海鞘内生真菌焦曲霉 *Aspergillus ustus* TK-5 的化学成分研究

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摘要: 焦曲霉(*Aspergillus ustus*)TK-5 是分离自土耳其海域海鞘(*Pyura momus*)新鲜组织中的一株内生真菌, 利用正相与反相硅胶柱层析、葡聚糖凝胶 Sephadex LH-20 柱层析以及高效液相制备等色谱方法从其发酵产物中分离得到 17 个化合物, 通过一维、二维核磁共振、质谱等技术鉴定了所有化合物的结构, 分别为血苋烷型倍半萜类化合物 strobilactone A(**1**), ustusolate E(**2**), ustusolate C(**3**), ustusolate D(**4**), 11-hydroustusolate E(**5**), 11, 6'-hydroustusolate E(**6**), (2'*E*, 4'*E*, 6'*E*)-6-(1'-carboxyocta-2', 4', 6'-triene)-11, 12-epoxy-9, 11-dihydroxydrim-7-ene(**7**), 12-hydroxy-6-epi-albrassitriol (**8**), ustusolate A (**9**), deoxyuvidin B (**10**)和二倍半萜类化合物 6-epi-ophiobolin G(**11**), (6*α*)-21, 21-*O*-dihydroophiobolin G(**12**), 6-epi- ophiobolin K(**13**), ophiobolin P(**14**) ophiobolin H(**15**), ophiobolin Q(**16**)及 ophiobolin R(**17**)。活性筛选表明化合物 **2**、**6**、**7**、**9**、**11** 和 **13** 对神经氨酸酶具有一定的抑制活性, 其半数抑制浓度(IC_{50}) 分别为 31.8、37.3、28.4、36.8、46.6 和 37.6 μmol/L。

关键词: 海鞘; 内生真菌; 焦曲霉; 萜类; 神经氨酸酶抑制活性

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海洋环境的复杂性和生物竞争的多样性造就了海洋生物独特的代谢途径和适应机制, 其中海洋微生物多与海洋动、植物共附生, 有利于激发其沉默基因从而代谢产生结构新颖、具有多种生物活性的次级代谢产物。越来越多的研究已证实在海洋无脊椎动物中分离到的活性物质的真正生产者是其体内共附生的微生物[1-2]。因此以海洋动物为宿主的微生物代谢产物研究引起了科学家们的广泛关注, 成为活性天然产物的主要来源之一[3-5]。

海鞘作为海洋微生物的重要宿主, 其内生真菌天然产物的研究却鲜有报道。本文报道从采自土耳其海域的海鞘(*Pyura momus*)组织中分离到一株内生真菌 *Aspergillus ustus* TK-5, 根据文献报道 *A. ustus* 主要分离自海绵和海鞘, 但其特征产物都是血苋烷型倍半萜和二倍半萜类化合物, 以此确定以上报道的代谢产物不是来自于其宿主, 而是 *A. ustus* 自身的代谢产物[6-10]。从 *A. ustus*TK-5 发酵培养物中分离鉴定了 17 个化合物(图 1), 通过一维、二维核磁共振、质谱等光谱技术鉴定了所有化合物的结构, 与文献报道相符主要是血苋烷型倍半萜类(**1-10**)和二倍半萜类化合物(**11-17**), 分别是 strobilactone A (**1**)[11], ustusolate E (**2**)[6], ustusolate C (**3**)[6], ustusolate D (**4**)[6], 11-hydroustusolate E (**5**)[12], 11, 6'-hydroustusolate E (**6**)[12], (2'*E*, 4'*E*, 6'*E*)-6-(1'-carboxyocta-2', 4', 6'- triene)-11, 12-epoxy-9, 11-dihydroxydrim-7-ene (**7**)[13], 12-hydroxy-6-epi-albrassitriol (**8**)[14], ustusolate A (**9**)[6], deoxyuvidin B (**10**)[14], 6-epi-ophiobolin G (**11**)[15], (6*α*)-21, 21-*O*-dihydroophiobolin G (**12**)[10], 6-epi-ophiobolin K (**13**)[16], ophiobolin P (**14**)[17], ophiobolin H (**15**)[10], ophiobolin Q (**16**)[17]和 ophiobolin R (**17**)[17]。对所有化合物进行了神经氨酸酶抑制活性测试。

1　材料与方法

1.1　仪器与试剂

Bruker Avance 500 MHz 核磁共振仪; Dionex 分析型和制备型高效液相色谱仪; 薄层色谱硅胶 GF254 和柱色谱硅胶(200~300 目)为青岛海洋化工厂分厂产品; Lobar LiChroprep RP-18 硅胶 (40~63 μm,

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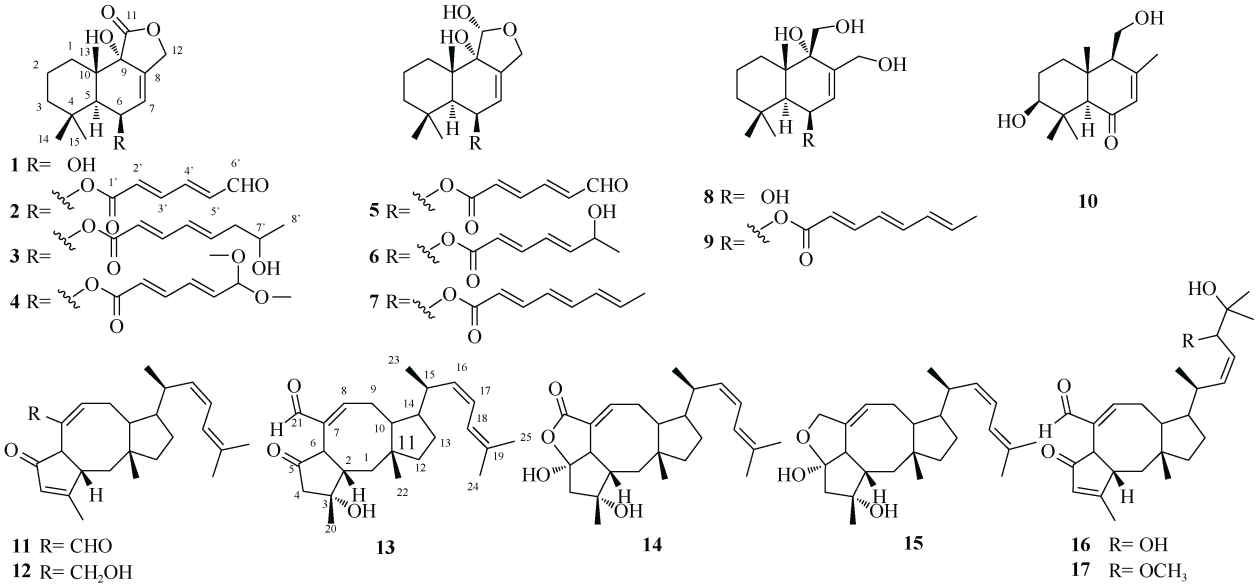

图 1　化合物的结构(**1-17**)

