

UNITED STATES PATENT OFFICE

2,629,734

N-OXYALKYL-p-AMINO BENZOYL
GLUTAMATES

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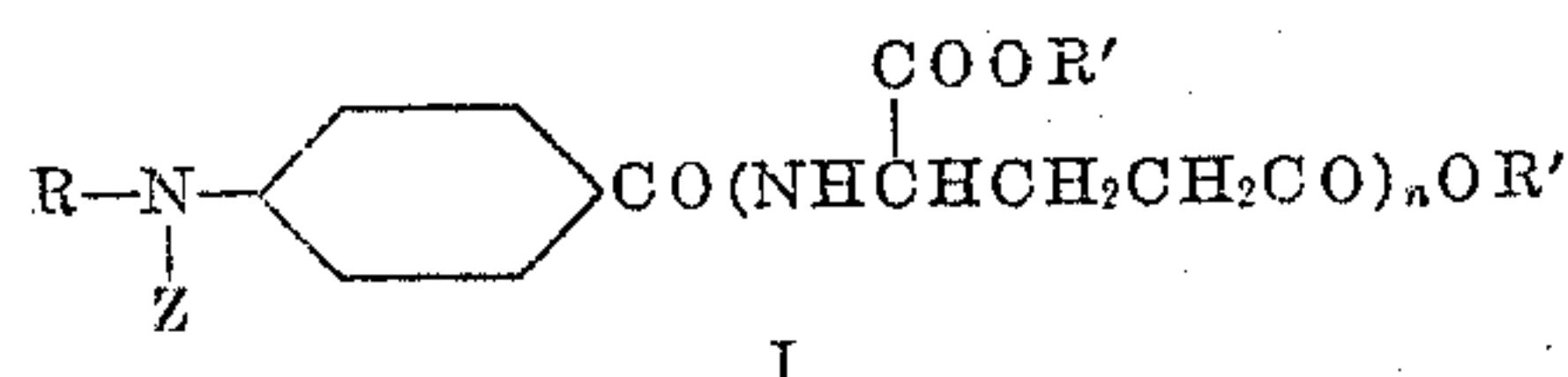
No Drawing. Application July 31, 1948,
Serial No. 41,890

13 Claims. (Cl. 260—470)

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This invention relates to a method for preparing certain N-propyl-p-aminobenzoate compounds containing substituents in the propyl radical, particularly to compounds containing substituents on both the second and third carbon atoms of the propyl radical, and to methods useful in their preparation.

The compounds which can be prepared by the method of the invention are herein defined as the "N-propyl-p-amino-benzoate compounds" and have the generic formula



wherein R' is from the group consisting of hydrogen and the alkyl radicals, Z is from the group consisting of hydrogen and the arylsulfonyl radicals, n is from the group consisting of zero and the positive integers 1 to 7 inclusive, and R is from the group consisting of the 3-chloro-2-hydroxypropyl, 3-bromo-2-hydroxypropyl, 3-iodo-2-hydroxypropyl, 3-alkoxy-2-hydroxypropyl, 3-aryloxy-2-hydroxypropyl, 3-aralkoxy-2-hydroxypropyl, 3-acyloxy-2-hydroxypropyl, 2,3-dihydroxypropyl radicals. These compounds are described and claimed and another method for their preparation is given in a concurrently filed copending application, Serial No. 41,884.

In the naming of the compounds of the invention and of other compounds mentioned herein when both a glutamic acid residue and a p-aminobenzoic acid residue are included in the molecule the nitrogen atom of the glutamic acid residue is, for convenience, herein referred to by the symbol "N" and the nitrogen atom of the p-aminobenzoic acid residue is referred to by the symbol "N."

As indicated by the formula given, compounds containing more than one glutamic acid or ester residue contemplated by the invention are those wherein only the gamma-carboxyl groups are involved in the peptide linkages, such as the residues derived from N'-(p-aminobenzoyl)-gamma-glutamylglutamic acid, N'-(p-aminobenzoyl)-gamma-glutamyl-gamma-glutamylglutamic acid, and the like. Preferred compounds of the invention are those wherein n represents the integer 1, i. e. those containing one glutamic acid or ester residue, and the invention will be described with particular reference thereto.

