

*Supporting Information for*

**6,6'-(methylazanediyl) bis (methylene) bis (2,4-dimethylphenol) Induces Autophagic Associated Cell Death Through mTOR-mediated Autophagy in Lung Cancer**

Nicharat Sriratanasak<sup>1,2</sup>, Worawat Wattanathana<sup>3</sup>, Pithi Chanvorachote<sup>1,2,\*</sup>

<sup>1</sup>Department of Pharmacology and Physiology, Faculty of Pharmaceutical Sciences, Bangkok 10330, Thailand

<sup>2</sup>Center of Excellence in Cancer Cell and Molecular Biology, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok 10330, Thailand

<sup>3</sup>Department of Materials Engineering, Faculty of Engineering, Kasetsart University, Lad Yao, Chatuchak, Bangkok, Thailand

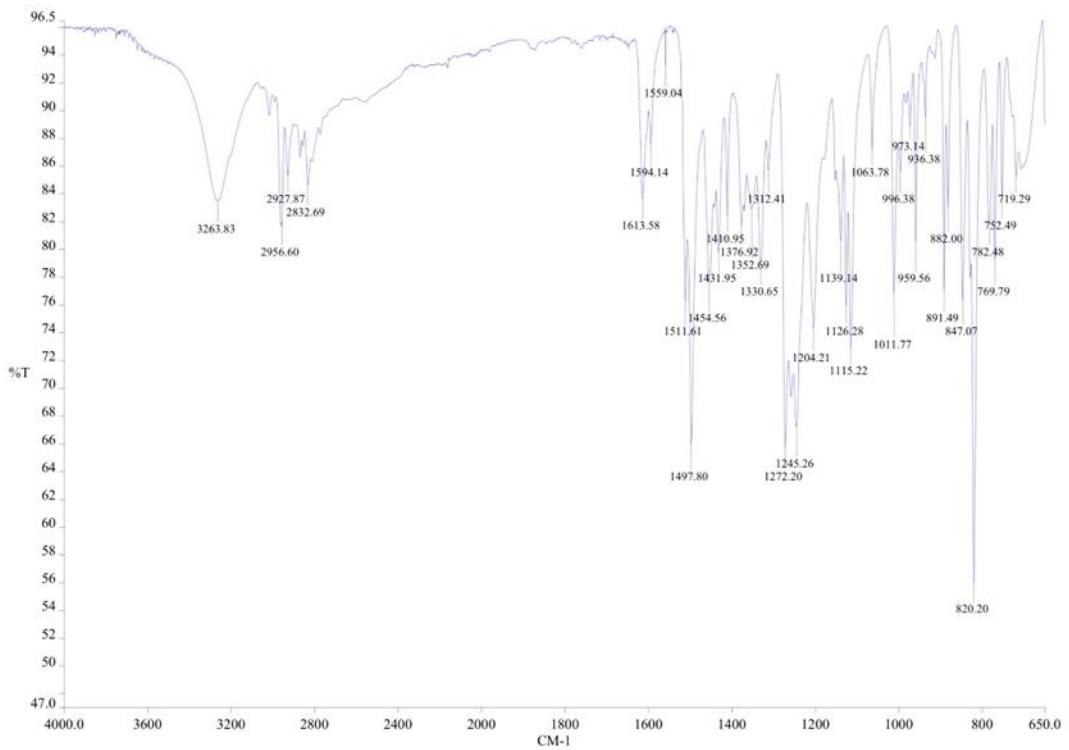
\*Correspondence: pithi.c@chula.ac.th.