Fig. 1　Structures of compounds **1-17**

Merck); 显色剂为茴香醛硫酸溶液和碘; 所用有机溶剂为重蒸的工业级溶剂。

1.2　菌株发酵

1.2.1　菌株

菌株 *A. ustus* 分离自海鞘(*Pyura momus*)的新鲜组织, 该样品于 2015 年 5 月 27 日采自土耳其海域。

1.2.2　菌株发酵

菌种以琼脂-麦芽膏培养基 4℃保存。发酵培养基采用的是大米培养基, 1000 mL 三角瓶作为发酵容器, 每瓶加入大米 70 g, 玉米浆 0.2 g, 蛋白胨 0.3 g, 酵母粉 0.5 g, 味精 0.6 g, 海水 100 mL。规模发酵 100 瓶, 在 121℃下高压灭菌 20 min, 待冷却后接种, 28℃静置培养 30 d。

1.3　提取与分离

发酵产物经乙酸乙酯萃取后减压浓缩得到粗提物 107.5 g, 将粗提物进行硅胶真空柱层析, 根据极性从小到大(石油醚/乙酸乙酯到二氯甲烷/甲醇)进行梯度洗脱, 经 TLC 和 HPLC 检测, 合并得到 10 个组分(Fr.1~10)。

其中, Fr.5(8.3 g)经反相硅胶柱层析、正相硅胶柱层析(二氯甲烷∶甲醇=150∶1–50∶1)、凝胶 SephadexLH-20(甲醇)柱层析和制备薄层层析分离得到化合物 **1** (8.8 mg)、**2** (10.2 mg)、**3** (22.4 mg)、**5** (15.3 mg)、**13** (8.0 mg); Fr.6(9.5 g)经反相硅胶柱层析、正相硅胶柱层析(二氯甲烷∶丙酮=100∶1~40∶1)、制备薄层层析和凝胶 SephadexLH-20(甲醇)柱层析分离得到化合物 **6** (8.2 mg)、**7** (7.9 mg)、**11** (26.4 mg)、**12** (6.1 mg)、**14** (7.3 mg)、**15** (6.1 mg); Fr.8(12.4 g)经反相硅胶柱层析、凝胶 Sephadex LH-20(甲醇)柱层析、制备薄层层析、高效液相制备分离得到化合物 **4** (6.8 mg)、**8** (11.9 mg)、**9** (9.9 mg)、**10** (17.2 mg)、**16** (21.1 mg)、**17** (16.3 mg)。

1.4　活性测试

利用神经氨酸酶抑制剂筛选试剂盒(包括神经氨酸酶检测缓冲液、神经氨酸酶、神经氨酸酶荧光底物、Milli-Q 水)进行神经氨酸酶抑制活性测试[18]。

1.4.1　样品的准备

将待测化合物和阳性对照奥司他韦用甲醇分别配制成浓度为 100 μmol/L 的溶液。

1.4.2　样品检测的准备

在 96 孔荧光酶标板内每孔依次加入 70 μL 神经氨酸酶检测缓冲液、10 μL 神经氨酸酶、上述配置的待筛选的神经氨酸酶抑制剂样品或阳性对照奥司他韦溶液(样品和对照分别加入 0、1、2、5、7.5、10 μL)及 Milli-Q 水(10、9、8、5、2.5、0 μL, 使每孔总体积为 90 μL), 每个样品做三个平行。

1.4.3　检测

振动混匀约 1 min; 37℃孵育 2 min 使抑制剂和神经氨酸酶充分相互作用; 每孔加入 10 μL 神经氨

酸酶荧光底物; 再振动混匀约 1 min; 37℃孵育 30 min 后进行荧光测定, 激发波长为 322 nm, 发射波长为 450 nm。

1.4.4 计算

酶标仪测定每孔的吸光值(*OD* 值)。取三孔平均 *OD* 值, 按 IR% =($OD_{空白对照}$–$OD_{样品}$)/$OD_{空白对照}$×100%式计算样品对神经氨酸酶的抑制率(IR%), 并得到 IC_{50}。

2 化合物结构鉴定和神经氨酸抑制活性结果

2.1 化合物结构鉴定

化合物 **1**: 无色油状液体, ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 175.0 (C, C-11), 132.0 (C, C-8), 127.3 (CH, C-7), 73.4 (C, C-9), 68.3 (CH_2, C-12), 63.3 (CH, C-6), 45.2 (CH, C-5), 44.4 (CH_2, C-3), 37.0 (C, C-10), 33.7 (C, C-4), 32.3 (CH_3, C-15), 29.7 (CH_2, C-1), 24.3 (CH_3, C-14), 18.4 (CH_3, C-13), 17.5 (CH_2, C-2); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 5.95 (1H, s, 9-OH), 5.80 (1H, s, H-7), 4.84 (1H, d, *J*=12.2 Hz, H-12), 4.72 (1H, d, *J*=12.2 Hz, H-12), 4.65 (1H, d, *J*=5.7 Hz, 6-OH), 4.31 (1H, s, H-6), 1.90 (1H, td, *J*=13.6, 3.9 Hz, H-1), 1.76 (1H, d, *J*=13.4 Hz, H-1), 1.65 (1H, d, *J*=4.9 Hz, H-5), 1.59 (1H, d, *J*=13.6 Hz, H-2), 1.43 (1H, d, *J*=13.3 Hz, H-2), 1.28 (1H, d, *J*=13.5 Hz, H-3), 1.25 (3H, s, H-14), 1.16 (1H, t, *J*=12.8 Hz, H-3), 1.03(3H, s, H-15), 0.96 (3H, s, H-13)。其波谱数据与 strobilactone A[11]的文献报道一致。化合物 **1** 的比旋光度为$[\alpha]_D^{20}$ –130.0 (*c* 0.10, $CHCl_3$)与文献报道$[\alpha]_D^{20}$–110.0 (*c* 0.70, $CHCl_3$)的接近, 说明绝对构型也相同。

化合物 **2**: 白色固体, ^{13}C NMR (125 MHz, $CDCl_3$) δ_C: 192.7 (CH, C-6'), 174.8 (C, C-11), 164.7 (C, C-1'), 146.7 (CH, C-4'), 141.4 (CH, C-3'), 137.6 (CH, C-5'), 135.7 (C, C-8), 129.6 (CH, C-2'), 123.4 (CH, C-7), 74.8 (C, C-9), 69.1 (CH_2, C-12), 67.5 (CH, C-6), 45.0 (CH, C-5), 45.0 (CH_2, C-3), 38.1 (C, C-10), 34.1 (C, C-4), 32.6 (CH_3, C-13), 30.5 (CH_2, C-1), 25.0 (CH_3, C-14), 18.6 (CH_3, C-15), 17.8 (CH_2, C-2); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 9.68 (1H, d, *J*=7.6 Hz, H-6'), 7.40 (1H, dd, *J*=15.4, 11.2 Hz, H-3'), 7.16 (1H, m, H-4'), 6.44 (1H, dd, *J*=15.5, 7.6 Hz, H-5'), 6.30 (1H, d, *J*=15.4 Hz, H-2'), 5.94 (1H, s, H-7), 5.79 (1H, s, H-6), 4.97 (1H, d, *J*=12.4 Hz, H-12), 4.74 (1H, d, *J*=12.5 Hz, H-12), 2.13 (1H, d, *J*=8.1 Hz, H-1), 2.06 (1H, d, *J*=4.6 Hz, H-5), 1.71 (1H, d, *J*=8.0 Hz, H-1), 1.60 (1H, m, H-2), 1.45 (1H, d, *J*=11.6 Hz, H-2), 1.32 (1H, m, H-3), 1.26 (1H, d, *J*=7.7 Hz, H-3), 1.20 (3H, s, H-13), 1.13 (3H, s, H-15), 1.01 (3H, s, H-14)。其波谱数据与 ustusolate E[6]文献报道一致。化合物 **2** 的比旋光度为$[\alpha]_D^{20}$ –300.0 (*c* 0.10, MeOH)与文献报道$[\alpha]_D^{20}$ –320.0 (*c* 0.10, MeOH)的接近, 说明绝对构型也相同。

