

Iriomoteolide-10a, a new 20-membered macrolides from dinoflagellate *Amphidinium* species

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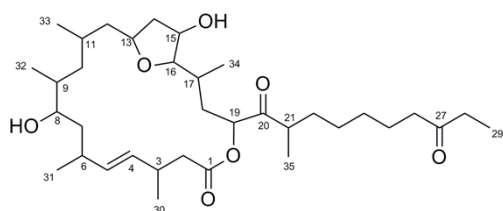
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Summary

Marine dinoflagellates of the genus *Amphidinium* are well-known as a producer of unique cytotoxic metabolites. During our investigation of bioactive substances from the *Amphidinium* dinoflagellates, we have isolated a new 20-membered macrolide, iriomoteolide-10a, from the strain collected off Iriomote Island, Japan.

Iriomoteolide-10a is a new 20-membered macrolide with a tetrahydropyran ring at C-13—C-16, six one-carbon branches, two ketone carbonyls, and two hydroxyl groups. Iriomoteolide-10a exhibited cytotoxicity against human epidermoid carcinoma KB cells (IC₅₀: 0.9 μg/mL). In this symposium, we will discuss the isolation and structural elucidation of these new macrolides.

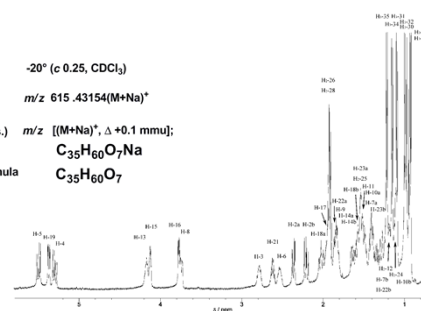


Iriomoteolide-10a

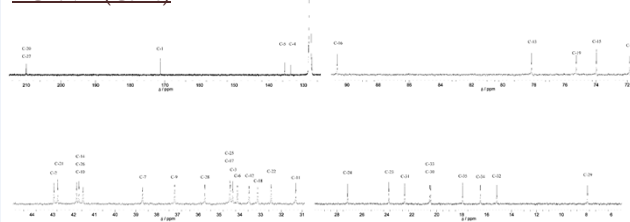
Structure Elucidation of Iriomoteolide-10a

¹H NMR (C₆D₆)

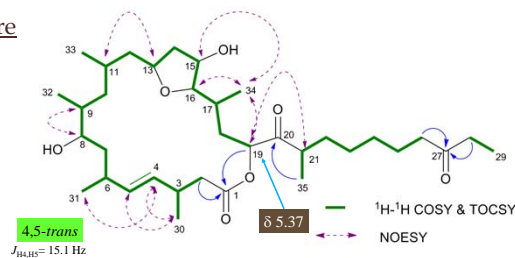
colorless oil
[α]_D²³ -20° (c 0.25, CDCl₃)
ESIMS (pos.) m/z 615.43154(M+Na)⁺
HRFABMS (pos.) m/z [(M+Na)⁺, Δ +0.1 mmu];
C₃₅H₆₀O₇Na
Molecular Formula C₃₅H₆₀O₇



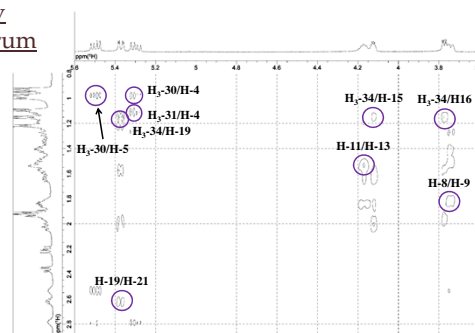
¹³C NMR (C₆D₆)



Planar Structure



Noesy spectrum



Isolation

Dinoflagellate *Amphidinium* sp. <strain KCA09053 >

Isolated from sea sand of Iriomote Island
25 °C, 2 weeks in seawater medium enriched with
1 % PES supplement, 16 h light 8 h dark

30.3 g dry cells from 350 L of culture

Ext. with toluene / MeOH, 1 : 3
partit. with toluene / H₂O

Toluene 7.01g H₂O

SiO₂ column (CHCl₃/MeOH, 95:5)

C₁₈ column (MeCN/H₂O, 70 : 30)

C₁₈HPLC (MeCN/H₂O, 70 : 30)



Amphidinium sp.
KCA09053 strain

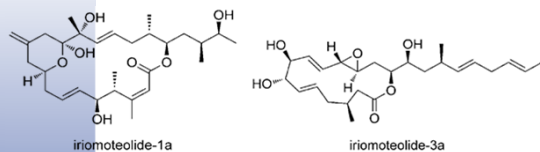


Iriomoteolide-10a
0.0165%

known macrolides

Iriomoteolide-1a 0.0074%

Iriomoteolide-3a 0.0083%



Reference

Amphidinium macrolides : Kobayashi, J. *Jpn. J. Antibiot.* **2009**, 62, 471-480.

Kobayashi, J.; Tsuda, M. *Nat. Prod. Rep.* **2004**, 21, 77-93

Iriomoteolide-1a : Tsuda, M.; Oguchi, K.; Iwamoto, R.; Okamoto, Y.; Kobayashi, J.;

Fukushi, E.; Kawabata, J.; Ozawa, T.; Masuda, A.; Kitaya, Y.; Omasa, K. *J. Org. Chem.* **2007**,

72, 4469-4474.

Iriomoteolide-3a : Oguchi, K.; Tsuda, M.; Iwamoto, R.; Okamoto, Y.; Kobayashi, J.;

Fukushi, E.; Kawabata, J.; Ozawa, T.; Matsuda, A.; Kitaya, Y.; Omasa, K. *J. Org. Chem.* **2008**, 73, 1567-1570

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