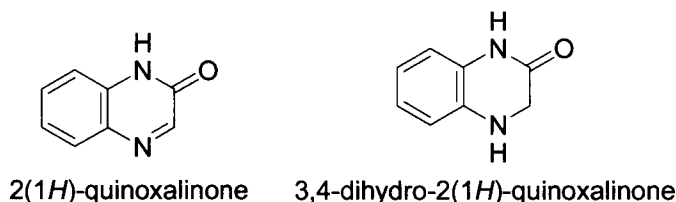


deprotection of the pyrazine below was done with hydrochloric acid at elevated temperatures. This then provides the aromatic alcohol that then tautomerizes to provide the unsaturated amide. The equilibrium between the pyrazine and the amide allows the alkylation of the nitrogen to provide tertiary amide in high yield. This alkylation prevents the tautomerization to reform the pyrazine.

### 12.3.2 Reactivity of the diazine ring

Quinoxaline is a by-product of cooking some food and can inhibit the growth of some ciliate protozoa and plan-pathogenic fungi.<sup>37</sup> The metabolism of this ring system by *Pseudomonas putida* can provide the quinoxaline *cis*-5,6-dihydrodiol, 5-hydroxyquinoxaline, and 2(1*H*)-quinoxalinone. When quinoxaline is metabolized by *Streptomyces badius*, two different products were isolated. Both of these two products, 2(1*H*)-quinoxalinone and 3,4-dihydro-2(1*H*)-quinoxalinone, were only isolated from the treatment of *Streptomyces badius* with quinoxaline. Six other *Streptomyces* species were tested and only produced 2(1*H*)-quinoxalinone. The mechanism for the formation of 3,4-dihydro-2(1*H*)-quinoxalinone was not determined.



The reaction of quinoxalines and pyrazines with radicals has been exploited to further develop the regioselective functionalization of these ring systems.<sup>38</sup> The substitution of protonated heteroaromatic bases by nucleophilic carbon radicals is a general reaction due to the variable radical sources and the high regioselectivity of the very simple experimental conditions. Using cerium ammonium nitrate (CAN), the nucleophilic carbamoyl radical was formed in a two-step process with *N*-hydroxyphthalimide (NHPI). It can reproduce many Friedel–Crafts aromatic substitutions but with the opposite regioselectivity. The high regioselectivity on the quinoxaline rings appears to be related to the low reversibility for the addition of the  $\cdot\text{CONH}_2$  radical to the ring under the reaction conditions.

Protonation of the heteroaromatic ring considerably increases the reactivity towards nucleophilic radicals (3–6 orders of magnitude) compared to the unprotonated base. The introduction of the carbonyl decreases the basicity of the heterocyclic ring, reducing the reactivity of the molecule and preventing disubstitution.