化合物 **3**: 白色固体, ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 174.3 (C, C-11), 165.4 (C, C-1'), 145.7 (CH, C-3'), 142.7 (CH, C-5'), 136.6 (C, C-8), 129.6 (CH, C-4'), 121.3 (CH, C-7), 119.0 (CH, C-2'), 73.1 (C, C-9), 68.2 (CH_2, C-12), 65.7 (CH, C-6), 65.4 (CH, C-7'), 44.4 (CH_2, C-3), 44.2 (CH, C-5), 42.5 (CH_2, C-6'), 37.2 (C, C-10), 33.3 (C, C-13), 32.9 (C, C-4), 29.5 (CH_2, C-1), 24.0 (CH_3, C-14), 23.2 (CH_3, C-8'), 18.2 (CH_3, C-15), 17.4 (CH_2, C-2); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 7.18 (1H, m, H-3'), 6.31 (1H, dd, *J*=15.4, 10.4 Hz, H-4'), 6.30 (1H, s, 9-OH), 6.27 (1H, dd, *J*=15.4, 7.1 Hz, H-5'), 5.88 (1H, d, *J*=15.4 Hz, H-2'), 5.78 (1H, s, H-7), 5.58 (1H, s, H-6), 4.88 (1H, d, *J*=12.6 Hz, H-12), 4.78 (1H, d, *J*=12.7 Hz, H-12), 4.61 (1H, s, 7'-OH), 3.70 (1H, dd, *J*=11.8, 5.9 Hz, H-7'), 2.21 (1H, t, *J*=5.3 Hz, H-6'), 2.02 (1H, dd, *J*=4.8 Hz, H-5), 1.96 (1H, dd, *J*=13.6, 3.5 Hz, H-1), 1.84 (1H, d, *J*=13.3 Hz, H-1), 1.60(1H, dd, *J*=17.8, 9.0 Hz, H-2), 1.47 (1H, d, *J*=13.3 Hz, H-2), 1.34 (1H, d, *J*=12.5 Hz, H-3), 1.21 (1H, m, H-3), 1.07 (3H, s, H-15), 1.06 (3H, s, H-13), 1.05 (3H, d, *J*=6.6 Hz, H-8'), 0.92 (3H, s, H-14)。其波谱数据与 ustusolate C[6]的文献报道一致。化合物 **3** 的比旋光度为$[\alpha]_D^{20}$–700.0 (*c* 0.10, MeOH)与文献报道$[\alpha]_D^{20}$–700.0 (*c* 0.10, MeOH)的完全一致, 说明绝对构型也相同。

化合物 **4**: 无色液体, ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 174.3 (C, C-11), 165.1 (C, C-1'), 143.9 (CH, C-3'), 138.8 (CH, C-5'), 136.7 (C, C-8), 130.4 (CH, C-4'), 122.7 (CH, C-7), 121.2 (CH, C-2'), 101.2 (CH, C-6'), 73.1 (C, C-9), 68.2 (CH_2, C-12), 66.0 (CH, C-6), 52.4 (CH_3, 6'-OCH_3), 52.4 (CH_3, 6'-OCH_3), 44.4 (CH_2, C-3), 44.1 (CH, C-5), 37.2 (C, C-10), 33.3 (C, C-4), 32.1 (CH_3, C-14), 29.5 (CH_2, C-1), 24.3 (CH_3, C-15), 18.3 (CH_3, C-13), 17.4 (CH_2, C-2); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 7.26 (1H, dd, *J*=15.2, 11.1 Hz, H-3'), 6.54 (1H, dd, *J*=15.5, 11.1 Hz, H-4'), 6.19 (1H, dd, *J*=15.5, 4.8 Hz, H-5'), 6.10 (1H, d, *J*=15.4 Hz, H-2'), 5.79 (1H, s, H-7), 5.59 (1H, s, H-6), 4.90 (1H, d, *J*=4.0 Hz, H-6'), 4.87 (1H, s, H-12), 4.80 (1H, m, H-12), 3.22 (6H, s, 6'-OCH_3), 2.03 (1H, d, *J*=4.3 Hz, H-5), 1.97 (1H, dd, *J*=11.7, 7.0 Hz, H-1), 1.83 (1H, d, *J*=21.2, 8.6 Hz, H-1), 1.48 (1H, m, H-2), 1.45 (1H, m, H-2), 1.34 (1H, d, *J*=12.3 Hz, H-3), 1.19 (1H, d, *J*=17.6 Hz, H-3), 1.07 (3H, s, H-13), 1.06 (3H, s, H-15), 0.92 (3H, s, H-14)。其波谱数据与 ustusolate D[6]的文献报道一致。化合物 **4** 的比旋光度为$[\alpha]_D^{20}$ –280.0 (*c* 0.10, MeOH)与文献报道$[\alpha]_D^{25}$–300.0 (*c* 0.10, MeOH)的数据接近, 说明绝对构型也相同。

化合物 **5**: 黄色油状液体, ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 194.2 (CH, C-6'), 164.6 (C, C-1'), 147.9 (CH, C-4'), 143.3 (C, C-8), 141.4 (CH, C-3'),

137.3 (CH, C-5'), 129.6 (CH, C-2'), 116.6 (CH, C-7), 97.2 (C, C-11), 76.3 (C, C-9), 67.4 (CH, C-6), 65.6 (CH_2, C-12), 44.9 (CH, C-5), 44.3 (CH_2, C-3), 37.9 (C, C-10), 33.1 (C, C-4), 32.4 (CH_3, C-14), 31.4 (CH_2, C-1), 24.3 (CH_3, C-15), 18.4 (CH_3, C-13), 17.6 (CH_2, C-2); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 9.63 (1H, d, *J*=7.9 Hz, H-6'), 7.46 (2H, ddd, *J*=33.2, 14.6, 11.2 Hz, H-3', 4'), 6.60 (1H, dd, *J*=14.8, 7.8 Hz, H-5'), 6.51 (1H, d, *J*=14.7 Hz, H-2'), 6.34 (1H, d, *J*=8.2 Hz, 9-OH), 5.51 (1H, s, H-6), 5.21 (1H, d, *J*=8.2 Hz, H-7), 4.85 (1H, s, 11-OH), 4.39 (1H, d, *J*=12.8 Hz, H-12), 4.09 (1H, d, *J*=12.9 Hz, H-12), 2.09 (1H, d, *J*=4.5 Hz, H-5), 1.87 (1H, t, *J*=14.0 Hz, H-1), 1.58 (1H, dd, *J*=26.7, 13.3 Hz, H-1), 1.43 (1H, d, *J*=12.9 Hz, H-2), 1.33 (1H, d, *J*=12.3 Hz, H-2), 1.22 (2H, d, *J*=5.0 Hz, H-3), 1.14 (3H, s, H-13), 1.08 (3H, s, H-15), 0.93 (3H, s, H-14)。其波谱数据与 11-hydroustusolate E[12]的文献报道基本一致。文献中没有该化合物的比旋光度报道，但化合物 **5** 的比旋光度为$[\alpha]_D^{20}$ –100.0 (*c* 0.10, MeOH)，与上述相似化合物的符号相同，提示其绝对构型与上述化合物相同。