---

**Spectral data for the synthesized organic compounds**

**(I) 2,2'-(methylazanediyl)bis(methylene)bis(4-ethylphenol) or EMD**

FTIR ( $\text{cm}^{-1}$ ): 3263 (br, O-H), 1497 (vs, C<sub>a</sub>-C<sub>a</sub>), 1454 (m, N-CH<sub>3</sub>), 1272 (m, C-O), 1204 (m, C-N-C), 820 (m, C-N-C); <sup>1</sup>H NMR ( $\delta_{\text{H}}$ , ppm): 1.29 (d,  $J = 8.0$  Hz, 6H), 2.36 (s, 3H), 2.64 (d,  $J = 7.5$  Hz, 4H), 3.81 (s, 4H), 6.85 (d,  $J = 8.0$  Hz, 2H), 6.99 (d,  $J = 2.2$  Hz, 2H), 7.05 (dd,  $J = 2.0, 8.0$  Hz, 2H); <sup>13</sup>C NMR ( $\delta_{\text{C}}$ , ppm): 15.89 (-CH<sub>3</sub>), 27.94 (-CH<sub>2</sub>-C<sub>a</sub>), 40.98 (CH<sub>3</sub>-NR<sub>2</sub>), 59.24 (-CH<sub>2</sub>-NR<sub>2</sub>), 115.80 (C<sub>a</sub>), 122.31 (C<sub>a</sub>), 128.22 (C<sub>a</sub>), 129.47 (C<sub>a</sub>), 135.16 (C<sub>a</sub>), 154.19 (C-OH). (Yield: 89%)



