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2,862,938

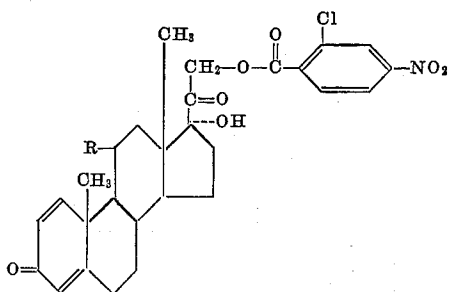
21-(2-CHLORO-4-NITROBENZOATE) OF PREDNISOLONE AND PREDNISONE

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3 Claims. (Cl. 260—397.45)

This invention is concerned with physiologically active steroid hormones and is more particularly concerned with 11 β ,17 α ,21 - trihydroxy - 1,4 - pregnadiene - 3,20 - dione and 17 α ,21 - dihydroxy - 1,4 - pregnadiene - 3,11,20 - trione 21 - (2 - chloro - 4 - nitrobenzoates), i. e. the 21 - (2 - chloro - 4 - nitrobenzoates) of prednisolone and prednisone represented by the following formula:



wherein R is selected from the group consisting of β -hydroxy and oxo.

It is an object of the present invention to provide the 21 - (2 - chloro - 4 - nitrobenzoate) of prednisolone and prednisone which are physiologically active agents of high potency having high anti-inflammatory activity, particularly locally and intra - articularly, anti - arthritic activity, low toxicity, and a superior therapeutic ratio. The compounds of the present invention are substitutable for other adrenal cortical steroid hormones in known adrenal cortical steroid hormone-containing pharmaceutical compositions such as tablets, lotions, ointments, injectables, and elixirs. Other objects and uses of the present invention will be apparent to one skilled in the art.

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The 21-(2-chloro-4-nitrobenzoate) esters of prednisolone and prednisone of the present invention are obtained by esterification of prednisolone and prednisone, respectively, to introduce the 21-(2-chloro-4-nitrobenzoate) radical, as more fully described in the following illustrative examples.

EXAMPLE 1

A solution of 11 parts of prednisolone in 110 parts of pyridine is prepared at forty degrees centigrade, 8 parts of ortho-chloro-para-nitrobenzoyl chloride is added, with stirring, at a rate to maintain the reaction temperature between twenty and thirty degrees centigrade, and the reaction mixture then stirred for an additional four hours. The mixture is then poured, with stirring into a mixture of 600 parts of ice and water and allowed to stand overnight at five degrees centigrade. The solid which had precipitated is removed by filtration, washed with water, dried, and recrystallized from an ethyl acetate-acetone mixture using Nuchar C-190 N decolorizing charcoal. The yield of purified prednisolone 21-(2-chloro-4-nitrobenzoate) is 63 percent; melting point 195.5 to 198 degrees centigrade; $[\alpha]_D^{24}$ is plus 139 degrees in chloroform.

Analysis.—Theoretical: C, 61.82; H, 5.56. Found: C, 62.09; H, 5.78.

EXAMPLE 2

Following the procedure of Example 1, but substituting prednisone for the prednisolone provides purified prednisone 21-(2-chloro-4-nitrobenzoate) in a yield of 59 percent; melting point 211 to 212 degrees centigrade; $[\alpha]_D^{24}$ is plus 192 degrees in chloroform.

Analysis.—Theoretical: C, 62.05; H, 5.21. Found: C, 62.29; H, 5.49.

I claim:

1. A compound selected from the group consisting of 11 β ,17 α ,21 - trihydroxy - 1,4 - pregnadiene - 3,20 - dione 21 - (2 - chloro - 4 - nitrobenzoate) and 17 α ,21 - dihydroxy - 1,4 - pregnadiene - 3,11,20 - trione 21 - (2 - chloro-4-nitrobenzoate).

2. 11 β ,17 α ,21 - trihydroxy - 1,4 - pregnadiene - 3,20 - dione 21-(2-chloro-4-nitrobenzoate).

3. 17 α ,21 - dihydroxy - 1,4 - pregnadiene - 3,11,20 - trione 21-(2-chloro-4-nitrobenzoate).

References Cited in the file of this patent

UNITED STATES PATENTS

2,183,589	Reichstein	Dec. 19, 1939
2,736,734	Sarett	Feb. 28, 1956