化合物 **6**: 白色固体，^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 165.5 (C, C-1'), 145.5 (CH, C-4'), 144.9 (CH, C-3'), 142.8 (C, C-8), 133.2 (CH, C-5'), 126.6 (CH, C-2'), 117.0 (CH, C-7), 97.4 (CH, C-11), 76.3 (C, C-9), 75.1 (CH, C-6'), 69.5 (CH, C-6), 65.8 (CH_2, C-12), 44.9 (CH, C-5), 44.3 (CH_2, C-3), 37.8 (C, C-10), 33.1 (C, C-4), 32.5 (CH_3, C-14), 31.4 (CH_2, C-1), 24.2 (CH_3, C-15), 18.4 (CH_3, C-13), 18.2 (CH_3, C-7'), 17.6 (CH_2, C-2); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 7.20 (1H, ddd, *J*=10.8, 5.8, 3.0 Hz, H-3'), 6.43 (1H, m, H-4'), 6.30 (1H, ddd, *J*=15.4, 10.1, 4.9 Hz, H-5'), 5.91 (1H, d, *J*=15.3 Hz, H-2'), 5.57 (1H, s, H-7), 5.48 (1H, s, H-6), 5.21 (1H, s, 11-OH), 4.38 (1H, d, *J*=12.6 Hz, H-12), 4.08 (1H, d, *J*=12.9 Hz, H-12), 2.07 (1H, d, *J*=4.5 Hz, H-5), 1.87 (1H, dd, *J*=13.7, 10.0 Hz, H-1), 1.59 (1H, d, *J*=12.8 Hz, H-1), 1.43 (1H, d, *J*=13.3 Hz, H-2), 1.32 (1H, d, *J*=12.1 Hz, H-2), 1.22 (2H, d, *J*=10.8 Hz, H-3), 1.13 (3H, s, H-14), 1.08 (3H, s, H-15), 1.03 (3H, d, *J*=6.2 Hz, H-7'), 0.92 (3H, s, H-13)。其波谱数据与 11, 6'-hydroustusolate E[12]的报道一致。文献中没有该化合物的比旋光度报道，但化合物 **6** 的比旋光度为$[\alpha]_D^{20}$ –60.0 (*c* 0.10, MeOH)，与上述相似化合物的符号相同，提示其绝对构型与上述化合物相同。

化合物 **7**: 黄色油状液体，^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 165.4 (C, C-1'), 145.1 (CH, C-4'), 142.6 (CH, C-3'), 141.6 (C, C-8), 135.4 (CH, C-5'), 131.2 (CH, C-6'), 127.4 (CH, C-2'), 120.0 (CH, C-7'), 117.1 (CH, C-7), 97.2 (CH, C-11), 76.3 (C, C-9), 66.4 (CH, C-6), 65.6 (CH_2, C-12), 44.9 (CH, C-5), 44.3 (CH_2, C-3), 37.8 (C, C-10), 33.1 (C, C-4), 32.5 (CH_3, C-14), 31.4 (CH_2, C-1), 24.2 (CH_3, C-15), 18.4 (CH_3, C-13), 18.2 (CH_3, C-8'), 17.6 (CH_2, C-2); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 7.21 (1H, dd, *J*=15.2, 11.3 Hz, H-3'), 6.69 (1H, dt, *J*=17.8, 8.9 Hz, H-5'), 6.34 (1H, dd, *J*=14.8, 11.4 Hz, H-4'), 6.22 (1H, dd, *J*=27.8, 12.8 Hz, H-6'), 6.01 (1H, dt, *J*=13.8, 6.8 Hz, H-7'), 5.91 (1H, d, *J*=15.2 Hz, H-2'), 5.57 (1H, d, *J*=4.3 Hz, H-7), 5.48 (1H, d, *J*=1.8 Hz, H-6), 5.20 (1H, s, 9-OH), 4.82 (1H, s, 11-OH), 4.38 (1H, d, *J*=12.8 Hz, H-12), 4.08 (1H, d, *J*=12.9 Hz, H-12), 2.07 (1H, d, *J*=4.6 Hz, H-5), 1.87 (1H, dd, *J*=13.6, 9.6 Hz, H-1), 1.80 (3H, d, *J*=6.8 Hz, H-8'), 1.57 (1H, m, H-1), 1.43 (1H, d, *J*=12.9 Hz, H-2), 1.32 (1H, d, *J*=12.2 Hz, H-2), 1.21 (2H, m, H-3), 1.13 (3H, s, H-13), 1.08 (3H, s, H-15), 0.92 (3H, s, H-14)。其波谱数据与(2'*E*, 4'*E*, 6'*E*)- 6-(1'-carboxyocta-2', 4', 6'-triene)-11, 12-epoxy- 9, 11-dihydroxydrim-7-ene[13]的文献报道一致。化合物 **7** 的比旋光度为$[\alpha]_D^{20}$ –260.0 (*c* 0.10, MeOH)与文献报道$[\alpha]_D^{20}$ –266.0 (*c* 0.10, MeOH)的数据接近，说明绝对构型也相同。

化合物 **8**: 白色固体，^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 138.1 (C, C-8), 131.9 (CH, C-7), 74.6 (C, C-9), 67.0 (CH, C-6), 61.9 (CH_2, C-11), 61.5 (CH_2, C-12), 48.2 (CH, C-5), 43.3 (CH_2, C-3), 42.0 (C, C-10), 36.5 (CH_3, C-14), 32.8 (C, C-4), 32.3 (CH_2, C-1), 22.9 (CH_3, C-15), 18.3 (CH_2, C-2), 17.4 (CH_3, C-13); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 5.65 (1H, s, H-7), 4.87 (1H, s, 12-OH), 4.61 (1H, s, 11-OH), 4.25 (1H, d, *J*=6.9 Hz, 6-OH), 4.07 (1H, s, 9-OH), 4.05 (1H, s, H-12), 4.02 (1H, s, H-6), 3.99 (1H, s, H-12), 3.48 (1H, m, H-11), 3.43 (1H, d, *J*=11.0 Hz, H-11), 1.72 (1H, d, *J*=10.2 Hz, H-5), 1.61 (1H, t, *J*=11.2 Hz, H-1), 1.46 (1H, d, *J*=12.7 Hz, H-1), 1.36 (2H, m, H-2), 1.25 (2H, t, *J*=13.1 Hz, H-3), 1.10 (3H, s, H-14), 1.01 (3H, s, H-15), 0.90 (3H, s, H-13)。其波谱数据与 12-hydroxy-6-epi-albrassitriol[14]的文献报道一致。文献中没有该化合物的比旋光度报道，但化合物 **8** 的比旋光度为$[\alpha]_D^{20}$ –140.0 (*c* 0.05, MeOH)，与上述相似化合物的符号相同，提示其绝对构型与上述化合物相同。