**Figure S1** Fourier-transform infrared spectrum of EMD

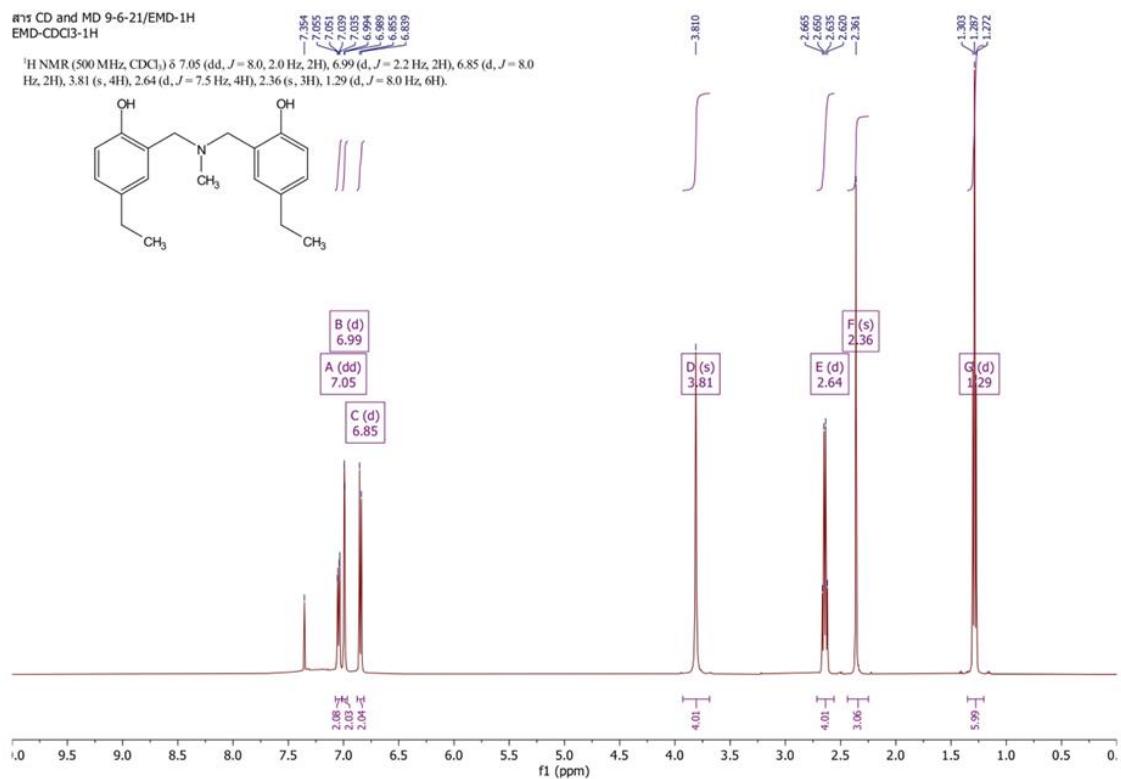


Figure S2 <sup>1</sup>H-NMR spectrum of EMD

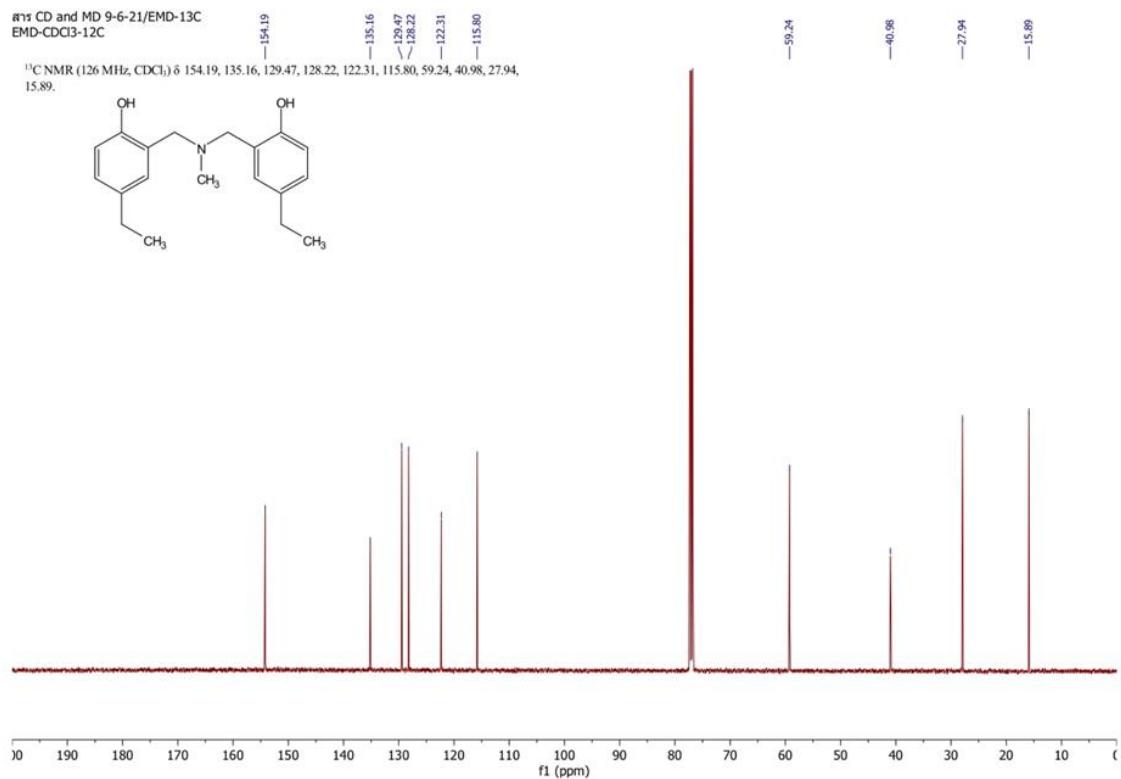
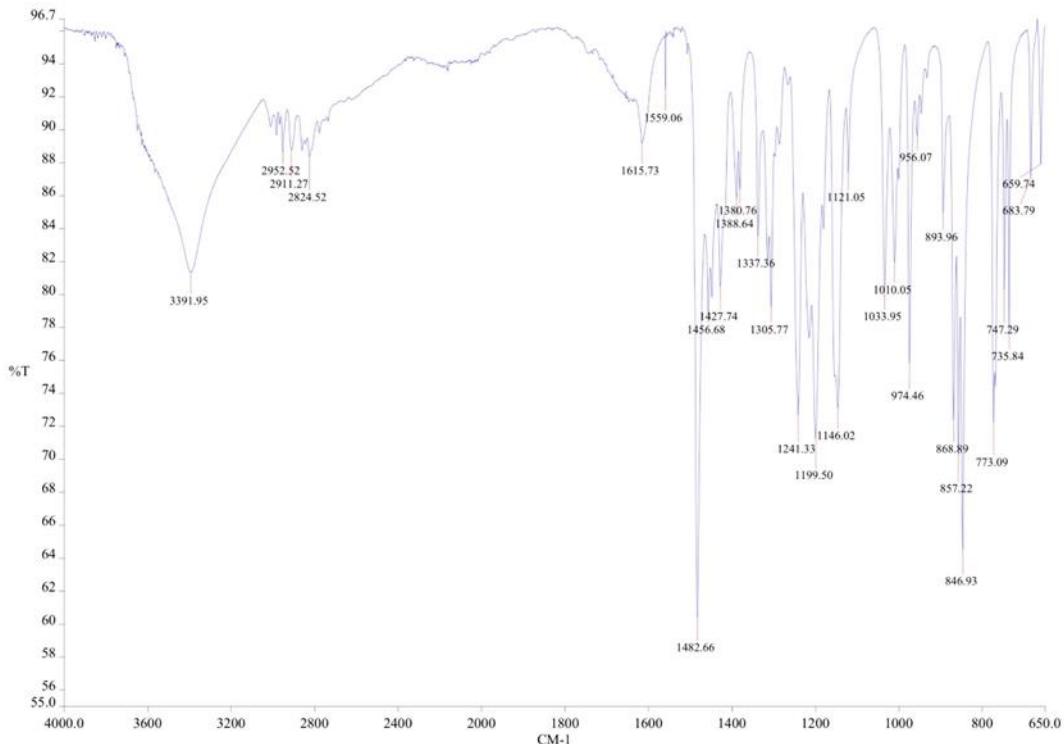


