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3,236,893
2-AMINOARYLALKYLENE-DIHYDROXY-BENZENES

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7 Claims. (Cl. 260—571)

This application is, in part, a continuation of our copending application Serial No. 612,051, filed September 25, 1956, now U.S. Patent No. 3,019,107, issued January 30, 1962.

This invention relates to novel chemical compounds and more particularly to certain novel chemical compounds useful as photographic developing agents.

One object of this invention is to provide novel chemical compounds and suitable syntheses for their preparation.

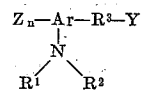
Another object of this invention is to provide novel photographic developing agents and novel compositions for the development of silver halide emulsions.

Other objects of this invention will in part be obvious and will in part appear hereinafter.

The invention accordingly comprises the several steps and the relation and order of one or more of such steps with respect to each of the others, and the products and compositions possessing the features, properties and the relation of elements which are exemplified in the following detailed disclosure, and the scope of the application of which will be indicated in the claims.

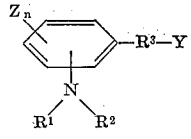
For a fuller understanding of the nature and objects of the invention, reference should be had to the following detailed description.

The novel compounds of this invention may be represented by the formula:



wherein R^1 and R^2 may be the same or different and may be hydrogen or alkyl, preferably lower alkyl such as methyl or ethyl; R^3 is an alkylene group, preferably an alkylene group containing no more than five carbons and more preferably an ethylene ($—CH_2CH_2—$) group; Ar is an aryl nucleus, such as a benzene or naphthalene nucleus; each Z is an alkyl group, preferably lower alkyl such as methyl or ethyl, an alkoxy group, preferably a lower alkoxy group such as methoxy, or halogen, such as chlorine; *n* is 0, 1 or 2; and Y is an ortho-dihydroxyphenyl or a para-dihydroxyphenyl group which may be substituted by alkyl groups, preferably lower alkyl, or by halogen, e.g., chlorine and bromine.

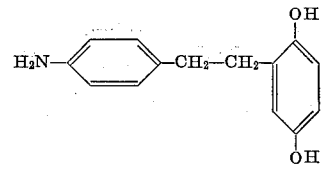
In the preferred embodiment, the aryl nucleus X is a benzene nucleus, and such compounds may be represented by the formula:



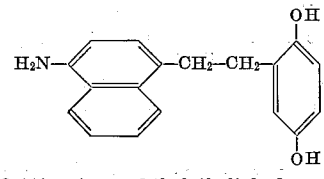
wherein Z, *n*, R^1, R^2, R^3 and Y have the same meaning as above.

The following are illustrative examples of compounds falling within the scope of this invention, and which have

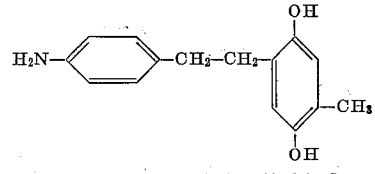
been synthesized by one or more of the procedures hereinafter described:



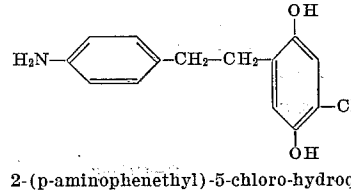
(I) p-aminophenethyl-hydroquinone



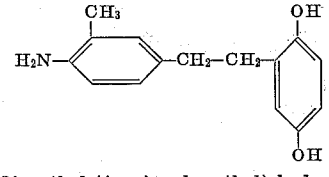
(II) 2-(4'-aminonaphthylethyl)-hydroquinone



(III) 2-(p-aminophenethyl)-5-methyl-hydroquinone



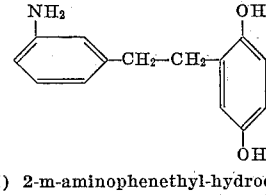
(IV) 2-(p-aminophenethyl)-5-chloro-hydroquinone



(V) 2-(3'-methyl-4'-aminophenethyl)-hydroquinone

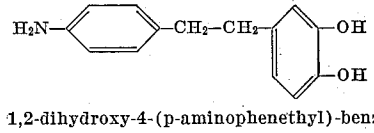
(VI) 2-(p-aminophenethyl)-5,6-dimethyl-hydroquinone