化合物 **9**: 无色油状液体，^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 165.6 (C, C-1'), 144.8 (CH, C-3'), 144.4 (C, C-8), 141.3 (CH, C-5'), 135.3 (CH, C-7'), 131.2 (CH, C-6'), 127.5 (CH, C-4'), 120.4 (CH, C-2'), 119.9 (CH, C-7), 74.1 (C, C-9), 66.2 (CH, C-6), 61.7 (CH_2, C-11), 60.6 (CH_2, C-12), 44.6 (CH, C-5), 44.0 (CH_2, C-3), 40.1 (C, C-10), 33.3 (C, C-4), 32.6 (CH_3, C-14), 31.8 (CH_2, C-1), 24.5 (CH_3, C-15), 18.6 (CH_3, C-13), 18.3 (CH_3, C-8'), 18.2 (CH_2, C-2); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 7.19(1H, dd, *J*=15.2, 11.3 Hz, H-3'), 6.67 (1H, m, H-5'), 6.33 (1H, m, H-4'), 6.22 (1H, dd, *J*=19.1, 8.1 Hz, H-6'), 6.01 (1H, td, *J*=14.0, 6.8 Hz, H-7'), 5.89 (1H, d, *J*=15.2 Hz, H-2'), 5.77 (1H,

dd, *J*=9.3, 5.1 Hz, H-7), 5.54 (1H, m, H-6), 4.87 (1H, s, 12-OH), 4.74 (1H, s, 11-OH), 4.46 (1H, s, 9-OH), 4.43 (2H, s, H-12), 5.32 (1H, d, *J*=10.1 Hz, H-11), 3.45 (1H, d, *J*=11.4 Hz, H-11), 1.98 (1H, dd, *J*=7.0, 4.3 Hz, H-5), 1.87(4H, dd, *J*=15.8, 7.1 Hz, H-8', 1), 1.60 (1H, d, *J*=14.2 Hz, H-2), 1.43 (2H, t, *J*=15.0 Hz, H-2, 1), 1.29 (1H, d, *J*=12.3 Hz, H-3), 1.23 (1H, s, H-3), 1.17 (3H, s, H-13), 1.05 (3H, s, H-15), 0.91 (3H, s, H-14)。其波谱数据与 ustusolate A[6]的一致。化合物 **9** 的比旋光度为$[\alpha]_D^{20}$ –70.0 (*c* 0.10, MeOH)与文献报道$[\alpha]_D^{20}$ –68.0 (*c* 0.10, MeOH)的数据接近，说明绝对构型也相同。

化合物 **10**: 白色固体，^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 198.8 (C, C-6), 158.9 (C, C-8), 127.8 (CH, C-7), 76.6 (CH, C-3), 61.8 (CH, C-5), 57.8 (CH_2, C-11), 57.1 (CH, C-9), 41.4 (C, C-10), 37.3 (C, C-4), 36.5 (CH_2, C-1), 28.3 (CH_3, C-14), 26.5 (CH_2, C-2), 21.4 (CH_3, C-12), 15.6 (CH_3, C-13), 15.3 (CH_3, C-15); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 5.70 (1H, s, H-7), 5.62 (1H, s, 11-OH), 4.38 (1H, d, *J*=4.8 Hz, 3-OH), 3.73 (1H, d, *J*=11.2 Hz, H-11), 3.60 (1H, m, H-11), 3.01 (1H, m, H-3), 2.24 (1H, s, H-9), 2.12 (1H, s, H-5), 1.65 (1H, d, *J*=4.9 Hz, H-5), 1.98 (3H, s, H-12), 1.90 (1H, d, *J*=12.4 Hz, H-2), 1.45 (3H, ddd, *J*=20.4, 10.3, 6.9 Hz, H-2, 1), 1.11 (3H, s, H-14), 0.99 (3H, s, H-15), 0.83 (3H, s, H-13)。其波谱数据与 deoxyuvidin B[15]的文献报道一致。文献中没有该化合物的比旋光度报道，但化合物 **10** 的比旋光度为$[\alpha]_D^{20}$ –85.0 (*c* 0.10, MeOH)，与上述相似化合物的符号相同，提示其绝对构型与上述化合物相同。

化合物 **11**: 白色透明固体，^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 207.1 (C, C-5), 193.1 (CH, C-21), 177.4 (C, C-3), 157.8 (CH, C-8), 140.3 (C, C-7), 136.6 (C, C-19), 135.9 (CH, C-16), 130.5 (CH, C-4), 124.2 (CH, C-17), 120.2 (CH, C-18), 52.3 (CH, C-14), 50.2 (CH, C-6), 49.3 (CH, C-2), 46.1 (CH_2, C-1), 45.6 (C, C-11), 44.5 (CH_2, C-12), 44.1 (CH, C-10), 32.8 (CH, C-15), 31.1 (CH_2, C-9), 27.9 (CH_2, C-13), 26.6 (CH_3, C-25), 23.1 (CH_3, C-22), 21.4 (CH_3, C-23), 18.4 (CH_3, C-24), 17.3 (CH_3, C-20); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 9.27 (1H, s, H-21), 6.80 (1H, d, *J*=6.2 Hz, H-8), 6.10 (1H, t, *J*=11.2 Hz, H-17), 6.02 (2H, d, *J*=15.4 Hz, H-18, 4), 5.12 (1H, t, *J*=10.0 Hz, H-16), 3.38 (1H, s, H-6), 2.92 (1H, d, *J*=20.5 Hz, H-9), 2.60 (3H, dd, *J*=31.9, 12.4 Hz, H-2, 10, 15), 2.21 (1H, m, H-9), 2.07 (3H, s, H-20), 2.03 (2H, d, *J*=3.4 Hz, H-2, 1), 1.90 (1H, m, H-14), 1.84 (3H, s, H-25), 1.77 (3H, s, H-24), 1.69 (1H, m, H-13), 1.44 (2H, dd, *J*=11.1, 8.9 Hz, H-12), 1.17 (2H, dd, *J*=24.1, 14.8 Hz, H-1, 13), 0.98 (3H, d, *J*=6.7 Hz, H-23), 0.87 (3H, s, H-22)。其波谱数据与 6-epi-ophiobolin G[16]的文献报道一致。化合物 **11** 的比旋光度为$[\alpha]_D^{20}$ +107.0 (*c* 0.10, MeOH)与文献报道$[\alpha]_D^{23}$ +117.0 (*c* 1.05 MeOH)的数据接近，说明绝对构型也相同。

