragment was analyzed by 1% agarose gel and visualized by ethidium bromide staining. Data shown are the means  $\pm$  SD from three independent experiments, \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001 vs LPS-treated group and ###p < 0.001 vs control group.

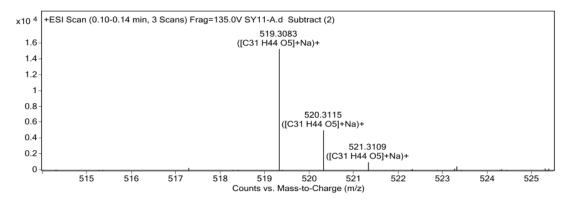


Figure S7. HRESIMS spectrum of compound 1

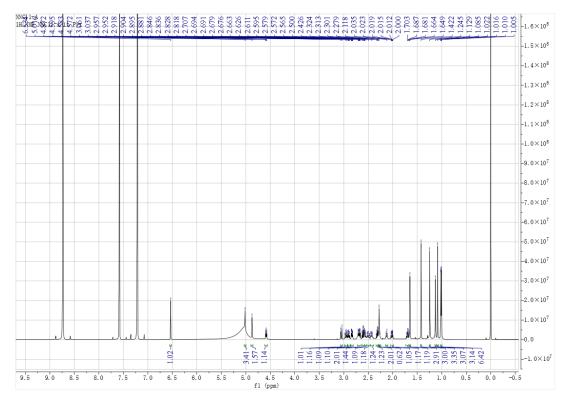


Figure S8. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 1

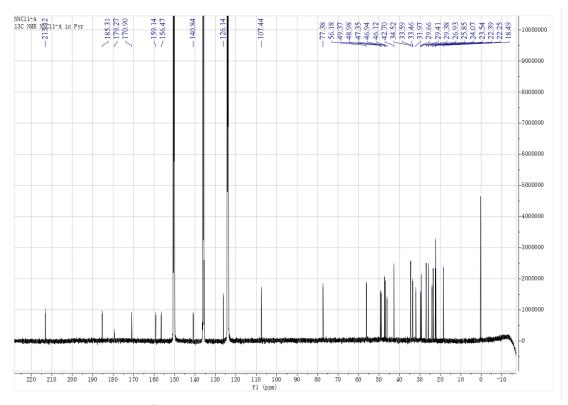


Figure S9. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 1

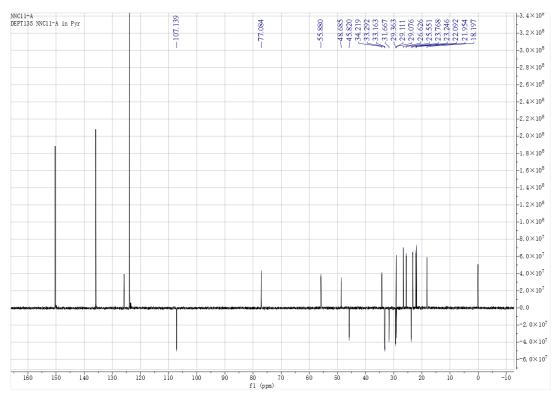


Figure S10. DEPT 135° spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 1

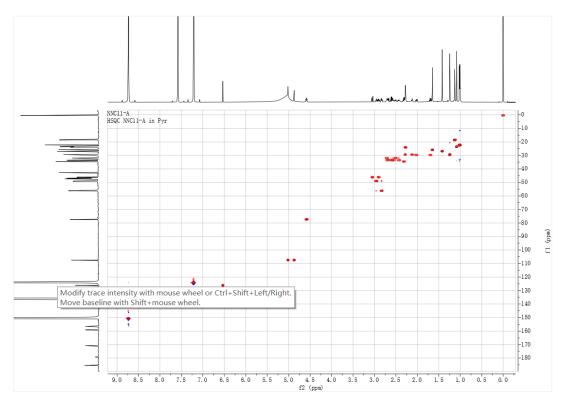


Figure S11. HSQC spectrum (600 MHz,  $C_5D_5N$ ) of compound 1

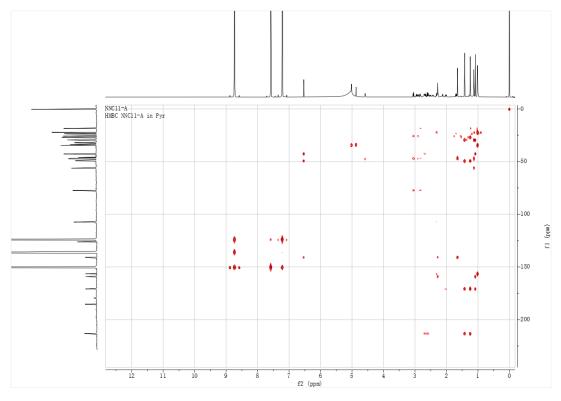


Figure S12. HMBC spectrum (600 MHz,  $C_5D_5N$ ) of compound 1

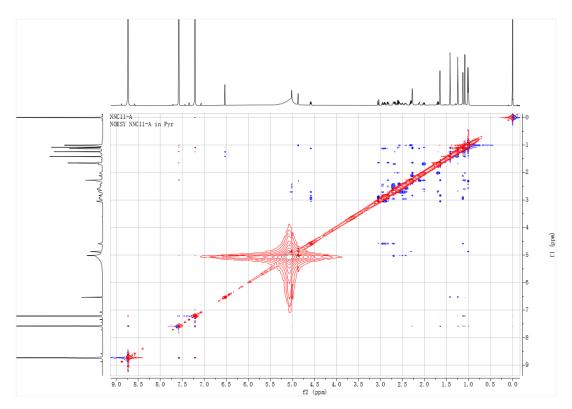


Figure S13. NOESY spectrum (600 MHz, C5D5N) of compound 1

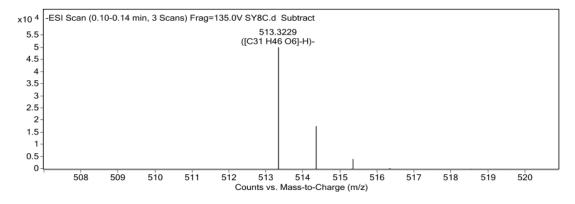


Figure S14. HRESIMS spectrum of compound 2

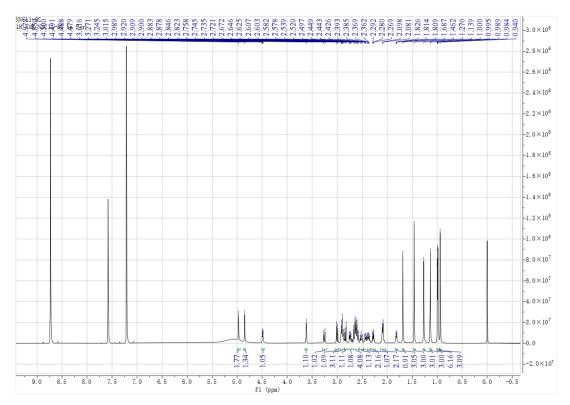


Figure S15. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 2

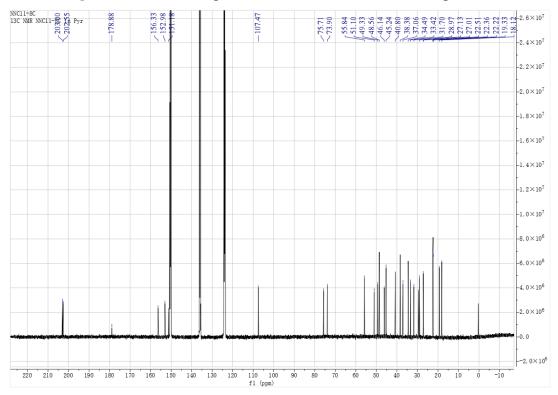


Figure S16. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 2

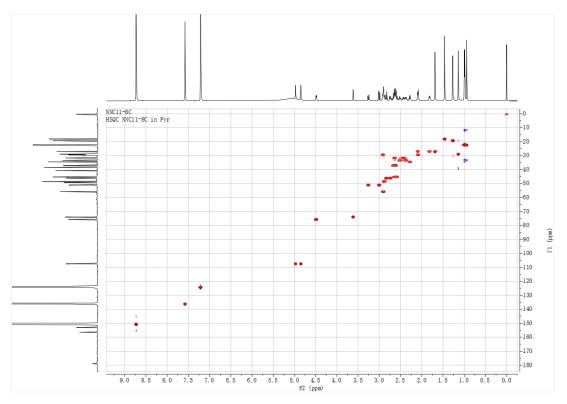


Figure S17. HSQC spectrum (600 MHz,  $C_5D_5N$ ) of compound 2

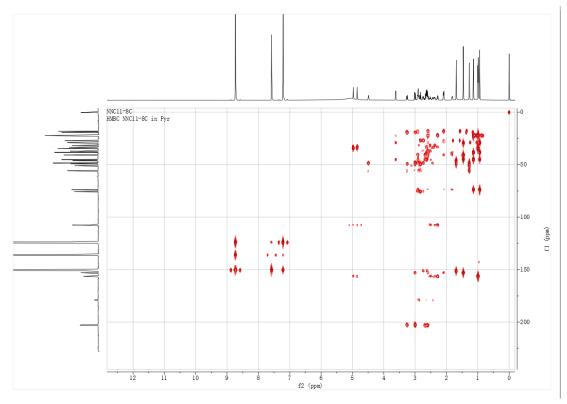


Figure S18. HMBC spectrum (600 MHz,  $C_5D_5N$ ) of compound 2

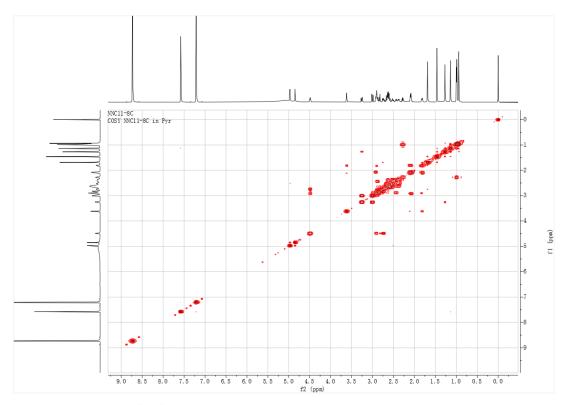


Figure S19.  $^{1}\text{H}$ - $^{1}\text{H}$  COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 2

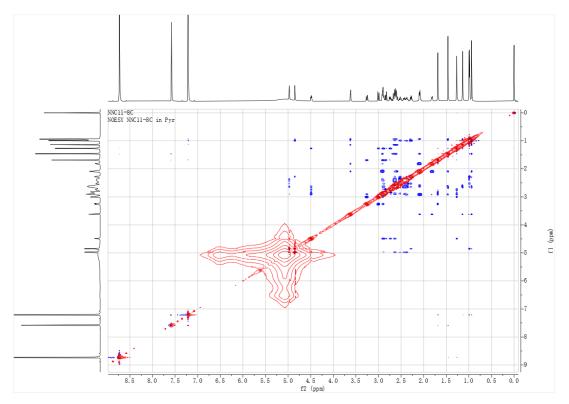


Figure S20. NOESY spectrum (600 MHz,  $C_5D_5N$ ) of compound 2

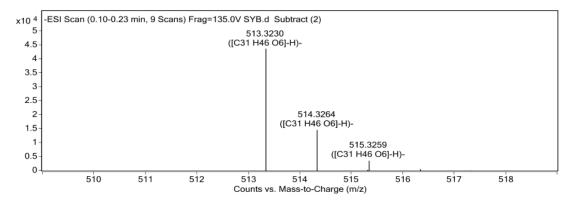


Figure S21. HRESIMS spectrum of compound 3

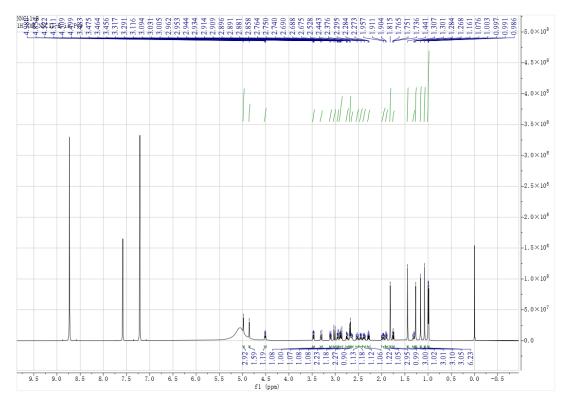


Figure S22. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 3

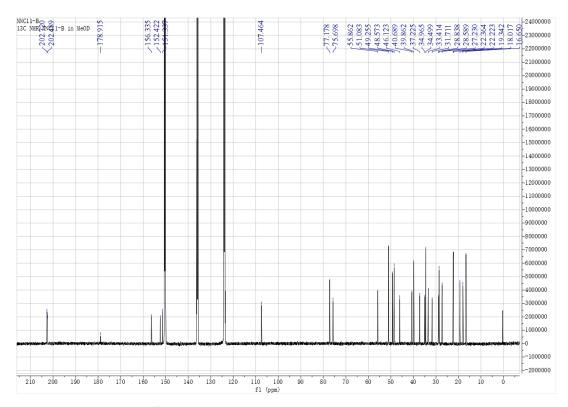


Figure S23. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 3

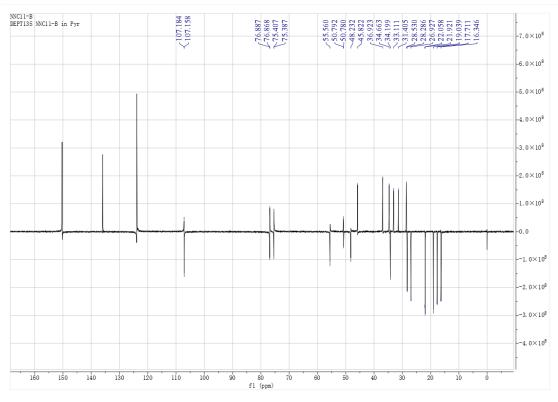


Figure S24. DEPT 135° spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 3

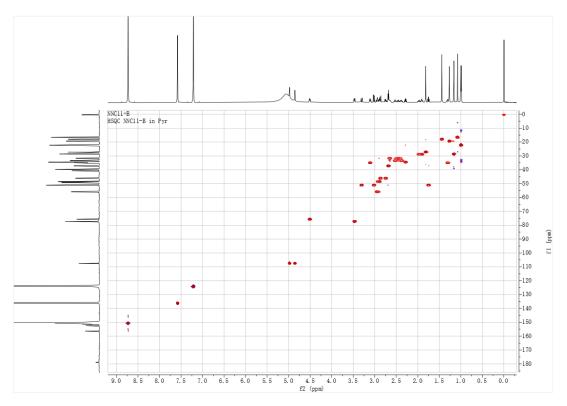


Figure S25. HSQC spectrum (600 MHz,  $C_5D_5N$ ) of compound 3

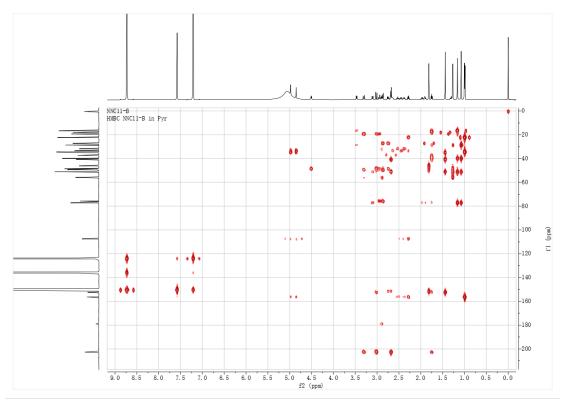
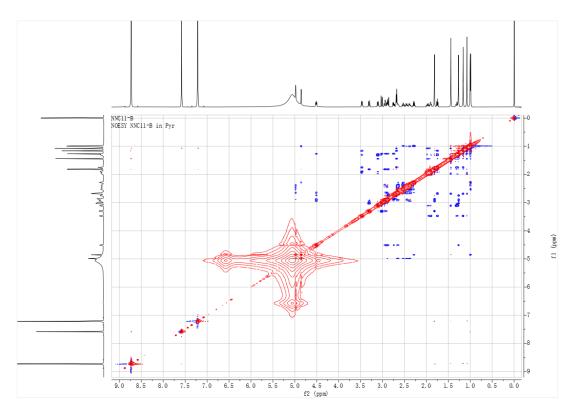
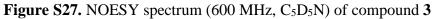


