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Effects of (+)-, (-)- and (\pm) -Indenestrols A and B on Microtubule Polymerization*

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Indenestrol A (IA) is a metabolite of diethylstilbestrol (DES), and indenestrol B (IB) is an analog of IA. IA was simply obtained from E,E-dienestrol in the presence of dilute sulfuric acid, and a mixture of IA and IB was formed by thermal cyclization of E,E-dienestrol. In order to elucidate the effects of optically active IA and IB on microtubule assembly, the IA and IB enantiomers were separated to>99% purity by high-pressure liquid chromatography using a chiral column. The di(4-bromobenzoate) of (-) IB was analyzed by X-ray crystallography and its absolute structure was determined as C(3)-S. The (+)-, (-)- and (\pm)- indenestrols A and B were shown to be inhibitors of microtubule assembly in vitro using microtubule proteins from porcine brain. (\pm)-IB is more active than (\pm)-IA, and the order of inhibitory activity of the enantiomers on microtubule assembly was (+)-IB>(+)-IA>(-)-IA>(-)-IB.

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