Many of the compounds of the invention are well defined crystalline substances soluble in alcohol and ether and in many other common or-

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ganic liquids. The amino acids and esters form addition salts with acids which are soluble in water while the arylsulfonylamino acids and esters are only sparingly soluble in water. The amino acids and esters also form quaternary ammonium compounds with alkyl halides.

The N-propyl-p-aminobenzoate compounds of the invention are useful as intermediates in the preparation of certain compounds generally referred to broadly as "folic acids." Thus, as described and claimed in a concurrently filed copending application, Serial No. 41,889, diethyl N'-(N-(3-methoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate can be oxidized, e. g. with chromic acid, to form diethyl N'-(N-(3-methoxy-2-ketopropyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate which can then be condensed with 2,4,5-triamino-6-hydroxypyrimidine, as described and claimed in a concurrently filed co-pending application Serial No. 41,882, now Patent No. 2,558,711, to form diethyl N'-(N-((2-amino-4-hydroxy-6-pteridyl)methyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate. Upon treatment of the latter compound with hydrogen bromide in an aliphatic acid medium, and in the presence of a bromine acceptor to prevent bromination in the benzene nucleus of the aminobenzoic acid residue according to the method described and claimed in a concurrently filed co-pending application, Serial No. 41,883, now Patent No. 2,562,222, and after subsequent hydrolysis of the ester groups, there is formed N'-(N-((2-amino-4-hydroxy-6-pteridyl)methyl)-p-aminobenzoyl)-glutamic acid (pteroylglutamic acid) generally recognized, when the glutamic acid residue has the same configuration as 1(+)-glutamic acid, as being identical with the "L. casei factor" or vitamin B₉ from liver.

Compounds similar to, or identical with, those of the folic acid group made by using compounds of the invention as intermediates, such as pteroylglutamic acid and pteroyl-gamma-glutamyl-gamma-glutamylglutamic acid, which are of greatest value as measured by their biological activity against *Lactobacillus casei* or *Streptococcus fecalis* R, are those wherein the glutamic acid residues possess the same configuration as 1(+)-glutamic acid and for this reason the preferred compounds of the invention are those having this same configuration. However, the invention also contemplates compounds having the dextro configuration as well as racemic mixtures.

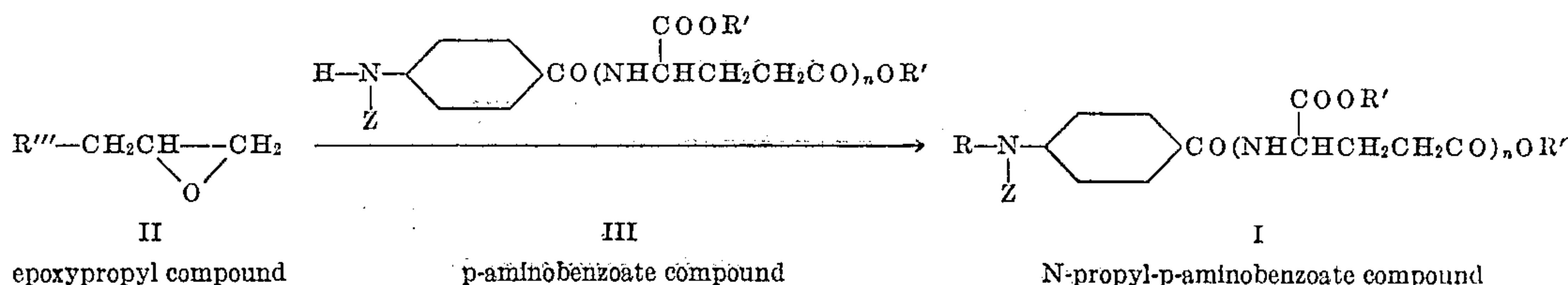
Compounds of the generic formula (I) wherein Z represents an arylsulfonyl radical are of

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particular value because of the protection afforded the aromatic amino group by the arylsulfonyl group. Compounds having the amino group thus protected are often not subject to decomposition

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be carried out and corresponding compounds prepared using other esters, such as the phenyl, tolyl, xylyl, cyclohexyl, benzyl and many other aryl, aralkyl or cycloalkyl esters.