Figure S26. HMBC spectrum (600 MHz,  $C_5D_5N$ ) of compound 3





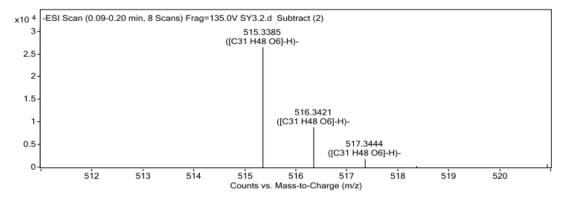


Figure S28. HRESIMS spectrum of compound 4

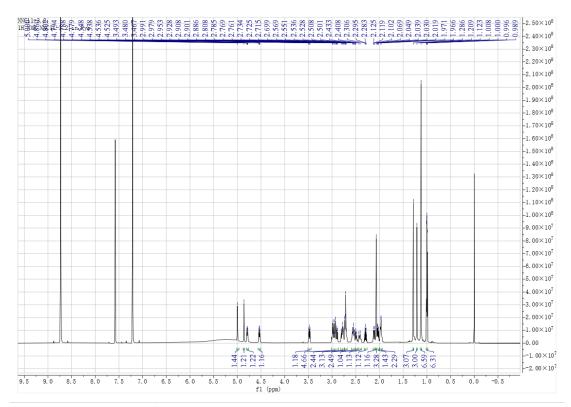


Figure S29. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 4

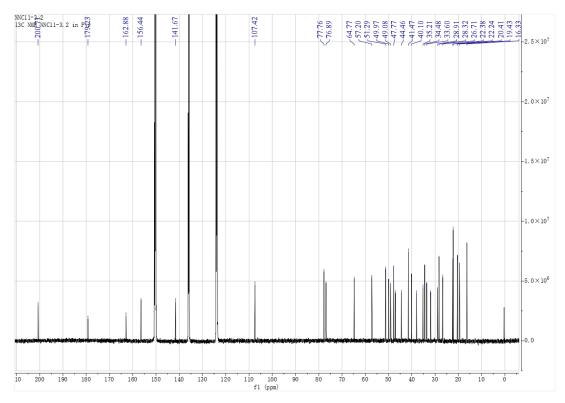


Figure S30. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 4

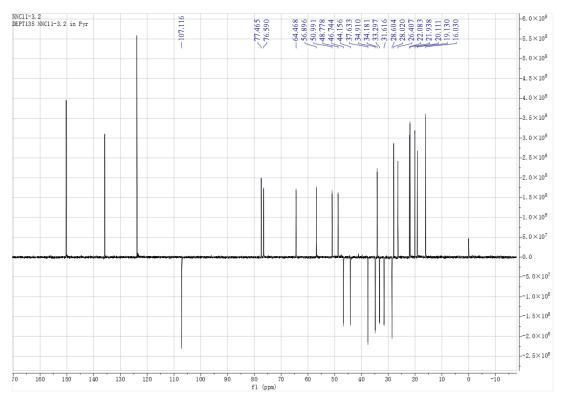


Figure S31. DEPT 135° spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 4

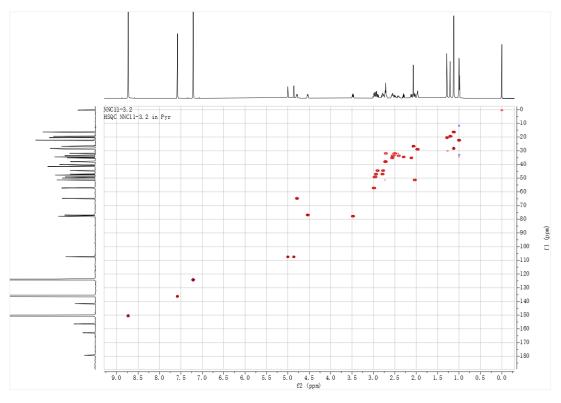


Figure S32. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 4

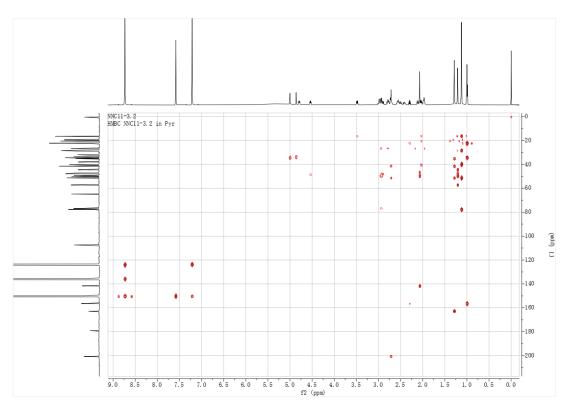


Figure S33. HMBC spectrum (600 MHz, C5D5N) of compound 4

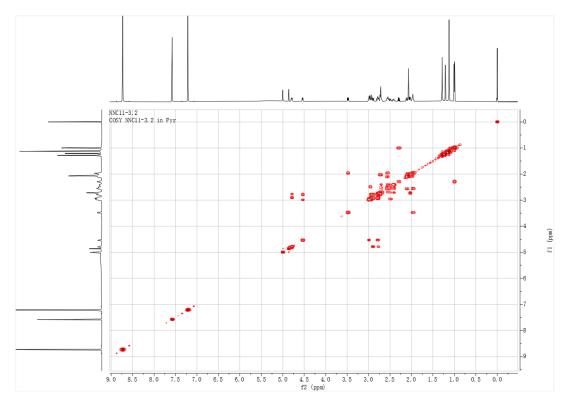


Figure S34. <sup>1</sup>H-<sup>1</sup>H COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 4

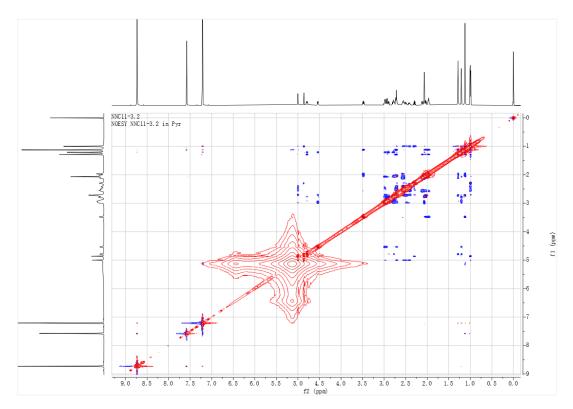


Figure S35. NOESY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 4

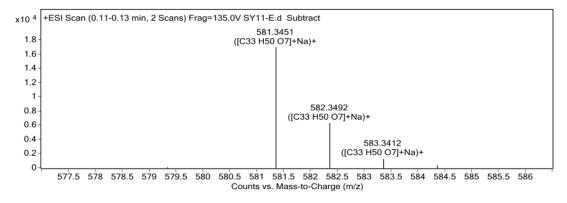


Figure S36. HRESIMS spectrum of compound 5

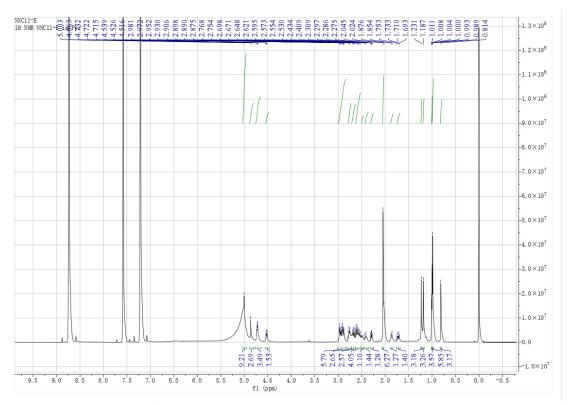


Figure S37. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 5

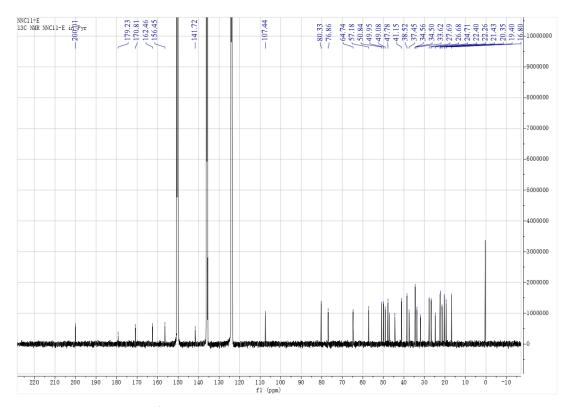


Figure S38. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 5

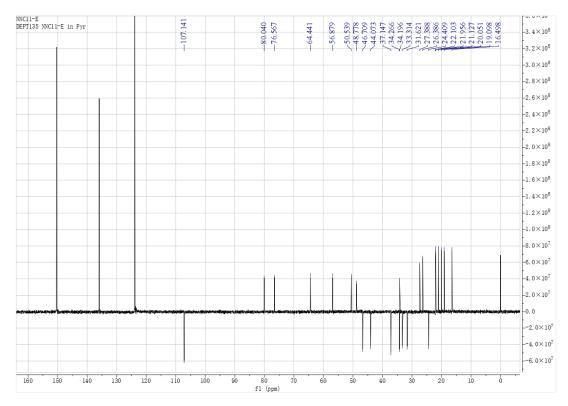


Figure S39. DEPT 135° spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 5

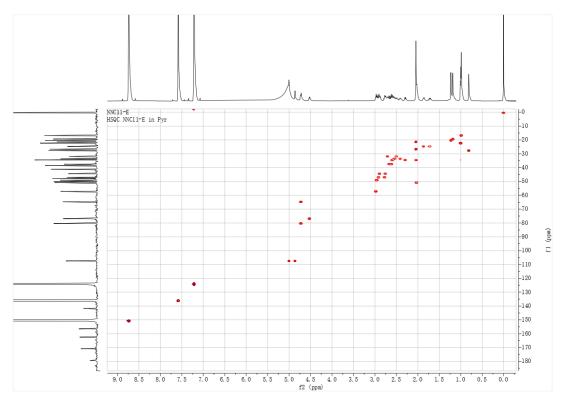


Figure S40. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 5

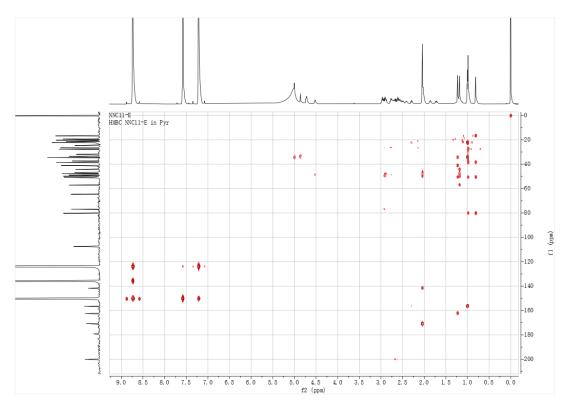


Figure S41. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 5

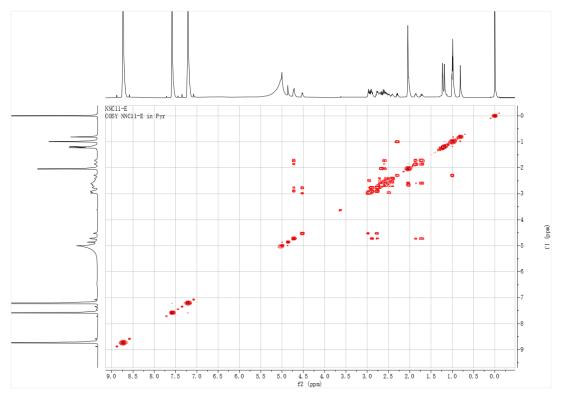


Figure S42. <sup>1</sup>H-<sup>1</sup>H COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 5

