Supplementary Materials

Discovery of Natural Dimeric Naphthopyrones as Potential Cytotoxic Agents Through ROS-mediated Apoptotic Pathway

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General procedure for ECD calculations

In general, conformational analyses of compounds 1 and 12 are carried out via systematic searching in the WaveFunction Spartan 14 (version 1.1.4) using the MMFF94 force field. Conformers with Boltzmann distribution over 1% are chosen as the beginning for ECD calculations. Ground-state geometries are optimized at the B3LYP/6-311+G(d,p) level in gas phase by the Gaussian 16 program (Gaussian Inc., Wallingford, CT, USA). All quantum computations are performed on an IBM cluster machine located at the High Performance Computing Center of Peking Union Medical College. The energies, oscillator strengths, and rotational strengths (velocity) of the first 50 electronic excitations are calculated using the TD-DFT methodology at the B3LYP/6-311+G(d,p) level in methanol. The ECD spectra are simulated by the overlapping Gaussian function (half the bandwidth at 1/e peak height, 0.25 eV). By comparison of the calculated and experimental ECD spectra, the absolute configurations of these compounds are established.

Table 1. The 3D conformers of 1 and 12 with Boltzmann distribution over 1%.

| Compounds no. | 3D Conformers | ΔG (kcal/mol) | Population (%) |
|---------------|---------------|---------------|----------------|
| 1             | ![3D conformer of 1](image1) | 0.00          | 79.7           |
| 2             | ![3D conformer of 12](image2) | 5.92          | 7.3            |
|   |   | ![Image](image1.png) |   |   |
|---|---|---|---|---|
| 3 | ![Image](image2.png) | 6.73 | 5.3 |
| 4 | ![Image](image3.png) | 7.48 | 3.9 |
| 5 | ![Image](image4.png) | 8.39 | 0.027 |
| 6 | ![Image](image5.png) | 10.54 | 1.1 |
| 12 | ![Image](image6.png) | 0.00 | 100.0 |
References:

1. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ó.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, Rev. C 01; Gaussian, Inc., Wallingford CT, 2009.

2. Stephens, P. J.; Harada, N. ECD cotton effect approximated by the Gaussian curve and other methods. Chirality 2010, 22, 229–233.
Analytical HPLC spectra for all isolated compounds (1–18)
### Shimadzu LCsolution 分析报告

#### 样品信息

- **样品名称**: Compound 16
- **样品浓度**: 1
- **样品体积**: 20 μL
- **溶剂**: 乙醇

#### 操作条件

- **溶剂**: 乙醇
- **流动相**: 水:乙醇=10:90
- **检测波长**: 254 nm
- **检测条件**: 210nm

#### 数据处理

- **数据处理**: 2019-07-18 15:27:05

#### 图表

- **UV Chromatogram**: Compound 16

| 分析器 | A | B |
|--------|---|---|
| 1 | 19.28 | 20.03 |
| 2 | 19.28 | 20.03 |
| 3 | 19.28 | 20.03 |
| 4 | 19.28 | 20.03 |
| 5 | 19.28 | 20.03 |

#### 表格

| 分析器 | A | B |
|--------|---|---|
| 1 | 19.28 | 20.03 |
| 2 | 19.28 | 20.03 |
| 3 | 19.28 | 20.03 |
| 4 | 19.28 | 20.03 |
| 5 | 19.28 | 20.03 |

#### 绘图

- **UV Chromatogram**: Compound 16

- **UV Chromatogram**: Compound 16
—— Shimadzu LCsolution 分析报告 ——

样品信息

样品名称：Compound 17

数据生成日期：2019-3-7

数据来源：11:34:58

图谱

Compound 17 E: HPLC谱图 (C20%甲醇-THF) 10000

1 检测器 A 流速1 / 35mm

峰表

峰号 峰面积 A (mm²) 峰面积 B (mm²) 峰面积 C (mm²) 峰面积 D (mm²)

1 15995 1123 0.3 0.002
2 126 1123 0.72 0.003
3 10.25 1123 0.725 0.003
4 10.25 1123 0.725 0.003

总计 119675 1123 0.725 0.003

图谱

Compound 17 S: UPLC谱图 (C20%甲醇-THF) 10000

1 检测器 A 流速1 / 35mm

峰表

峰号 峰面积 A (mm²) 峰面积 B (mm²) 峰面积 C (mm²) 峰面积 D (mm²)

1 1531 1000 99.0 0.002
2 1531 1000 99.0 0.002
3 1531 1000 99.0 0.002
4 1531 1000 99.0 0.002

总计 119675 1123 0.725 0.003
