

## Introduction

Zoanthamine-type alkaloids from *Zoanthus vietnamensis* with potential bioactivities, including anticancer, anti-lymphangiogenic, antiangiogenic, antiplatelet aggregation, and anti-osteoporotic activities. Herein, the details of extraction, isolation, structural elucidation, and anti-angiogenic activity of four major compounds **12–15** are reported. These secondary metabolites (**1–17**) were identified by NMR, MS spectroscopic data, and the single-crystal X-ray diffraction analyses were used to determine the absolute configuration of **1**. In addition, the biosynthetic route of zoanide A (**1**) from precursor 28-deoxyzoanthamine (**15**) was proposed.

## Materials

Kingdom	Animalia
Phylum	Cnidaria
Class	Anthozoa
Subclass	Hexacorallia
Order	Zoantharia
Family	Zoanthidae
Genus	<i>Zoanthus</i>
Species	<i>vietnamensis</i>



Fig. 1 *Zoanthus vietnamensis*.

## Extraction and Isolation

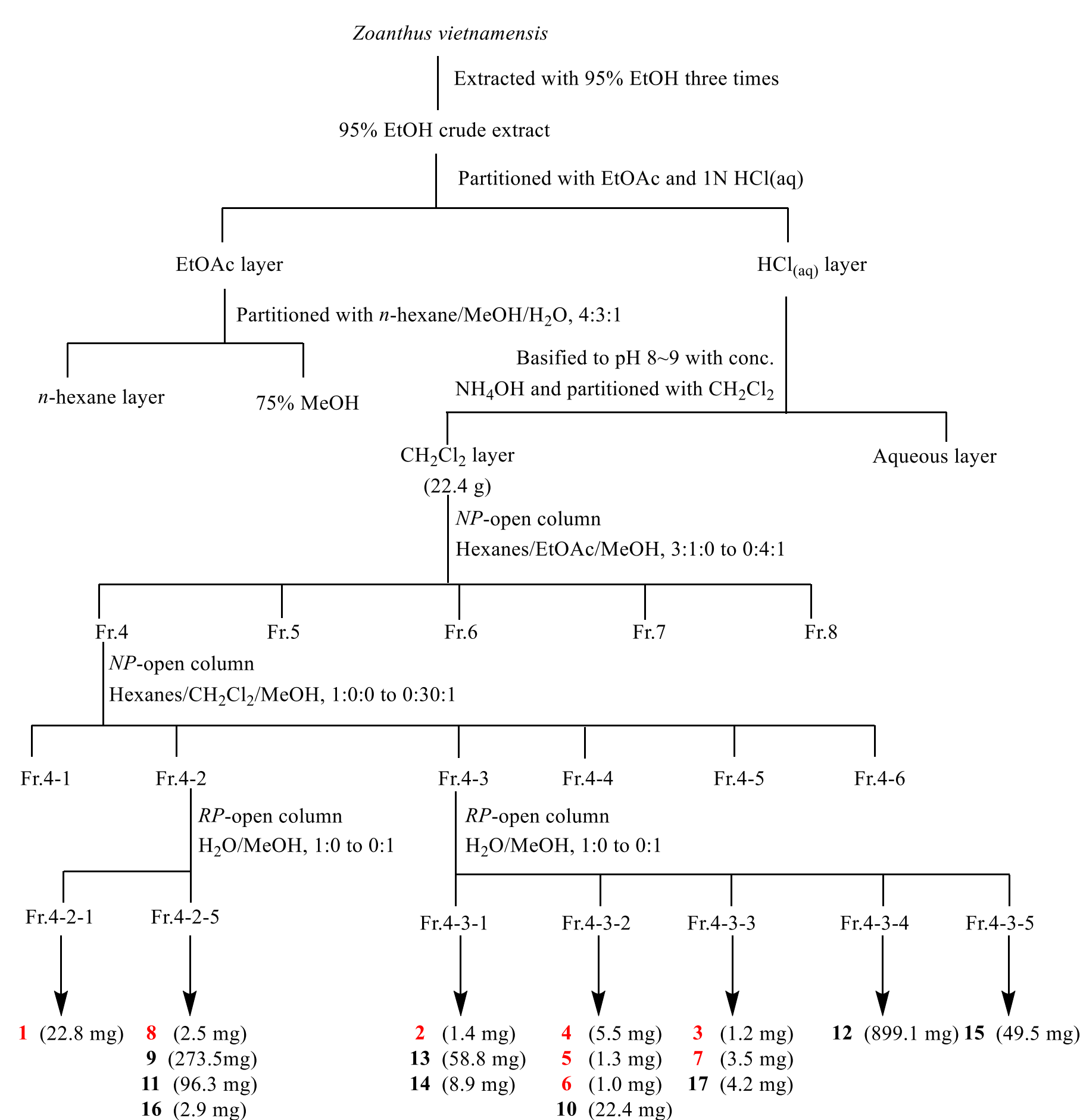


Fig. 2 The flow chart of extraction and isolation.

## Results and Discussion

A novel skeleton compound, zoanide A (**1**), seven new compounds, kuroshine L (**2**), kuroshine M (**3**), 1-keto-kuroshine A (**4**), 1-keto-11-dehydrokuroshine A (**5**), 1-keto-zoanthamine (**6**), 26-norzoanthamine (**7**), 10-*epi*-1-keto-2-hydroxykuroshine K (**8**), and nine known compounds, kuroshine E (**9**), 18-*epi*-kuroshine A (**10**), kuroshine A (**11**), zoanthamine (**12**), zoanthamine (**13**), 26-norzoanthamine (**14**), 28-deoxyzoanthamine (**15**), kuroshine H (**16**), and kuroshine J (**17**) were isolated from the *Z. vietnamensis*.