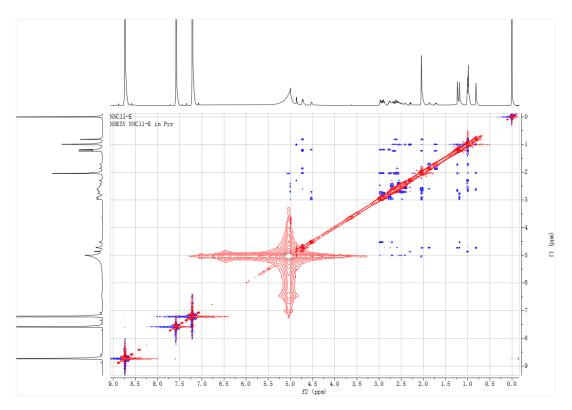


Figure S43. NOESY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 5

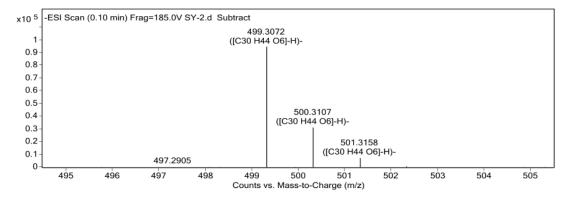


Figure S44. HRESIMS spectrum of compound 6

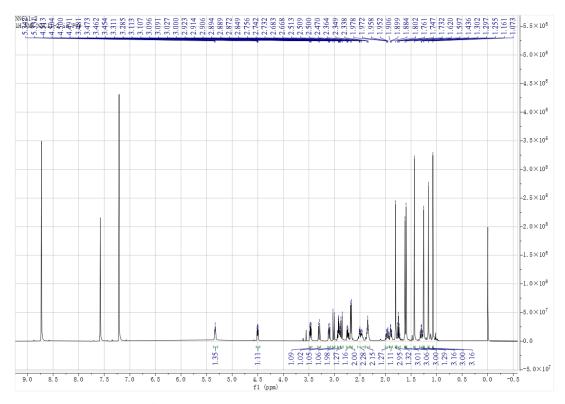


Figure S45. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 6

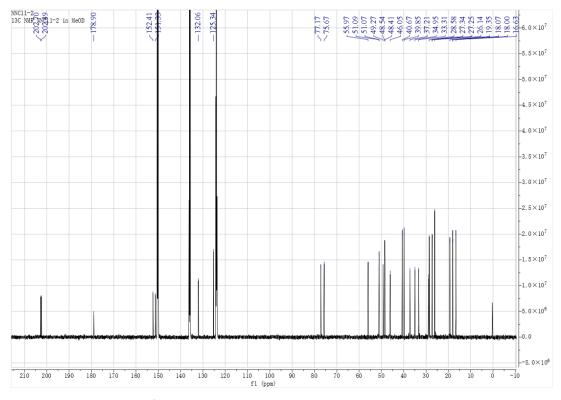


Figure S46. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 6

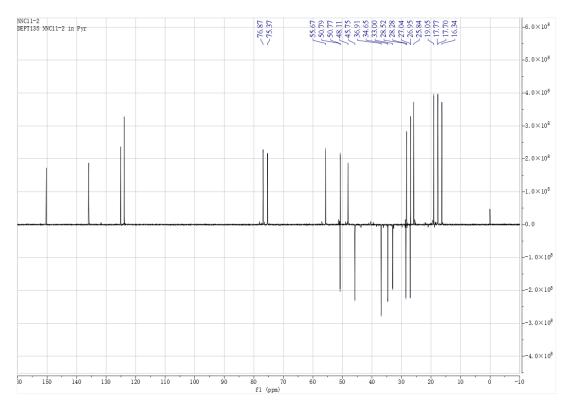


Figure S47. DEPT 135° spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 6

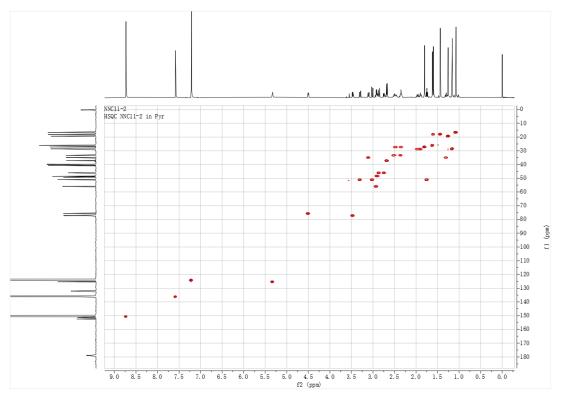


Figure S48. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 6

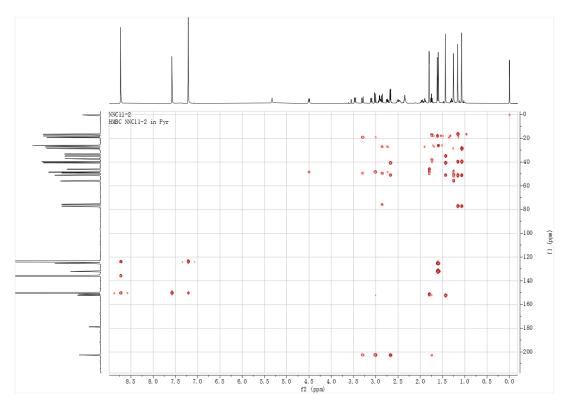


Figure S49. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 6

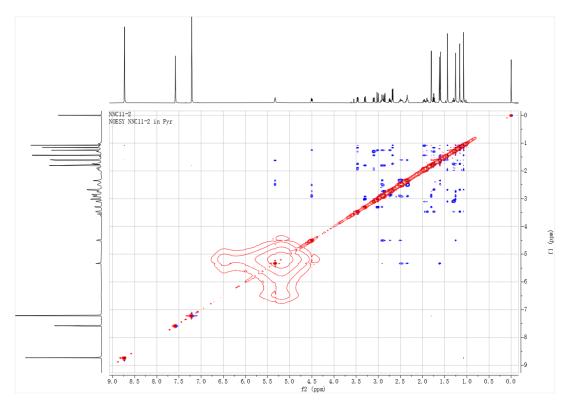


Figure S50. NOESY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 6

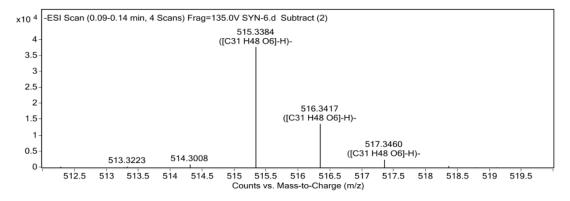


Figure S51. HRESIMS spectrum of compound 7

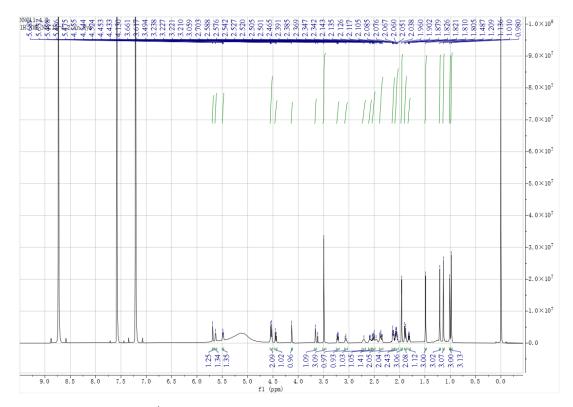


Figure S52. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 7

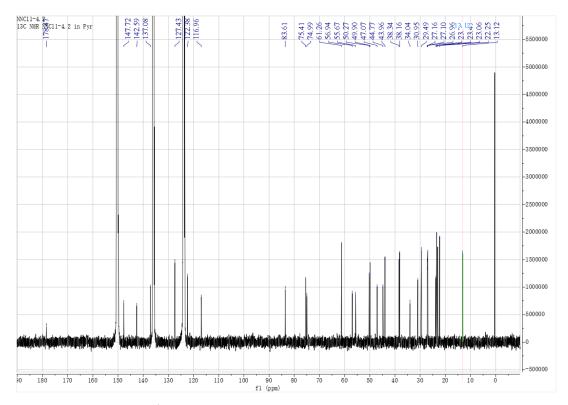


Figure S53. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 7

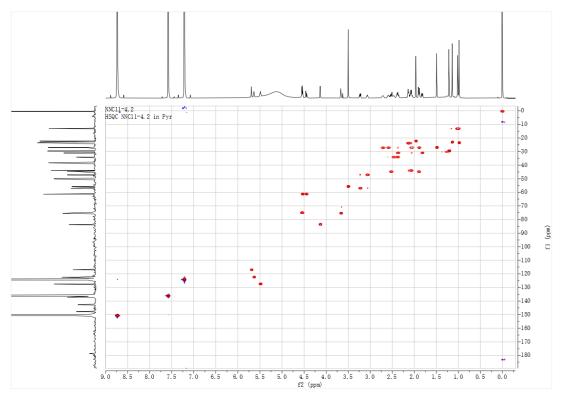


Figure S54. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 7

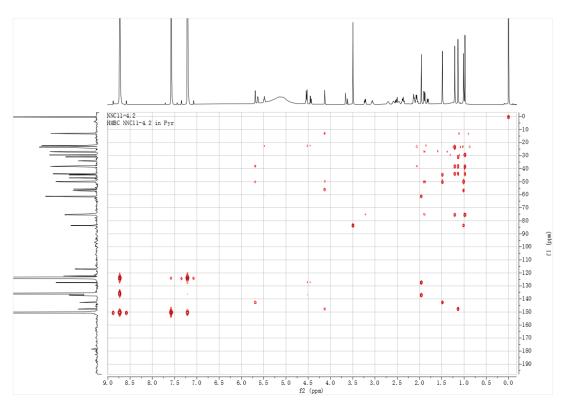


Figure S55. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 7

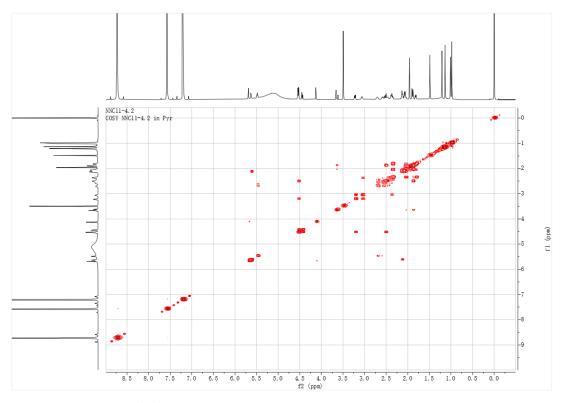


Figure S56. <sup>1</sup>H-<sup>1</sup>H COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 7

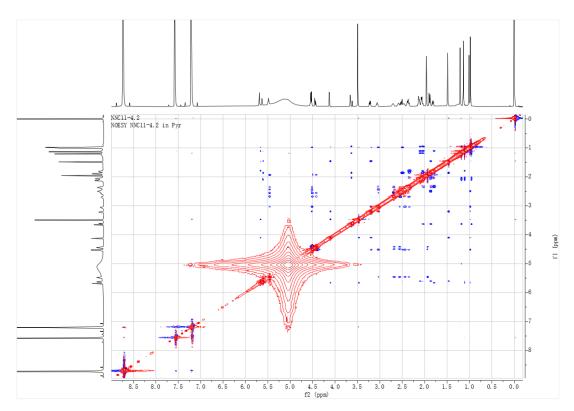


Figure S57. NOESY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 7

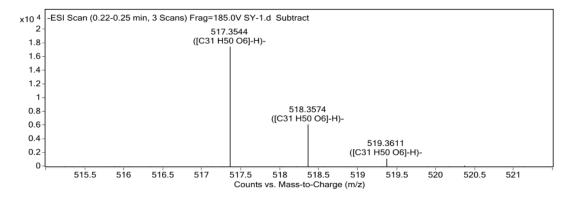


Figure S58. HRESIMS spectrum of compound 8

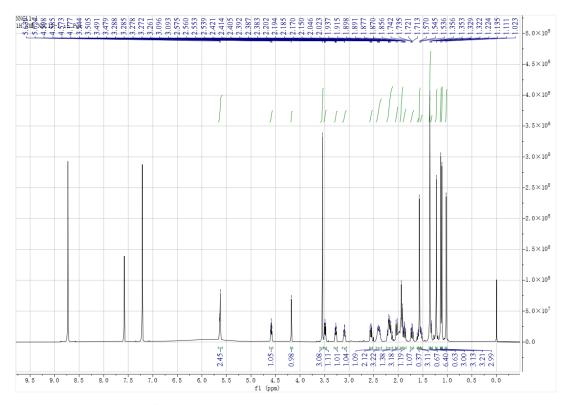


Figure S59. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 8

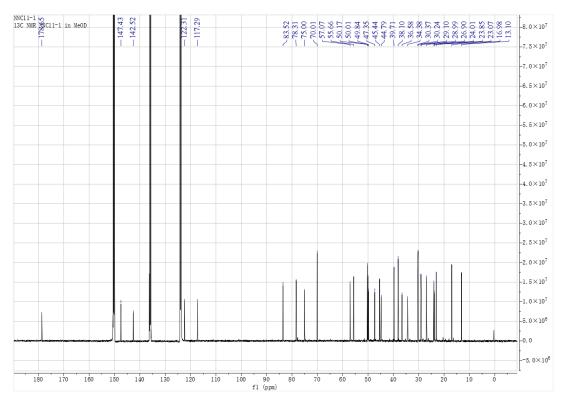


Figure S60. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 8

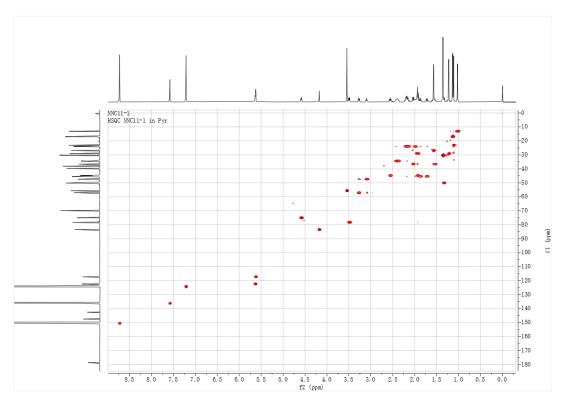


Figure S61. HSQC spectrum (600 MHz,  $C_5D_5N$ ) of compound 8

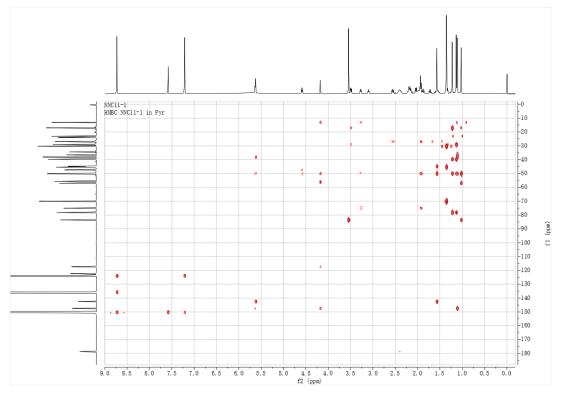


Figure S62. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 8

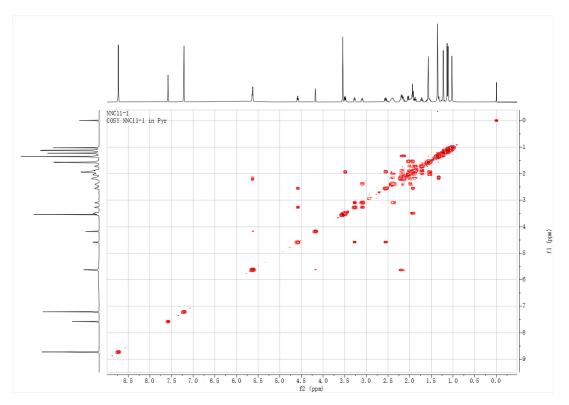


Figure S63.  $^{1}\text{H}\text{-}^{1}\text{H}$  COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 8

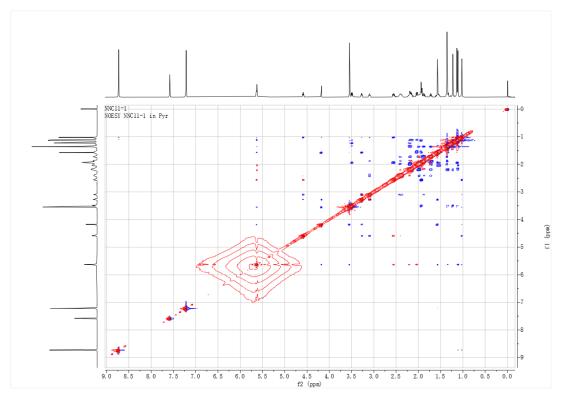


Figure S64. NOESY spectrum (600 MHz, C5D5N) of compound 8

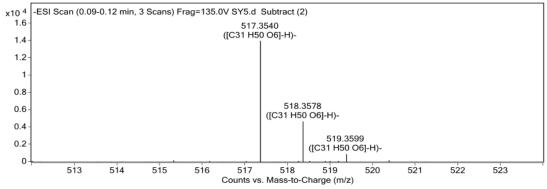


Figure S65. HRESIMS spectrum of compound 9

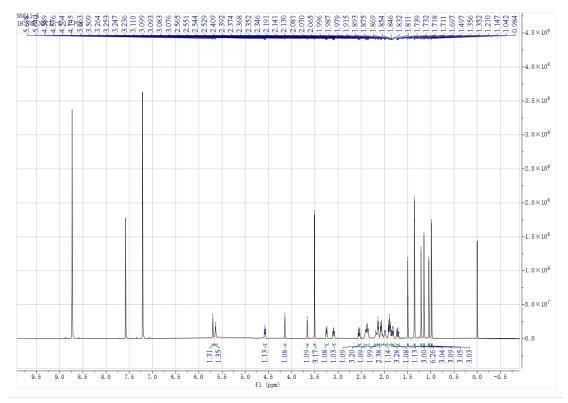


Figure S66. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 9

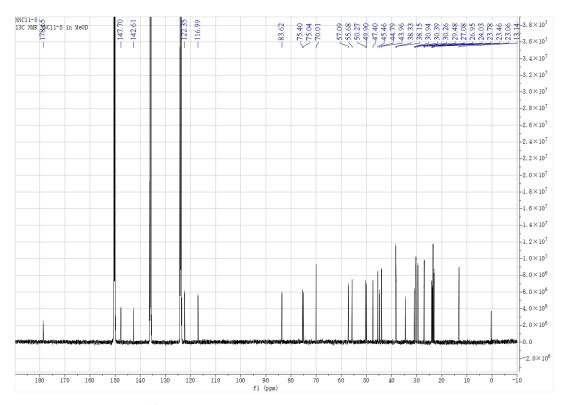


Figure S67. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 9

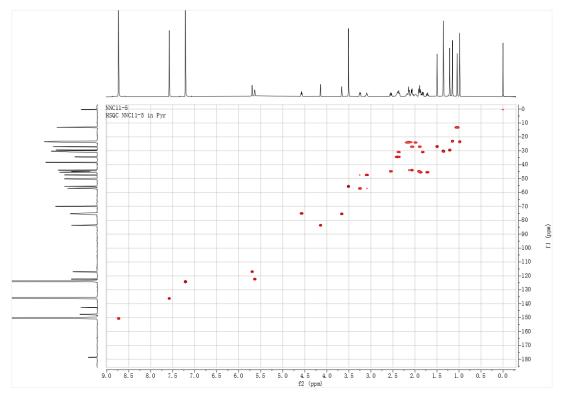


Figure S68. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 9

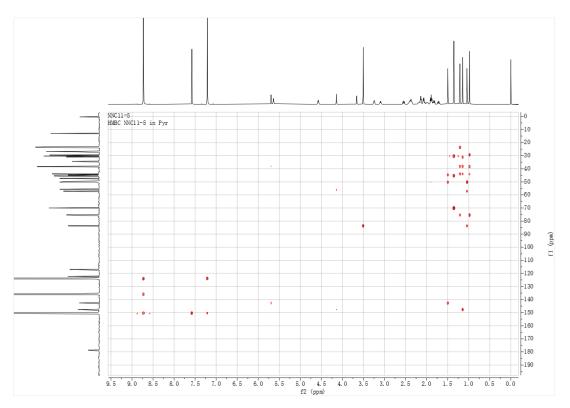


Figure S69. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 9

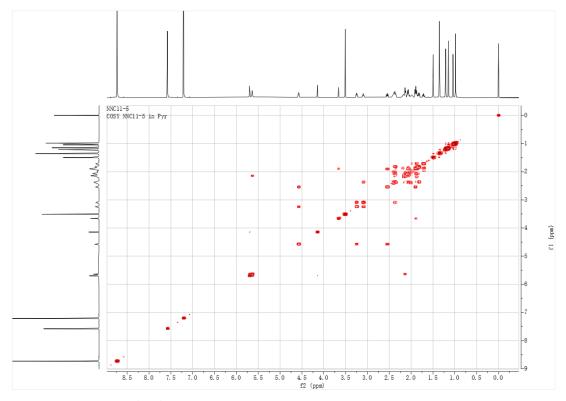
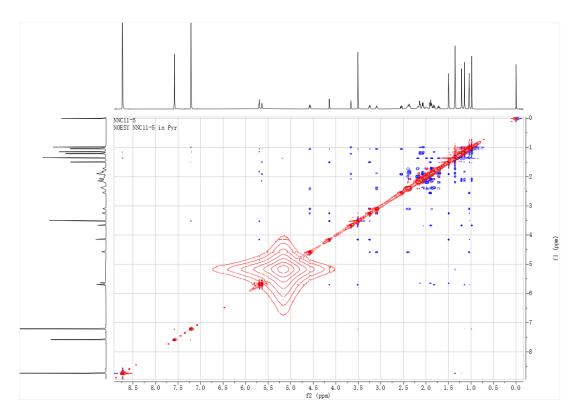
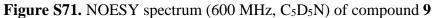


Figure S70. <sup>1</sup>H-<sup>1</sup>H COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 9





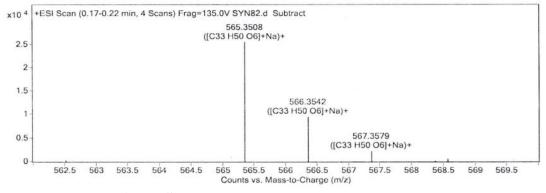


Figure S72. HRESIMS spectrum of compound 10

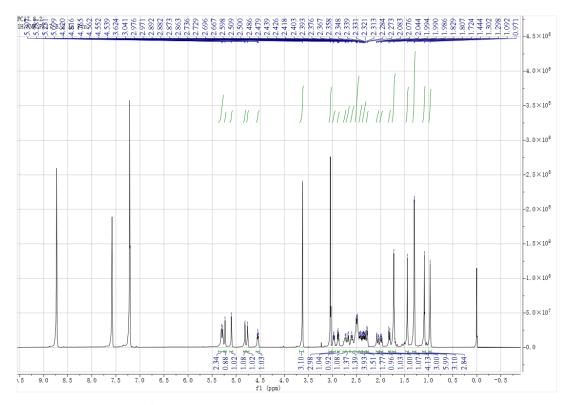


Figure S73. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 10

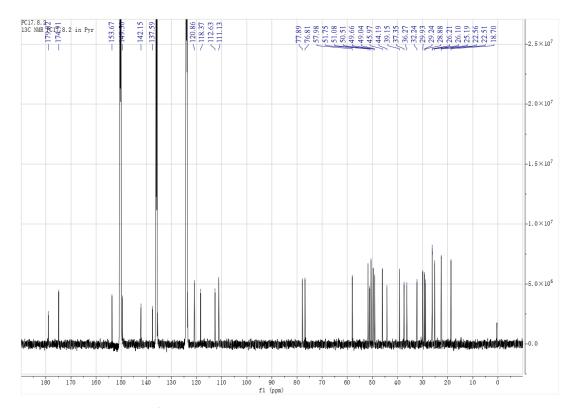


Figure S74. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 10

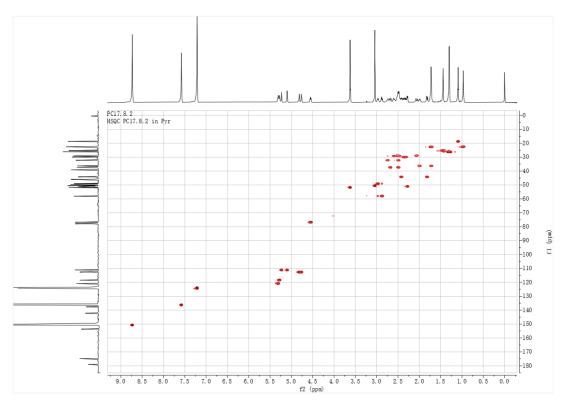


Figure S75. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 10

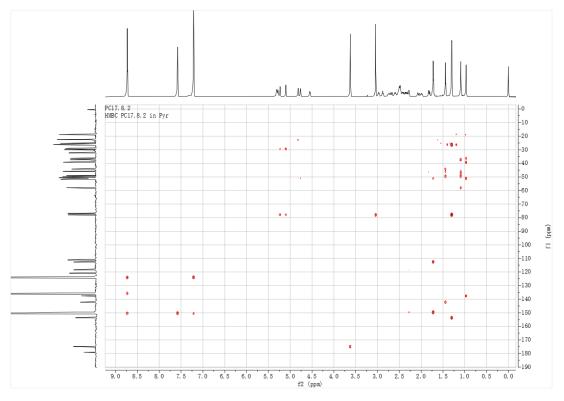


Figure S76. HMBC spectrum (600 MHz, C5D5N) of compound 10

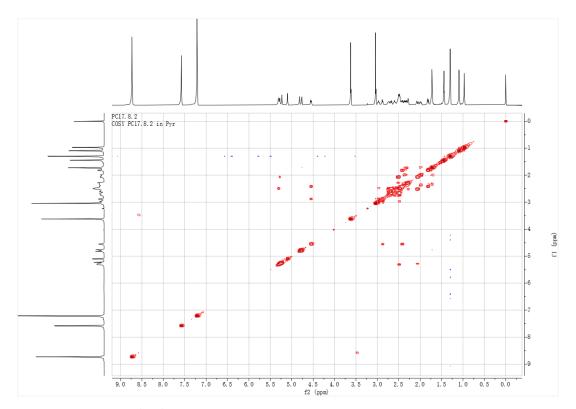


Figure S77. <sup>1</sup>H-<sup>1</sup>H COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 10

