caused by heroin. Methadone can be given twice daily and tapered over 7 to 10 days. Methadone use, in both therapeutic doses and overdoses, has been associated with QTc interval prolongation and torsade de pointes, which, in some cases, has been fatal. Alternatively, buprenorphine, a partial agonist, can be given; it is combined with naloxone in a formulation (Suboxone) developed to decrease the potential for abuse. Clonidine reduces autonomic hyperactivity and is particularly effective if combined with a benzodiazepine. Patients with repeated relapses can be maintained on methadone or buprenorphine.

Naltrexone, a long-acting opioid antagonist that blocks impulsive opioid use, is an option for maintenance treatment to prevent relapse. It can be given orally daily or via injectable depot and implantable formulations every 60 to 90 days. It should only be administered after the patient is thoroughly detoxified because it may precipitate withdrawal. Pharmacotherapy must be combined with psychotherapy and structured rehabilitation to achieve an optimal outcome.

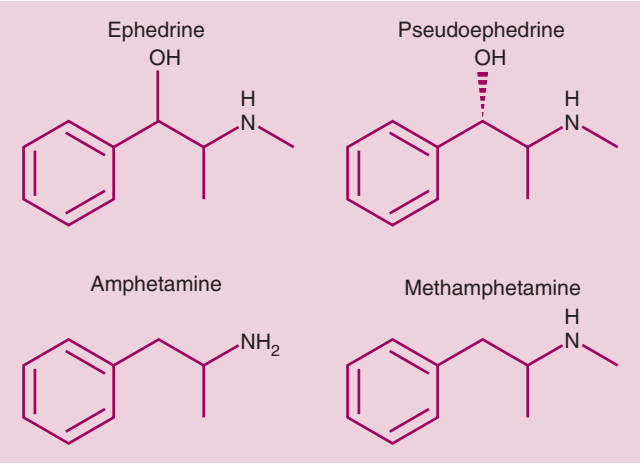

FIGURE 126-4 The chemical structures of amphetamine and methamphetamine, which can be easily manufactured from ephedrine or pseudoephedrine given that they are structurally similar and widely available.

Amphetamines

Amphetamines have been used therapeutically for weight reduction and treatment of attention-deficit disorder and narcolepsy. Similar to cocaine, they cause a release of monoamine neurotransmitters (dopamine, norepinephrine, and serotonin) from presynaptic neurons. In addition, however, they have neurotoxic effects on dopaminergic and serotonergic neurons. Their euphoric and reinforcing effects are mediated through dopamine and the mesolimbic system, whereas their cardiovascular effects are caused by the release of norepinephrine. Chronic use leads to neuronal degeneration in dopamine-rich areas of the brain, which may increase the risk for the eventual development of Parkinson's disease.

Amphetamines can be abused orally, intranasaly, intravenously, or by smoking. The most frequently used drugs are dextroamphetamine (Dexedrine), methamphetamine (Desoxyn), and methylphenidate (Ritalin). Methamphetamine is known on the street as *ice, crank, meth, crystal, tina, glass, and yaba.* Illicit use of amphetamines has increased substantially, in part because (a) it is easily and quickly synthesized from ephedrine or pseudoephedrine (Fig. 126-4), and (b) its psychotropic effects persist for up to 24 hours. The anorexiants, phenmetrazine and phentermine, which are structurally and pharmacologically similar to amphetamine, also have been used illicitly.

Tolerance to the stimulant effects of amphetamines develops rapidly, and toxic effects can occur with higher doses. Acute amphetamine toxicity is characterized by excessive sympathomimetic effects, including tachycardia, hypertension, hyperthermia, cardiac tachyarrhythmia, tremors, seizures, and coma. The patient may experience irritability, hypervigilance, paranoia, stereotyped compulsive behavior, and tactile, visual, or auditory hallucinations. The clinical picture may simulate an acute schizophrenic psychosis. The symptoms of withdrawal are similar to those seen with cocaine (see discussion of cocaine), but the acute psychosis and paranoia are often pronounced.

The treatment of amphetamine abuse centers on a quiet environment, benzodiazepines for anxiety, and sodium nitroprusside for severe hypertension. Antipsychotics, such as haloperidol, can reduce the agitation and psychosis by blocking the effect of dopamine on the CNS receptor. Urine acidification with ammonium chloride accelerates amphetamine excretion.

ILLICIT DRUG ABUSE

Cocaine

Among individuals 12 years old or older in 2011, 1.4 million had used cocaine within the previous month, and 670,000 had used it for the first time within the previous 12 months. Cocaine can be taken orally or intravenously; alternatively, because it is well absorbed through all mucous membranes, abusers may achieve a high blood concentration after intranasal, sublingual, vaginal, or rectal administration. Its freebase form (called *crack* because of the popping sound it makes when heated) is heat stable, and it can be smoked. Crack cocaine is considered to be the most potent and addictive form of the drug. Euphoria occurs within seconds after crack cocaine is smoked, and is short lived. Compared with smoking crack cocaine or intravenous injection of the drug, mucosal administration results in a slower onset of action, a later peak effect, and a longer duration of action. The blood half-life is approximately 1 hour. The drug's major metabolite is benzoylecgonine, which can be detected in the urine for 2 to 3 days after a single dose.

An intense, pleasurable reaction lasting 20 to 30 minutes occurs after cocaine use, after which rebound depression, agitation, insomnia, and anorexia occur, which are then followed by fatigue, hypersomnolence, and hyperphagia (the *crash*). This crash usually lasts 9 to 12 hours but occasionally may last up to 4 days. Users often ingest the drug repetitively at relatively short intervals to recapture the euphoric state and to avoid the crash. On occasion, sedatives or alcohol are ingested concomitantly to reduce the intensity of anxiety and irritability associated with the crash. The combination of cocaine and intravenously administered heroin (so-called *speedball, snowball, blanco, boy-girl, Bombita, Belushi,* or *dynamite*) is often used so that the abuser can experience the cocaine-induced euphoria and then *float* down on the opiate. Unfortunately, this combination has been reported to cause sudden death. People who use cocaine in temporal