Figure S3 <sup>13</sup>C-NMR spectrum of EMD

(II) **6,6'-(methylazanediyl)bis(methylene) 409 bis(2,4-dimethylphenol) or 24MD**  
 FTIR ( $\text{cm}^{-1}$ ): 3391 (*br*, O–H), 1482 (*vs*, C<sub>a</sub>–C<sub>a</sub>), 1456 (*m*, N–CH<sub>3</sub>), 1241 (*m*, C–O), 1199 (*m*, C–N–C), 846 (*m*, C–N–C); <sup>1</sup>H NMR ( $\delta_{\text{H}}$ , ppm): 2.32 (*s*, 12H), 2.34 (*s*, 3H), 3.77 (*s*, 4H), 6.83 (*d*,  $J = 2.5$  Hz, 2H), 6.98 (*d*,  $J = 2.5$  Hz, 2H); <sup>13</sup>C NMR ( $\delta_{\text{C}}$ , ppm): 15.86 (–CH<sub>3</sub>), 20.42 (–CH<sub>3</sub>), 41.06 (CH<sub>3</sub>–NR<sub>2</sub>), 59.35 (–CH<sub>2</sub>–NR<sub>2</sub>), 121.41 (C<sub>a</sub>), 124.54 (C<sub>a</sub>), 128.40 (C<sub>a</sub>), 128.59 (C<sub>a</sub>), 131.15 (C<sub>a</sub>), 151.95 (C–OH). (Yield: 80%)



**Figure S4** Fourier-transform infrared spectrum of 24MD

ans CD and MD 9-6-21/24MD-1H  
24-MD-CDCl<sub>3</sub>-1H

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 6.98 (d, *J* = 2.5 Hz, 2H), 6.83 (d, *J* = 2.5 Hz, 2H), 3.77 (s, 4H), 2.34 (s, 3H), 2.32 (s, 12H).