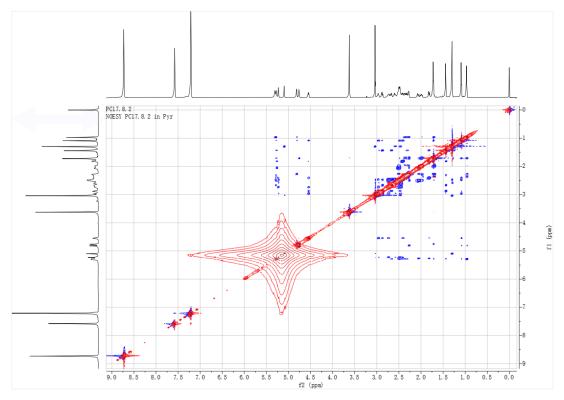


Figure S78. NOESY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 10

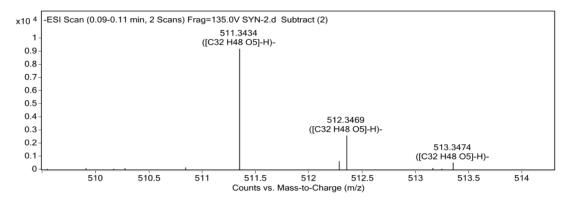


Figure S79. HRESIMS spectrum of compound 11

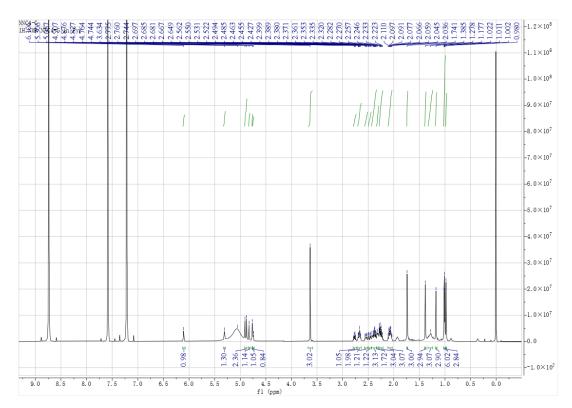


Figure S80. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 11

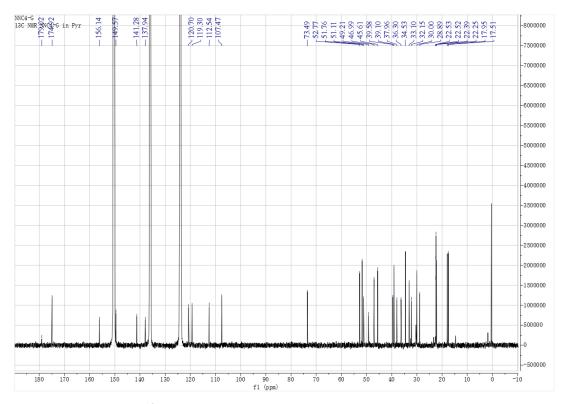


Figure S81. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 11

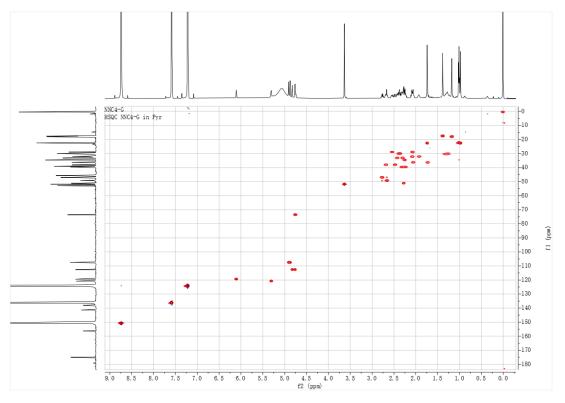


Figure S82. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 11

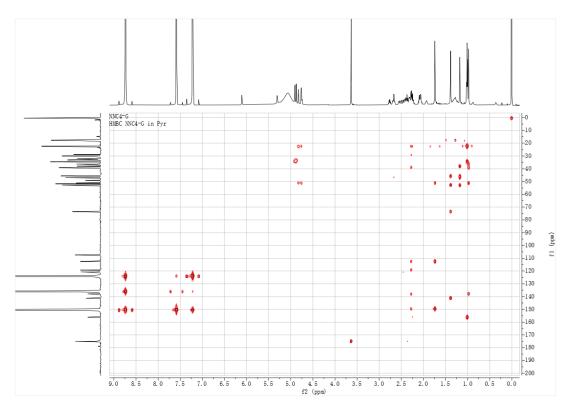


Figure S83. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 11

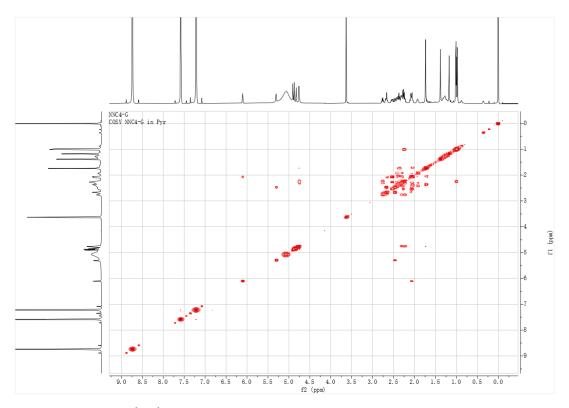


Figure S84. <sup>1</sup>H-<sup>1</sup>H COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 11

