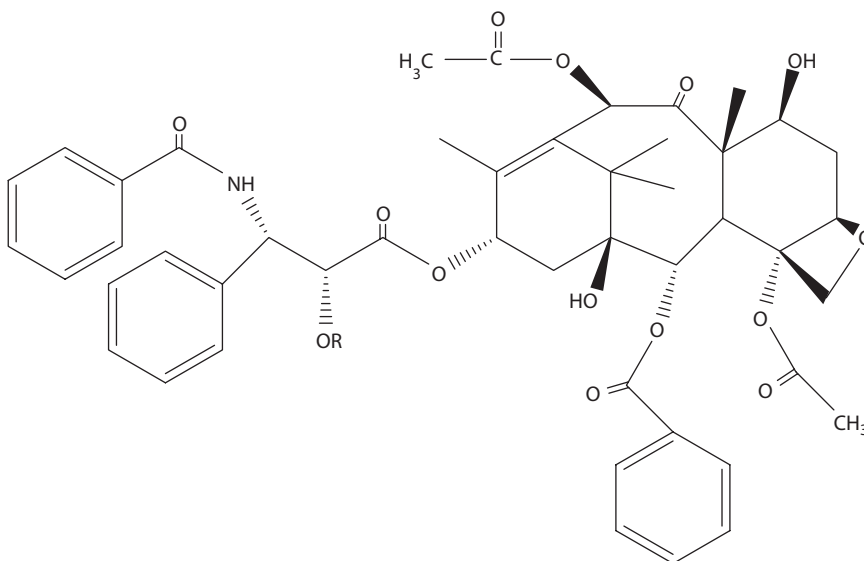


TABLE 16.1
Taxol, Its Reactant Form, and the Possible Products from Reactions
Catalyzed by *Candida Antarctica* Lipase



Substance

Taxol

Modified Taxol as a reactant

Potential adipic acid product

Potential adipolyglucose product

R Group

H —

$\text{H}_2\text{C}=\text{CH}_2-\text{O}-\text{C}(=\text{O})-(\text{CH}_2)_4-\text{C}(=\text{O})-$

$\text{HO}-\text{C}(=\text{O})-(\text{CH}_2)_4-\text{C}(=\text{O})-$

$\text{CH}_2-\text{O}-\text{C}(=\text{O})-(\text{CH}_2)_4-\text{C}(=\text{O})-$

keeping in mind that following hydrolysis of the ester, the hydroxymethyl group is rapidly hydrolyzed in aqueous media to yield the parent drug and formaldehyde. Formaldehyde toxicity does not appear to be a concern at the low levels expected with the use of prodrugs because pivampicillin and methenamine, each of which are marketed as safe drugs, also release formaldehyde on administration (Bansai et al., 1981b). Formaldehyde toxicity, however, will depend on the dose, the dosing frequency, and the duration of the therapy. The *N*-hydroxymethyl derivative usually demonstrates a higher aqueous solubility and dissolution rate, attributed to a lower melting point because hydroxymethylation interferes with hydrogen-bonding capability with the nitrogen in the crystalline state (Bansai et al., 1981a,b).

For drugs that possess an acidic NH functionality, such as amides, imides, carbamates, hydantoins, and urea derivatives, as well as for drugs that have aliphatic and aromatic amines, water-soluble