and the formation of by-products when employed as a reactant, e. g. when oxidized by chromic acid, to nearly the same extent as are compounds in which the aromatic amino group is unprotected. Following the carrying out of a reaction using a compound containing such an arylsulfonyl-amino group, the arylsulfonyl radical can be split readily from the molecule formed, as mentioned previously, by treating the compound with hydrogen bromide in an aliphatic acid medium and in the presence of a bromine acceptor. By such treatment, the arylsulfonyl radical is split from the molecule to give a high yield of the amine, and bromination in the benzene nucleus is effectively prevented. The final and intermediate compounds of the method of the present invention wherein Z is an arylsulfonyl radical can also be converted to the corresponding final or intermediate compounds wherein Z is hydrogen by splitting the arylsulfonyl radical from the molecule in the manner just described.

Although the invention will be described in the case of arylsulfonyl compounds with particular reference to p-toluene-sulfonyl compounds, it is understood that the invention contemplates compounds and intermediates containing other arylsulfonyl radicals, such as the o-toluenesulfonyl, benzene-sulfonyl, and naphthalenesulfonyl radicals as well as many others. Arylsulfonyl radicals having substituents, such as chlorine, bromine, or a nitro group, on the aromatic nucleus can also be used provided only that the substituent is nonreactive under the reaction conditions.

The preferred arylsulfonyl radical is the p-toluenesulfonyl radical because the compounds formed are generally well defined crystalline solids and because it has been found that higher yields of amine are often formed when splitting a p-toluenesulfonylamino compound than when splitting certain other arylsulfonyl derivatives of the same amino compound. It should be mentioned, furthermore, that the method involved in the present invention can be carried out and the corresponding intermediate and final compounds prepared using starting compounds wherein the arylsulfonyl group is replaced by an alkylsulfonyl, aralkylsulfonyl or cycloalkylsulfonyl group, such as the methanesulfonyl, alpha-toluenesulfonyl or cyclohexylsulfonyl radicals, respectively.

Although the benzoic acid ester or glutamic acid ester residues present in the compounds prepared by the method of the invention can comprise as alkyl ester, such as the methyl, ethyl, n-propyl, iso-propyl, n-butyl, tert.-butyl, amyl lauryl, dodecyl and many other esters, the preferred ester is the ethyl ester due to matters of convenience and economy.

Although the invention is directed particularly, in case of esters of the glutamic acid residues, to alkyl esters, the process of the invention can also

The N-propyl-p-aminobenzoate compounds (I) can be prepared readily, as indicated in the accompanying chart wherein R', n, Z and R have the values previously given, by reacting an epoxypropyl compound having the formula (II) with a p-aminobenzoate compound having the formula (III). Epoxypropyl compounds which can be used are, as indicated by the formula (II), the 1,2-epoxypropanes having a substituent, R''', on the third carbon atom of the propane chain which can be chlorine, bromine or iodine or an alkoxy, aryloxy, aralkoxy, hydroxy or acyloxy radical. Among the epoxypropyl compounds (II) which can be used in the process to produce the corresponding N-propyl-p-aminobenzoate compounds are included compounds wherein R''' of formula given is the methoxy, ethoxy, butoxy, amyloxy, dodecyloxy, phenoxy, tolyloxy, naphthylloxy, cyclohexyloxy, phenylmethoxy, tolylethoxy, acetoxo, formoxo, propionoxo, acryloxy, cinnamylloxy, benzoxy or toluoxy radical as well as many others.

The reaction can be carried out conveniently by mixing the epoxypropyl compound and the p-aminobenzoate compound with a small proportion of pyridine, quinoline, triethylamine, tributylamine or other tertiary amine to catalyze the reaction and heating the mixture. The reaction proceeds rapidly and smoothly and is usually substantially complete in from a few minutes to an hour or more. Inert diluents can be employed, if desired, although they are not usually necessary. Heating can be carried out over a wide range of temperatures, preferably from 30° to about 150° C.

Following the heating of the mixture, the entire reaction mass can be diluted with benzene, ether, or other suitable solvent for the N-propyl-p-aminobenzoate compound and the solution washed with dilute mineral acid and then with water to remove the pyridine or other tertiary amine. Upon drying the washed solution and evaporating the solvent, the N-propyl-p-aminobenzoate compound remains as a residue which is generally oily in nature in the case of esters but which may be crystalline in the case of some of the acids. The N-propyl-p-aminobenzoate compounds are generally thus obtained in a form sufficiently pure for further use but they can usually be purified further, if desired, either by chromatography or, in some instances, by crystallization, e. g. from alcohol or a mixture of ether and hexane.

