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(21) International Application Number: PCT/US96/05831 (22) International Filing Date: 26 April 1996 (26.04.96) (30) Priority Data: 08/458,950 2 June 1995 (02.06.95) US (71) Applicant: WARNER-LAMBERT COMPANY [US/US]; 201 Tabor Road, Morris Plains, NJ 07950 (US). (72) Inventors: HUCKABEE, Brian, Keith; Apartment 3A, 2975 Millpond Drive East, Holland, MI 49424 (US). SOBIERAY, Denis, Martin; 2178 South Bristol, Holland, MI 49424 (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>
(54) Title: METHODS OF MAKING (S)-3-(AMINOMETHYL)-5-METHYLHEXANOIC ACID (57) Abstract The present invention provides a method of making (S)-(+)-3-(aminomethyl)-5-methylhexanoic acid which comprises condensing isovaleraldehyde with an alkyl cyanoacetate to form a 2-cyano-5-methylhex-2-enoic acid alkyl ester; reacting the 2-cyano-5-methylhex-2-enoic acid alkyl ester with a dialkyl malonate to form 3-isobutylglutaric acid; forming the anhydride of 3-isobutylglutaric acid; reacting the anhydride with ammonia to form (±)-3-(carbamoylmethyl)-5-methylhexanoic acid; reacting (±)-3-(carbamoylmethyl)-5-methylhexanoic acid with (R)-(+)-α-phenylethylamine to obtain the (R)-(+)-α-phenylethylamine salt of (R)-(-)-3-(carbamoylmethyl)-5-methylhexanoic acid; combining the salt with an acid to obtain (R)-(-)-3-(carbamoylmethyl)-5-methylhexanoic acid; and reacting the (R)-(-)-3-(carbamoylmethyl)-5-methylhexanoic acid with a Hofmann reagent to obtain (S)-(+)-3-(aminomethyl)-5-methylhexanoic acid.		