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AMINOPHENYL UREAS

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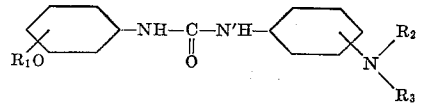
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This invention relates to new urea derivatives. More particularly our invention relates to N-aminophenyl ureas containing N'-hydroxyphenyl or N'-alkoxyphenyl radicals. This application is in part a continuation of S. N. 135,043, filed December 24, 1949, and S. N. 200,114, filed December 9, 1950, now both abandoned.

We have discovered that our novel ureas comprise an entirely novel class of powerful antioxidants, which inhibit the deterioration of organic materials caused by oxygen or ozone.

It is, therefore, an object of this invention to provide a new class of antioxidant materials. One particular object of our invention is to provide a new class of materials which prevents the deterioration by oxygen of petroleum hydrocarbons, hydrocarbon fuels, elastomers and other organic products.

In accordance with our invention we provide new ureas which contain the fundamental structure



wherein R_1, R_2 and R_3 are hydrogen or hydrocarbon radicals. In a preferred embodiment the groups R_1O—, and —NR_2R_3 are in the para position with respect to the urea nitrogen atoms.

Examples of hydrocarbon groups which we can employ include alkyl, cycloalkyl, or aralkyl, such as, for example, methyl, ethyl, propyl, n-butyl, sec.-butyl, isobutyl, n-amyl, 2-methylbutyl, hexyl, octyl, dodecyl, cyclobutyl, cyclohexyl, benzyl, or phenylethyl. Thus, when R_1 is hydrocarbon, we provide hydrocarbyloxyphenyl ureas, such as alkoxy-, cycloalkoxy- for aralkoxy-phenyl ureas.

Certain of our novel series of compounds possess a relatively low degree of solubility in petroleum hydrocarbons. Therefore, in order to incorporate such antioxidants in gasoline, for example, a solubilizing agent, must be employed. Typical of such solubilizing agents are methanol, ethanol, isopropanol, dimethylether of diethylene glycol, dimethyl formamide, methyl ethyl ketone, acetone and ethyl acetate. However, by substituting the alkyl groups as described heretofore on the amine nitrogen, in accordance with our invention, we can likewise increase the solubility in petroleum hydrocarbons. In addition, however, we thus obtain the completely unexpected result that we thereby also increase the antioxidant effectiveness of our compounds, as

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will be illustrated hereinafter. Conversely, we can likewise obtain high hydrocarbon solubility by introducing the alkoxy group as described above, but do not necessarily improve the antioxidant effectiveness thereby. It is likewise surprising that in the N-(p-hydroxyphenyl) embodiments of our invention we obtain unusually high hydrocarbon solubility, although such radicals are ordinarily considered as being useful in imparting the property of solubility in polar solents. Thus, whether solubility, miscibility, ease of manufacture, or antioxidant effectiveness is the primary concern in selecting the particular embodiment of our invention, we have provided means for choosing a combination such that the needs of the particular application can be supplied. The effect of structure on the two properties, antioxidant effectiveness and solubility, are further illustrated by the data presented in Tables I and II.

In general the compounds of our invention can be prepared readily and in good yield by two methods as illustrated in the following typical examples. In the examples which follow all parts and percentages are by weight.

EXAMPLE I

N-(p - hydroxyphenyl) -N'- (p - aminophenyl) - urea.—To a vessel provided with an agitator, means for returning reflux, means for introducing solid and liquid reactants, and means for supplying heat, was added 100 parts p-aminophenol and 300 parts of benzene. To this stirred mixture was added 135 parts of p-nitrophenylisocyanate over a period of 30 minutes maintaining the reaction temperature at 50° C. The mixture was stirred and heated at this temperature for an additional period of 6 hours. The product which separated at this stage was N-(p-hydroxyphenyl) - N' - (p - nitrophenyl) urea. This material was recovered by filtration and added to a vessel provided with means for carrying out reaction under pressure. To this vessel was added 300 parts of ethanol and 5 parts of platinum black catalyst. The temperature of the reactants was raised to 50° C. and hydrogen was admitted to a pressure of 10 pounds per square inch gauge. The reduction was complete in 30 minutes as evidenced by the drop in the hydrogen pressure. After venting off the excess hydrogen the catalyst was removed by filtration and the reduced product N-(p-hydroxyphenyl) - N' - (p - aminophenyl) urea was recovered by concentrating the solution by evaporation. The precipitated product was removed