As mentioned previously, p-aminobenzoate compounds having the formula (III) which can be used in the process include those wherein n is zero, i. e. p-aminobenzoic acid, the arylsulfonyl-p-aminobenzoic acids and alkyl esters thereof, and also those wherein n is an integer from 1 to 7, inclusive, such as N'-(p-aminobenzoyl)-glutamic acid, N'-(p-aminobenzoyl)-gamma-glutamylglutamic acid, N'-(arylsulfonyl-p-aminobenzoyl)-

gamma-glutamyl-gamma-glutamylglutamic acid and their alkyl esters.

The p-aminobenzoate compounds wherein n is an integer from the group 1 to 7, inclusive, can be obtained as described in a concurrently filed co-pending application, Serial No. 41,888. According to the method of the co-pending application a p-aminobenzoate compound having one glutamic acid residue in the molecule is prepared by reacting glutamic acid or an alkyl ester thereof with an arylsulfonyl-p-aminobenzoyl halide or with a p-nitrobenzoyl halide. The halides referred to in this connection are the chlorides and the bromides. When a p-nitrobenzoyl halide is used, an N'-(p-nitrobenzoyl)-glutamic acid or ester is first obtained which, upon reduction, e. g. with hydrogen using platinum oxide as a catalyst, yields an N'-(p-aminobenzoyl)-glutamic acid or ester. The latter compound can be converted readily by means of an arylsulfonyl halide to an N'-(arylsulfonyl-p-aminobenzoyl)-glutamic acid or ester. When an arylsulfonyl-p-aminobenzoyl halide is reacted with glutamic acid or its ester, an N'-(arylsulfonyl-p-aminobenzoyl)-glutamic acid or ester is formed directly. The latter compound can, if desired, be treated with hydrogen bromide and a bromine acceptor, such as phenol or catechol, in an aliphatic acid medium to split the arylsulfonyl radical from the molecule and form an N'-(p-aminobenzoyl)-glutamic acid or its ester according to the method described and claimed in the concurrently filed co-pending application, Serial No. 41,883, now Patent No. 2,562,222, mentioned previously. Furthermore, the N'-(p-aminobenzoyl)-glutamic acid and the N'-(arylsulfonyl-p-aminobenzoyl)-glutamic acids can, if desired, be converted to the corresponding alkyl esters, e. g. by treatment with an alkanol and an esterification catalyst in known manner, or the esters can be hydrolyzed to the corresponding acids. In similar manner, other p-aminobenzoate compounds can be prepared having up to seven glutamic acid residues in the molecule by starting with the corresponding gamma-glutamylglutamic acids or esters containing the requisite number of peptide linkages.

Certain of the epoxypropyl compounds used as starting materials in the present method have not been described previously and are of particular advantage in the process herein described. The 2,3-epoxypropyl formate, the preparation of which is described in an appended example, is one such compound. It has been found this compound reacts smoothly with the p-aminobenzoate compounds to form N-(3-formoxy-2-hydroxypropyl)-p-aminobenzoate compounds which in turn are of particular value because of the ease with which they can be oxidized to corresponding 3-formoxy-2-ketopropyl compounds and the latter condensed with 2,4,5-triamino-6-hydroxypyrimidine to give high yields of compounds of the folic acid type. The 2,3-epoxypropyl formate is superior to the 2,3-epoxypropyl esters of acetic and higher molecular weight acids in this respect.

Certain advantages of the invention are apparent from the following examples which are given by way of illustration only and are not to be construed as limiting.

Example 1. Diethyl N'-(p-nitrobenzoyl)-1-glutamate

One hundred eleven grams of p-nitrobenzoyl chloride was added at about 0° C. over a period

of about one hour to a solution of 95.8 grams of crude diethyl 1(+)-glutamate hydrochloride and 80 milliliters of pyridine in 200 milliliters of benzene. The mixture was stirred for five hours, extracted first with dilute hydrochloric acid, then with aqueous sodium bicarbonate and the benzene removed under reduced pressure. The 110 grams of pasty, neutral fraction remaining consisted largely of diethyl N'-(p-nitrobenzoyl)-1-glutamate. After recrystallization from dilute ethanol, the ester melted at 93° to 95° C. It had a specific rotation of $\alpha_D^{25} = -18^\circ$. The sodium bicarbonate extract upon acidification yielded 42 grams of p-nitrobenzoic acid.

