Chronic actinic dermatitis and sequiterpene lactones : investigation toward the mechanism of photosensitivity

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Chronic actinic dermatitis, one of the most extreme form of photosensitivity, is highly associated to a heavy sensitization background to sesquiterpene lactones.[1] Even if histological analysis suggest that endogenous chromophore such as DNA or RNA may be involved, the pathway from allergic contact dermatitis to chronic actinic dermatitis remains unknown. However, it has been shown that the α-methylene-γ-butyrolactone group, which is responsible for the sensitizing potential of sesquiterpene lactones, can also photoreact with thymidine to form several [2+2] photoadducts.[2]

To better understand the molecular basis of this pathology, we have developed a stereoselective synthesis of the four stereoisomers of an α-methylene-γ-butyrolactone to investigate their photoreactivity toward thymidine.[3] We showed a high photoreactive potential of these molecules toward thymidine in solution with a high *syn* regioselectivity for all [2+2] photoadducts (Fig. 1).[4] Moreover, mass spectroscopy results revealed for the first time the formation of photoadducts between our model lactones and an oligonucleotide. These results further supports the proposal that photocycloaddition of sesquiterpene lactones on thymidine could be at the origin of chronic actinic dermatitis development.

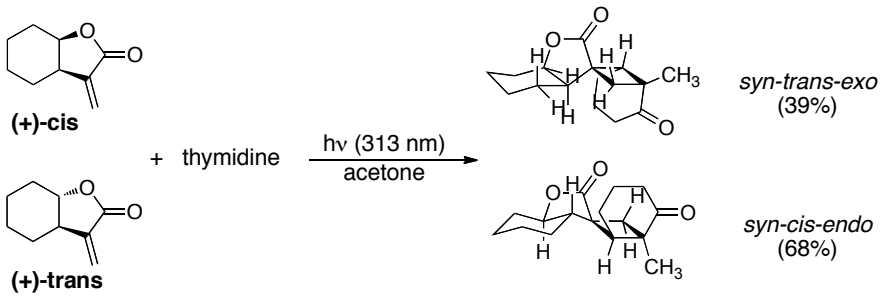

Figure 1. Intermolecular photoreaction between α–methylene-γ-butyrolactone and thymidine

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