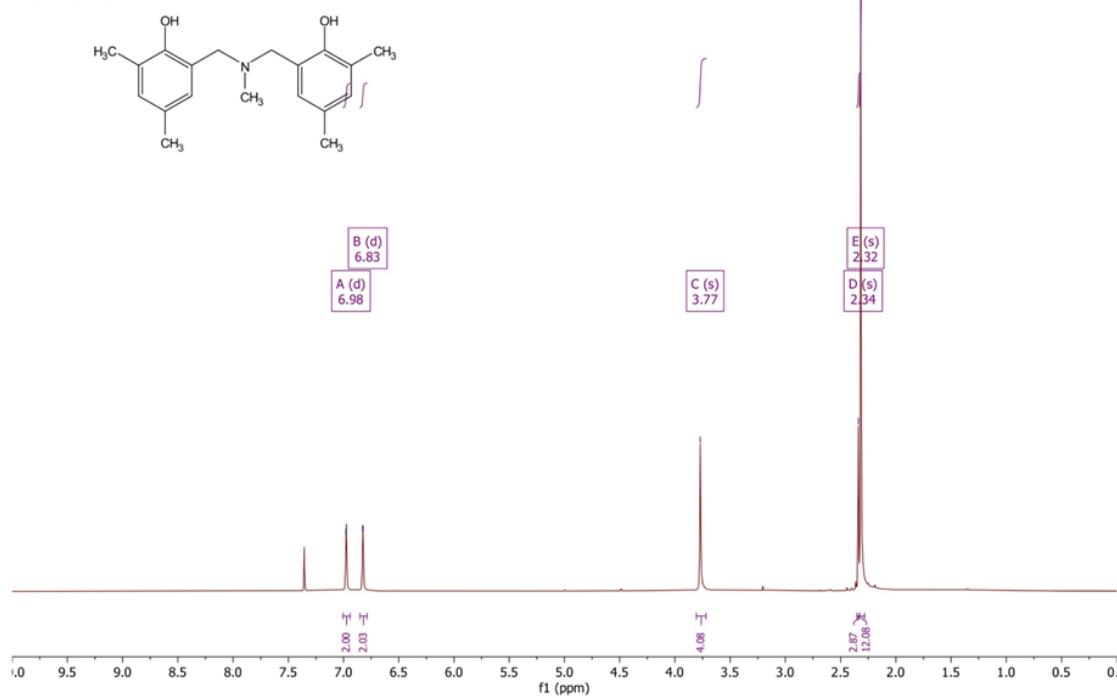


Figure S5 <sup>1</sup>H-NMR spectrum of 24MD

11-09-2021.19.fid  
24-MD-CDCl<sub>3</sub>-12C

<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 151.95, 131.15, 128.59, 128.40, 124.54, 121.41, 59.35, 41.06, 20.42, 15.86.