(VII) 2-(p-aminophenethyl)-3,5,6-trimethyl-hydroquinone

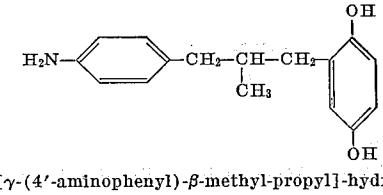


(VIII) 2-m-aminophenethyl-hydroquinone

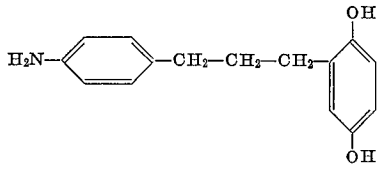
(IX) 2-(m-aminophenethyl)-5-methyl-hydroquinone



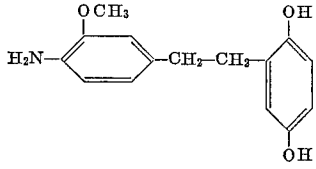
(X) 1,2-dihydroxy-4-(p-aminophenethyl)-benzene



(XI) 2-[γ-(4'-aminophenyl)-β-methyl-propyl]-hydroquinone



(XII) 2-[γ-(4'-aminophenyl)-propyl]-hydroquinone



(XIII) 2-(4'-amino-3'-methoxy-phenethyl)-hydroquinone

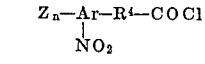
(XIV) 2-[γ-(3'-amino-4'-methyl-phenyl)-propyl]-hydroquinone

(XV) 2-(p-aminophenethyl)-6-methyl-hydroquinone

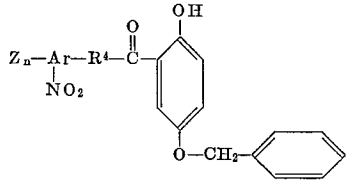
(XVI) 2-(p-aminophenethyl)-5-bromo-hydroquinone

(XVII) 2-(5'-aminonaphthylethyl)-hydroquinone

One method of preparing compounds within the scope of this invention is by condensing a suitable acid chloride of the formula:



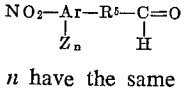
wherein R^4 is an alkylene group, Ar, Z and n have the same meaning as above, e.g., p-nitrophenylacetyl chloride, with a suitable dihydroxybenzene, which preferably has one hydroxyl group protected, e.g., monobenzyloxyhydroquinone, rearranging the product by a Fries rearrangement to:



followed by reduction and removal of any protective group to regenerate the hydroxyl group. If desired, the alkylene group R^4 may be omitted by using the acid chloride of the corresponding benzoic acid.

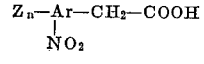
Another method of preparing compounds within the scope of this invention, and a preferred method for preparing some of these compounds, is to acylate the appropriate hydroquinone, or a suitable mono or dialkoxy derivative thereof, e.g., p-dimethoxy benzene, with an acid or acid chloride within the above formula using a Friedel-Crafts catalyst, e.g., BF_3, followed by reduction and, where an alkoxy derivative was used, dealkylation to the free hydroquinone.

One may also prepare compounds within the scope of this invention by condensing a compound of the formula:



wherein Ar, Z and n have the same meaning as above, and R^5 is a single valence bond or an alkylene group, with a suitably protected dihydroxyphenyl ketone, reducing the product and removing the protective groups.

Another method of preparing compounds within the scope of this invention, and particularly applicable to the preferred embodiment, comprises reacting an appropriate derivative of a dihydroxy aryl aldehyde, e.g., a dialkoxy derivative, with the appropriate compound of the formula:



wherein Ar, Z and n have the same meaning as above, after which the nitro group and the double bond of the product are reduced and the protective groups removed from the hydroxyl groups. If desired, one may use the free dihydroxy aryl aldehyde.

Where the secondary or tertiary alkylated amine derivatives are desired, the amino group may be suitably alkylated in accordance with well-known alkylating procedures, preferably before removing the protective groups.