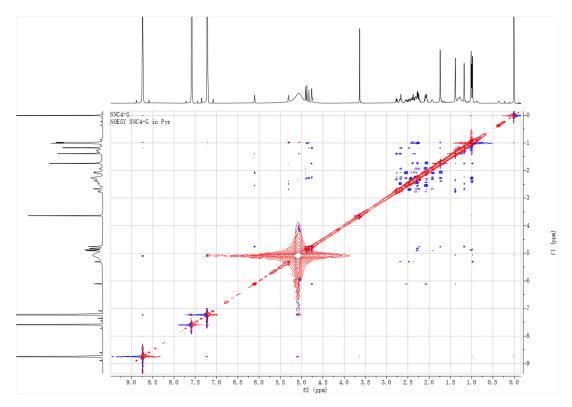


Figure S85. NOESY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 11

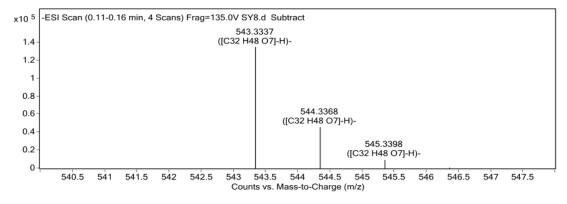


Figure S86. HRESIMS spectrum of compound 12

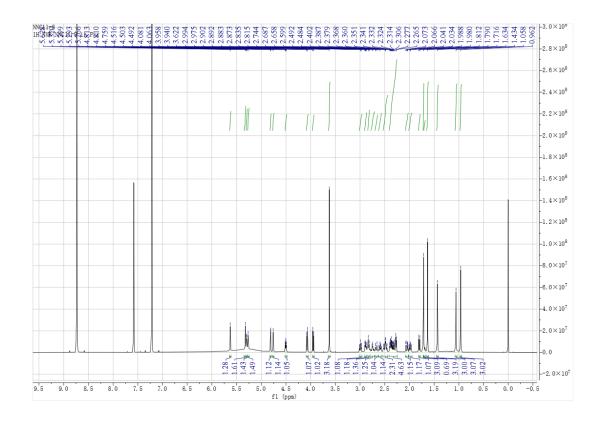


Figure S87. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 12

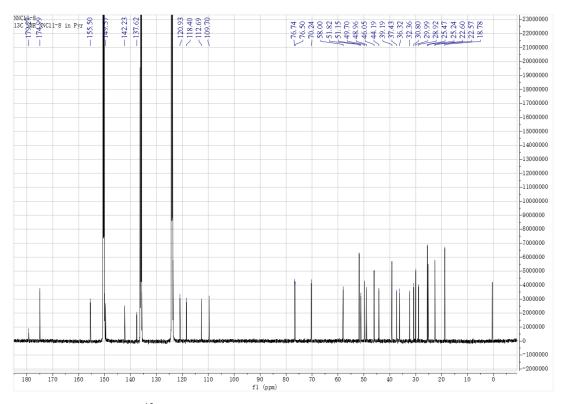


Figure S88. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 12

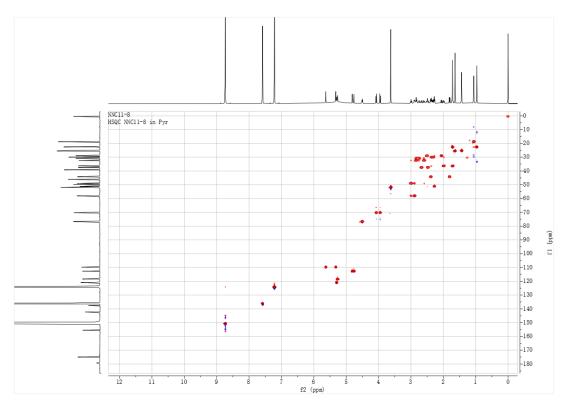


Figure S89. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 12

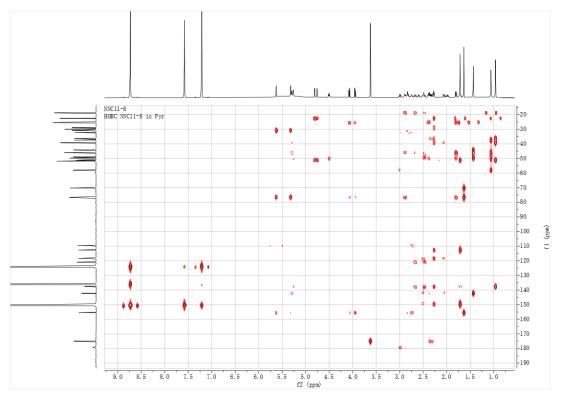


Figure S90. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 12

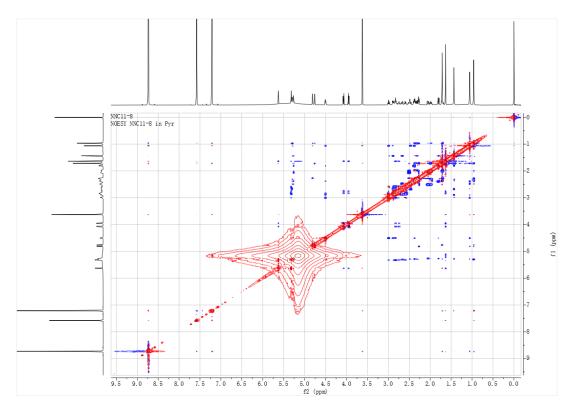


Figure S91. NOESY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 12

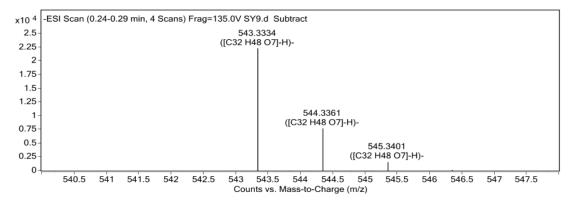


Figure S92. HRESIMS spectrum of compound 13

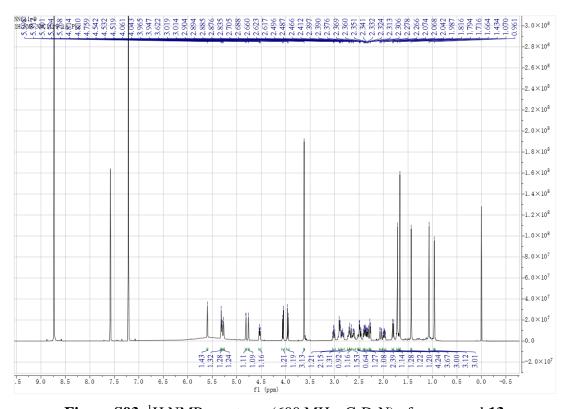


Figure S93. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 13

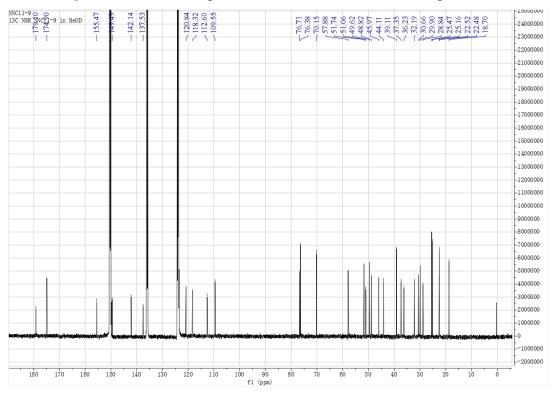


Figure S94. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 13

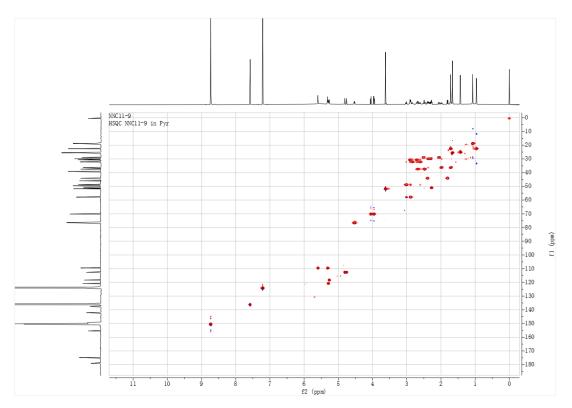


Figure S95. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 13

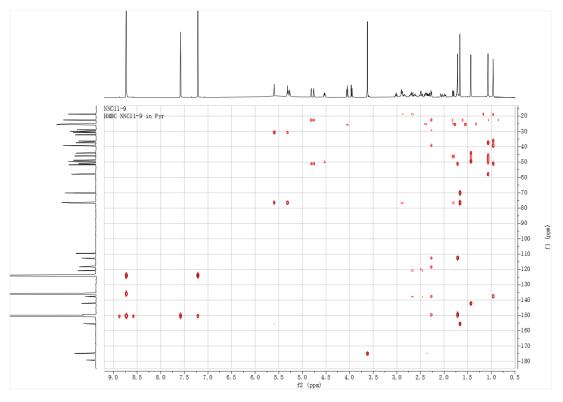


Figure S96. HMBC spectrum (600 MHz,  $C_5D_5N$ ) of compound 13

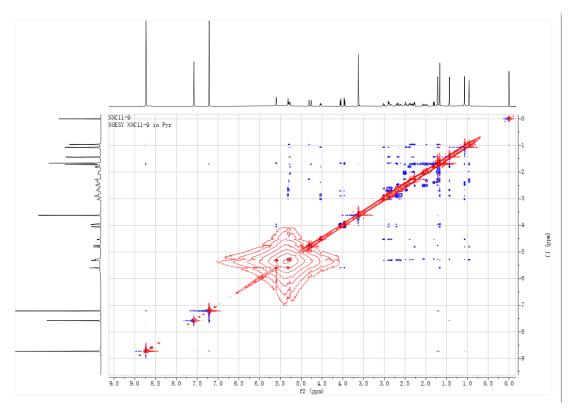


Figure S97. NOESY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 13

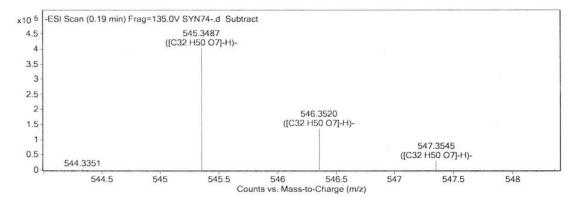


Figure S98. HRESIMS spectrum of compound 14

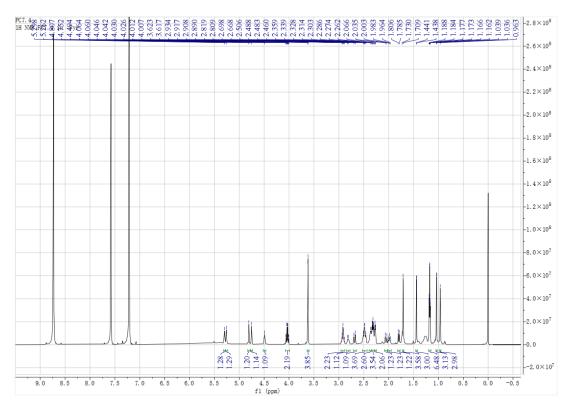


Figure S99. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 14

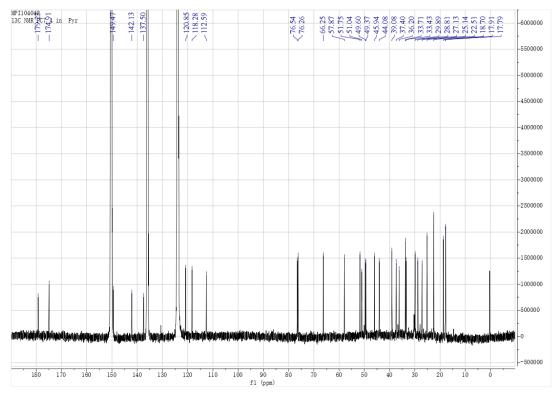


Figure S100. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 14

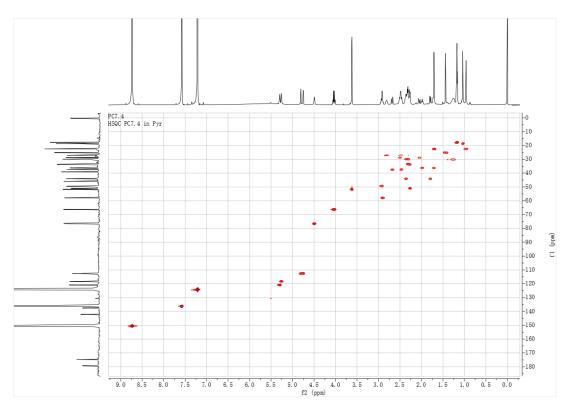


Figure S101. HSQC spectrum (600 MHz, C5D5N) of compound 14

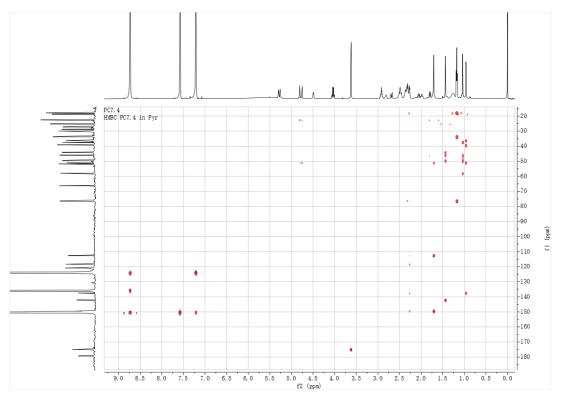


Figure S102. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 14

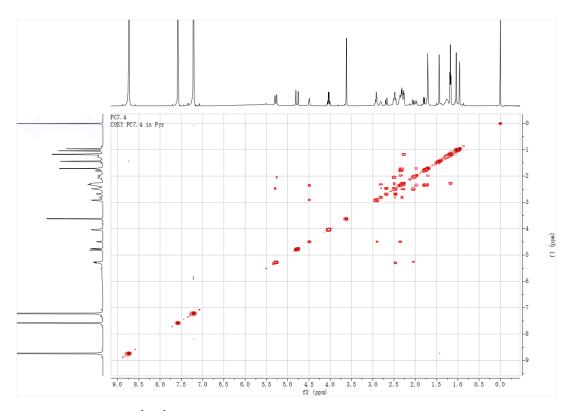


Figure S103. <sup>1</sup>H-<sup>1</sup>H COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 14

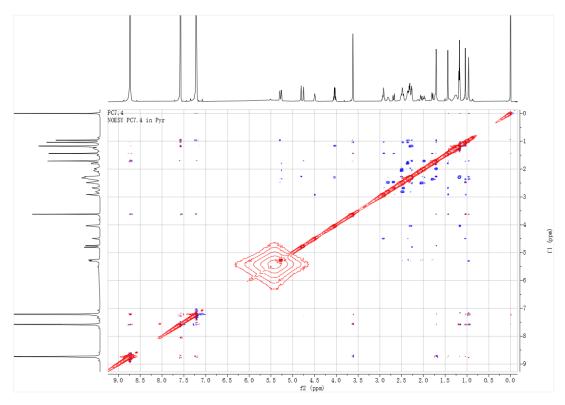


Figure S104. NOESY spectrum (600 MHz, C5D5N) of compound 14

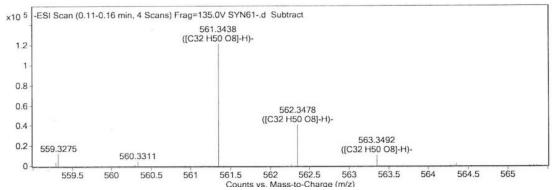


Figure S105. HRESIMS spectrum of compound 15

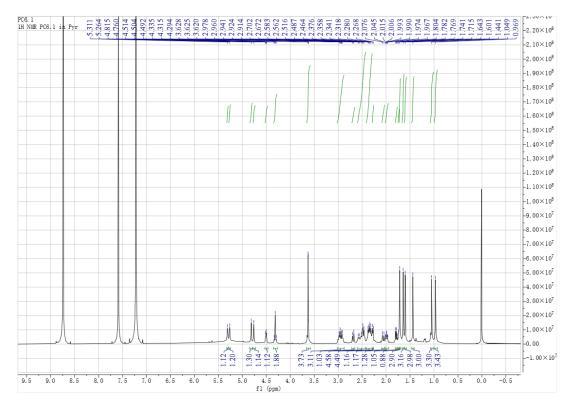


Figure S106. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 15

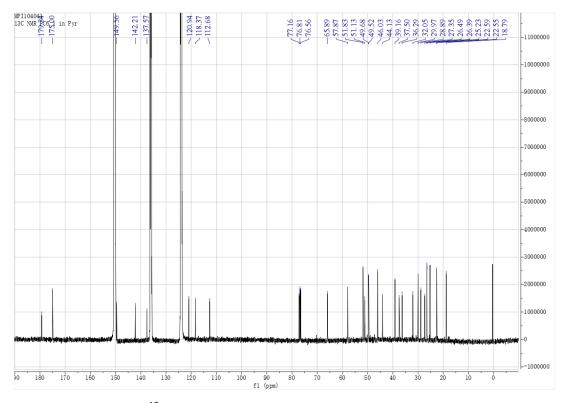


Figure S107. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 15

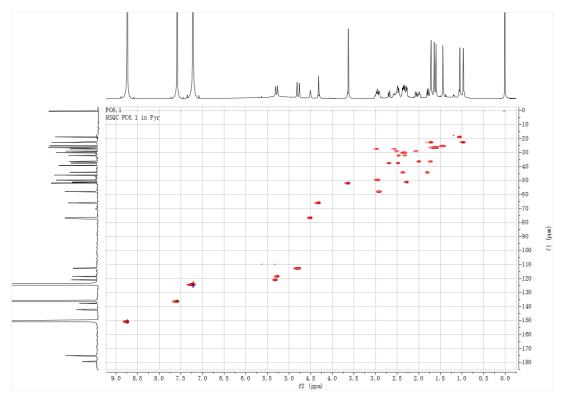


Figure S108. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 15

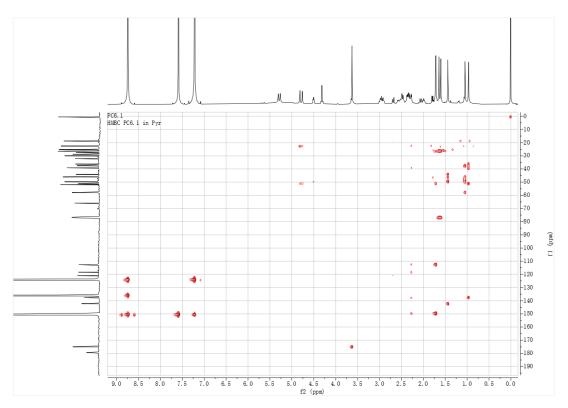


Figure S109. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 15

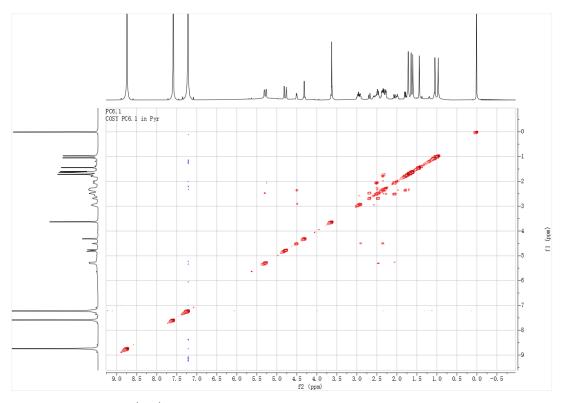


Figure S110.  $^{1}\text{H}$ - $^{1}\text{H}$  COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 15

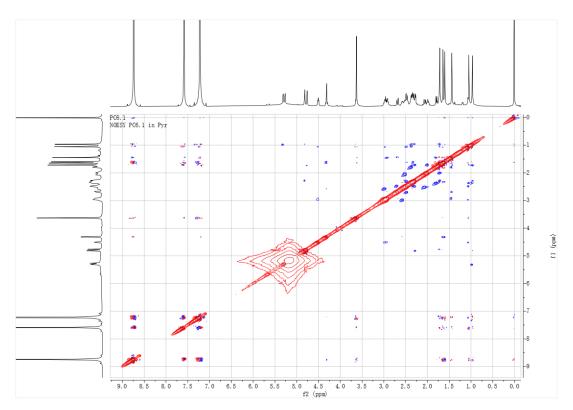


Figure S111. NOESY spectrum (600 MHz, C5D5N) of compound 15

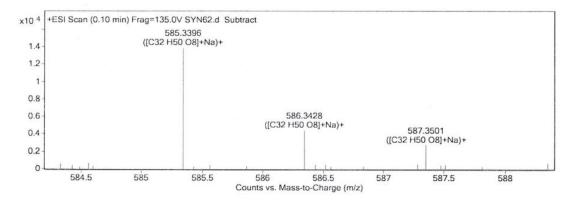


Figure S112. HRESIMS spectrum of compound 16

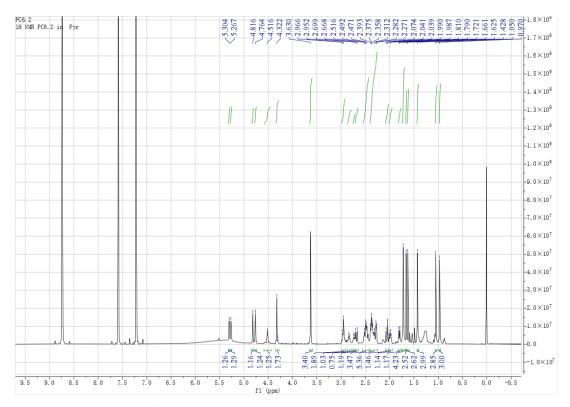


Figure S113. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 16

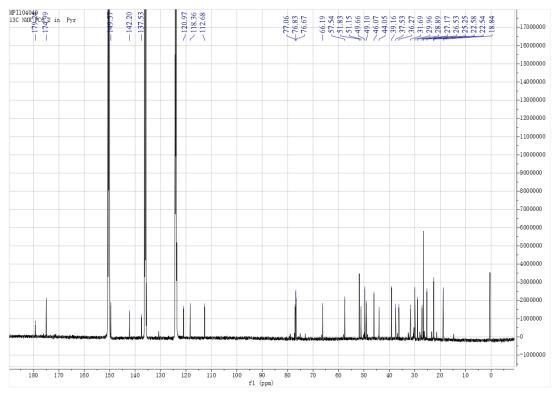


Figure S114. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 16

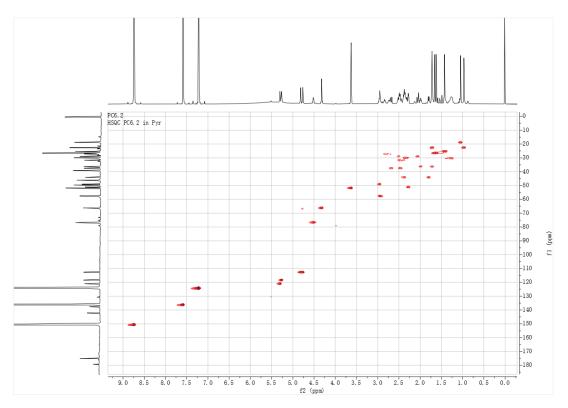


Figure S115. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 16

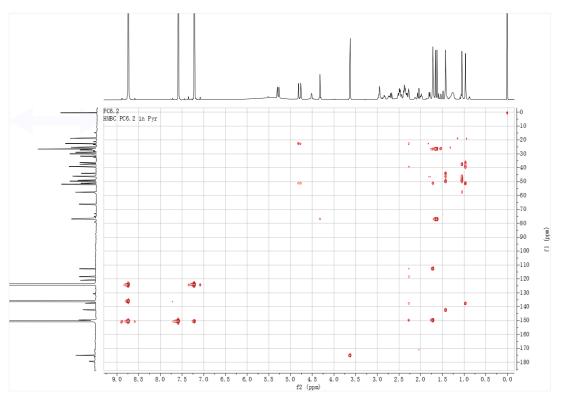


Figure S116. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 16

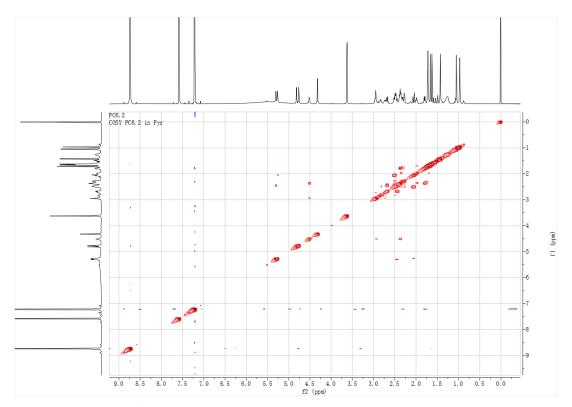


Figure S117.  $^{1}\text{H}$ - $^{1}\text{H}$  COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 16

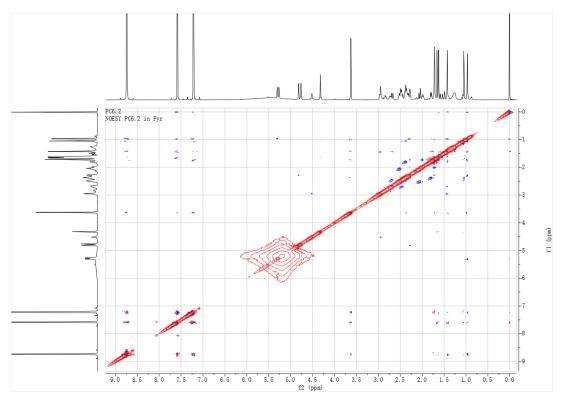


Figure S118. NOESY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 16

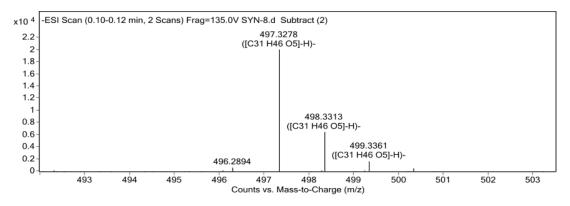


Figure S119. HRESIMS spectrum of compound 17

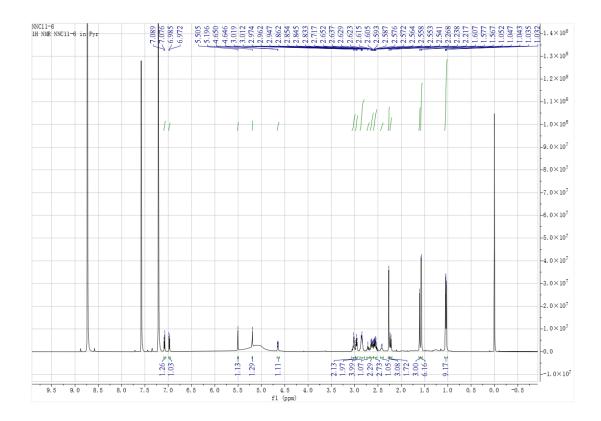


Figure S120. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 17

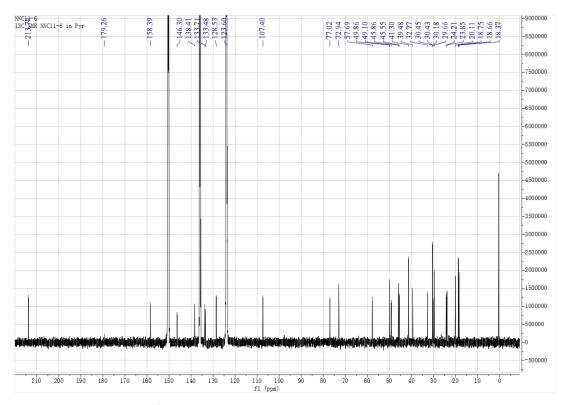


Figure S121. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 17

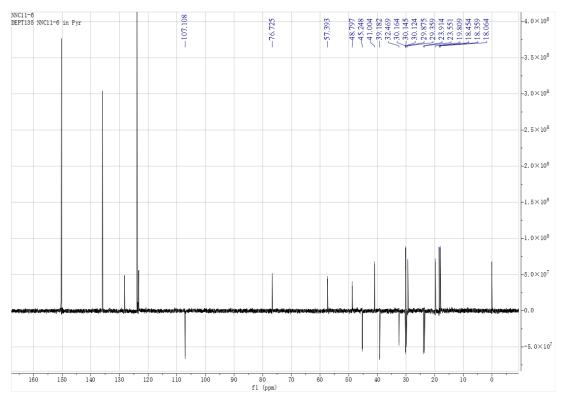


Figure S122. DEPT 135° spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 17