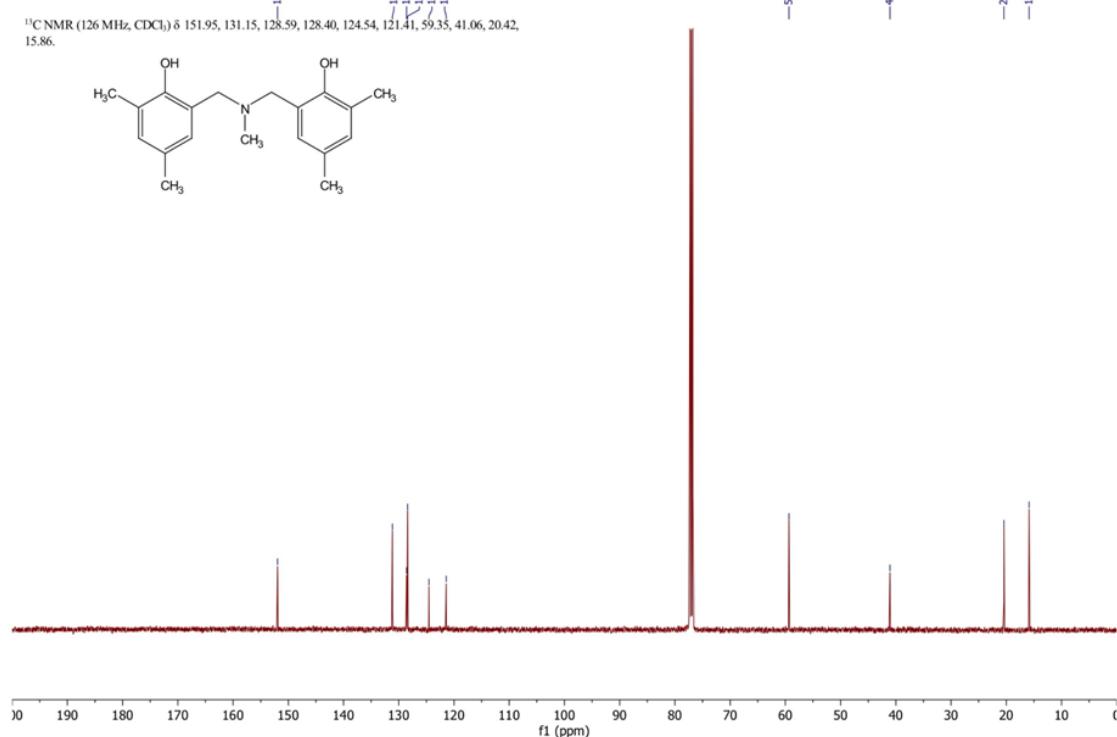
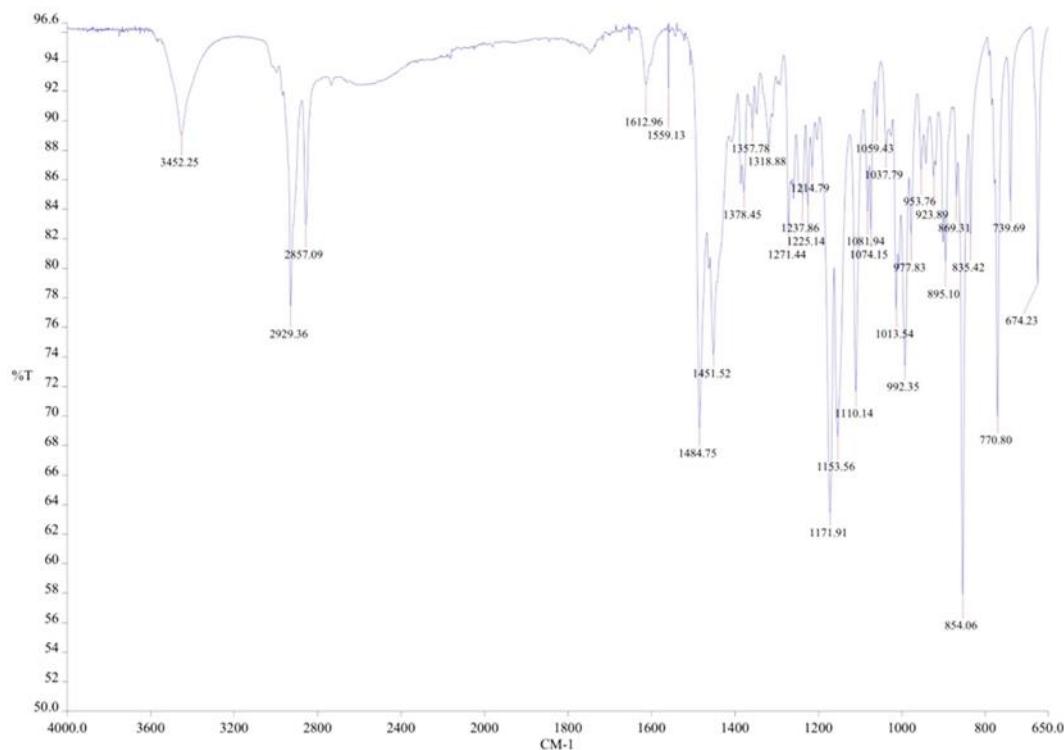