The following examples illustrate the preparation of compounds within the scope of this invention and are given as illustrations only:

Example 1

A mixture of 100 g. of p-nitrophenyl acetic acid, 80 g. of 2,5-dimethoxy benzaldehyde and 20 cc. of piperidine is heated at 160° C. for 6 hours and allowed to cool overnight. The product is taken up in 100 cc. of acetic acid and poured into 500 cc. of water, giving a dark red oil. Supernatant liquid is decanted, and the oil is triturated with 100 cc. of ethanol. The resultant solid is filtered and crystallized from 2,000 cc. of ethanol, giving 52.5 g. of 2,5-dimethoxy-4'-nitrostilbene in the form of red crystals melting at 114–116° C.

The above product is hydrogenated in 450 cc. of ethyl acetate using 15 g. of 5% palladinized barium sulfate. The solvent is then evaporated off, giving p-(2',5'-dimethoxy-phenethyl)-aniline in the form of an oil.

The thus prepared p-(2',5'-dimethoxy-phenethyl)-aniline is demethylated by refluxing under nitrogen in 500 cc. of 48% HBr for 4 hours. Excess HBr is then removed in vacuo, water added and the evaporation repeated. Ethanol is then added and the evaporation repeated again. The residual solid is dried over potassium hydroxide, giving 54.5 g. of p-aminophenethyl-hydroquinone hydrobromide in the form of a tan solid melting at 215° C.

Analysis of the product shows:

	C	H	N
Calculated	54.2	5.2	4.5
Found	54.3	5.4	4.7

Example 2

A flask was charged with 500 cc. of 1,2-dichloroethane and 47.1 g. of anhydrous aluminum chloride. After the resultant mixture had cooled to −5 to −10° C., 53.7 g. of 2,5-dimethoxytoluene diluted with 100 cc. of 1,2-dichloroethane was added, dropwise with stirring, while maintaining this temperature range. Stirring was continued for another 10 minutes after which 70.5 g. of p-nitrophenylacetyl chloride dissolved in 100 cc. of 1,2-dichloroethane was added, dropwise with stirring, over a 30-minute period. The reaction mixture was then poured, with stirring, into a beaker containing 500 g. of ice and stirred for 30 minutes. The organic layer which separated was washed with 500 cc. of 5% sodium carbonate solution followed by 500 cc. of distilled water. An additional 500 cc. of distilled water was added and the resulting mixture was steam distilled. A brown oil which separated in the steam distillation flask solidified on cooling to 5° C. to give a brown solid. This solid was filtered by suction, partially dried between filter paper, and then was recrystallized from 1500 cc. boiling 95% ethanol to give an almost white, fluffy crystalline solid. The filtered crystals were washed with cold 95% ethanol, and dried in air at room temperature to give 61.0 g. (55% yield) of p-nitrophenylacetyl-5-methyl-hydroquinone dimethyl ether, M.P. 120–121° C.

10.0 g. of the p-nitrophenylacetyl-5-methyl-hydroquinone dimethyl ether was dissolved in 200 cc. of glacial acetic acid containing 1.0 g. of 10% palladium on charcoal catalyst and hydrogenated at room temperature at an intial pressure of 45 p.s.i. until the theoretical hydrogen uptake was observed. Hydrogenation was then stopped and the acetic acid solution filtered directly by suction into 5 cc. of acetic anhydride. The solvent was re-

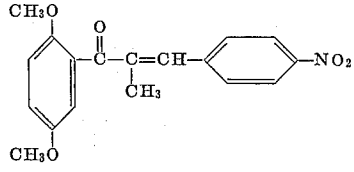
moved in vacuo on a steam bath. An additional 5 cc. of acetic anhydride was thoroughly mixed with the straw colored oil and the evaporation process repeated. The oil was then dissolved in 100 cc. of absolute ethanol. Removal of the ethanol in vacuo on a steam bath gave a white solid (M.P. 133–138° C.). This solid was dissolved in 100 cc. of hot methanol. Water was added to the cloud point and the resultant solution was set aside to cool slowly. The white crystals were filtered and dried in air at room temperature to give 9.3 g. (91% yield) of 2-(4'-acetamidophenylacetyl)-5-methylhydroquinone dimethyl ether, M.P. 139–142° C.

