

EXAMPLE XIX

16.86 gm (0.1 mol) of L-ornithine hydrochloride is dissolved in 200 ml of 1M NaOH. To the clear solution is added 5.71 gm of methyl isocyanate (0.1 mol) dropwise at room temperature. The pH is maintained at 9.5-10.5 by occasional cautious addition of 1M NaOH. After stirring overnight at room temperature, the reaction mixture is reduced to dryness by rotary evaporation at reduced pressure. The residue is suspended in concentrated HCl and the precipitate of NaCl is filtered off. The filtrate, which contains N^ω-methyl-L-citrulline is evaporated to dryness under reduced pressure and redissolved in a small volume of water. That solution is applied to a column 2.0 by 50 cm of Dowex 50 (Na⁺ form). The column is washed with 2 L of distilled water and fractions of approximately 25 ml are collected sequentially. Under these conditions of chromatography, N^ω-methyl-L-citrulline is eluted and residual unreacted L-ornithine remains bound to the Dowex resin. Fractions containing N^ω-methyl-L-citrulline (detected using a conventional ninhydrin spot assay) are pooled, rotary evaporated to dryness under reduced pressure, and the residual oil is crystallized from ethanol/water. The overall yield is approximately 75% based on the amount of ornithine used.

N^ω-Alkyl-L-citrullines with different N^ω-alkyl groups from methyl are prepared by substituting an equivalent molar amount of the corresponding alkyl isocyanate for the methyl isocyanate.

Many variations will be obvious to those skilled in the art. Thus, the invention is defined by the claims.

What is claimed is:

1. A method of prophylaxis or treatment of a subject for inflammation caused by induced nitric oxide production from arginine in cells, said method comprising administering to a subject at risk for or having such inflammation, a

therapeutically effective amount of an argininosuccinate synthetase activity reducing agent.

2. The method of claim 1 wherein the argininosuccinate synthetase activity reducing agent is an argininosuccinate synthetase induction blocking agent.

3. The method of claim 2 wherein the argininosuccinate synthetase induction blocking agent is also a nitric oxide synthase induction blocking agent and is an antibiotic that binds to DNA sequences present in the upstream regulatory region of the argininosuccinate synthetase gene.

4. The method of claim 3 wherein the antibiotic is selected from the group consisting of mithramycin, chromomycins and olivomycins.

5. The method of claim 4 wherein the antibiotic is mithramycin.

6. The method of claim 1 wherein the argininosuccinate synthetase activity reducing agent is an argininosuccinate synthetase inhibitor.

7. The method of claim 6 wherein the argininosuccinate synthetase inhibitor is an L-citrulline antagonist.

8. The method of claim 7 wherein the L-citrulline antagonist is not L-thiocitrulline or L-homothiocitrulline.

9. The method of claim 8 wherein the L-citrulline antagonist is N^ω-alkyl-L-citrulline wherein the alkyl contains 1 to 6 carbon atoms.

10. The method of claim 9 wherein the L-citrulline antagonist is N^ω-methyl-L-citrulline.

11. The method of claim 6 wherein the argininosuccinate synthetase inhibitor is an L-aspartate antagonist.

12. The method of claim 11 wherein the L-aspartate antagonist is D-aspartate.

13. N^ω-C₁₋₆-alkyl-L-citrulline.

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