isolated from the marine sponge species *Halichondria okadai* (Hirata and Uemura 1986). The total synthesis was achieved soon thereafter (Aicher et al. 1992). Fragment-based screening and further derivatization then resulted in Eribulin (**23**, Yeung 2011).

2.2 Unexplored Sources of Natural Products

From the currently established sources for natural products, the potential of finding new natural products seems virtually limitless, when one considers that our knowledge on the plant, bacterial, and fungal kingdoms is still very limited; it is estimated that only 10% of all-known plant species have been tested for the presence of bioactive compounds (Verpoorte 1998) and about 1% of all microbes have been cultured and investigated (Hugenholtz et al. 1998). Besides these established sources, there are unexplored potential sources for natural products which have only recently received recognition from the academic community. A few examples of sources which have been shown to contain new natural products are discussed below.

2.2.1 Extremophiles, Pathogenic, and Non-cultivable Microorganisms

Extremophiles are organisms which have managed to survive in extreme environments in which the majority of life on Earth would perish. Groups of extremophiles include acidophiles and alkaliphiles living in extreme pH environments, anaerobes requiring the absence of oxygen to survive, thermophiles living in high temperature environments, and halophiles living in environments that contain high concentrations of salts.

Because extremophiles have managed to survive in these extreme environments, they have evolved unique metabolisms and survival strategies which no doubt involve the synthesis of interesting secondary metabolites. As a result of this, various natural products with a wide variety of biological activities have been discovered, such as the ribosomally synthesized lantipeptide curvopeptin from bacterial species *Thermomonospora curvata* (Krawczyk et al. 2012), cytotoxic agents variecolorquinones A and B from the halotolerant marine fungal species *Aspergillus variecolor* (Wang et al. 2007), the cytotoxic berkelic acid from an acidophilic fungal *Penicillium* species (Stierle and Stierle 2005; Stierle et al. 2006), and the antimicrobial and cytotoxic agent naphthospironone A from alkaliphilic bacterial strain *Nocardiopsis* sp. YIM DT266 (Ding et al. 2010). Not only does this demonstrate the potential of extremophiles as sources for natural products, it is also curious to note that berkelic acid and naphthospironone were in fact not isolated from naturally occurring extreme environments but from heavily polluted mining areas.

Likewise an interesting source of new structural diversity could be pathogenic microorganisms which use small molecules in host–pathogen interactions. Recent examples have been reported for the honey bee and the bacterium *Paenibacillus larvae*, the causative agent of the American Foulbrood. Bacterial spores are