N'-(p-nitrobenzoyl)-1-glutamic acid can be prepared in similar fashion from p-nitrobenzoyl chloride and 1(+)-glutamic acid.

Example 2.—Diethyl N'-(p-aminobenzoyl)-1-glutamate

Crude diethyl N'-(p-nitrobenzoyl)-1-glutamate prepared as in Example 1 was dissolved in ethanol and reduced with hydrogen under a pressure of about 50 pounds per square inch using platinum oxide as a catalyst. The mixture was then filtered to recover platinum and the ethanol evaporated under reduced pressure. There was thus obtained a 52 per cent yield of diethyl N'-(p-aminobenzoyl)-1-glutamate melting at 135° to 138° C. Upon recrystallization from dilute ethanol, the ester melted at 140° to 141° C. and had a specific rotation $(\alpha)_D^{25} = -9.5$.

N'-(p-nitrobenzoyl)-1-glutamic acid is reduced in similar fashion to form N'-(p-aminobenzoyl)-1-glutamic acid.

Example 3.—Diethyl N'-(p-toluenesulfonyl-p-aminobenzoyl)-1-glutamate

A mixture of 407 grams of p-toluenesulfonyl-p-aminobenzoic acid and 3,450 milliliters of toluene was dried by distilling the mixture until 350 milliliters of distillate had been collected. A few drops of pyridine and 50 milliliters of thionyl chloride were then added to the dry toluene solution and the mixture stirred and refluxed for one-half hour. The solution was then cooled with agitation for two hours and the solid which precipitated was recovered by filtering and washing with toluene and then with mixed pentanes and drying. There was thus obtained 387 grams of p-toluenesulfonyl-p-aminobenzoyl chloride melting at 141° to 142° C.

A mixture of 48 grams of diethyl 1(+)-glutamate hydrochloride, 68 grams of p-toluenesulfonyl-p-aminobenzoyl chloride, 19 grams of magnesium oxide, 250 milliliters of ethylene dichloride and 100 milliliters of water was stirred with cooling for about 4 hours. The mixture was filtered and the organic layer was separated from the filtrate and washed successively with water, ice cold dilute hydrochloric acid, water and dilute aqueous sodium bicarbonate. The washed organic layer was then dried and diluted with mixed hexanes until slightly turbid and allowed to crystallize. Upon filtering the mixture, there was obtained 78 grams of diethyl N'-(p-toluenesulfonyl-p-aminobenzoyl)-1-glutamate melting at 125° to 126° C. and having a specific rotation $(\alpha)_D^{25} = -13.2^\circ$.

Example 4.—2,3-epoxypropyl acetate (glycidol acetate)

A mixture of 98 grams of anhydrous potassium acetate, 10 grams of potassium carbonate and 250 milliliters of dry epichlorohydrin was refluxed for 25 hours. The mixture was cooled,

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filtered, and the filtrate fractionally distilled. A first fraction of unreacted epichlorohydrin was recovered and the fraction consisting of 73 grams of 2,3-epoxypropyl acetate boiling at 82° to 84° C. under a pressure of 40 millimeters was collected separately. The compound had an index of refraction $N_D^{20}=1.4201$.

Example 5.—2,3-epoxypropyl formate

Nine hundred twenty-five grams of epichlorohydrin was added slowly while keeping the temperature below 20° C. to 2.2 liters of 90 per cent formic acid. The mixture was held at about 20° C. for a total of five hours and the excess formic acid then distilled under a pressure of about 100 millimeters. The residue was then fractionally distilled *in vacuo* and there was obtained 1,175 grams of 3-chloro-2-hydroxypropyl formate boiling at 94° to 96° C. under a pressure of 6 millimeters of mercury and having an index of refraction $N_D^{23}=1.4585$.