化合物 **12**: 棕红色透明固体，^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 210.6 (C, C-5), 181.0 (C, C-3), 136.4 (CH, C-16), 135.8 (C, C-19), 133.4 (C, C-7), 133.1 (CH, C-4), 130.2 (CH, C-8), 123.7 (CH, C-17), 120.4 (CH, C-18), 67.9 (CH_2, C-21), 53.5 (CH, C-6), 52.3 (CH, C-14), 51.1 (CH, C-2), 46.6 (CH_2, C-1), 45.1 (C, C-11), 44.4 (CH_2, C-12), 43.9 (CH, C-10), 32.6 (CH, C-15), 29.3 (CH_2, C-13), 28.0 (CH_2, C-9), 26.6 (CH_3, C-24), 23.0 (CH_3, C-23), 21.3 (CH_3, C-22), 18.3 (CH_3, C-25), 17.6 (CH_3, C-20); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 6.02 (2H, m, H-18, 17), 5.94 (1H, s, H-8), 5.73 (1H, d, *J*=5.2 Hz, H-4), 5.11 (1H, t, *J*=9.9 Hz, H-16), 4.15 (1H, d, *J*=11.9 Hz, H-21), 3.87 (1H, d, *J*=11.8 Hz, H-21), 3.60 (1H, d, *J*=2.6 Hz, H-6), 2.77 (1H, d, *J*=12.8 Hz, H-2), 2.51 (3H, m, H-10, 15, 9), 2.07 (3H, s, H-20), 2.03 (1H, dd, *J*=13.1, 3.4 Hz, H-9), 1.87 (2H, m, H-14, 1), 1.80 (3H, s, H-25), 1.74 (3H, s, H-24), 1.63 (1H, s, H-13), 1.50 (1H, dd, *J*=11.8, 4.3 Hz, H-12), 1.39 (1H, ddd, *J*=10.8, 8.9, 4.4 Hz, H-12), 1.27 (1H, m, H-13), 1.12 (1H, t, *J*=13.0 Hz, H-1), 0.98 (3H, s, H-22), 0.94 (3H, d, *J*=6.7 Hz, H-23)。其波谱数据与(6*α*)-21, 21-*O*-dihydroophiobolin G[10]的文献报道一致。化合物 **12** 的比旋光度为$[\alpha]_D^{20}$ +35.0 (*c* 0.05, $CHCl_3$)与文献报道$[\alpha]_D^{20}$ +49.0 (*c* 0.10, $CHCl_3$)的数据相近，说明绝对构型与文献一致。

化合物 **13**: 白色固体，^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 216.0 (C, C-5), 194.6 (CH, C-21), 159.7 (CH, C-8), 141.5 (C, C-7), 136.1 (CH, C-16), 135.3 (C, C-19), 123.3 (CH, C-17), 120.1 (CH, C-18), 74.6 (C, C-3), 54.7 (CH_2, C-4), 51.4 (CH, C-14), 49.6 (CH, C-2), 48.3 (CH, C-6), 44.9 (CH_2, C-12), 44.3 (C, C-11), 43.2 (CH, C-10), 41.0 (CH_2, C-1), 31.9 (CH, C-15), 30.0 (CH_2, C-9), 27.1 (CH_2, C-13), 26.1 (CH_3, C-25), 25.2 (CH_3, C-20), 22.9 (CH_3, C-22), 21.1 (CH_3, C-23), 17.9 (CH_3, C-24); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 9.13 (1H, s, H-21), 6.97 (1H, d, *J*=5.3 Hz, H-8), 6.11 (2H, m, H-17, 18), 5.27 (1H, m, H-16), 4.68 (1H, s, 3-OH), 3.05 (1H, d, *J*=10.7 Hz, H-6), 2.77 (1H, d, *J*=16.1 Hz, H-4), 2.63 (2H, dd, *J*=28.7, 14.6 Hz, H-9), 2.47 (1H, d, *J*=10.5 Hz, H-10), 2.29 (2H, m, H-15, 2), 2.21 (1H, d, *J*=16.0 Hz, H-4), 1.97 (2H, m, H-14, 1), 1.80 (3H, s, H-24), 1.71 (3H, s, H-25), 1.66 (1H, dd, *J*=13.7, 4.3 Hz, H-13), 1.59 (1H, m, H-1), 1.41 (2H, m, H-12), 1.27 (3H, s, H-20), 1.09 (1H, dd, *J*=14.9, 7.1 Hz, H-13), 0.93 (3H, d, *J*=6.6 Hz, H-23), 0.93 (3H, s, H-22)。其波谱数据与 6-epi-ophiobolin K[17]的文献报道一致。化合物 **13** 的比旋光度为$[\alpha]_D^{20}$ +170.0 (*c* 0.10, MeOH)，与文献报道$[\alpha]_D^{23}$ +155.0 (*c* 0.08 MeOH)的数据接近，说明绝对构型也相同。

化合物 **14**: 无色透明固体, ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 171.1 (C, C-21), 145.2 (CH, C-8), 136.4 (C, C-19), 135.6 (CH, C-16), 126.2 (C, C-7), 124.1 (CH, C-17), 120.2 (CH, C-18), 112.2 (C, C-5), 80.5 (C, C-3), 54.0 (CH_2, C-4), 53.0 (CH, C-2, 6), 52.1 (CH, C-14), 44.8 (CH_2, C-12), 44.1 (C, C-11), 42.5 (CH, C-10), 41.7 (CH_2, C-1), 33.1 (CH, C-15), 29.7 (CH_2, C-9), 28.1 (CH_2, C-13), 26.6 (CH_3, C-25), 24.9 (CH_3, C-20), 23.7 (CH_3, C-22), 21.4 (CH_3, C-23), 18.3 (CH_3, C-24); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 6.97 (1H, s, H-8), 6.03 (2H, m, H-17, 18), 5.13 (1H, t, *J*=9.9 Hz, H-16), 3.33 (1H, m, H-6), 2.58 (1H, d, *J*=20.7 Hz, H-15), 2.50 (1H, dd, *J*=16.2, 9.5 Hz, H-9), 2.36 (1H, d, *J*=12.3 Hz, H-10), 2.30 (1H, d, *J*=14.6 Hz, H-4), 2.19 (1H, d, *J*=14.4 Hz, H-4), 2.04 (1H, m, H-9), 1.89 (1H, dd, *J*=18.7, 7.9 Hz, H-14), 1.83 (3H, s, H-24), 1.69 (3H, s, H-25), 1.69 (2H, dd, *J*=12.7, 9.0 Hz, H-1, 2), 1.49 (2H, m, H-12, 1), 1.30 (3H, s, H-20), 1.21 (2H, m, H-13), 0.98 (3H, d, *J*=6.7 Hz, H-23), 0.79 (3H, s, H-22)。其波谱数据与 ophiobolin P[18]的文献报道一致。化合物 **14** 的比旋光度为$[\alpha]_D^{20}$ +100.0 (*c* 0.05, MeOH)与文献报道$[\alpha]_D^{25}$ +93.8 (*c* 0.67, MeOH)的数据相近, 说明绝对构型与文献一致。