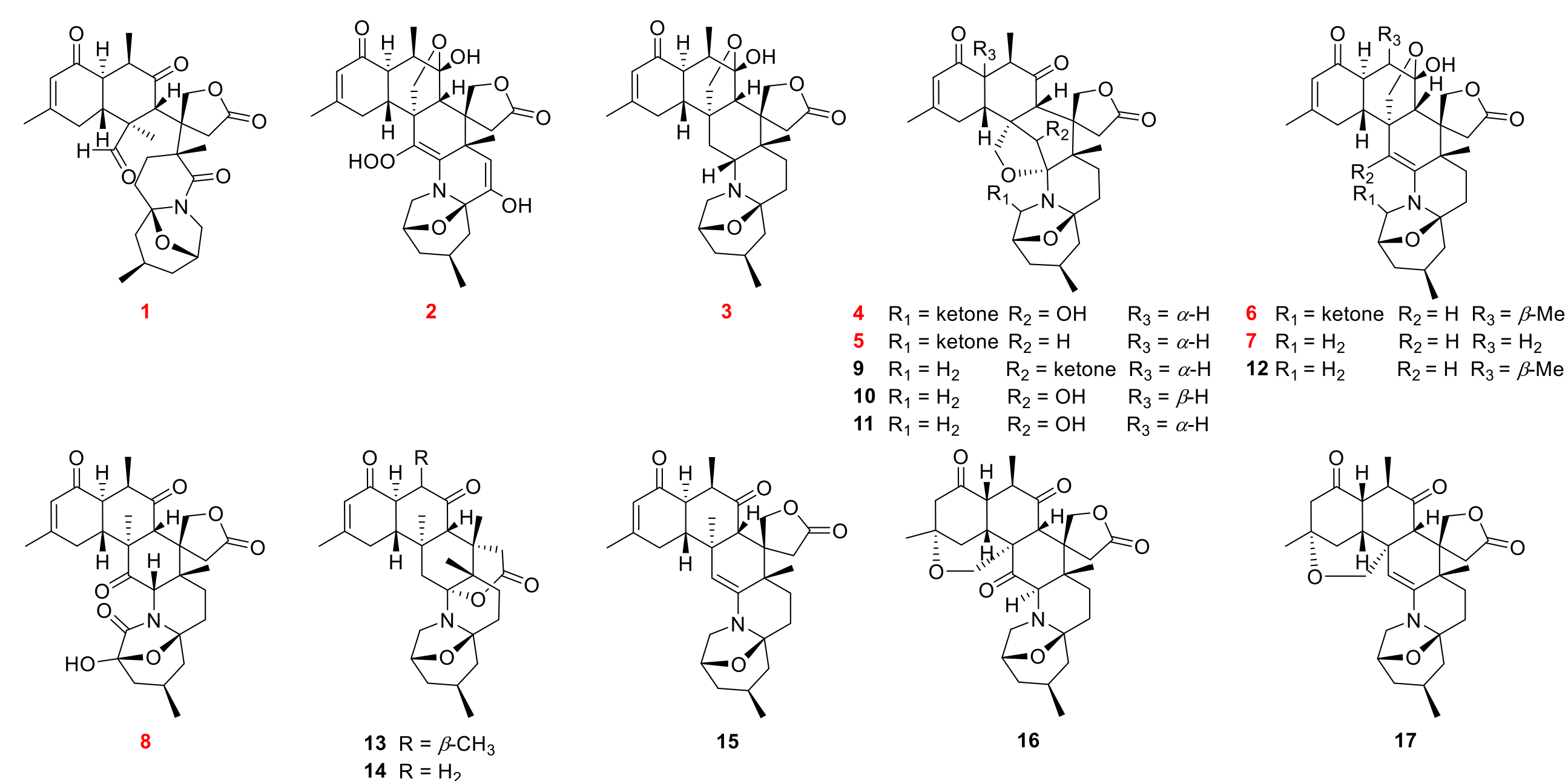


Fig. 3 Structures of compounds **1–17**.