Forty-eight grams of sodium hydride was added over a period of about 50 minutes and at a temperature below about 20° C. to a solution of 276 grams of 3-chloro-2-hydroxypropyl formate in 1 liter of absolute ether. After stirring for three hours, the mixture was filtered and the ether evaporated from the filtrate. Fractional distillation of the residue gave 134 grams of 2,3-epoxypropyl formate boiling at 63° to 64° C. at a pressure of 22 millimeters and having an index of refraction $N_D^{23}=1.4206$.

2,3-epoxypropyl butyrate, propionate, hexoate and valerate are prepared in similar manner using potassium or sodium butyrate, propionate, hexoate or valerate, respectively, in place of sodium formate.

Example 6.—Diethyl N'-(N-(3-formoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoyl)-1-glutamate

A mixture of 9.5 grams of diethyl N'-(p-toluenesulfonyl-p-amino-benzoyl)-1-glutamate and 2.25 grams of 2,3-epoxypropyl formate was heated at 135° C. and a few drops of pyridine added. The mixture was stirred and heated at 130° to 135° C. for several minutes and then cooled and dissolved in benzene. The benzene solution was washed with dilute hydrochloric acid and with water and then dried and treated with decolorizing charcoal. Upon evaporation of the benzene there was obtained 8.88 grams of diethyl N'-(N-(3-formoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate in the form of a clear, viscous liquid.

The corresponding benzenesulfonyl and naphthalenesulfonyl compounds are prepared in similar manner using diethyl N'-(benzenesulfonyl-p-aminobenzoyl)-1-glutamate and diethyl N'-(naphthalenesulfonyl-p-aminobenzoyl)-1-glutamate respectively, instead of diethyl N'-(p-toluenesulfonyl-p-aminobenzoyl)-1-glutamate.

Example 7.—Ethyl N-(3-acetoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoate

A mixture of 31.9 grams of ethyl p-toluenesulfonyl-p-aminobenzoate, 12.3 grams of 2,3-epoxypropyl acetate and 5 drops of pyridine was heated at about 145° C. for twenty minutes. The brown mass thus obtained was dissolved in ether and washed first with water and then with dilute hydrochloric acid. The washed ethereal solution was treated with decolorizing carbon and the ether then evaporated. The residue consisted of 32.5 grams of ethyl N-(3-acetoxy-2-hydroxypro-

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pyl)-p-toluenesulfonyl-p-aminobenzoate in the form of a light yellow oil having an index of refraction $N_D^{45}=1.5457$.

N-(3-acetoxy-2-hydroxypropyl)-p-aminobenzoic acid and ethyl N-(3-acetoxy-2-hydroxypropyl)-p-aminobenzoate are prepared in similar fashion using p-aminobenzoic acid and ethyl p-aminobenzoate, respectively, instead of ethyl p-toluenesulfonyl-p-aminobenzoate.

Example 8.—Diethyl N'-(N-(3-acetoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate

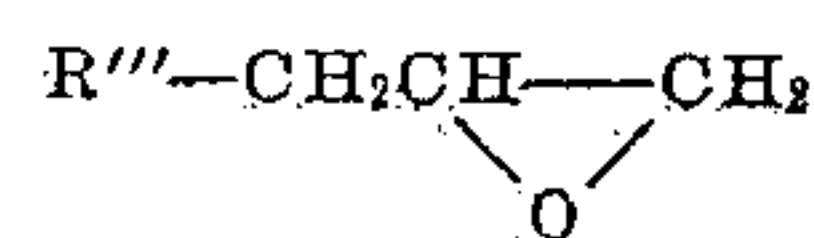
A mixture of 59.3 grams of diethyl N'-(p-toluenesulfonyl-p-aminobenzoyl)-glutamate and 12.7 grams of 2,3-epoxypropyl acetate was heated at 150° C. until a clear melt was formed. Five drops of pyridine was then added and the mixture heated at 145 to 150 C. for about one-half hour. The syrupy reaction mixture was then dissolved in 100 milliliters of benzene and the solution washed with water and dilute hydrochloric acid. The solution was dried and chromatographed on 1200 grams of alumina. The product was eluted with a solution of 5 per cent of ethanol in benzene. Evaporation of the alcohol and benzene gave a residue consisting of 66 grams of diethyl N'-(N-(3-acetoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate in the form of an oil having an index of refraction $N_D^{45}=1.5396$. The corresponding 3-butyroxy, 3-valeroxy and 3-hexoxy compounds are prepared in similar manner using 2,3-epoxypropyl butyrate, valerate or hexoate, respectively, instead of 2,3-epoxypropyl acetate.