by filtration and recrystallized from the mixture of ethanol and water.

Conversely, we can prepare the identical compound described above by treating, according to the procedure of Example I, p-nitroaniline with p-hydroxyphenylisocyanate, isolating the same intermediate, and reducing the nitro group thereof.

EXAMPLE II

N-(p-hydroxyphenyl)-N'-(p - n - butylaminophenyl) urea.—In accordance with the procedure of Example I, 100 parts of p-aminophenol and 138 parts of p-nitrophenylisocyanate were reacted to produce N-(p-hydroxyphenyl)-N'-(p-nitrophenyl) urea. This urea, 172 parts, was added along with 515 parts of zinc dust, 132 parts of absolute ethanol and 140 parts of 20 volume per cent of sulfuric acid to a vessel equipped with a mechanical stirrer, means for returning reflux and means for adding liquid reactants. The reaction mixture was heated and refluxed at atmospheric pressure with a mixture of n-butyraldehyde in aqueous ammonia, added over a period of one hour. The mixture was further heated at the reflux temperature for two hours and allowed to stand at a temperature of 25° C. over a period of 15 hours. The zinc and other solids were removed by filtration and the filtrate was made alkaline with ammonium hydroxide, sufficient excess being added to redissolve the zinc oxide which is formed initially. This mixture was further cooled to 0° C. and the resulting precipitate removed by filtration. This product was recrystallized from a mixture of water, ethanol and ethyl acetate. The purified product was 86 parts corresponding to an overall yield of 50 per cent, based upon the p-nitrophenylisocyanate employed.

In a similar manner, N-(p-hydroxyphenyl-N'-(p-n-butylaminophenyl) urea can be produced by treating, according to the procedure of Example III, the reaction product of p-nitroaniline and p-hydroxyphenylisocyanate with zinc, n-butyraldehyde and ammonia.

Similarly, when we treat, for example, the N-(p-hydroxyphenyl) - N' - (p-nitrophenyl) urea of Example II with zinc and either isobutyaldehyde, propionaldehyde, formaldehyde, acetaldehyde, benzaldehyde, cyclopentanone, methylcyclohexanone or n-octadecanal in ammonia we obtain N-(p-hydroxyphenyl)-N'-(p-i-butylaminophenyl) urea, -N'- (p - n - propylaminophenyl) urea, -N'-(p-methylaminophenyl) urea, -N'-(p-ethylaminophenyl) urea, - N' - (p-benzylaminophenyl) urea, -N'-(p-cyclopentylaminophenyl)-urea, -N'-(p-methylcycloxylaminophenyl) urea, or -N'-(p-n-octadecylaminophenyl) urea, respectively.

EXAMPLE III

N-(p-hydroxyphenyl)-N' - (p-sec.-butylaminophenyl) urea.—In accordance with the procedure of Example II, N-(p-hydroxyphenyl)-N'-(p-nitrophenyl) urea was treated with methylethyl ketone to produce the corresponding N-p-hydroxyphenyl-N'-(p - sec.-butylaminophenyl) urea.