Figure S6 <sup>13</sup>C-NMR spectrum of 24MD

**(III) 6,6'-(cyclohexylazanediyl)bis(methylene) 410 bis(2,4-dimethylphenol) or 24CD**

FTIR ( $\text{cm}^{-1}$ ): 3452 (*br*, O–H), 1484 (*vs*, C<sub>a</sub>–C<sub>a</sub>), 1451 (*m*, N–C<sub>cy</sub>), 1171 (*m*, C–O), 1153 (*m*, C–N–C), 854 (*m*, C–N–C); <sup>1</sup>H NMR ( $\delta_{\text{H}}$ , ppm): 1.14–1.23 (*m*, 1H), 1.24–1.34 (*m*, 2H), 1.46–1.61 (*m*, 2H), 1.73 (*dt*,  $J = 3.5$ , 13.0 Hz, 1H), 1.91 (*dt*,  $J = 3.5$ , 13.0 Hz, 2H), 2.03 (*dd*,  $J = 3.5$ , 9.0 Hz, 2H), 2.30 (*d*,  $J = 4.5$  Hz, 12H), 2.81 (*tt*,  $J = 3.5$ , 12.0 Hz, 1H), 3.83 (*s*, 4H), 6.79 (*d*,  $J = 2.0$  Hz, 2H), 6.95 (*d*,  $J = 2.0$  Hz, 2H); <sup>13</sup>C NMR ( $\delta_{\text{C}}$ , ppm): 15.90 (–CH<sub>3</sub>), 20.45 (C<sub>cy</sub>), 25.78 (–CH<sub>3</sub>), 26.15 (C<sub>cy</sub>), 27.45 (C<sub>cy</sub>), 51.48 (–CH<sub>2</sub>–NR<sub>2</sub>), 57.43 (C<sub>cy</sub>–NR<sub>2</sub>), 121.69 (C<sub>a</sub>), 124.83 (C<sub>a</sub>), 128.45 (C<sub>a</sub>), 128.50 (C<sub>a</sub>), 130.90 (C<sub>a</sub>), 152.06. (Yield: 89%)