Example 9.—Diethyl N'-(N-(3-methoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate

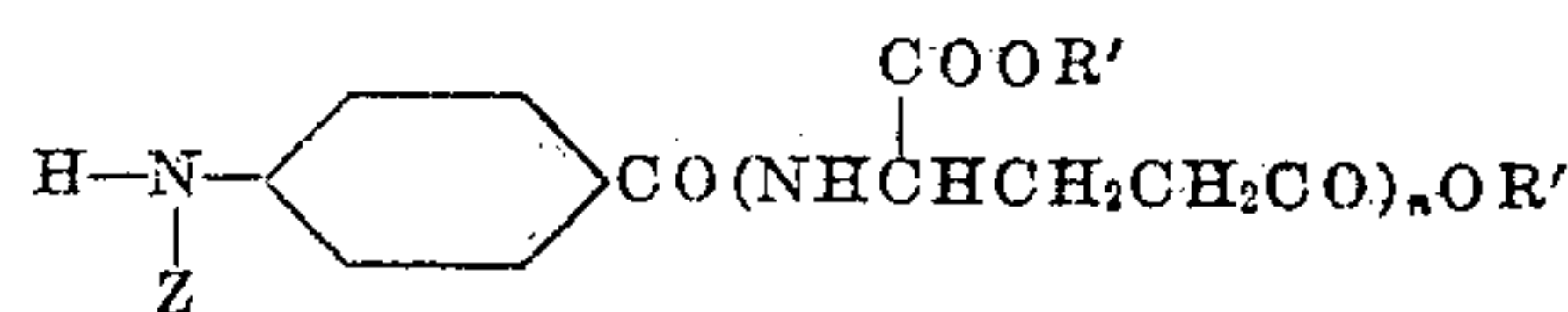
A mixture of 7.2 grams of diethyl N'-(p-toluenesulfonyl-p-aminobenzoyl)-glutamate and 1.45 grams of 1,2-epoxy-3-methoxy-propane was heated in an oil bath at 145° C. until melted and five drops of pyridine then added. The mixture was stirred at 145° to 150° C. for thirty minutes and then dissolved in 50 milliliters of benzene. The benzene solution was washed three times with 20 milliliter portions of dilute sulfuric acid and then with water until the washings were neutral. The benzene solution was then dried with anhydrous sodium sulfate, treated twice with 0.5 gram portions of decolorizing charcoal and filtered. The benzene was then evaporated from the filtrate under reduced pressure and there was thus obtained 8.0 grams of diethyl N'-(N-(3-methoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate as an almost colorless, somewhat viscous liquid having an index of refraction $N_D^{50}=1.538$.

We claim:

1. The method which includes heating a mixture comprising a compound having the formula



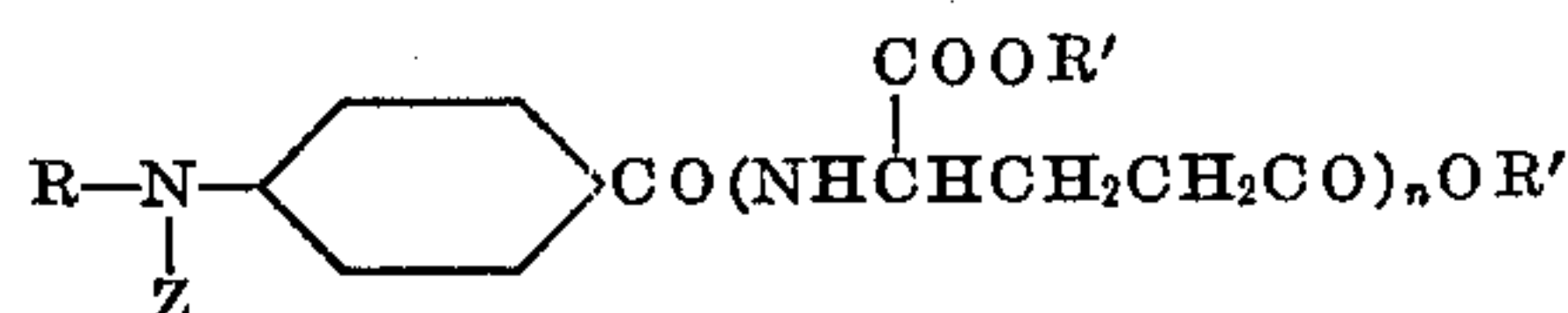
wherein R''' is a member of the group consisting of the alkoxy and aliphatic carboxylic acid acyloxy radicals, a compound having the formula