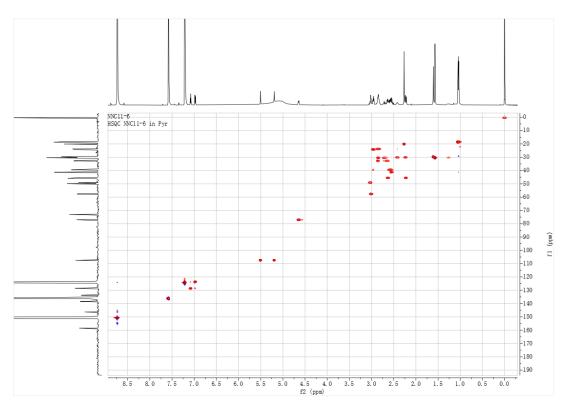


Figure S123. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 17

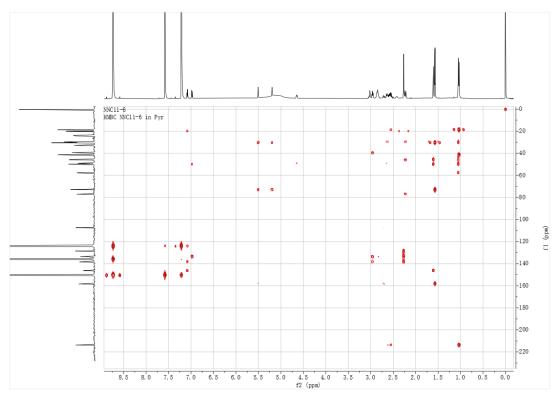


Figure S124. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 17

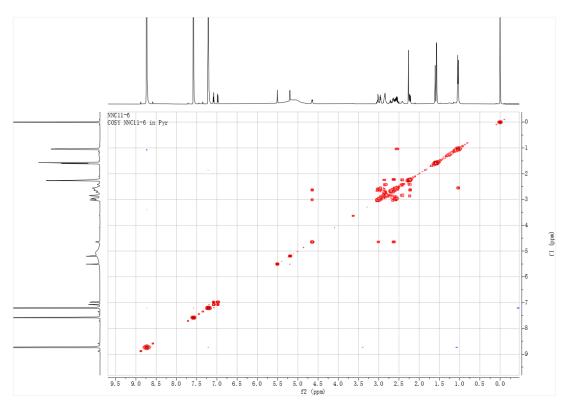


Figure S125. <sup>1</sup>H-<sup>1</sup>H COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 17

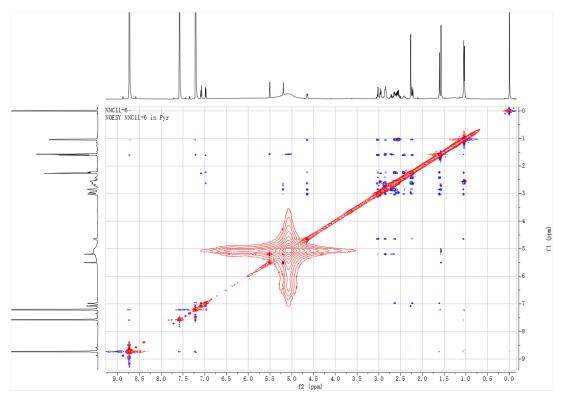


Figure S126. NOESY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 17

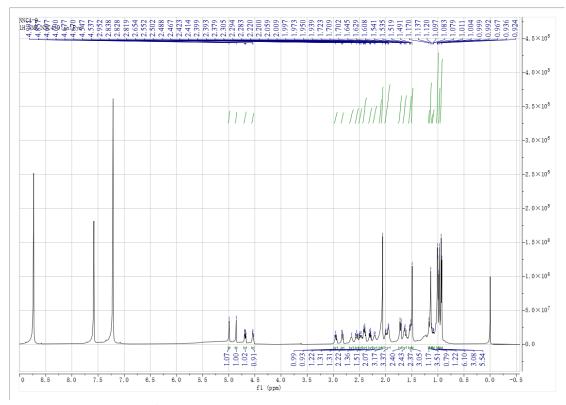


Figure S127. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 18

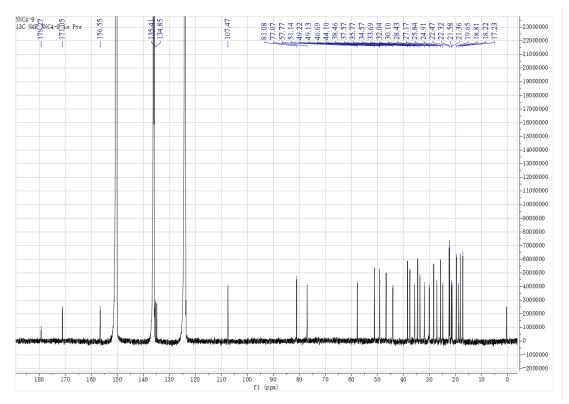


Figure S128. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 18

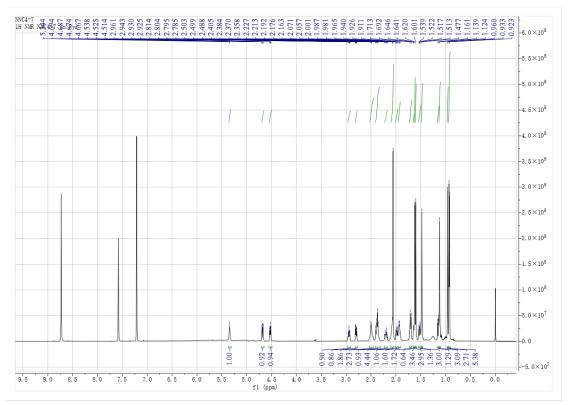


Figure S129. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 19

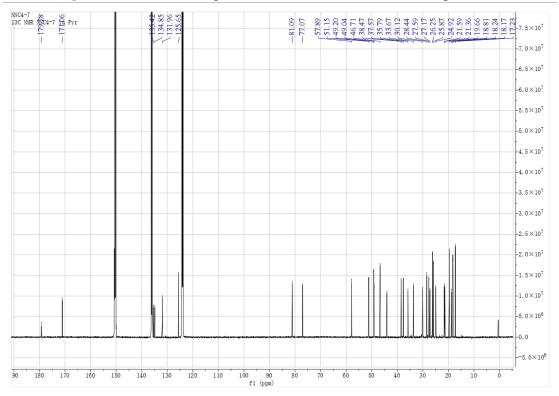


Figure S130. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 19

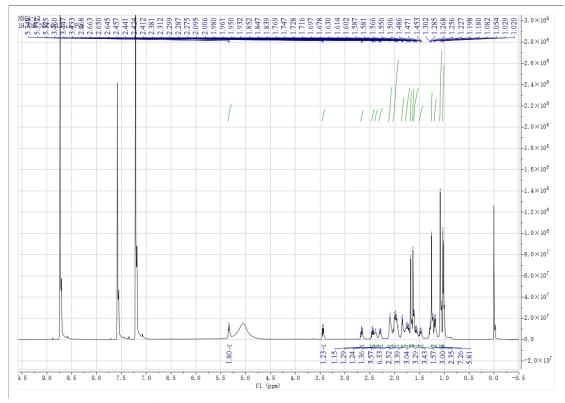


Figure S131. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 20

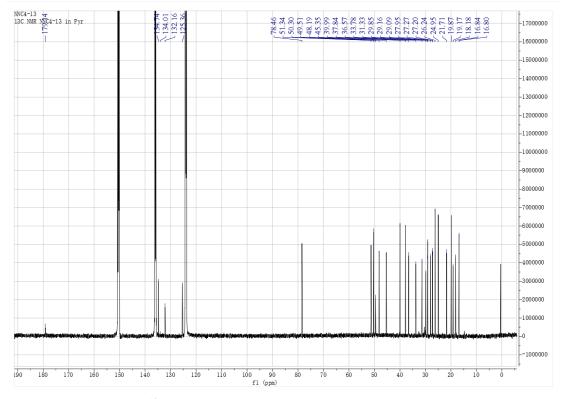


Figure S132. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 20

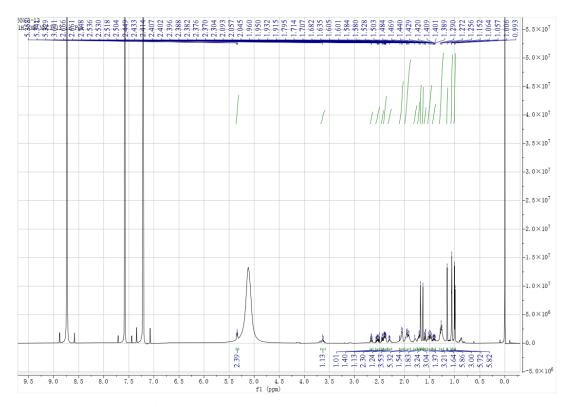


Figure S133. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 21

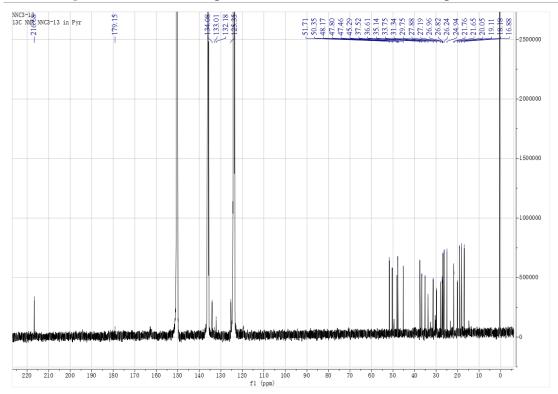


Figure S134. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 21

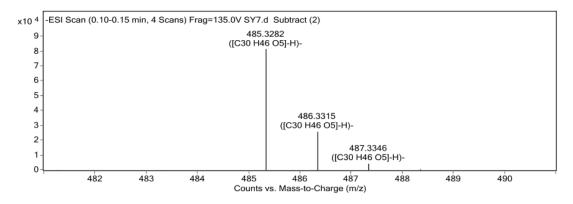


Figure S135. HRESIMS spectrum of compound 22

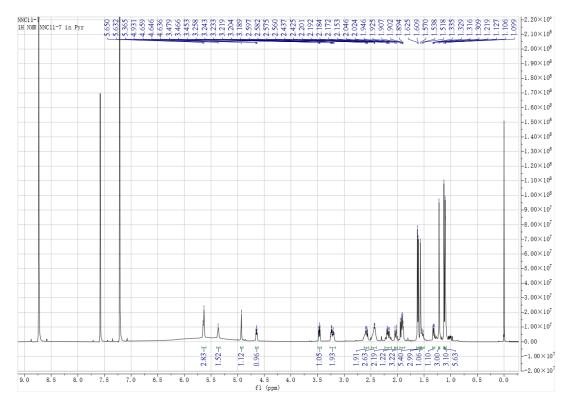


Figure S136. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 22

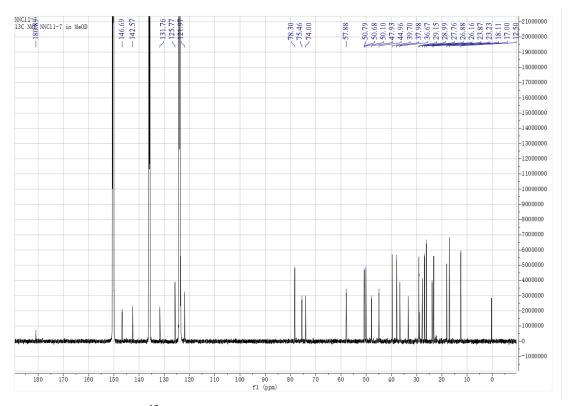


Figure S137. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 22

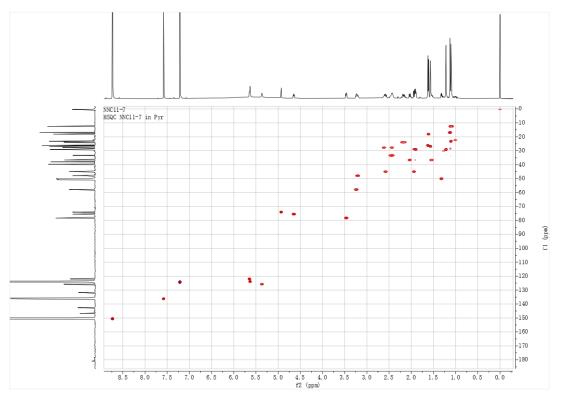


Figure S138. HSQC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 22

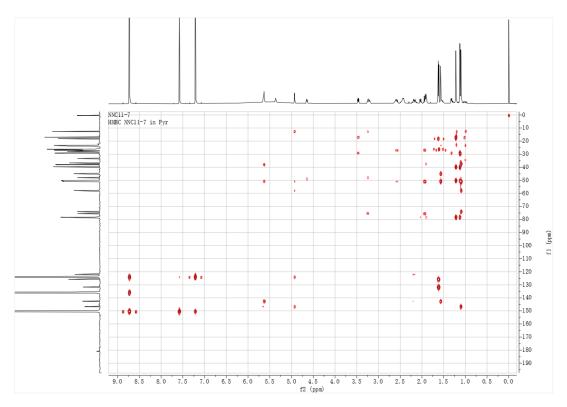


Figure S139. HMBC spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 22

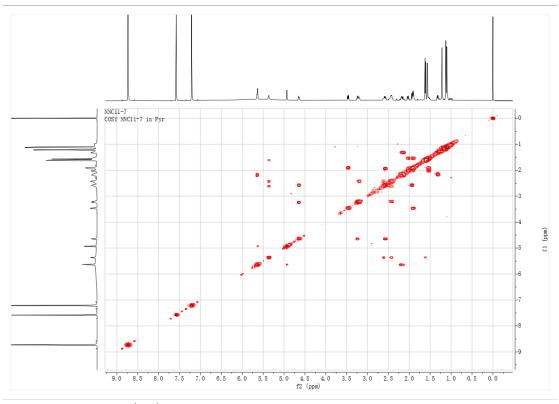


Figure S140. <sup>1</sup>H-<sup>1</sup>H COSY spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 22

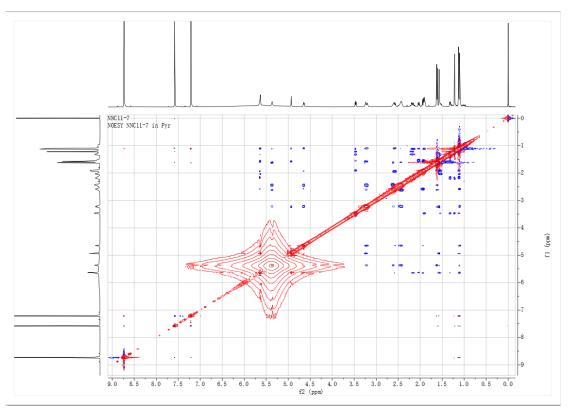


Figure S141. NOESY spectrum (600 MHz, C5D5N) of compound 22

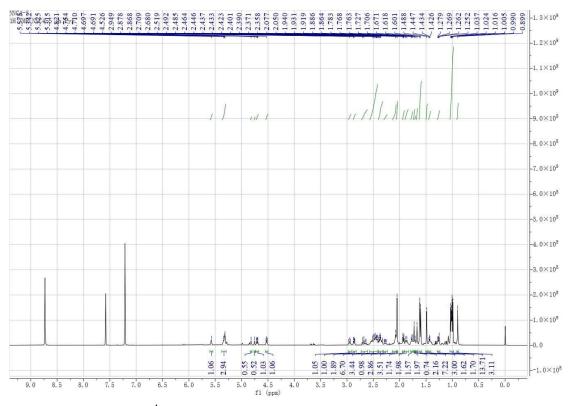


Figure S142. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 23

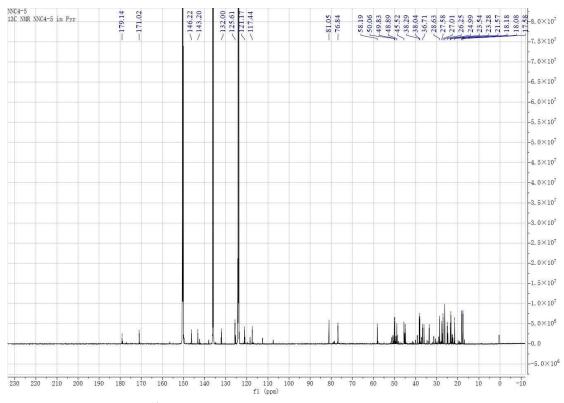


Figure S143. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 23

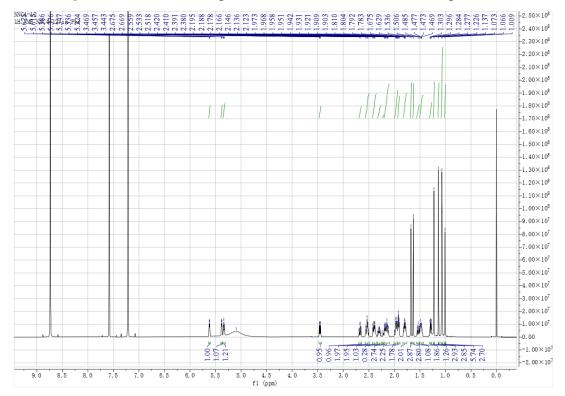
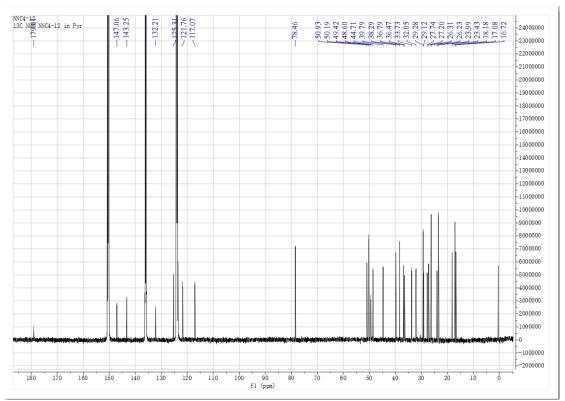