**Figure S7** Fourier-transform infrared spectrum of 24CD

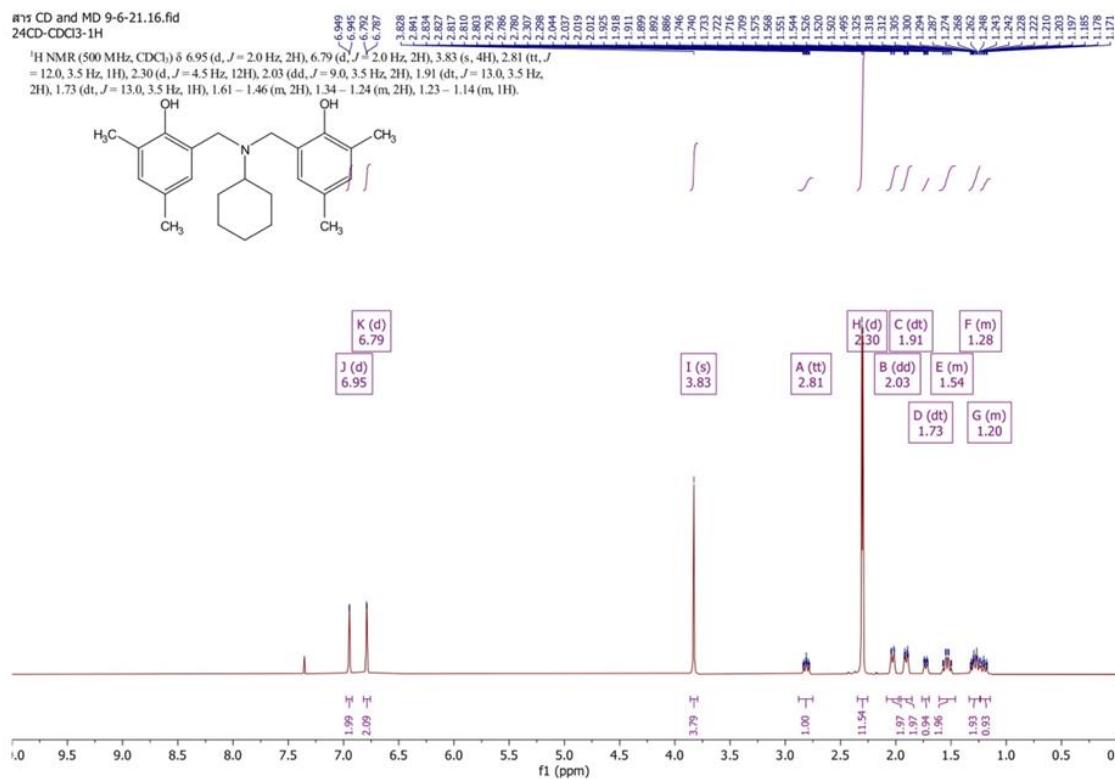


Figure S8 <sup>1</sup>H-NMR spectrum of 24CD

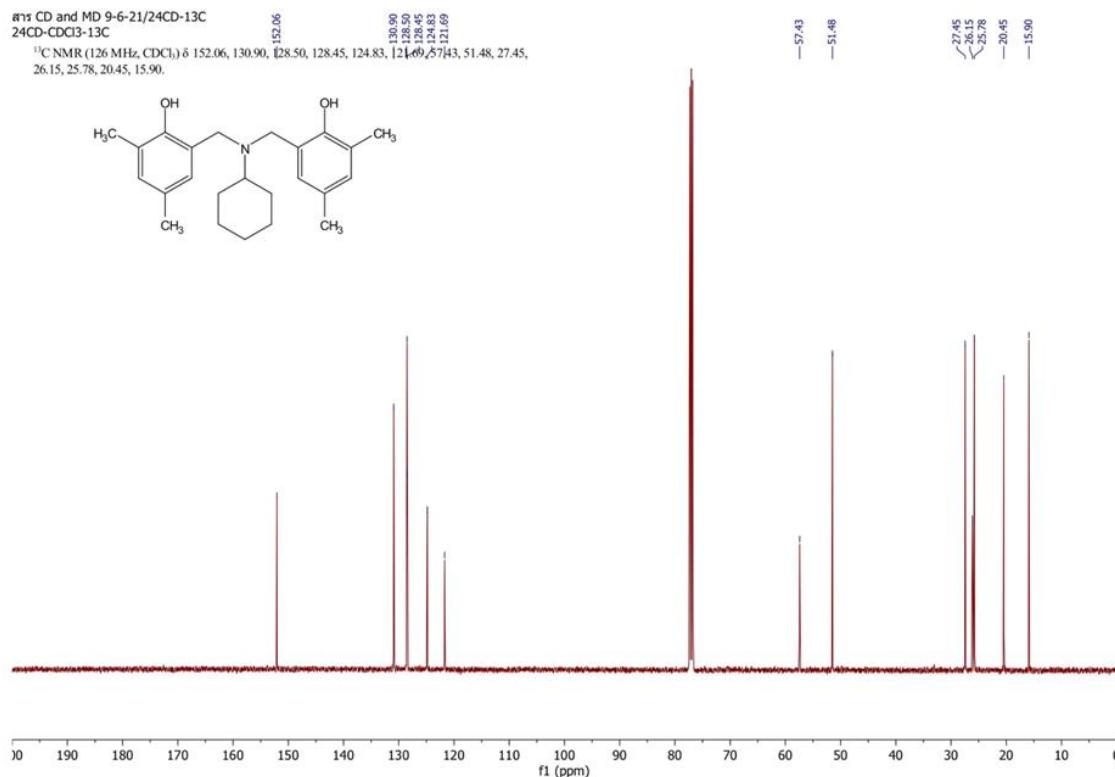


Figure S9 <sup>13</sup>C-NMR spectrum of 24CD