Furthermore, when we treat, for example, N-(p-hydroxyphenyl)-N'-(p-nitrophenyl) urea in accordance with the procedure of Example III with zinc, ammonia and the following ketones: acetone, cyclohexanone, methylpropyl ketone, dipropyl ketone, acetophenone, or benzophenone we obtain, respectively, N-(p-hydroxyphenyl)-N'-(p-isopropylaminophenyl) urea, -N'-(p-cyclohexylaminophenyl) urea, -N'-(p-methylpropylcarbylaminophenyl) urea, -N' - (p-di-n-propylcarbylaminophenyl) urea, -N'-(p-methylphenylcarbylaminophenyl) urea, and -N'-(p-diphenylcarbyl aminophenyl) urea.

EXAMPLE IV

N-(p-ethoxyphenyl) - N'-(p-dimethylaminophenyl) urea.—To a vessel provided with an agitator, means for returning reflux, means for introducing solid and liquid reactants, and means for supplying heat, was added 100 parts of p-ethoxyphenylisocyanate and 300 parts of benzene. To this stirred mixture was added 110 parts of N,N - dimethyl-p-phenylenediamine, while maintaining the reaction temperature at 50° C. The mixture was stirred and heated at this temperature for an additional period of 3 hours, at the end of which time N-(p-ethoxyphenyl)-N'-(p-dimethylaminophenyl) urea separated and was recovered by filtration.

Other typical hydrocarbyloxyphenylisocyanates which can be treated with N,N-dialkylphenylenediamines according to the foregoing example or with p-nitroaniline according to the procedure of Examples I, II and III include p-methoxyphenylisocyanate, p-phenoxyphenylisocyanate, p-isopropoxyphenylisocyanate, p - butoxyphenylisocyanate, p-cyclohexoxyphenylisocyanate and p-dodecyloxyphenylisocyanate.

Thus when, for example, N,N-diethyl-p-phenylenediamine is treated with p-methoxyphenylisocyanate, p-benzyloxyphenylisocyanate, p-n-butoxyphenylisocyanate or p-cyclohexoxyphenylisocyanate we obtain, respectively, N-(p-methoxyphenyl)-N'-(p-diethylaminophenyl) urea, N-(p - benzyloxyphenyl) - N' - (p-diethylaminophenyl) urea, N - (p-n-butoxyphenyl)-N'-(p-diethylaminophenyl) urea, and N-(p-cyclohexoxyphenyl)-N'-(p-diethylaminophenyl) urea.

Likewise N - methyl-N-ethyl-p-phenylenediamine, N,N-di-n-butyl-p-phenylenediamine, N-methyl-N-cyclohexyl - p - phenylenediamine, and the like, are treated with p-hydroxyphenylisocyanate or p-hydrocarbyloxpyhenylisocyanates the corresponding N-hydroxyphenyl- and N-hydrocarbyloxyphenyl-N'-(p - dialkylaminophenyl) ureas result.

EXAMPLE V

N-(p - cyclohexoxyphenyl)-N' - (p-n-butylaminophenyl) urea.—This compound is prepared according to the procedure of Example II wherein N - (p-cyclohexoxyphenyl)-N'-(p-nitrophenyl) urea was treated with n-butyraldehyde.

Similarly, when N-(p-ethoxyphenyl)-N'-(p-nitrophenyl) urea is treated with zinc and either propionaldehyde, formaldehyde, benzaldehyde or cyclohexanone, we obtain N-(p-ethoxyphenyl)-N' - (p-n-propylaminophenyl) urea, -N' - (p-methylaminophenyl) urea, -N'-(p-benzylaminophenyl) urea or -N'-(p-cyclohexylaminophenyl)-urea.

EXAMPLE VI

N-(p-ethoxyphenyl) - N' - (p-aminophenyl)-urea.—By treating p-ethoxyphenylisocyanate with p-nitroaniline according to the procedure of Example I, N-(p-ethoxyphenyl)-N'-(p-nitrophenyl) urea was obtained in good yield. On reduction with hydrogen in the presence of platinum black at a temperature of 50° C. in ethanol solution the N-(p-ethoxyphenyl)-N'-(p-aminophenyl) urea was obtained.

