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(21) International Application Number: PCT/US96/06819 (22) International Filing Date: 13 May 1996 (13.05.96) (30) Priority Data: 08/474,874 ✓ 7 June 1995 (07.06.95) ✓ US (71) Applicant: WARNER-LAMBERT COMPANY [US/US]; 201 Tabor Road, Morris Plains, NJ 07950 (US). (72) Inventors: GROTE, Todd, Michel; 1105 Whispering Dunes Drive, Holland, MI 49424 (US). HUCKABEE, Brian, Keith; Apartment 3A, 2975 Millpond Drive East, Holland, MI 49424 (US). MULHERN, Thomas; 5571 Hughes Drive, Hudsonville, MI 49426 (US). SOBIERAY, Denis, Martin; 2178 South Bristol, Holland, MI 49424 (US). TITUS, Robert, Daniel; 3631 Pleasant Lake Drive, Indianapolis, IN 46227 (US). (74) Agents: RYAN, M., Andrea; Warner-Lambert Company, 201 Tabor Road, Morris Plains, NJ 07950 (US) et al.		(81) Designated States: AU, CA, CZ, EE, HU, JP, LT, LV, MX, NZ, PL, RO, SG, SI, SK, Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: METHOD OF MAKING (S)-3-(AMINOMETHYL)-5-METHYLHEXANOIC ACID (57) Abstract A method of making (±)-3-(aminomethyl)-5-methylhexanoic acid that comprises condensing isovaleraldehyde with (II) to form primarily (III); reacting the (III) with a cyanide source to form (IV); decarboxylating the (IV) to form (V); hydrolyzing the (V) with an alkali or alkaline earth metal hydroxide to form an alkali or alkaline earth metal carboxylate salt; and hydrogenating the alkali or alkaline earth metal carboxylate salt to form (±)-3-(aminomethyl)-5-methylhexanoic acid, wherein R₁ and R₂ are the same or different and are hydrogen, C₁-C₆ alkyl, aryl, benzyl, or C₃-C₆ cycloalkyl. The present invention also provides a method of making (±)-3-(aminomethyl)-5-methylhexanoic acid that comprises condensing isovaleraldehyde with (II) to form primarily (III); reacting the (III) with a cyanide source to form (IV); decarboxylating the (IV) to form an alkali or alkaline earth metal carboxylate salt; and hydrogenating the alkali or alkaline earth metal carboxylate salt to form (±)-3-(aminomethyl)-5-methylhexanoic acid. $\begin{array}{c} \diagup \text{CO}_2\text{R}_1 \\ \diagdown \text{CO}_2\text{R}_2 \end{array} \quad \text{(II)}$ $\begin{array}{c} \text{CO}_2\text{R}_1 \\ \\ \text{CH}_3-\text{CH}_2-\text{CH}=\text{CH}-\text{CO}_2\text{R}_2 \end{array} \quad \text{(III)}$ $\begin{array}{c} \text{CN} \\ \\ \text{CH}_3-\text{CH}_2-\text{CH}-\text{CH}-\text{CO}_2\text{R}_2 \\ \\ \text{R}_1\text{O}_2\text{C} \end{array} \quad \text{(IV)}$ $\begin{array}{c} \text{CN} \\ \\ \text{CH}_3-\text{CH}_2-\text{CH}-\text{CH}-\text{CO}_2\text{R}_1 \\ \\ \text{CH}_3 \end{array} \quad \text{(V)}$		