Figure S144. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 24



-7.0×107 -6.5×10<sup>7</sup> -6.0×10<sup>7</sup>  $-5.5 \times 10^{7}$  $-5.0 \times 10^{7}$  $-4.5 \times 10^{7}$  $-4.0 \times 10^{7}$  $-3.5 \times 10^{7}$  $-3.0 \times 10^{7}$ -2.5×10<sup>7</sup> -2.0×10<sup>7</sup> -1.5×10<sup>7</sup>  $-1.0 \times 10^{7}$ -5.0×10<sup>6</sup> ł -0.0 0.98<del>.</del> 2.09.<u>∓</u> --5. 0×10<sup>6</sup> 5.5 5.0 4.5 fl (ppm) 6.5 6.0 4.0 3.0 2.5 2.0 1.5 1.0 0.5 0.0 9.5 9.0 8.5 8.0 7.5 7. 0 3. 5

Figure S145. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 24

Figure S146. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 25

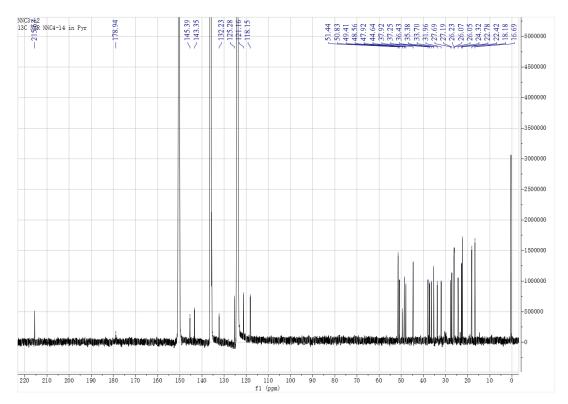


Figure S147. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 25

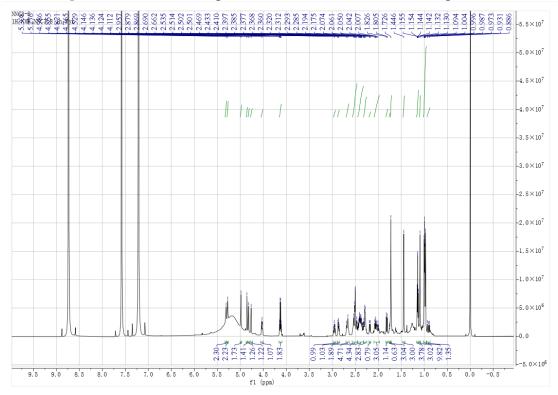


Figure S148. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 26

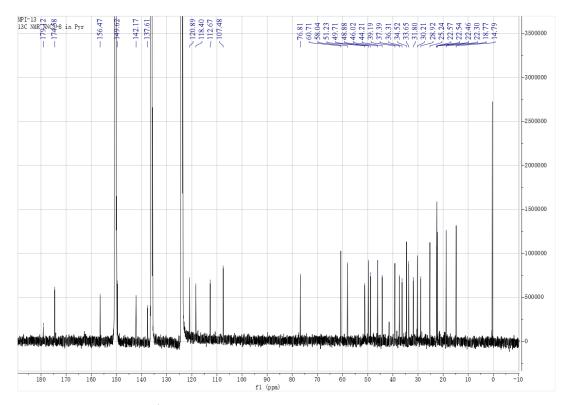


Figure S149. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 26

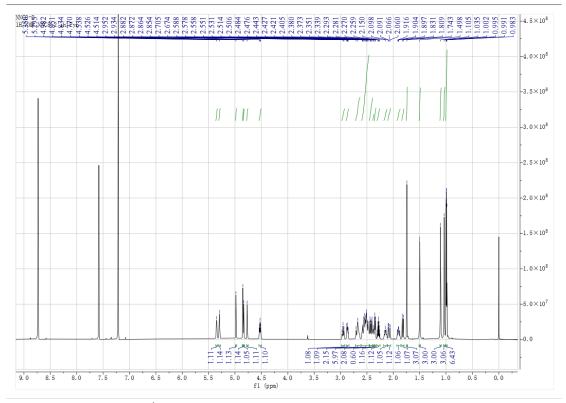


Figure S150. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 27

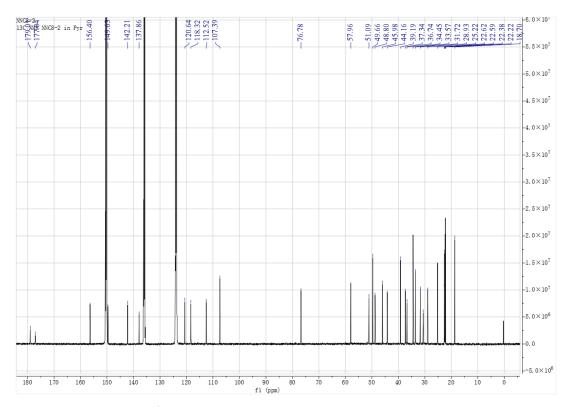


Figure S151. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 27

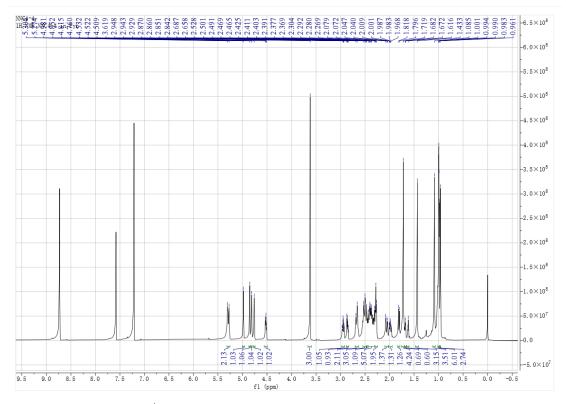


Figure S152. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 28

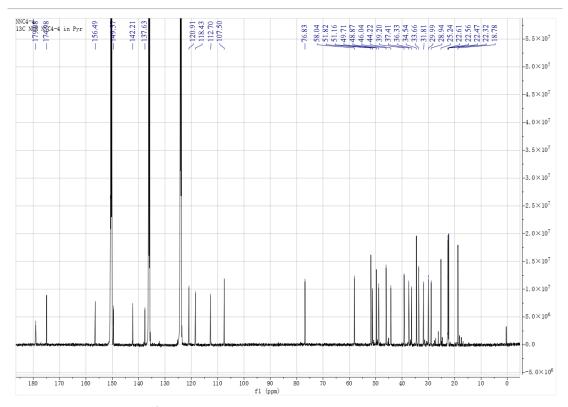


Figure S153. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 28

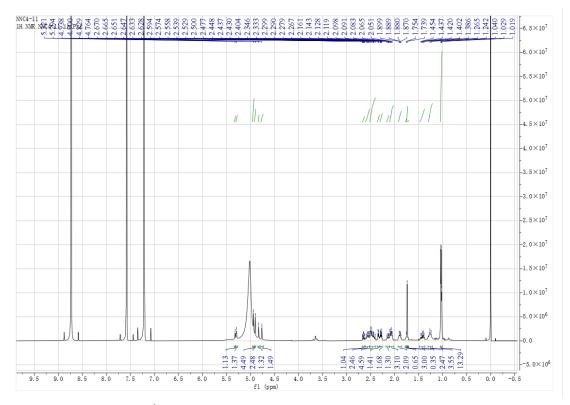


Figure S154. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 29

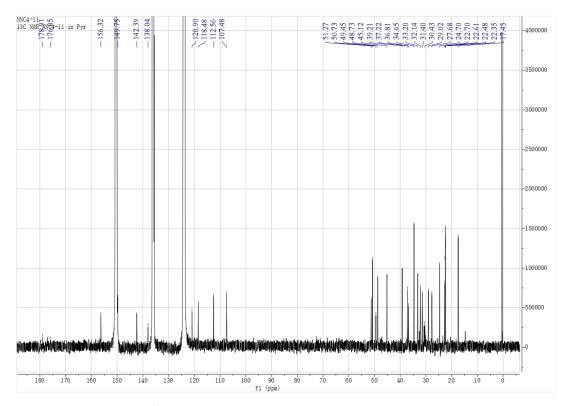


Figure S155. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 29

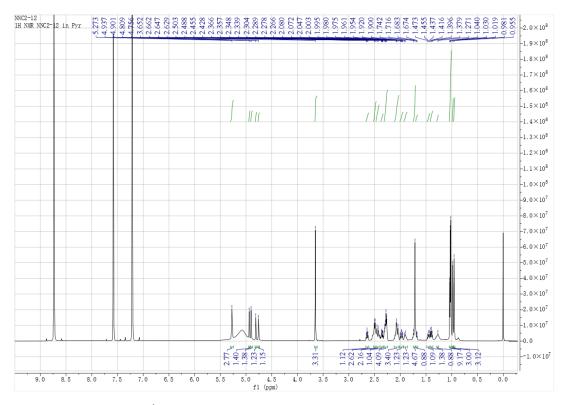


Figure S156. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 30

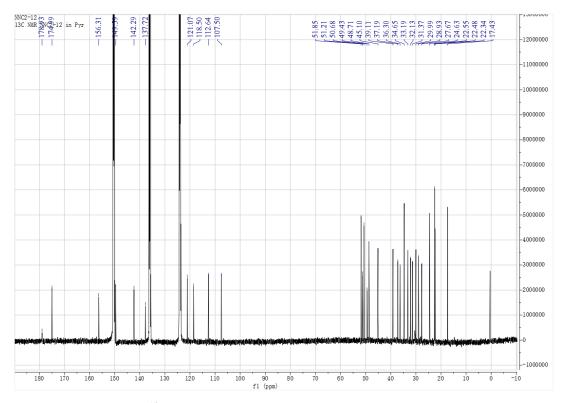


Figure S157. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 30

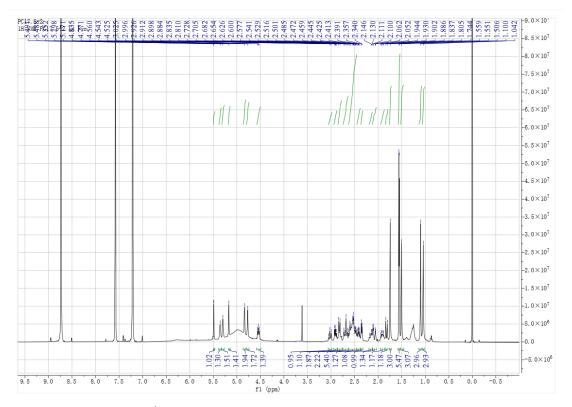


Figure S158. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 31

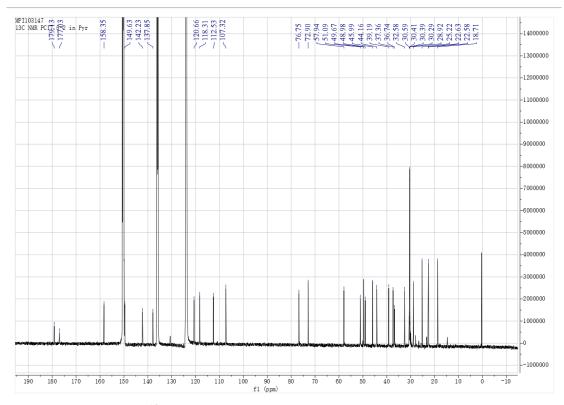


Figure S159. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 31

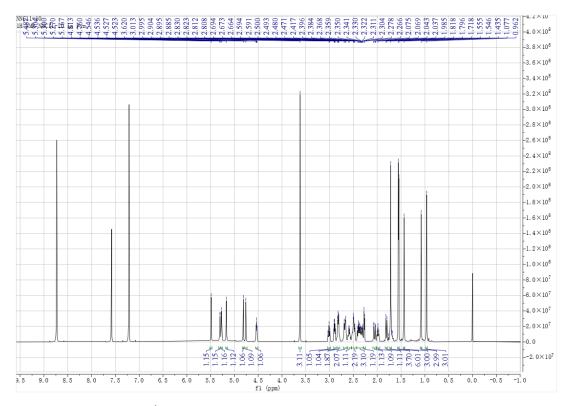


Figure S160. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 32

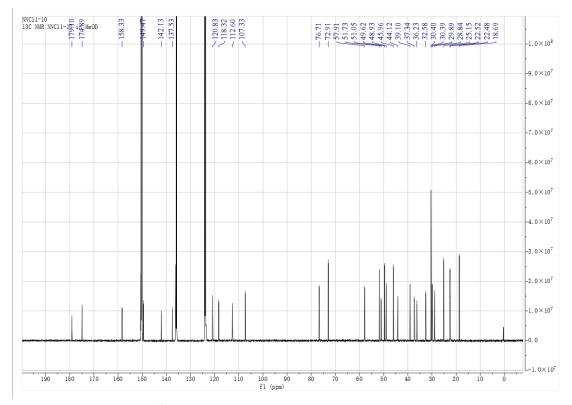


Figure S161. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 32

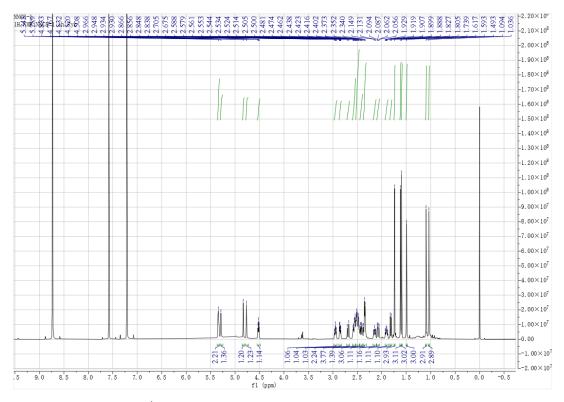


Figure S162. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 33

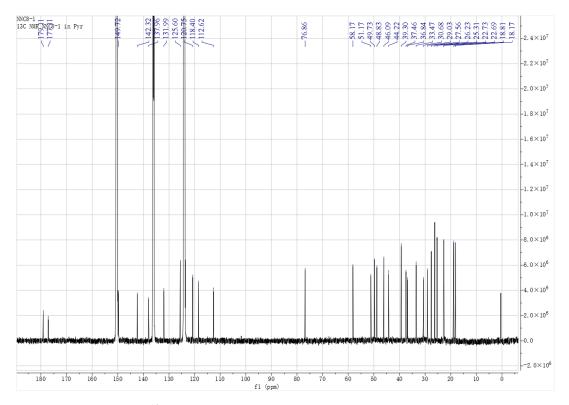


Figure S163. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 33

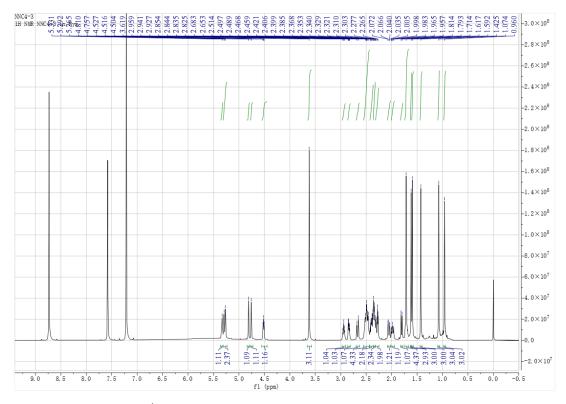


Figure S164. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 34

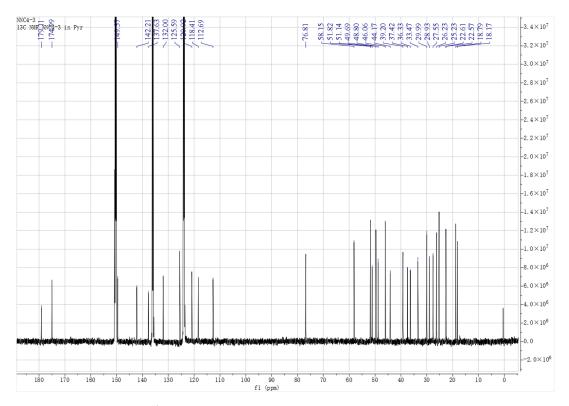


Figure S165. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 34