## X-ray Data

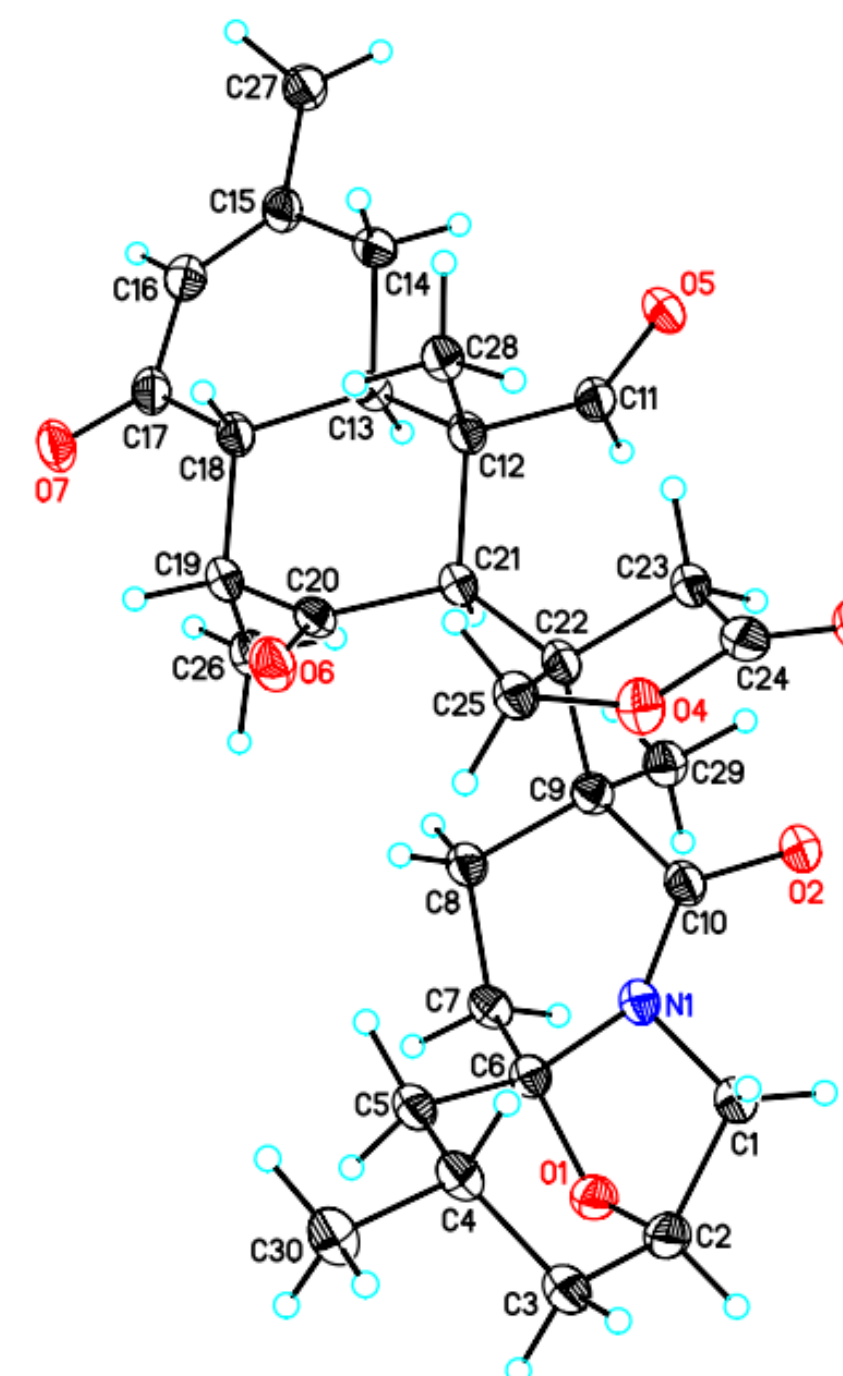


Fig. 4 X-ray ORTEP drawing of **1**.