wherein R' is a member of the group consisting

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of hydrogen and the alkyl radicals, n is a member of the group consisting of zero and the positive integer 1 and Z is a member of the group consisting of hydrogen and the arylsulfonyl radicals, and a catalytic proportion of a free tertiary amine and separating a compound having the formula



wherein R' , n and Z have the values given and R is a member of the group consisting of the 3-alkoxy-2-hydroxypropyl, and 3-aliphatic carboxylic acid acyloxy-2-hydroxypropyl radicals.

2. The method of claim 1 wherein the tertiary amine is pyridine.

3. The method of claim 1 wherein the mixture is heated at between about 80° and about 150° centigrade.

4. The method of claim 1 wherein R''' is the methoxy radical, R is the 3-methoxy-2-hydroxypropyl radical, n is 1, R' is ethyl, and Z is p-toluenesulfonyl.

5. The method of claim 1 wherein R''' is the formoxy radical, R is the 3-formoxy-2-hydroxypropyl radical, n is 1, R' is ethyl, and Z is arylsulfonyl.

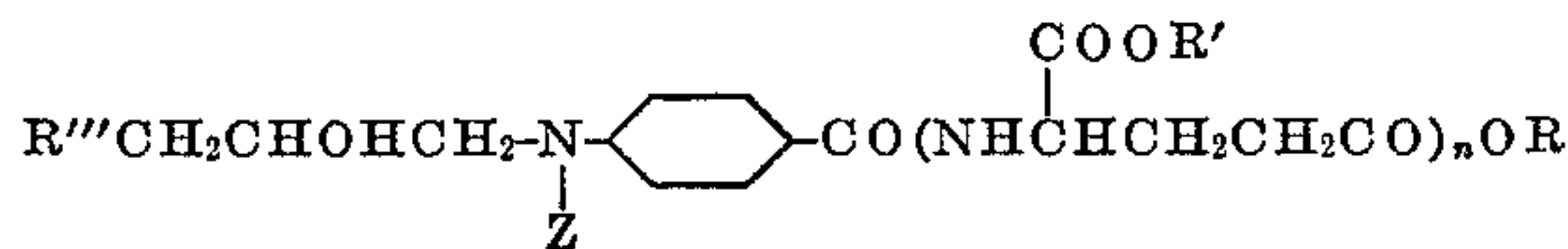
6. The method which includes: heating a mixture comprising 2,3-epoxypropyl formate, diethyl N' -(p-toluenesulfonyl-p-aminobenzoyl)-glutamate and tertiary amine as a catalyst; and separating diethyl N' -(N-(3-formoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate from the reaction mixture.

7. The process of claim 1, wherein R''' is an alkoxy radical, R is a 3-alkoxy-2-hydroxypropyl radical, n is 1, R' is alkyl, and Z is arylsulfonyl.

8. The process of claim 1, wherein R''' is an aliphatic carboxylic acid acyloxy radical, R is a 3-aliphatic carboxylic acid acyloxy-2-hydroxypropyl radical, n is 1, R' is alkyl, and Z is arylsulfonyl.

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9. A compound having the formula



wherein R' is a member of the group consisting of hydrogen and the alkyl radicals, Z is a member of the group consisting of hydrogen and the arylsulfonyl radicals, n is a member of the group consisting of zero and the positive integer 1 and R''' is a member of the group consisting of the alkoxy and the aliphatic carboxylic acid acyloxy radicals.

10. Diethyl N' -(N-(3-methoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate.

11. Ethyl N -(3-acetoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoate.

12. Diethyl N' -(N-(3-acetoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate.

13. Diethyl N' -(N-(3-formoxy-2-hydroxypropyl)-p-toluenesulfonyl-p-aminobenzoyl)-glutamate.

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