化合物 **15**: 白色透明固体, ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 139.4 (C, C-7), 138.0 (CH, C-16), 135.1 (C, C-19), 123.0 (CH, C-8), 121.9 (CH, C-17), 120.5 (CH, C-18), 119.7 (C, C-5), 79.8 (C, C-3), 71.7 (CH_2, C-21), 55.3 (CH, C-10), 52.8 (CH, C-6), 50.1 (CH, C-2), 50.3 (CH_2, C-4), 47.4 (CH, C-14), 43.7 (C, C-11), 43.2 (CH_2, C-12), 36.2 (CH_2, C-1), 35.7 (CH, C-15), 26.8 (CH_2, C-13), 26.5 (CH_3, C-25), 25.9 (CH_3, C-20), 25.2 (CH_2, C-9), 20.4 (CH_3, C-23), 18.9 (CH_3, C-22), 18.2 (CH_3, C-24); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 5.96 (2H, m, H-18, 17), 5.60 (1H, dd, *J*=8.2, 6.3 Hz, H-8), 5.20 (1H, m, H-16), 4.47 (2H, s, H-21), 3.01 (1H, d, *J*=9.8 Hz, H-6), 2.68 (1H, dd, *J*=15.9, 9.2 Hz, H-15), 2.48 (1H, dd, *J*=13.8, 8.5 Hz, H-9), 2.24 (1H, d, *J*=13.3 Hz, H-4), 2.19 (1H, dd, *J*=16.8, 7.0 Hz, H-2), 2.05 (1H, dt, *J*=18.4, 9.4 Hz, H-14), 1.91 (1H, d, *J*=13.3 Hz, H-4), 1.90 (3H, s, H-25), 1.72 (3H, s, H-24), 1.67 (2H, m, H-13, 9), 1.55 (3H, m, H-12, 10, 1), 1.38 (3H, m, H-13, 12, 1), 1.23 (3H, s, H-20), 0.89 (3H, s, H-22), 0.89 (3H, d, *J*=6.7 Hz, H-23)。其波谱数据与 ophiobolin H[10]的文献报道一致。化合物 **15** 的比旋光度为$[\alpha]_D^{20}$ +17.0 (*c* 0.10, MeOH)与文献报道$[\alpha]_D^{20}$ +25.0 (*c* 0.10, $CHCl_3$)的数据接近, 说明绝对构型也相同。

化合物 **16**: 无色透明液体, ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 205.8 (C, C-5), 193.1 (CH, C-21), 177.1 (C, C-3), 158.3 (CH, C-8), 139.6 (CH, C-16), 138.6 (C, C-7), 129.4 (CH, C-4), 128.0 (CH, C-17), 73.5 (CH, C-18), 71.4 (C, C-19), 51.2 (CH, C-14), 49.1 (CH, C-6), 48.6 (CH, C-2), 44.9 (C, C-11), 44.8 (CH_2, C-1), 43.7 (CH_2, C-12), 42.8 (CH, C-10), 32.1 (CH, C-15), 30.2 (CH_2, C-9), 27.1 (CH_2, C-13), 26.0 (CH_3, C-25), 25.2 (CH_3, C-24), 22.4 (CH_3, C-22), 20.1 (CH_3, C-23), 16.6 (CH_3, C-20); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 9.21 (1H, s, H-21), 6.92 (1H, d, *J*=4.5 Hz, H-8), 5.93 (1H, s, H-4), 5.32 (2H, m, H-17, 16), 4.48 (1H, d, *J*=4.9 Hz, H-18), 4.01 (1H, d, *J*=9.7 Hz, H-6), 3.08 (1H, d, *J*=20.4 Hz, H-9), 2.68 (1H, dd, *J*=17.4, 6.9 Hz, H-2), 2.59 (1H, m, H-15), 2.27 (2H, ddd, *J*=20.7, 14.4, 6.5 Hz, H-9, 10), 2.03 (3H, s, H-20), 1.97 (1H, m, H-1), 1.94 (1H, m, H-14), 1.57 (1H, m, H-13), 1.45 (1H, dd, *J*=11.5, 4.6 Hz, H-12), 1.38 (1H, td, *J*=11.1, 4.5 Hz, H-12), 1.27 (1H, m, H-13), 1.16 (1H, m, H-1), 1.06 (3H, s, H-24), 1.04 (3H, s, H-25), 0.92 (3H, d, *J*=6.5 Hz, H-23), 0.81 (3H, s, H-22)。其波谱数据与 ophiobolin Q[18]的文献报道一致。化合物 **16** 的比旋光度为$[\alpha]_D^{20}$ +140.0 (*c* 0.10, MeOH)与文献报道$[\alpha]_D^{25}$ +126.0 (*c* 0.39, MeOH)的数据相近, 说明绝对构型与文献一致。

化合物 **17**: 无色透明液体, ^{13}C NMR (125 MHz, DMSO-d_6) δ_C: 205.8 (C, C-5), 193.1 (CH, C-21), 177.0 (C, C-3), 157.8 (CH, C-8), 141.9 (CH, C-16), 139.8 (C, C-7), 129.4 (CH, C-4), 126.4 (CH, C-17), 82.9 (CH, C-18), 71.8 (C, C-19), 56.7 (CH_3, 18-OCH_3), 51.6 (CH, C-14), 49.1 (CH, C-6), 48.7 (CH, C-2), 44.9 (CH_2, C-1), 44.8 (C, C-11), 43.7 (CH_2, C-12), 42.7 (CH, C-10), 31.6 (CH, C-15), 31.3 (CH_2, C-9), 27.1 (CH_2, C-13), 26.8 (CH_3, C-25), 24.8 (CH_3, C-24), 22.3 (CH_3, C-22), 21.1 (CH_3, C-23), 16.6 (CH_3, C-20); ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 9.20 (1H, d, *J*=6.7 Hz, H-21), 6.81 (1H, m, H-8), 5.93 (1H, s, H-4), 5.66 (1H, m, H-16), 5.20 (1H, t, *J*=10.6 Hz, H-17), 3.67 (1H, d, *J*=9.9 Hz, H-18), 3.25 (3H, s, 18-OCH_3), 3.08 (1H, d, *J*=20.7 Hz, H-6), 2.74 (1H, t, *J*=12.4 Hz, H-2), 2.61 (1H, m, H-9), 2.53 (1H, m, H-15), 2.24 (1H, m, H-9), 2.05 (1H, m, H-1), 2.03 (3H, s, H-20), 1.98 (1H, m, H-14), 1.94 (1H, m, H-13), 1.59 (1H, m, H-12), 1.46 (1H, m, H-12), 1.39 (1H, m, H-10), 1.29 (1H, m, H-13), 1.17 (1H, m, H-1), 1.14 (3H, s, H-25), 1.05 (3H, s, H-24), 1.02 (3H, d, *J*=6.6 Hz, H-23), 0.80 (3H, s, H-22)。其波谱数据与 ophiobolin R[18]的文献报道一致。化合物 **17** 的比旋光度为$[\alpha]_D^{20}$ +70.0 (*c* 0.10, MeOH)与文献报道$[\alpha]_D^{25}$ +60.8 (*c* 0.24, MeOH)的数据相近, 说明绝对构型与文献一致。

2.2 神经氨酸酶抑制活性结果

实验结果显示化合物 **2**、**6**、**7**、**9**、**11**、**13** 对神经氨酸酶具有明显的抑制活性, 其半数抑制浓度(IC_{50}) 分别为 31.8、37.3、28.4、36.8、46.6、37.6 μM,

而阳性对照的 IC_{50} 则为 1.2 μM。根据实验结果和化合物结构可知, 对于倍半萜类化合物, 11-OH 和 C-6 所连侧链的不饱和程度可提高其神经氨酸酶抑制活性, 而二倍半萜类化合物则是 C-21 的醛基取代可提高其神经氨酸酶抑制活性。

参考文献:

[1] Unson M D, Holland N D, Faulkner D J. A brominated secondary metabolite synthesized by the cyanobacterial symbiont of a marine sponge and accumulation of the crystalline metabolite in the sponge tissue[J]. Marine Biology, 1994, 119(1): 1-11.