## NMR Data

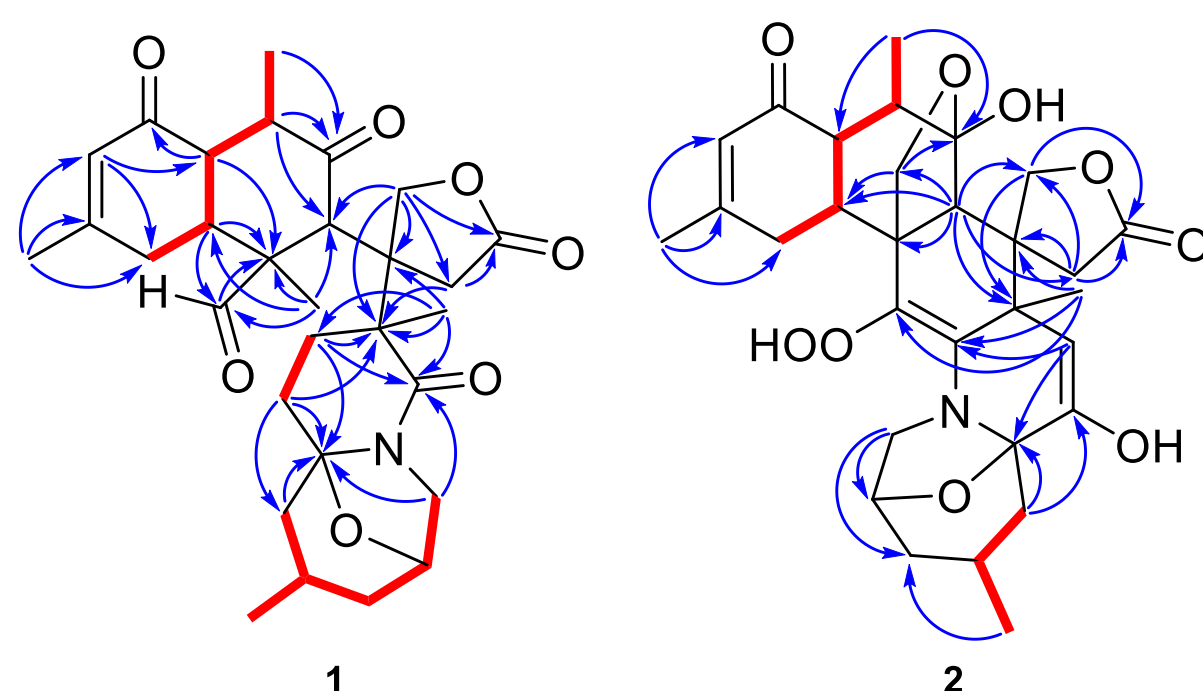


Fig. 5 COSY (bold bond) and HMBC (arrow) correlations of **1** and **2**.

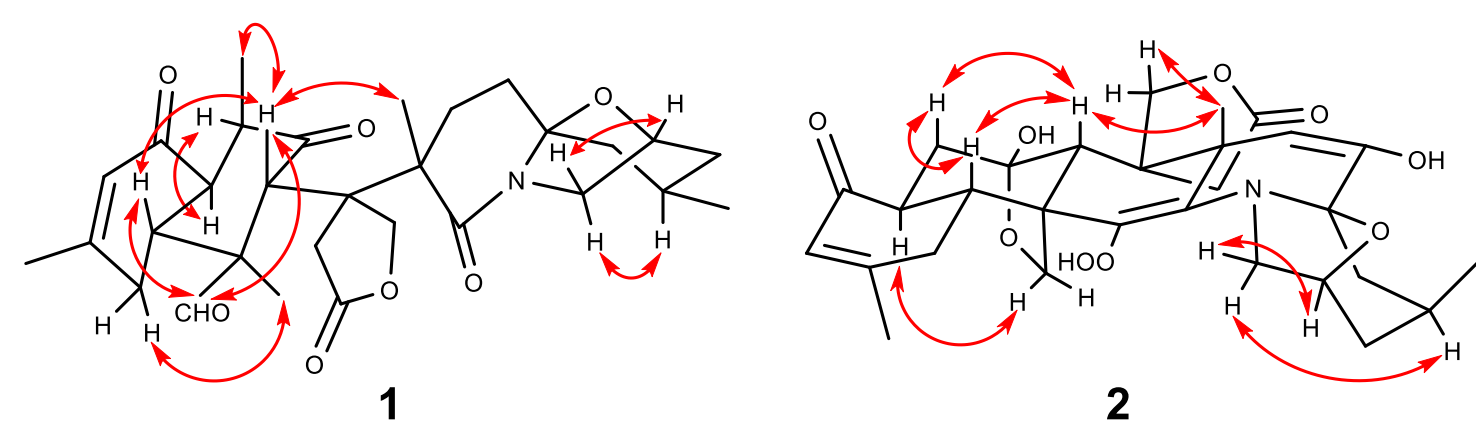


Fig. 6 Key NOESY (left right arrow) correlations of **1** and **2**.

