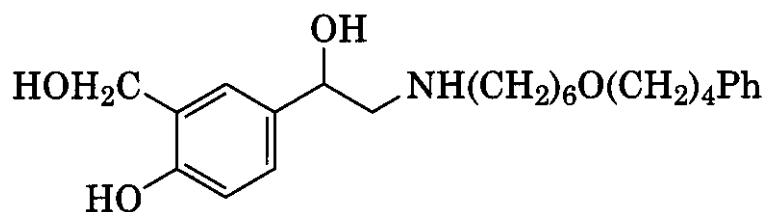


(149)

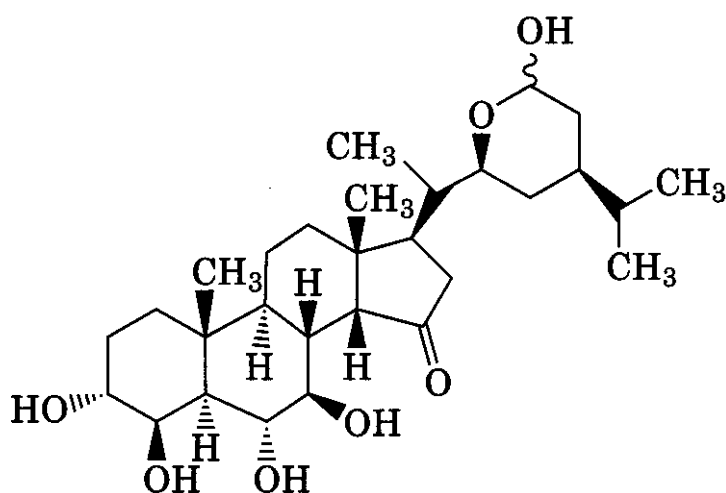


(150)

to have originated from the naturally occurring compounds, adrenaline and ephedrine.

7.3 Contignasterol

The use of inhaled corticosteroids such as **fluticasone** propionate to treat asthma and **rhinitis** has been well documented and will not be repeated here. Less well known is an unusual, highly oxygenated marine-derived steroid isolated from the sponge *Petrosia contignata* that possesses a unique cyclic hemiacyl side-chain (151). The compound was isolated by Andersen and coworkers (195) at the University of British Columbia and found to possess anti-inflammatory properties *in vivo*. Contignasterol is being developed by Inflazyme, in collaboration with Aventis, for the treatment of asthma and other inflammatory diseases and has progressed to phase II clinical trials.



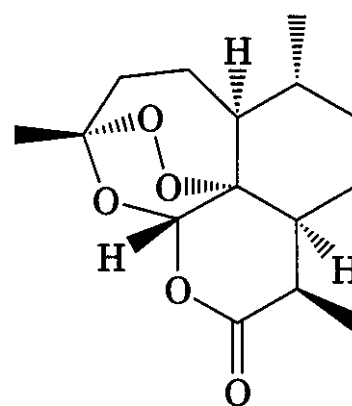
(151) Contignasterol

8 ANTIPARASITIC DRUGS

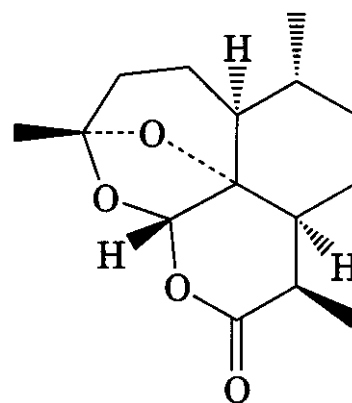
8.1 Artemisinin, Artemether, and Arteether

Artemisia annua (sweet wormwood, qing hao) has been used in Chinese medicine for well over 1000 years. The earliest recommendation is for the treatment of hemorrhoids, but there is a written record of use in fevers dated 340 A.D. Modern development dates from the isolation of a highly active antimalarial, **artemisinin** (qinghaosu), in 1972, and has been carried out almost entirely in China. Much of the original literature is therefore in Chinese, but there is an excellent review on qinghaosu by Trigg (196) and an account of the uses of *A. annua* (197). This section is largely a summary of these two articles.

Artemisinin (152) is a sesquiterpene lactone with an unusual peroxide bridge. One of the earliest modifications involved catalytic reduction of the peroxide, resulting in loss of one oxygen and total loss of antimalarial activity (196) in the **adduct** (153). The role of the peroxide bridge in producing antimalarial effects was not fully understood, but it appeared essential for activity, so much of the early work on analogs conserved this structural feature as an empirical finding. The mechanism



(152) artemisinin



(153)