[2] Bewley C A, Holland N D, Faulkner D J. Two classes of metabolites from *Theonella swinhoei* are localized in distinct populations of bacterial symbionts[J]. Experientia, 1996, 52(7): 716-722.

[3] Hu G P, Yuan J, Sun L, et al. Statistical research on marine natural products based on data obtained between 1985 and 2008[J]. Marine drugs, 2011, 9(4): 514-519.

[4] Zhao C H, Zhu T G, Zhu W M. New marine natural products of microbial origin from 2010 to 2013[J]. Chinese Journal of Organic Chemistry, 2013, 33(6): 1195-1234.

[5] Blunt J W, Copp B R, Keyzers R A, et al. Marine natural products[J]. Natural Product Reports, 2016, 33(3): 382-431.

[6] Lu Z Y, Wang Y, Miao C D, et al. Sequiterpenoids and benzofuranoids from the marine-derived fungus *Aspergillus ustus* 094102[J]. Journal of Natural Products, 2009, 72(10): 1761-1767.

[7] Liu X H, Miao F P, Qiao M F, et al. Terretonin, ophiobolin, and drimane terpenes with absolute configurations from an algicolous *Aspergillus ustus*[J]. RSC Advances, 2013, 3(2): 588-595.

[8] Zhou H N, Zhu T J, Cai S X, et al. Drimane sesquiterpenoids from the mangrove-derived fungus *Aspergillus ustus*[J]. Chemical pharmaceutical bulletin, 2011, 59(6): 762-766.

[9] Liu H B, Edrada-Ebel R A, Ebel R, et al. Drimane sesquiterpenoids from the fungus *Aspergillus ustus* isolated from the marine sponge *Suberites domuncula*[J]. Journal of Natural Products, 2009, 72(9): 1585-1588.

[10] Liu H B, Edrada-Ebel R A, Ebel R, et al. Ophiobolin sesterterpenoids and phyrrolidine alkaloids from the sponge-derived fungus *Aspergillus ustus*[J]. Helvetica Chimica Acta, 2011, 94(4): 623-631.

[11] Shionoa Y, Hiramatsua F, Murayamaa T, et al. Two drimane-type sesquiterpenes, strobilactones A and B, from the liquid culture of the edible mushroom *Strobilurus ohshimae*[J]. Z. Naturforsch, 2007, 62b: 1585-1589.

[12] 路新华, 郑智慧, 可爱兵, 等. 一类倍半萜酯化合物及其制备方法和用途[P]. 发明专利 ZL201110153948.7, 2014.
Lu Xinhua, Zheng Zhihui, Ke Aibing, et al. A group of sesquiterpene ester compounds, their preparation method and application[P]. Patent ZL201110153948.7, 2014.

[13] Hayes M A, Wrigley S K, Chetland I, et al. Novel drimane sesquiterpene esters from *Aspergillus ustus* var. pseudodeflectus with endothelin receptor binding activity.[J]. Journal of Antibiotics, 1996, 27(47): 505-512.

[14] Grabley S, Thiericke R, Zerlin M, et al. New albrassitriols from *Aspergillus* sp. (FH-A 6357)[J]. Journal of Antibiotics, 1996, 49(6): 593-595.

[15] Ayer W A, Pena-Rodriguez L M. Metabolites produced by *Alternarza brasszcae*, the black spot pathogen of canola, part 2, sesquiterpenoid metabolites[J]. Journal of Natural Products, 1987, 50(3): 408-417.

[16] Wei H, Itoh T, Kinoshita M, et al. Cytotoxic sesterterpenes, 6-epi-ophiobolin G and 6-epi-ophiobolin N, from marine derived fungus *Emericella variecolor*, GF10[J]. Tetrahedron, 2004, 60(28): 6015-6019.

[17] Singh S B, Smith J L, Sabnis G S, et al. ChemInform abstract: structure and conformation of ophiobolin K and 6-epiophiobolin K from *Aspergillus ustus* as a nematocidal agent[J]. Tetrahedron, 1991, 47(34): 6931-6938.

[18] Wang Q X, Bao L, Yang X L, et al. Ophiobolins P-T, five new cytotoxic and antibacterial sesterterpenes from the endolichenic fungus *Ulocladium* sp. [J]. Fitoterapia, 2013, 90(20): 220-227.

[19] Dao T T, Tung B T, Nguyen P H, et al. C-methylated flavonoids from *Cleistocalyx operculatus* and their inhibitory effects on novel influenza a (H1N1) neuraminidase[J]. Journal of Natural Products, 2010, 73(10): 1636-1642.

Chemical constituents of *Aspergillus ustus* TK-5, an endophytic fungus derived from the ascidian *Herdmania momus*

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Abstract: Cultivation of the fungal strain *Aspergillus ustus* TK-5, an endophytic fungus which was isolated from the fresh tissue of ascidian *Herdmania momus*, resulted in the identification of 17 compounds. These compounds were isolated by a combination of silica gel, Sephadex LH-20, and Lobar LiChroprep RP-18 column chromatography as well as by preparative high-performance liquid chromatography (pHPLC). The structures were elucidated to be drimane sesquiterpenoids (**1**–**10**) and sesterterpenes (**11**–**17**) by analysis of their spectroscopic data, including strobilactone A (**1**), ustusolate E (**2**), ustusolate C (**3**), ustusolate D (**4**), 11-hydroustusolate E (**5**), 11, 6'- hydroustusolate E (**6**), (2'*E*, 4'*E*, 6'*E*)-6-(1'-carboxyocta-2', 4', 6'-triene)-11, 12-epoxy-9, 11-dihydroxydrim-7-ene (**7**), 12-hydroxy-6-epi-albrassitriol (**8**), ustusolate A (**9**), deoxyuvidin B (**10**), 6-epi-ophiobolin G (**11**), (6α)-21, 21-*O*-dihydroophiobolin G (**12**), 6-epi-ophiobolin K (**13**), ophiobolin P (**14**), ophiobolin H (**15**), ophiobolin Q (**16**), and ophiobolin R (**17**). Regarding to the neuraminidase inhibitory activity, compounds **2**, **6**, **7**, **9**, **11**, and **13** were found to possess moderate activity, with IC_{50} values of 31.8, 37.3, 28.4, 36.8, 46.6, and 37.6 μmol/L.

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