Claims

1. A process for preparing a crystalline form of (2R,S)-, (2S)- or (2R)-DOTAP chloride

which crystalline (2R,S)-DOTAP chloride has one of the following characteristics:
2 theta values comprising at least values of about 12.6, about 19.5, about 20.2, about 21.5 and about 25.2; or
2 theta values comprising at least values of about 6.5, about 12.6, about 13.4, about 19.5, about 20.2, about 21.5, about 25.2 and about 29.8; or an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 1; or

which crystalline (2S)-DOTAP chloride has one of the following characteristics:
2 theta values comprising at least values of about 12.8, about 19.5, about 19.8, about 20.2, and about 21.6;
2 theta values comprising at least values of about 6.5, about 12.8, about 19.5, about 19.8, about 20.2, about 20.7, about 21.6 and about 25.3; or an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 2; or

which crystalline (2R)-DOTAP chloride has one of the following characteristics:
2 theta values comprising at least values of about 12.8, about 19.5, about 19.8, about 20.3, and about 21.6;
2 theta values comprising at least values of about 6.6, about 12.8, about 19.5, about 19.8, about 20.3, about 20.8, about 21.6 and about 25.3; or an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 3;
comprising crystallizing (2R,S)-, (2S)- or (2R)-DOTAP chloride from one or more aprotic solvents wherein the crystallizing takes place by slow cooling at a rate of 0.001 °C to 0.1 °C per minute to -12 °C for 10 to 30 hours, wherein the one or more aprotic solvents comprise one or more protic solvents.

2. The process according to claim 1, wherein the crystalline (2R.S)-, (2S)- or (2R)-DOTAP chloride, has a stability of higher than 99% by weight and Area-% determined by HPLC when stored at 25°C for 36 months or at 40°C for 12 months.

3. The process according to claim 1, wherein the crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride has a chemical purity of at least about 95% determined by HPLC.

4. The process according to any one of claims 1-3, wherein the crystalline (2R.S)-, (2S)- or (2R)-DOTAP chloride has a melting point of higher than 160°C and a melting enthalpy of more than -130 J/g.

5. The process according to any one of claims 1-4, wherein the crystallizing takes place under an inert atmosphere.

6. The process according to any one of claims 1-5, where crystallisation is carried out directly from a reaction solution without prior purification, which reaction solution is from a process of preparing (2R,S)-, (2S)- or (2R)-DOTAP chloride.

7. The process according to any one of claims 1-6, which further comprises a recrystallization of crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride.

Claims

1. A process for preparing a crystalline form of (2R,S)-, (2S)- or (2R)-DOTAP chloride

which crystalline (2R,S)-DOTAP chloride has one of the following characteristics:

2 theta values comprising at least values of about 12.6, about 19.5, about 20.2, about 21.5 and about 25.2; or

2 theta values comprising at least values of about 6.5, about 12.6, about 13.4, about 19.5, about 20.2, about 21.5, about 25.2 and about 29.8; or an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 1; or

which crystalline (2S)-DOTAP chloride has one of the following characteristics:

2 theta values comprising at least values of about 12.8, about 19.5, about 19.8, about 20.2, and about 21.6;

2 theta values comprising at least values of about 6.5, about 12.8, about 19.5, about 19.8, about 20.2, about 20.7, about 21.6 and about 25.3; or an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 2; or

which crystalline (2R)-DOTAP chloride has one of the following characteristics:

2 theta values comprising at least values of about 12.8, about 19.5, about 19.8, about 20.3, and about 21.6;

2 theta values comprising at least values of about 6.6, about 12.8, about 19.5, about 19.8, about 20.3, about 20.8, about 21.6 and about 25.3; or an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 3;

comprising crystallizing (2R,S)-, (2S)- or (2R)-DOTAP chloride from one or more aprotic solvents wherein the crystallizing takes place by slow cooling from 35°C to -12°C over a period of 12 hours or slow cooling from lower temperature than 35°C over a period from 10 to 50 hours wherein the one or more aprotic solvents comprise one or more protic solvents.

2. The process according to claim 1, wherein the crystalline (2R.S)-, (2S)- or (2R)-DOTAP chloride, has a stability of higher than 99% by weight and Area-% determined by HPLC when stored at 25°C for 36 months or at 40°C for 12 months.

3. The process according to claim 1, wherein the crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride has a chemical purity of at least about 95% determined by HPLC.

4. The process according to any one of claims 1-3, wherein the crystalline (2R.S)-, (2S)- or (2R)-DOTAP chloride has a melting point of higher than 160°C and a melting enthalpy of more than -130 J/g.

5. The process according to any one of claims 1-4, wherein the crystallizing takes place under an inert atmosphere.

6. The process according to any one of claims 1-5, where crystallisation is carried out directly from a reaction solution without prior purification, which reaction solution is from a process of preparing (2R,S)-, (2S)- or (2R)-DOTAP chloride.

7. The process according to any one of claims 1-6, which further comprises a recrystallization of crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride.