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(12) **United States Patent**
Müller et al.(10) **Patent No.: US 6,271,374 B1**
(45) **Date of Patent: *Aug. 7, 2001**(54) **STABLE CRYSTALLINE (6S)- AND (6R)-TETRAHYDROFOLIC ACID**(75) Inventors: **Hans Rudolf Müller**, Schaffhausen;
Martin Ulmann, Dachsen; **Rudolf Moser**, Schaffhausen; **Thomas Ammann**, Marthalen, all of (CH)(73) Assignee: **Eprova AG**, Schaffhausen (CH)

(*) Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/013,266**(22) Filed: **Jan. 26, 1998****Related U.S. Application Data**

(63) Continuation of application No. 08/437,716, filed on May 9, 1993, now abandoned.

(30) **Foreign Application Priority Data**

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(51) **Int. Cl.⁷** **C07D 475/04**(52) **U.S. Cl.** **544/258**(58) **Field of Search** 544/258(56) **References Cited**

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Primary Examiner—John M. Ford(74) *Attorney, Agent, or Firm*—Millen, White, Zelano & Branigan, P.C.(57) **ABSTRACT**Pure and extremely stable crystalline (6S)- and (6R)-tetrahydrofolic acids, absolutely inert even when exposed to air and elevated temperature without stabilizers being added, are prepared by a crystallization process at a pH of ≥ 3.5 for the preparation of crystalline (6S)-tetrahydrofolic acid and at a pH of ≥ 2 for the preparation of crystalline (6R)-tetrahydrofolic acid.**17 Claims, No Drawings**