The above product (9.3 g.) was hydrogenated over palladium on charcoal as described earlier in this example. The theoretical amount of hydrogen was taken up in 2 hours at 80° C. and an initial pressure of 45 p.s.i. The reaction flask was allowed to cool to room temperature, the catalyst filtered off, and the solvent evaporated on a steam bath in vacuo to 100 cc. About 100 cc. of distilled water was added to the acetic acid solution and the resultant milky solution was allowed to crystallize slowly overnight at room temperature. The white crystals were filtered, washed with water, and dried in air at room temperature to give 7.85 g. (88% yield) of 2-(4'-acetamidophenethyl)-5-methylhydroquinone dimethyl ether, M.P. 120–123° C. This product was hydrolyzed as in Example 1 to give 2-(4'-aminophenethyl)-5-methyl-hydroquinone.

Example 3

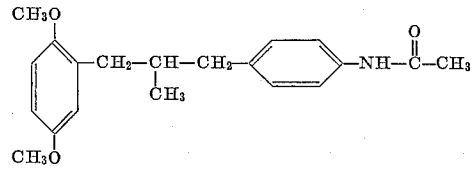
180 g. of $AlCl_3$ was added, over a period of 1½ to 2 hours, to a mechanically stirred mixture of 165 g. of p-dimethoxybenzene, 123.5 g. of propionyl chloride, 200 cc. of tetrachloroethane and 50 cc. of nitrobenzene contained in a flask held in an ice bath. The temperature of the reaction mixture was kept below 5° C. during the $AlCl_3$ addition. After stirring for 4 hours, the reaction mixture was placed in the refrigerator overnight. The reaction mixture was then poured onto a mixture of ice and hydrochloric acid and stirred thoroughly. The resulting aqueous and organic layers were separated, and the aqueous layer was extracted with ether. The ether extract was combined with the organic layer, washed twice with 3 N sodium hydroxide and once with water. After drying over magnesium sulfate, the ether was driven off and the residue distilled on a water aspirator. The resulting product, 2,5-dimethoxy-propiophenone, is a pale yellow liquid (B.P. 160–162° C. at 12 mm. Hg) which darkens on standing.

A flask was charged with 97 g. of 2,5-dimethoxy propiophenone and 75.5 g. of p-nitrobenzaldehyde dissolved in 1500 cc. of 2B ethanol (dry). The flask was chilled in an ice bath and 20 g. of NaOH in 100 cc. of water were added slowly with stirring. After a few minutes, the desired 4-nitro-2',5'-dimethoxy-β-methyl-chalcone:



crystallized out. The filtered crude product was washed with cold 80% ethanol and recrystallized from ethanol to give yellow needles, M.P. 144–150° C.

A Parr shaker bottle was charged with 10 g. of 4-nitro-2',5'-dimethoxy-β-methyl-chalcone, 1 g. of 10% palladium on charcoal catalyst, 100 cc. of acetic acid and 40 cc. of acetic anhydride. Hydrogen was passed in and the mixture was shaken until the theoretical quantity of hydrogen for the nitro group and the double bond was absorbed. The reaction mixture was filtered through a Celite pad and evaporated. Methanol was added to the oily residue and this solution was evaporated. The resulting oil was taken up in 100 cc. of acetic acid and returned to the shaker bottle with 1 g. of 10% Pd/C catalyst. Hydrogen was passed in and the mixture was shaken at about 80° C. until the theoretical hydrogen uptake was observed. The reaction mixture was then filtered, the filtrate slowly added with stirring to cold water containing some seed material and placed in the refrigerator overnight. The resulting solid was filtered off, washed with cold water and dried in a vacuum desiccator over P_2O_5. The crude material was recrystallized from ether-hexane to give 2-[α-(4'-acetamidophenyl) - β-methyl-propyl]-hydroquinone dimethyl ether:



as a white powder, M.P. 99–101° C. 5 g. of this product, 50 cc. of acetic acid and 100 cc. concentrated hydrochloric acid were refluxed, under nitrogen, for about 20 hours. The reaction was evaporated, 2B ethanol added to the residue and the solution evaporated again. The resulting oil was taken up in ethanol and precipitated with ether. The ether was removed and the flask containing the oil was warmed and placed under aspirator vacuum. The oily material solidified, and the solid was scraped from the flask and dried in a vacuum desiccator to give 3.4 g. (80% yield) of 2-[α-(4'-aminophenyl)-β-methyl-propyl]-hydroquinone hydrochloride as a light tan material melting, with decomposition, at 150° C.

