



Enediynes have a double mechanism of action that involves binding to DNA by interaction of parts of the molecule with the minor groove⁹⁹ and activation to DNA-cleaving biradical species, either by reaction with thiols or by reduction.

The chemical basis for enediyne activation is the Bergmann reaction,¹⁰⁰ through which enediyne systems **4.40** undergo cycloaromatization to benzene derivatives, with the intermediacy of the highly reactive 1,4-benzenoid biradical species **4.41** (Figure 4.33a). In the related Myers–Saito reaction, one of the triple bonds can be replaced by an allene unit (**4.42**), leading to biradical **4.43** (Figure 4.33b). These processes do not take place in the natural products because their spacial arrangement prevents coplanarity of the three bonds involved in Bergmann-type chemistry, and therefore an activation reaction or cascade of reactions that alters the compound geometry is necessary.