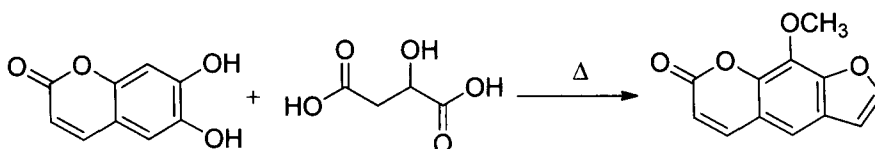


Methoxsalen and trioxsalen are derived from a family of benzofuran-containing plant natural products known as psoralens. Both methoxsalen and trioxsalen act as photosensitizers that decompose in the presence of UV light into active metabolites that crosslink DNA. These compounds have found significant use in the treatment psoriasis, eczema, and vitiligo.<sup>70–72</sup>



Spath and Pailer reported the first synthesis of methoxsalen in 1936.<sup>73</sup> Their original report involved the condensation of a dihydroxy coumarin derivative with malic acid to afford trace amounts of methoxsalen.



Mai and co-workers later published an improved synthesis of methoxsalen.<sup>70</sup> Anionic [4 + 2]-cycloaddition followed by a retro-Diels-Alder reaction and esterification formed the key tricyclic intermediate in low yield. Two additional steps were required to reach the target compound.

