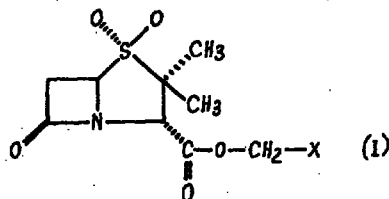


SPECIFICATION

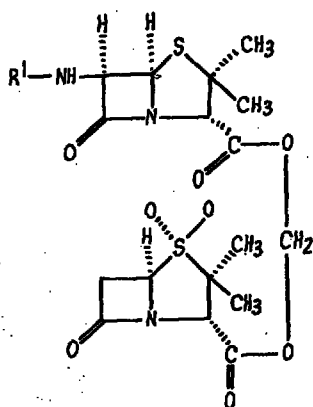
Penicillanic Acid Derivatives

- 5 The present invention relates to new penicillanic acid derivatives. In particular, the present invention relates to a compound having the formula:—

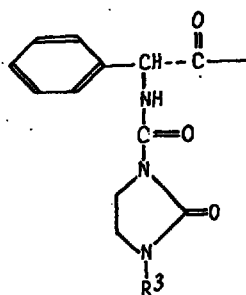


- 10 wherein X is selected from alkylsulfonyloxy having from one to four carbon atoms in the alkyl group, benzenesulfonyloxy and toluenesulfonyloxy.

The compounds of the present invention are useful as intermediates in the preparation of methanediol bisesters having the formula



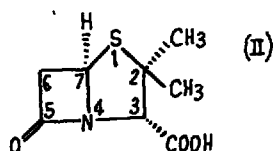
- 15 and pharmaceutically-acceptable salts thereof wherein R¹ is selected from 2-phenylacetyl, 2-phenoxyacetyl, 2-carboxy-2-(2-thienyl)acetyl, 2-(4-ethyl-2,3-dioxopiperazinocarbonylamino)-2-phenylacetyl and a group of the formula



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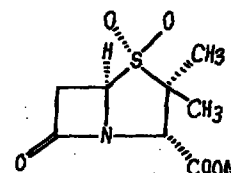
- wherein R³ is selected from hydrogen, 2—4C alkanoyl and 1—3C alkylsulfonyl, which compounds are valuable antibacterial agents and form the subject of our published British Patent Application 2051057.

- 25 This invention relates to derivatives of penicillanic acid, which is represented by the following structural formula



- 30 In formula II, broken line attachment of a substituent to the bicyclic nucleus indicates that the substituent is below the plane of the bicyclic nucleus. Such a substituent is said to be in the alpha-configuration. Conversely, solid line attachment of a substituent to the bicyclic nucleus indicates that the substituent is attached above the plane of the nucleus. This latter configuration is referred to as the beta-configuration.

- 40 The compounds of formula I can be prepared by reacting a compound of the formula



- wherein M is a carboxylate-salt forming cation with a compound of the formula X—CH₂—Y, wherein X and Y are each alkylsulfonyloxy having one to four carbons in the alkyl group, benzene-sulfonyloxy or toluenesulfonyloxy. A variety of cations can be used to form the carboxylate salt but salts which are commonly used include: alkali metal salts, such as sodium and potassium salts; alkaline earth metal salts, such as calcium and barium salts; and tertiary amine salts, such as trimethylamine, triethylamine, tributylamine, diisopropylethylamine, *N*-methylmorpholine, *N*-methylpiperidine, *N*-methylpyrrolidine, *N,N*-dimethylpiperazine and 1,2,3,4-tetrahydroquinoline.

- The reaction between the compounds above is usually carried out by contacting the reagents in a polar, organic solvent, at a temperature in the range from about 0° to about 80°C., and preferably from 25° to 50°C. The compounds can be contacted in substantially equimolar proportions, but preferably the compound X—CH₂—Y is used as an excess (e.g. a fourfold excess). A wide variety of solvents can be used, but it is usually advantageous to use a relatively polar solvent, since this has the effect of speeding up the reaction. Typical solvents which can be used include *N,N*-dimethylformamide, *N,N*-dimethylacetamide, *N*-methylpyrrolidone, dimethylsulfoxide and hexamethylphosphoramide. The reaction time varies according to a number of factors, but at about 25°C. reaction times of several hours, e.g. 12 to 24 hours, are commonly used.

Example 1

Methylsulfonyloxymethyl Penicillanate 1,1-Dioxide

- 80 To a stirred solution of 24 g. of penicillanic acid, 1,1-dioxide in 125 ml. of *N,N*-dimethylformamide is added 9.5 ml. of diisopropylethylamine, followed by 67.1 g. of di(methylsulfonyloxy)methane. Stirring is continued overnight and then the reaction mixture is added to 300 ml. of water. The pH is adjusted to 8.5, and then the

mixture is extracted with ethyl acetate. The extract is washed with water, followed by saturated sodium chloride solution and then it is dried over sodium sulfate. The dried extract is concentrated to dryness *in vacuo* to give the crude product.

The procedure above is repeated, except that the di(methylsulphonyloxy)methane used therein is replaced by an equimolar amount of (1) di(isobutylsulfonyloxy)methane, (2) di(benzenesulfonyloxy)methane and (3) di(4-toluenesulfonyloxy)methane. This affords:

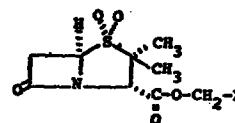
(1) isobutylsulfonyloxymethyl penicillanate 1,1-dioxide,

(2) benzenesulfonyloxymethyl penicillanate 1,1-dioxide, and

(3) 4-toluenesulfonyloxymethyl penicillanate 1,1-dioxide, respectively.

Claims

1. A compound of the formula



wherein X is selected from the group consisting of alkylsulfonyloxy having from one to four carbons, benzenesulfonyloxy and toluenesulfonyloxy.

2. The compound according to claim 1, wherein X is methylsulfonyloxy.

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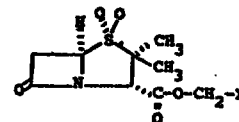
The procedure above is repeated, except that the di(methylsulphonyloxy)methane used therein is replaced by an equimolar amount of (1) di(isobutylsulfonyloxy)methane, (2) di(benzenesulfonyloxy)methane and (3) di(4-toluenesulfonyloxy)methane. This affords:

- (1) isobutylsulfonyloxymethyl penicillanate
1,1-dioxide,
15 (2) benzenesulfonyloxymethyl penicillanate
1,1-dioxide, and

(3) 4-toluenesulfonyloxymethyl penicillanate
1,1-dioxide, respectively.

Claims

- 20 1. A compound of the formula



wherein X is selected from the group consisting of alkylsulfonyloxy having from one to four carbons, benzenesulfonyloxy and toluene-sulfonyloxy.

- 25 2. The compound according to claim 1, wherein X is methylsulfonyloxy.

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