## Plausible Biosynthetic Pathway

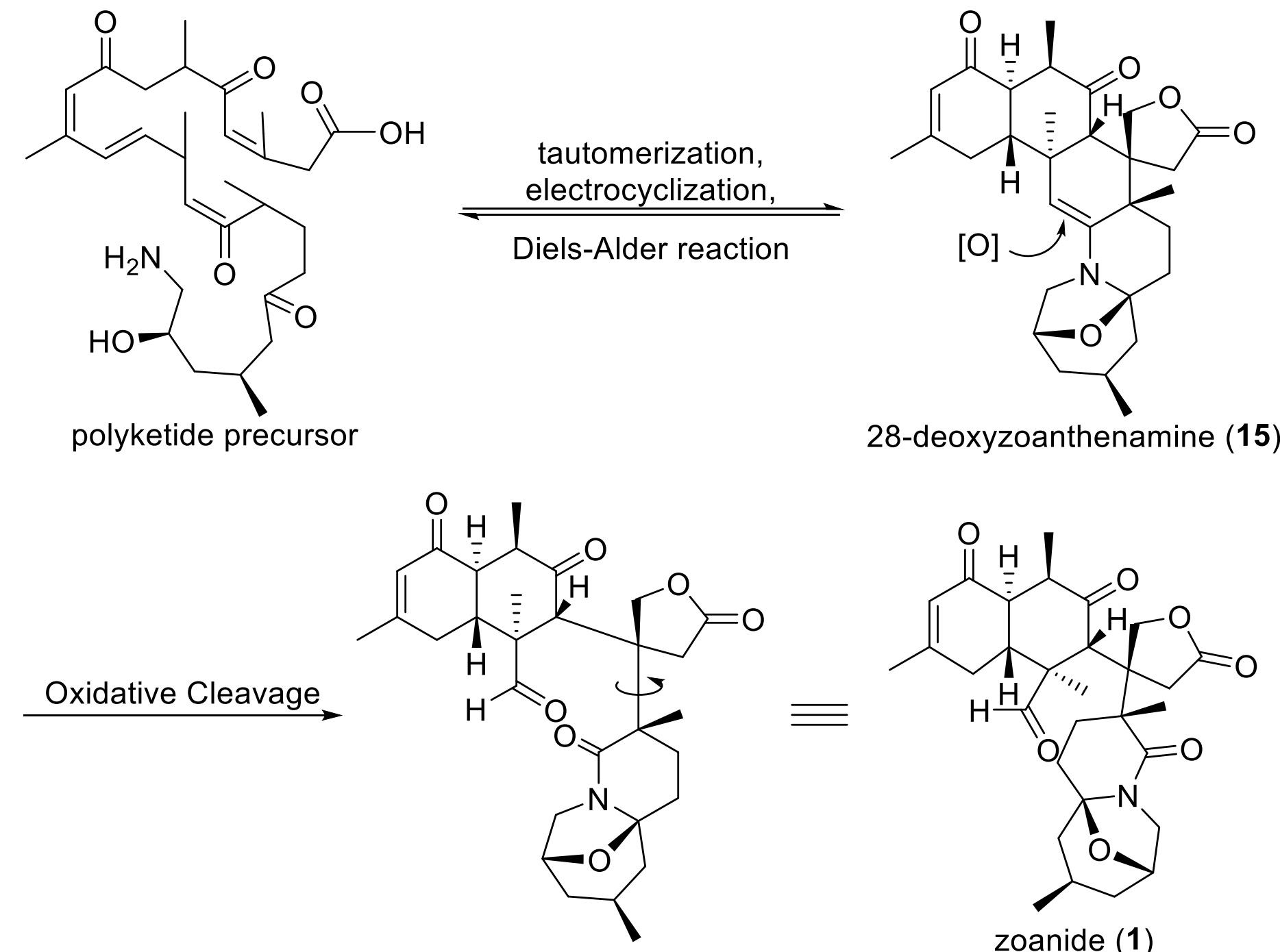


Fig. 7 Plausible Biosynthetic pathway of **1**.

