3''-Hydroxymethyl-butyrolactone II from Aspergillus sp.

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Abstract

In continuation of the search for new compounds from the terrestrial fungus Aspergillus sp., one new butyrolactone, 3''-hydroxymethyl-butyrolactone II (1) was isolated. The chemical structure of 1 was confirmed by extensive 1D and 2D NMR and HR-ESI mass data analysis, and by comparison with literature data. The absolute configuration was also determined by ECD calculations.

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Experimental Section

1.1. General Experimental Procedure

UV spectra was measured on a Shimadzu UV-1601 (Shimadzu, Tokyo, Japan). IR spectra was measured on a Bruker IFS-55 infrared spectrophotometer (Bruker Co., Zurich, Switzerland). The optical rotation was measured on a PerkinElmer 241 polarimeter (PerkinElmer Co., Jena, Germany). The NMR spectral data were recorded on a Bruker AV spectrometer (400 MHz for $^1$H and 100 MHz for $^{13}$C) with TMS (tetramethylsilane) as the internal standard (Bruker Co.). The HR-ESI-MS data was obtained on the MicrosMass AutoSpec-UltimaE TOF mass spectrophotometer (Bruker Co.). Chromatography was carried out on silica gel (200-300 mesh; Qingdao Haiyang Chemical Factory, Qingdao, China), Sephadex LH-20 (Pharmacia, Piscataway, NJ, USA), and reversed phase HPLC (Shimadzu LC-8A vp, Kyoto, Japan).

1.2. Isolation and Taxonomy of the producing strain

Isolation and taxonomy of the terrestrial Aspergillus sp. was reported recently (An et al., 2016).

1.3. Fermentation, Extraction and Isolation

The fermentation and extraction was described previously (An et al., 2016). Briefly, the EtoAc extraction was subjected to silica column with CHCl$_3$: MeOH (100:1-1:100) as the eluent. An application of sub-fraction F delivered on Sephadex LH-20 (DCM/50% MeOH) and then RP-18 column (Water/Methanol [80:20]) afforded (4R)-3”-hydroxymethyl-butyrolactone II (5.2 mg) as yellow oil.

(4R)-3”-hydroxymethyl-butyrolactone II (1)

Yellow oil. $[\alpha]_D^{20} +11.6$ (c 0.60, MeOH), UV (MeOH) $\lambda_{\text{max}}$: 208 nm; IR (KBr) $\nu_{\text{max}}$ (cm$^{-1}$) 3345, 2988, 1685, and 1225; HR-ESI-MS $m/z$ 409.0889; $^1$H-NMR (400 MHz, DMSO-$d_6$) and $^{13}$C-NMR (100 MHz, DMSO-$d_6$): see Table S1.

1.4. Antimicrobial, anti-inflammatory, and DHHP/ABTS assays
See An et al. 2016, An et al. 2017, and Gao et al. 2017

1.5. Quantum-mechanical calculations

The least-energy conformations of the investigated compounds were determined with systematic methods implemented in Discovery studio 2013 package. The possible conformers were optimized using DFT at the B3LYP/6-31G (d) level in the GAUSSIAN 09 program. The optimized isomer was calculated using DFT at the B3LYP/6-311G (d, p) in the GAUSSIAN 09 program to generate its ECD property.

References

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An X, Feng BM, Chen G, Chen SF, Bai J, Hua HM, Wang HF, Pei YH. 2017. Isolation and identification of phase I metabolites of butyrolactone I in rats. Xenobiotica. 47: 236-244.

Gao Y, Rao H, Mao LJ, Ma QL. 2017. Chemical composition, antioxidant, antibacterial and cytotoxic activities of essential oil of Leontopodium leontopodioides (Willd.) Beauverd. Nat Prod Res. 17:1-4.
Table S1. $^1$H (400 MHz) and $^{13}$C NMR (100 MHz) data of 1 in DMSO-$d_6$

| position | $\delta_H$ (J in Hz) | $\delta_C$ |
|----------|----------------------|-----------|
| 1        | -                    | 168.4     |
| 2        | -                    | 138.5     |
| 3        | -                    | 128.1     |
| 4        | -                    | 85.2      |
| 5        | 3.35 (d, 16.4); 3.42 (d, 16.4) | 38.7 |
| 6        | -                    | 170.2     |
| 1'       | -                    | 121.4     |
| 2'       | 7.51 (d, 8.8)        | 129.3     |
| 3'       | 6.88 (d, 8.8)        | 116.3     |
| 4'       | -                    | 158.3     |
| 5'       | 6.88 (d, 8.8)        | 116.3     |
| 6'       | 7.51 (d, 8.8)        | 129.3     |
| 1''      | -                    | 123.4     |
| 2''      | 6.79 (d, 2.0)        | 130.1     |
| 3''      | -                    | 128.1     |
| 4''      | -                    | 153.6     |
| 5''      | 6.50 (d, 8.4)        | 114.3     |
| 6''      | 6.47 (dd, 8.4, 2.0)  | 129.5     |
| 7''      | 4.31 (2H, s)         | 58.6      |
| 6-OCH$_3$| 3.74 (3H, s)         | 53.9      |
Figure S1: The key HMBC correlations of 1.
Figure S2: Main conformers of (4S)- (left) and (4R) (right), determined by DFT calculations (B3LYP/6-311G (d, p) of 1.
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**Figure S7**: The HMBC spectrum of 1.
Figure S8: The HR-ESI-MS spectrum of 1.