Example 4

In a modification of the procedure described in Example 3, 9.7 g. of 2,5-dimethoxy-propiophenone, 8.15 g. of p-acetamidobenzaldehyde and 100 cc. of methanol were placed in a flask and heated on a steam bath to effect solution. 2.7 g. of sodium methoxide in about 20 cc. of methanol was added, and the flask was plugged with glass wool and allowed to stand at room temperature for 3 days. At this point, crystals started to form. The separated yellow solid (M.P. 148–153° C.) was recrystallized from methanol/water. Heating of the reaction mixture on a steam bath for 15 to 20 minutes after it had been standing for 24 hours was found to hasten precipitation of the product chalcone. This chalcone was hydrogenated overnight in glacial acetic acid using a Pd/c catalyst following the procedure described in Example 3.

Example 5

2-[α-(4'-aminophenyl)-propyl]-hydroquinone was prepared in a manner similar to that described in Example 3, except that the intermediate chalcone, i.e., 2,5-dimethoxy-4'-nitrochalcone, was prepared as follows: 25 g. each of p-nitroacetophenone and 2,5-dimethoxy-benzaldehyde in 500 cc. of 2B ethanol (dry) was stirred in a flask until solution was effected. The flask was cooled below 10° C. and a mixture of 50 cc. of 3 N NaOH and 50 cc. of 2B ethanol was added slowly. Stirring was continued at this temperature for 3 hours after the addition was completed. The reaction mixture was brought to room temperature slowly and then filtered. The solids were washed with water and recrystallized from ethanol. Hydrogenation of this chalcone was effected in acetic acid over Pd/C catalyst; the theoretical hydrogen uptake was absorbed after about 2 hours. The catalyst was filtered off, acetic anhydride added and the flask stoppered and allowed to stand overnight at room temperature. Upon addition of water, a cloud appeared; upon scratching, a white solid precipitated out and was filtered off and washed with water. Hydrolysis of the product (recrystallized from the same solvent mixture, M.P. 116–118° C.) gave the desired product.

Example 6

2 - (4'-amino-3'-methoxy-phenethyl)-hydroquinone was prepared as follows: m-cresol was nitrated according to

the procedure in Annalen, vol. 259, p. 208 (1890), giving a mixture of isomers, from which 2-nitro-5-methyl-phenol was separated. This compound then was treated with dimethyl sulfate in the usual manner to give 3-methoxy-4-nitro-toluene, which was converted into 3-methoxy-4-nitro-phenylacetic acid as follows: to a 500 cc. flask containing 50 cc. of 2B ethanol was added 81 g. of sodium methoxide. 19.0 cc. of ethyl oxalate was added to the stirred solution, followed by 18.1 g. of 3-methoxy-4-nitrotoluene. The solution was refluxed for 15 minutes, cooled, 100 cc. of water added, the alcohol removed in vacuo and the solution filtered. To the filtrate (kept at 30° C. or lower) was added 6 cc. of 30% hydrogen peroxide, and the solution was stirred until there was no further evolution of gas. The solution was then filtered, and the filtrate was acidified and extracted with ether. After drying, the ether was removed. The product could be crystallized from either water or ether-hexane. Analysis of the product (M.P. 119–121° C.) as $C_9H_9NO_5$ showed:

	C	H	N
Calculated	51.2	4.3	6.6
Found	51.1	4.3	6.5

Gentisaldehyde dibenzyl ether was prepared as follows: a mixture of 121 g. of benzenesulfonylgentisyl hydrazide dibenzyl ether and 1360 cc. of ethylene glycol was heated with stirring in a 5 liter flask to 160 C.° at which temperature solution was complete. The heating mantle was removed and 160 g. of anhydrous sodium carbonate was added at once. There was vigorous frothing, lasting several minutes. When this frothing had subsided, 750 cc. of water was cautiously added to the hot mixture, and the flask was cooled. The cooled solution was poured into 3750 cc. of ice and water, to which was then added 190 cc. of 3 N sodium hydroxide. The solids were filtered off and desiccated over P_2O_5. The dried product (91 g.) was crystallized from hexane by extraction with three 2.5-liter portions of boiling solvent, followed by filtration (hot), concentration of the clear filtrate to about 500 cc., chilling, and filtration of the precipitate that separated. 50 g. of yellow powder, M.P. 87–91° C., was obtained (64% yield).

