Total Synthesis of Neurymenolide A

Significance: Neurymenolide A is an unusual α-pyrene macroclide that was isolated in 2009 from the Fijian red alga *Neurymenia fraxinifolia*, exhibiting a broad scope of biological activity. This work represents the first total synthesis of the natural product and features a series of remarkably selective transition metal-catalyzed transformations to build up the highly sensitive cyclophane scaffold.

Comment: The route is based on a novel gold-catalyzed pyrone synthesis that allowed for selective alkyne activation within intermediate F. α-Pyrene H was subjected to efficient alkyne metathesis to construct macrocycle J. Neurymenolide A acetate (K) exists as a mixture of interchanging atropisomers and the synthetic material obtained was identical to a sample derived from natural sources. Deprotection of K led to rapid degradation.

Category: Synthesis of Natural Products and Potential Drugs

Key words: neurymenolide, α-pyrone, alkyne metathesis, gold, molybdenum

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Synfacts 2012, 8(10), 1047 Published online: 19.09.2012 DOI: 10.1055/s-0032-1317279; Reg-No.: C00612SF