Similarly we obtain N-(p-cyclohexoxyphen-

yl)-, N - (p-β-phenylethoxyphenyl)-, N - (p-methoxyphenyl)-, N - (p-sec.-butoxyphenyl)-, and N-(p-octyloxyphenyl)-N'-(p-aminophenyl)-urea by reducing the corresponding -N'-(p-nitrophenyl) urea as in the foregoing example.

The compounds of our invention are excellent antioxidants and we have illustrated this property in Table I, wherein we have listed the results obtained by determining the oxidation stability of gasoline according to the Induction Period Method, ASTM designation: D525–46, as fully described in part III–A, ASTM Standards for 1946. We have employed gasoline in this determination since it is representative of an important class of industrial products which are susceptible to deterioration, and for which it is important to provide stabilizing materials. The column headed IPI lists the induction period increase in the presence of 6 milligrams of our compounds per 100 milliliters of gasoline over that of the gasoline in the absence of the antioxidants of our invention. Thus, this period is that in which the period of no absorption of oxygen by gasoline is increased over the period for which no absorption takes place in the absence of our materials, and under the same conditions of test.

TABLE I

Effect of induction period increase of gasoline

No.	Additive	IPI, Min.
1	N-(p-Hydroxyphenyl)-N'-(p-n-butylaminophenyl)urea.	540
2	N-(p-Ethoxyphenyl)-N'-(p-dimethylaminophenyl)urea.	60

To illustrate the solubility characteristics of the novel compounds of our invention, we have listed in Table II the solubility expressed as milligrams of compound per 100 millimeters of solvent of representative members of our compounds in isooctane, representative of a typical petroleum product. Thus, we have found that a hydroxy group on the phenyl radical surprisingly increase the hydrocarbon solubility compared to the unsubstituted compound No. 4.

TABLE II

Hydrocarbon solubility of N-aryl-N'-(p-aminophenyl) ureas

No.	Material	Solubility, mg./100 ml.
1	N-(p-Hydroxyphenyl)-N'-(p-n-butylaminophenyl)urea.	4.4.
2	N-(p-Hydroxyphenyl)-N'-(p-aminophenyl)-urea.	11.0.
3	N-(p-Hydroxyphenyl)-N'-(p-i-butylaminophenyl)urea	11.2.
4	N-phenyl-N'-(p-Aminophenyl)urea	Slight.

While we have illustrated the utility of various representative members of our novel class of compounds in protecting gasoline from deterioration by oxygen, it is to be understood that our invention resides in the compounds which we have provided, not in the particular application illustrated herein. Thus, there are many other materials which are susceptible to such deterioration, and it is contemplated, and within the scope of our invention, to employ our compounds for such application. To list only a few of the important organic materials susceptible of such protection we can cite elastomers, both natural and synthetic, soaps, foodstuffs, synthetic or naturally occurring organic chemicals, particularly those which contain a degree of unsaturation or which tend to polymerize by oxygen-induced reactions, and certain pharmaceutical preparations.

We have disclosed a number of embodiments of our invention and illustrated several methods whereby these materials can be prepared. However, our invention is not intended to be limited to the specific examples herein or to the means described herein for obtaining our novel compounds.

We claim:

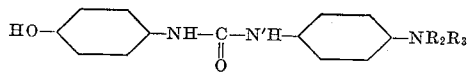
1. As a new composition of matter, N-(p-hydroxyphenyl)-N'-(p-alkylaminophenyl) urea.

2. As a new composition of matter, N-(p-hydroxyphenyl)-N'-(p-aminophenyl) urea.

3. As a new composition of matter, N-(p-hydroxyphenyl)-N'-(p-n-butylaminophenyl) urea.

4. As a new composition of matter, N-(p-hydroxyphenyl)-N'-(p-i-butylaminophenyl) urea.

5. As new compositions of matter, compounds having the general formula



wherein R_2 and R_3 are selected from the group consisting of hydrogen, alkyl and cycloalkyl.

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