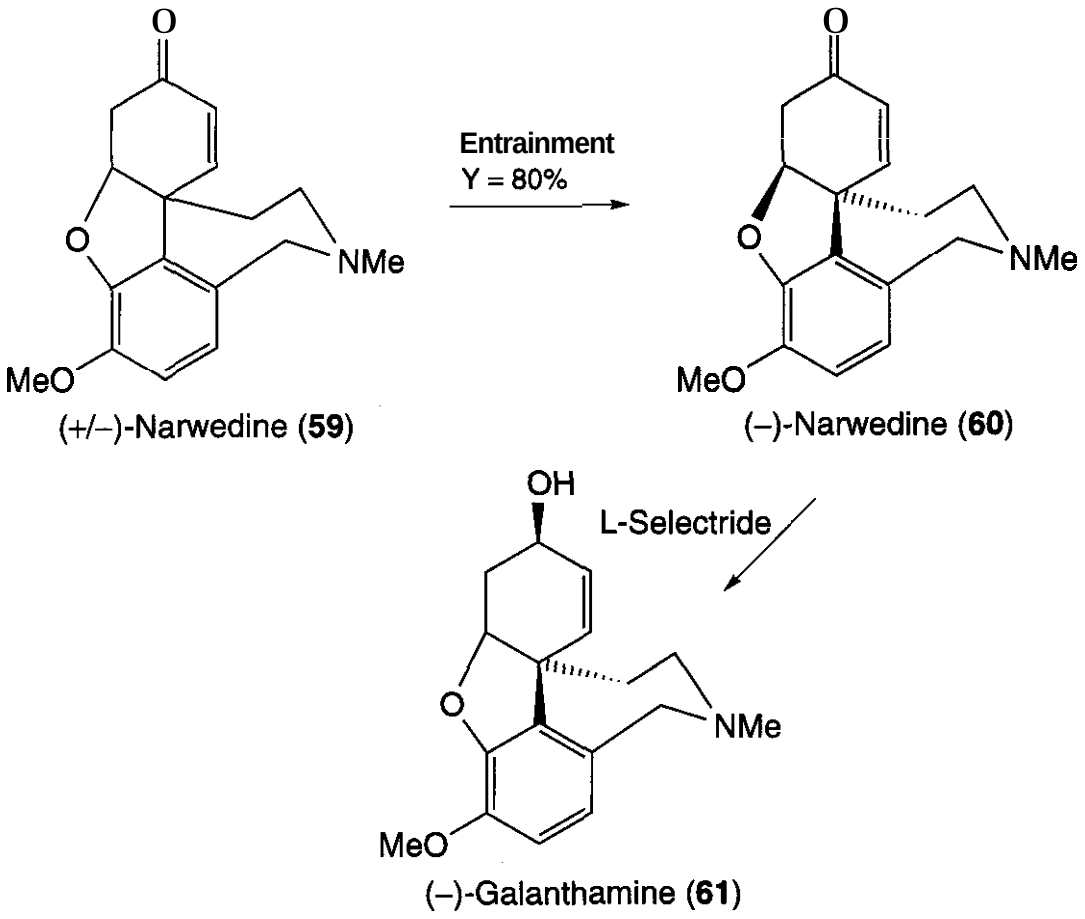
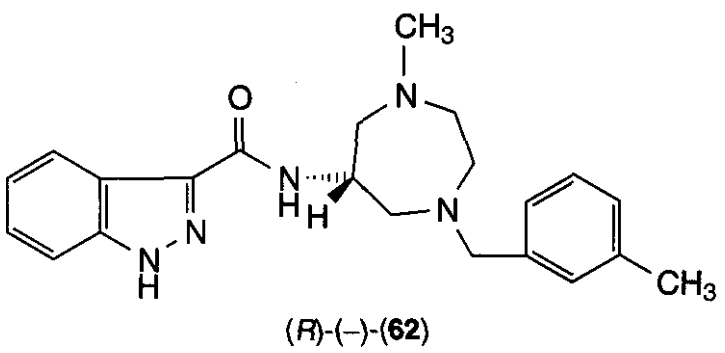



**Figure 18.25.**

raiwa et al. have described the preferential crystallization of racemic methionine hydrochloride (106). The obtained D- or L-methionine hydrochloride was, however, only —75% optically pure, requiring a further recrystallization to furnish enantiopure product. Shiraiwa et al. have also recently disclosed the resolution of (2*RS*, 3*SR*)-2-amino-3-chlorobutanoic acid HCl again using entrainment (107). Here it was shown to be necessary to conduct the crystallization in an ethanol15 M hydrochloric acid solvent mixture for optimal results. By careful control of the conditions, high levels of enantiomeric excess were obtained in the crystalline salt.

Chemists in Japan have developed an excellent approach to (+)-Diltiazem, which is a coronary vasodilator (108). An intermediate




(*R*)-(–)-(**62**)

**Figure 18.26.**

is successfully resolved using preferential crystallization. The glycidic acid–substituted phenylesters were prepared; of the 30 synthesized, only one exhibited conglomerate properties (109). This was the 3-(4-methoxyphenyl)glycidic acid 4-chloro-3-methylphenyl ester (63). Table 18.2 summarizes the physical data collected, which is illustrative of the conglomerate nature of this compound.

The obtained single enantiomer (–)-epoxide (64) is then converted into the required (+)-isomer of Diltiazem (**65**) in several steps, as highlighted in Fig. 18.27.

Taxol is a natural product isolated in very low yield from *Taxus* brevifolia and is used in the treatment of cancer (110). The extreme chemical complexity of Taxol makes production by total synthesis uneconomical. However, a semisynthetic approach using the naturally derived 10-deacetylbaccatin III (**66**) condensation with *N*-benzoyl-(2*R*, 3*S*)-3-phenylisoserine (67) does provide an alternative and economic approach (111). *N*-benzoyl-(2*R*, 3*S*)-3-phenylisoserine (67) is also commonly known as the Taxol side-chain and has been prepared in optically active form using chiral auxiliaries or resolving agents (112). It has been shown that the Taxol side-chain is a conglomerate and can therefore be cheaply and