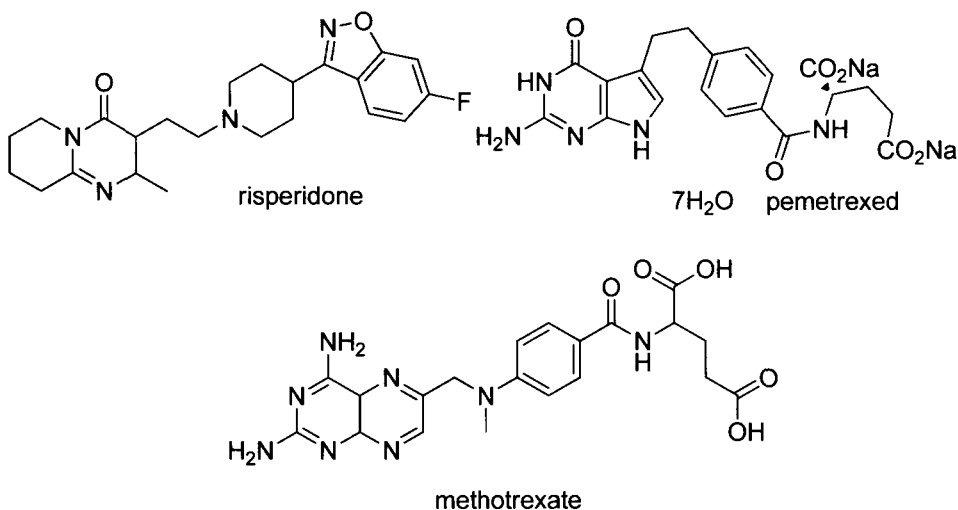


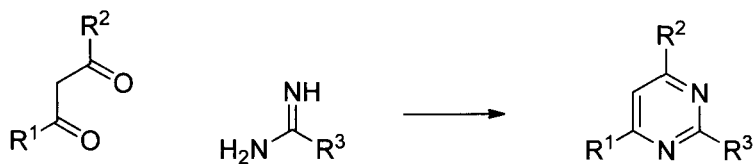
medical abortions. It acts by inhibiting the metabolism of folic acid, thereby blocking folic acid-dependent steps in the synthesis of purines and pyrimidines.<sup>6</sup> Methotrexate began to replace the more toxic antifolate aminopterin starting in the 1950s.



Given the extensive presence of the pyrimidine ring in numerous compounds of medicinal value, this chapter will primarily focus on the contemporary methods to construct pyrimidine rings and pyrimidine-fused systems. In addition, the syntheses of a few commercial drugs are discussed to showcase the preparations of pyrimidines in industrial settings.

## 13.2 Construction of the Pyrimidine Ring

### 13.2.1 Synthesis Involving Formation of Two Bonds



Condensation of an amidine with a 1,3-diketone is a popular method for the direct preparation of the six-membered-ring pyrimidine. Numerous methods exist for the synthesis of the prerequisite diketone and other dicarbonyl compounds, making this a very attractive strategy for the preparation of substituted pyrimidines.