## Neuroprotective Activity

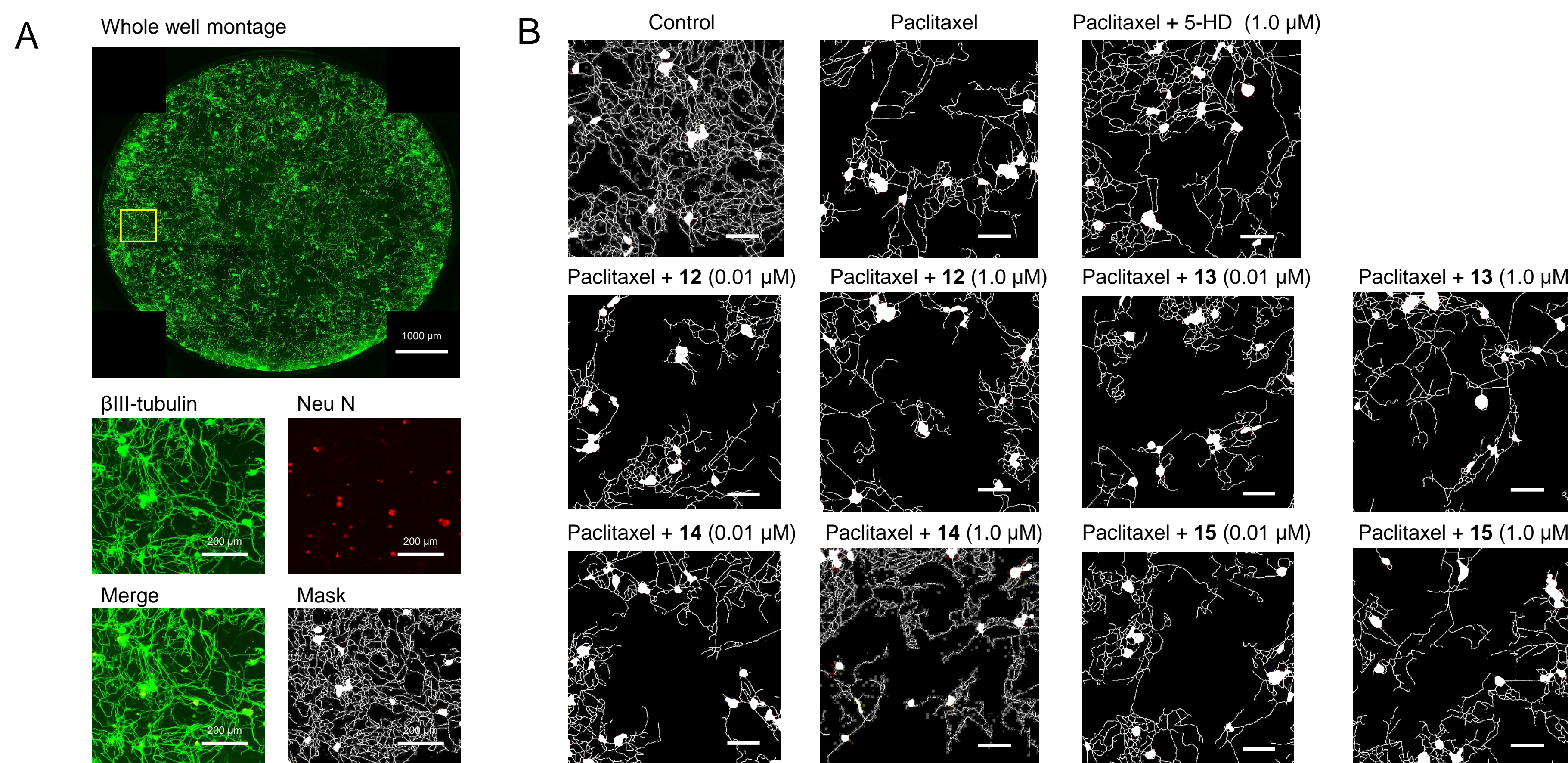


Fig. 8 The neuroprotective effects of four major compounds **12–15** on the neurite outgrowth of dorsal root ganglion (DRG) neurons. To evaluate neuroprotective effects, primary culture of DRG neurons from 6 or 7-weeks-old C57/B6J mice were pre-treated with vehicle control or testing compounds for 24 hours and then exposed to 0.1  $\mu$ M paclitaxel for another 24 hours.

## Conclusion

Zoanide A (**1**) was identified to possess an unprecedented functionalized skeleton derived from zoanthamine alkaloids that contain the aldehyde group at C-10 and the carbonyl group at C-11. Moreover, the carbonyl group at C-1 (**4–6** and **8**) and the hemiketal group at C-2 (**8**) were first reported in zoanthamine alkaloids. Our findings suggest that *Zoanthus* can produce diverse marine natural products with unique carbon skeletons. This research is still in progress, and eight new compounds will be tested for neuroprotective activity in the future.