

# STUDIES TOWARDS THE TOTAL SYNTHESIS OF HETEROCLITIN F AND TAIWANSCHIRIN A, B, C AND D

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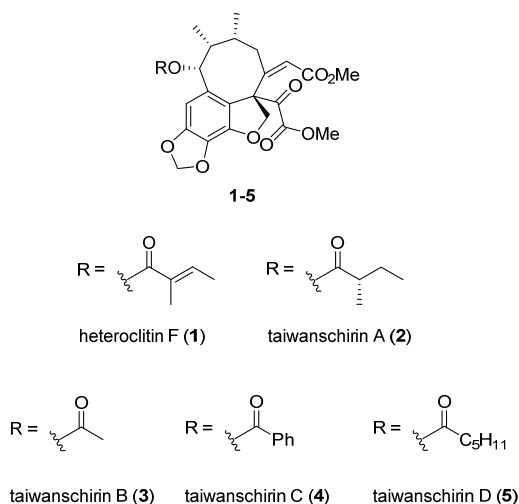


Figure 1: heteroclitin F and taiwanschirins A-D

Isolated by Yang and Chen in 1992 from the stems of *Kadsura heteroclita*, heteroclitin F (**1**) was the first member of the taiwanschirin family to be discovered (Figure 1).<sup>1</sup> In 1999, Kuo reported the isolation of taiwanschirins A (**2**), B (**3**) and C (**4**) from *Schizandra arisanensis*,<sup>2</sup> later followed by taiwanschirin D (**5**) from *Kadsura matsudai* in 2000.<sup>3</sup>

The therapeutic properties of closely related *Kadsura* and *Schizandra* have long been known and applied in traditional Chinese medicine.<sup>4,5</sup> More recently, *in vitro* hepatoma cytotoxicity and activity against human type B hepatitis has been demonstrated by taiwanschirins C and D respectively.<sup>2,3</sup>

This work describes model studies towards the total synthesis of the taiwanschirin family, none of which have been previously synthesised. An original approach has been developed to enable the installation of the (*Z*)-enone as a single diastereomer. Furthermore, these studies have led to the assembly of the 8-membered macrocycle in high yield. With methods developed for the incorporation of the three contiguous stereocentres on the macrocycle, in addition to the aromatic methylenedioxy substitution pattern, we present here a novel approach towards the first total synthesis of the taiwanschirin family.

[1] Yang, X-W., Chen, D-F. et. Al., *Chem. Pharm. Bull.*, 1992, 1510-1516.

[2] Kuo, Y-H.; Huang, H-C.; Kuo, L-M. Y.; Chen, C-F., *J. Org. Chem.*, 1999, 7023-7027.

[3] Kuo, Y-H.; Huang, R-L. et. al., *Chem. Pharm. Bull.*, 2000, 1992-1993.

[4] Ookawa, N.; Ikeya, Y.; Taguchi, H.; Yosiokam I., *Chem. Pharm. Bull.*, 1981, 123-127.

[5] Shen, Y-C.; Lin, Y-C.; Cheng, Y-B.; Kuo, Y-H.; Liaw, C-C., *Org. Lett.*, 2005, 5297-5300.