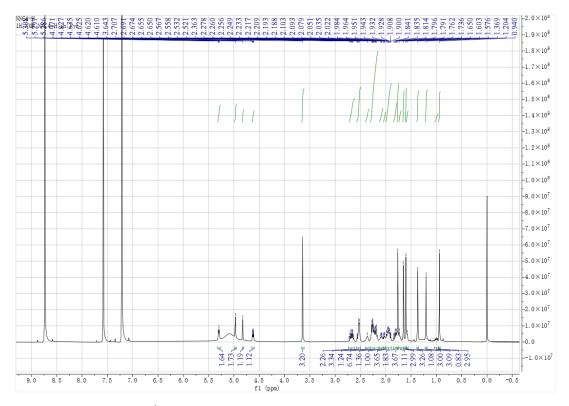


Figure S166. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 35

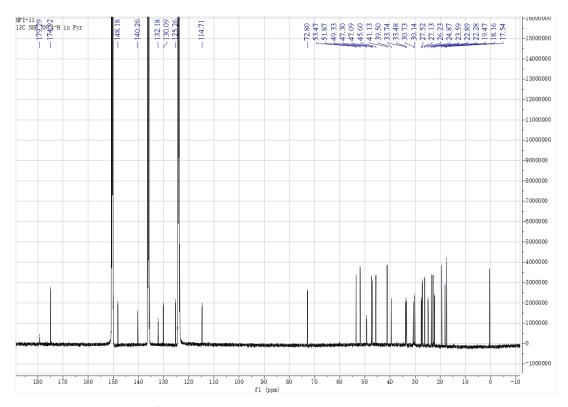


Figure S167. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 35

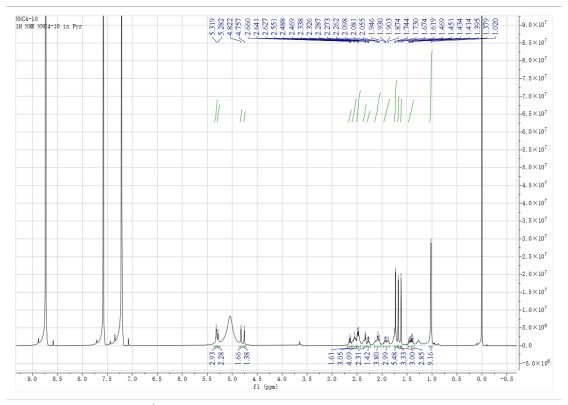


Figure S168. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 36

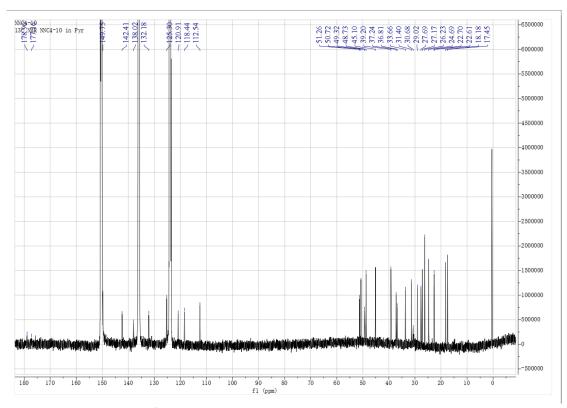


Figure S169. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 36

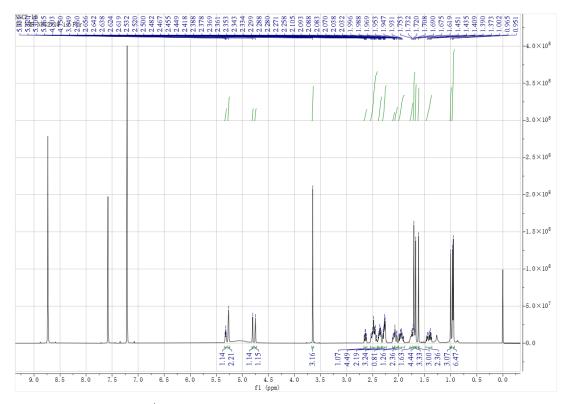


Figure S170. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 37

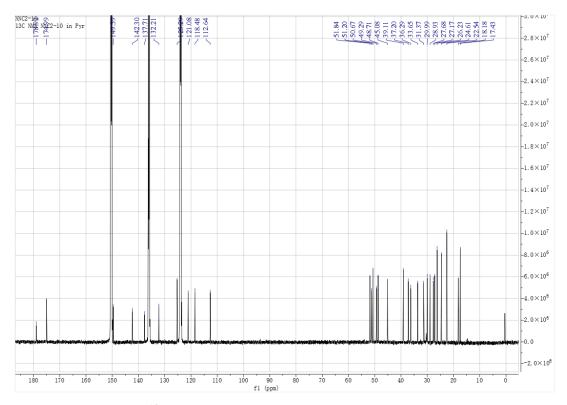


Figure S171. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 37

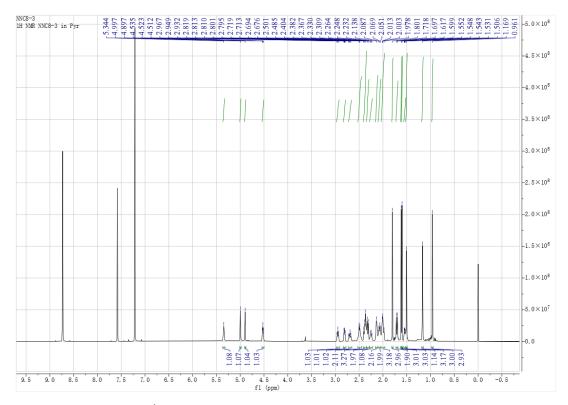


Figure S172. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 38

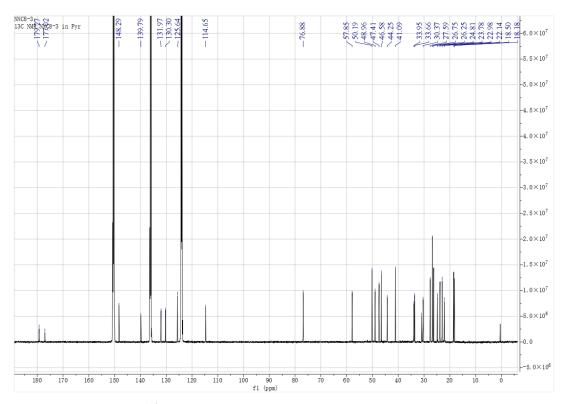


Figure S173. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 38

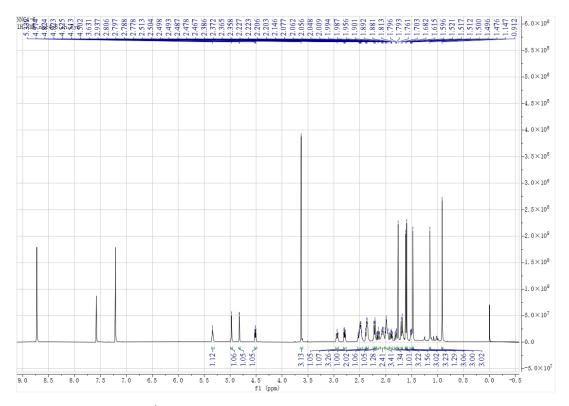


Figure S174. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 39

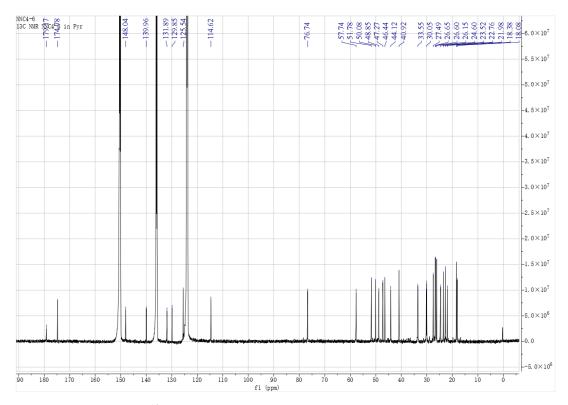


Figure S175. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 39

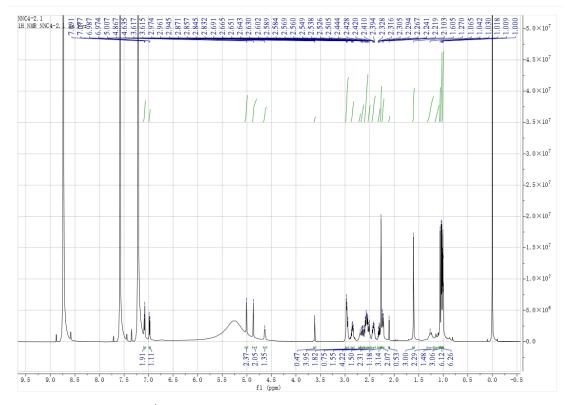


Figure S176. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 40

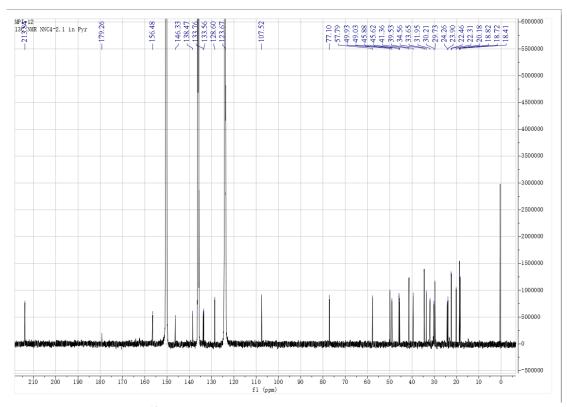


Figure S177. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 40

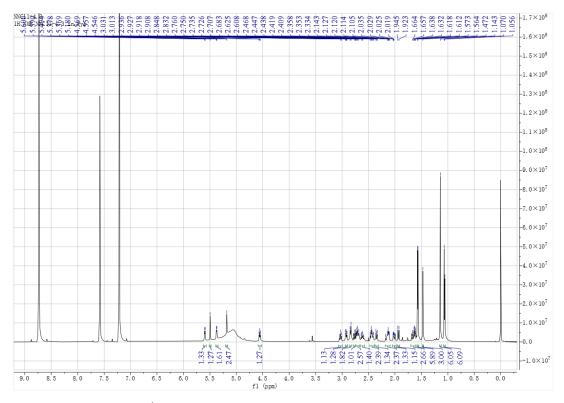


Figure S178. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 41

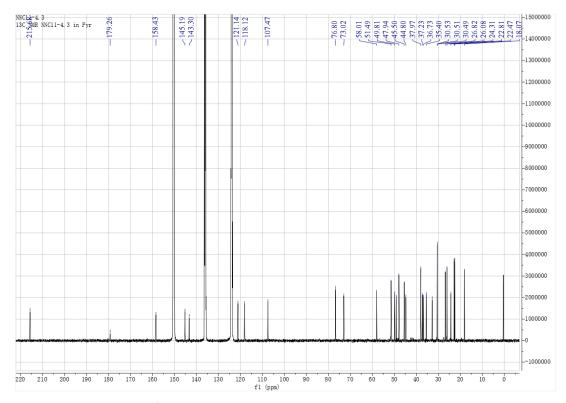


Figure S179. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 41

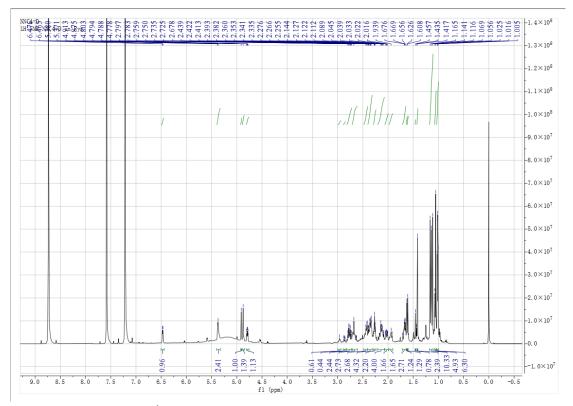


Figure S180. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 42

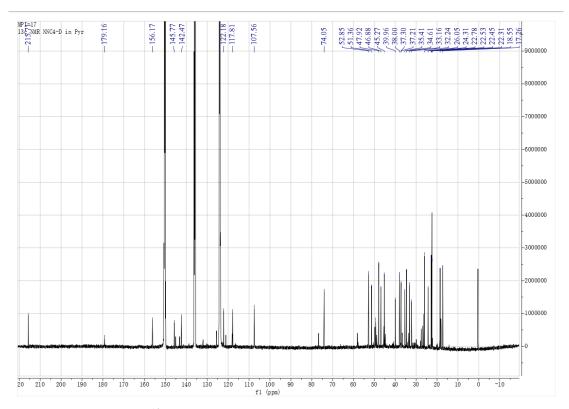


Figure S181. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 42

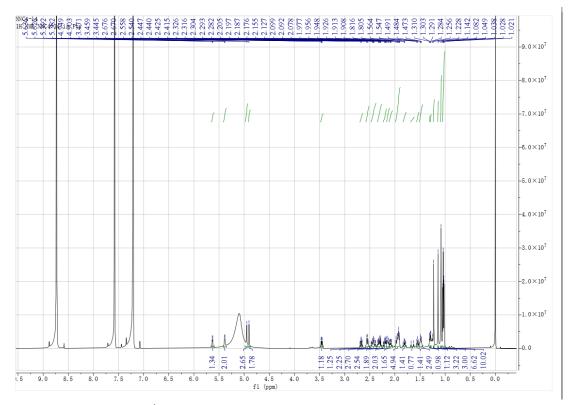


Figure S182. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 43

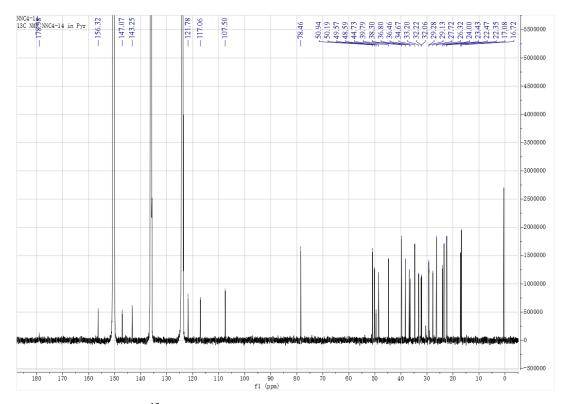


Figure S183. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 43

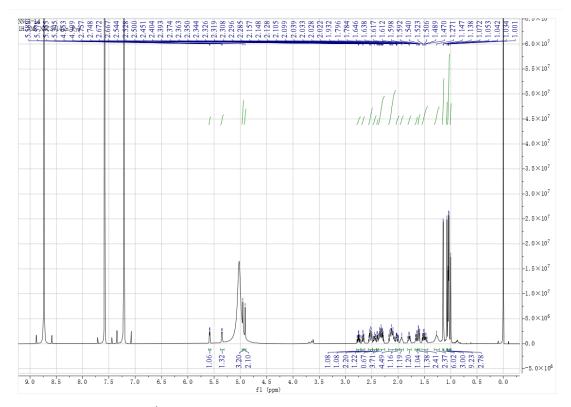


Figure S184. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 44

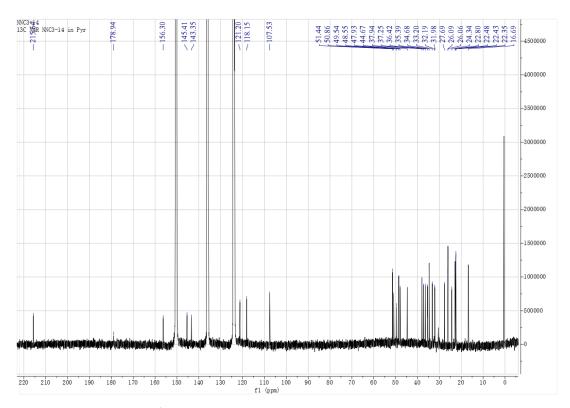


Figure S185. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 44

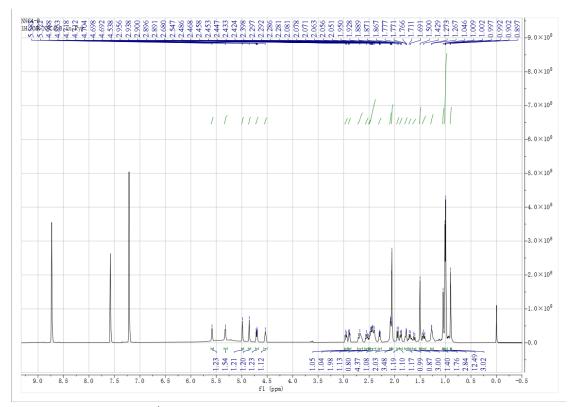


Figure S186. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 45

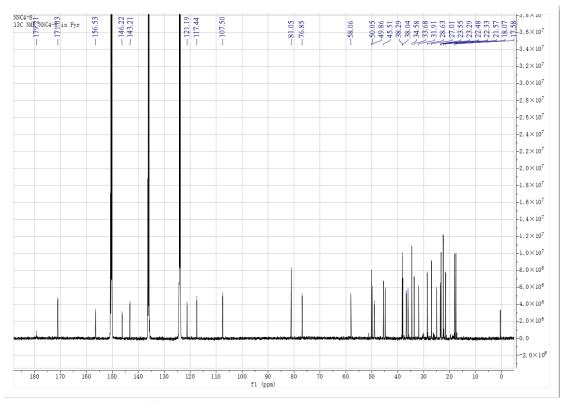


Figure S187. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 45

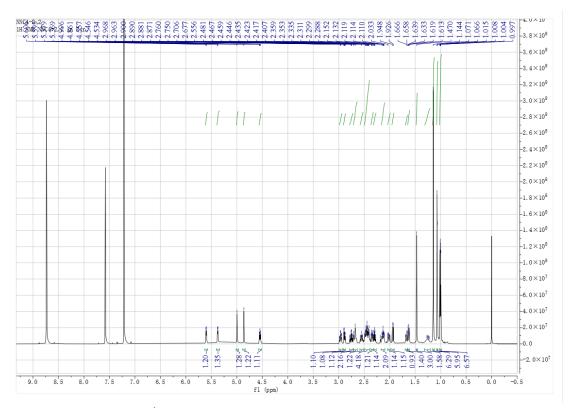


Figure S188. <sup>1</sup>H NMR spectrum (600 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 46

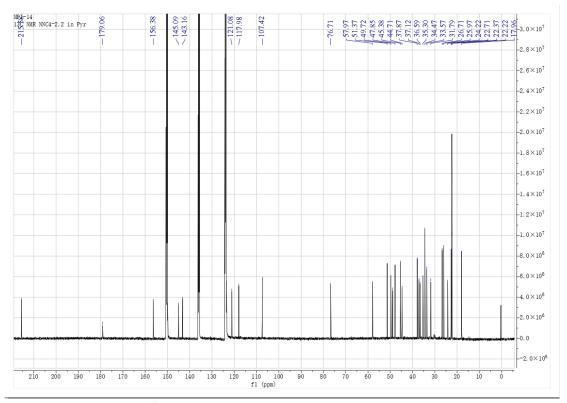


Figure S189. <sup>13</sup>C NMR spectrum (150 MHz, C<sub>5</sub>D<sub>5</sub>N) of compound 46