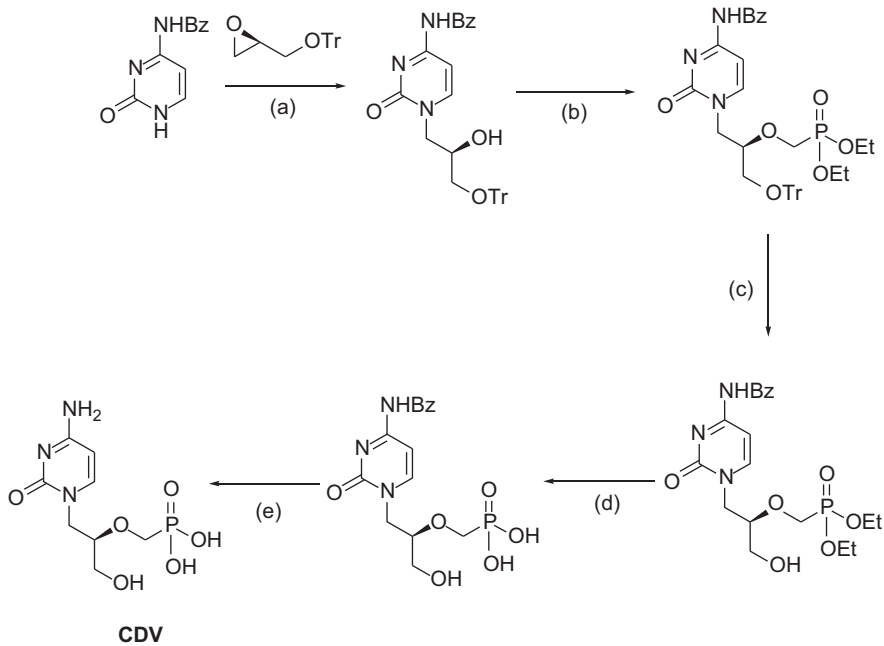
ST-246 is a new chemical entity discovered by high-throughput screening of chemical libraries to identify compounds the inhibited OPV replication. This unbiased or target neutral approach has proven successful for discovery of novel inhibitors of OPV replication.[51] Cell-based assays have been designed to measure virus replication and can be optimized for high-throughput screening of compound libraries to identify inhibitors of OPV replication. Simple assays have been developed that measure virus-induced cytopathic effects (CPEs) and can be easily conducted in 96- or 384-well formats. Vaccinia virus is often used as a prototype OPV in these assays because it is replicates to high levels in cell culture producing robust CPEs and can be handled safely in biosafety level 2 containment.

4.4.1 Cidofovir

CDV {(*S*)-1-[3-hydroxy-2-(phosphonomethoxy)propyl]cytosine, Vistide] is an acyclic nucleoside phosphonate analog that exhibits broad-spectrum antiviral activity against DNA-containing viruses (Figure 4.2).[52] The acyclic nucleoside



(a) NaH (0.22 equiv.), DMF, 105 °C, 5 h
(b) $TsOCH_2P(O)(OEt)_2$, NaH (3 equiv.), DMV, 0 °C, 6 h
(c) HCl, CH_2Cl_2, 0–5 °C, 10 min.
(d) TMSBr, CH_2Cl_2, r.t., 18 h
(e) Concentrated NH_4OH, r.t., 4 h

Figure 4.2 Synthesis of cidofovir (CDV). Chemical synthesis adapted from Brodfuehrer *et al.*[119]