In a 300 cc. three-necked flask were placed 6.36 g. of gentisaldehyde dibenzyl ether, 4.22 g. of 3-methoxy-4-nitro-phenylacetic acid, and 2 cc. of piperidine. The mixture was heated in a Wood's metal bath to a bath temperature of 160° C., maintained at that temperature for an hour and forty-five minutes, and then cooled. The product was extracted with ether, the ether solution washed with dilute hydrochloric acid, water, 3 N sodium hydroxide and water. The product then was dried, filtered, and the solvent removed. The 2,5-dibenzyloxy-3′-methoxy-4′-nitrostilbene solid product, after crystallization from acetic acid-water, melted at 87–90° C. and gave a nitrogen analysis of 2.9% (calculated 3.0%). 3.7 g. of this stilbene product in 50 cc. of ethyl acetate was reduced in a Parr shaker over 1 g. of 5% palladium-on-barium sulfate catalyst until the theoretical hydrogen uptake (for reduction of the nitro group, the double bond, and cleavage of the benzyl ethers) was observed. The desired 2-(4′-amino-3′-methoxy-phenethyl)-hydroquinone was then recovered in a manner similar to that described in the previous examples.

As previously noted, the novel compounds of this invention are useful as photographic developing agents, and this use is disclosed and claimed in our previously mentioned copending application, Serial No. 612,051.

The novel compounds of this invention are also useful as anti-oxidants in petroleum products. The compounds wherein R^1 and R^2 both are hydrogen are useful as intermediates, for example, in the preparation of the corresponding O-acylated compounds disclosed and claimed in the copending application of Milton Green and Helen P. Husek, Serial No. 805,673, filed April 13, 1959, as a continuation-in-part of Serial No. 612,063, filed September 25, 1956 (now abandoned), which copending application issued as U.S. Patent No. 3,019,254 on January 30, 1962. These O-acylated compounds, in turn, are useful as intermediates in the preparation of azo dyes, as disclosed and claimed in the copending application of Elkan R. Blout, Milton Green and Howard G. Rogers, Serial No. 612,045, filed September 25, 1956, now abandoned and replaced by Serial No. 145,978, filed October 18, 1961, now U.S. Patent No. 3,134,764.

It will be noted that the dialkyl ether intermediates, e.g., p-(2,5-dimethoxyphenethyl)-aniline, as well as the N-acylated dialkyl ether intermediates, e.g., 2-[α-(4′-acetamidophenyl)-β-methyl-propyl]-hydroquinone dimethyl ether, also are novel compounds.

3-methyl-2,5-dimethoxybenzaldehyde, an intermediate useful in the synthesis of compounds within the scope of this invention, may be prepared according to the procedures described in the copending application of Milton Green, Adnan A. Sayigh and Henri Ulrich, Serial No. 25,559, filed April 29, 1960.

Since certain changes may be made in the above processes, products and compositions without departing from the scope of the invention herein involved, it is intended that all matter contained in the above description shall be interpreted as illustrative and not in a limiting sense.

What is claimed is:

1. Compounds selected from the group consisting of compounds within the formula:

$$Z_n-\underset{\displaystyle NH_2}{\underset{|}{Ar}}-R^3-Y$$

wherein R^3 is an alkylene group containing no more than 5 carbons, each Z is selected from the group consisting of lower alkyl, lower alkoxy and chlorine groups, *n* is selected from the group consisting of 0 and 1, Ar is an aryl nucleus selected from the group consisting of benzene and naphthalene nuclei, and Y is selected from the group consisting of unsubstituted, lower alkyl-substituted, chlorine-substituted and bromine-substituted o-dihydroxyphenyl and p-dihydroxyphenyl groups and unsubstituted, lower-alkyl substituted, chlorine-substituted and bromine-substituted o-di-lower alkoxyphenyl and p-di-lower alkoxyphenyl groups.

2. Compounds as defined in claim **1**, wherein Ar is a benzene nucleus.

3. p-Aminophenethyl-hydroquinone.

4. 2-[γ-(4′-aminophenyl)-propyl]-hydroquinone.

5. 2-(p-aminophenethyl)-5-methyl-hydroquinone.

6. 2-(3′-methyl-4′-aminophenethyl)-hydroquinone.

7. 2-(4′-aminonaphthylethyl)-hydroquinone.

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