

PATENT SPECIFICATION

(11) 1 564 023

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- (21) Application No. 43752/76 (22) Filed 21 Oct. 1976
 (31) Convention Application No. 51/021 987
 (32) Filed 1 March 1976
 (31) Convention Application No. 51/028 995
 (32) Filed 17 March 1976 in
 (33) Japan (JP)
 (44) Complete Specification published 2 April 1980
 (51) INT CL³ C07C 93/14
 (52) Index at acceptance
 C2C 220 227 22Y 30Y 321 32Y 364 36Y 500 50Y 610 620
 624 660 662 FC LG



(54) PROCESS FOR PRODUCING ALKOXYANILINES

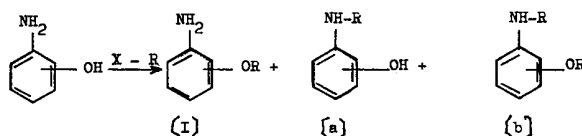
(71) We, IHARA CHEMICAL INDUSTRY CO. LTD., a Japanese company of 4-26, Ikenohata 1-chome, Taitoh-ku, Tokyo, Japan, do hereby declare the invention, for which we pray that a patent may be granted to us and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to a process for producing alkoxy anilines which are useful as intermediates for medicines and dyes and as raw materials for various chemical compounds.

More particularly, it relates to a process for selectively producing alkoxyanilines in high yield and high efficiency by directly reacting hydroxyaniline with an alkyl halide.

It is difficult to produce the alkoxyaniline [I] selectively by directly reacting hydroxyaniline with an alkyl halide because N-alkylhydroxyaniline [a] and N-alkyl alkoxyaniline [b] tend to be formed as by products as shown in the following reaction formula [A].

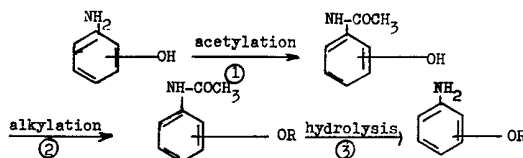
Reaction formula A:



Accordingly, the alkoxyanilines have until now been produced by the process (1) which comprises protecting the amino group (—NH_2) of hydroxyaniline as an acetamide group (—NHCOCH_3) by an acetylation and the alkylating it with an alkyl halide and hydrolyzing it.

<Journal of the Pharmaceutical Society of Japan Vol. 74 Pages 872 to 875 and Journal für Praktische Chemie Vol. 4 No. 1 Pages 57 to 86 (1954)>

Process (1):

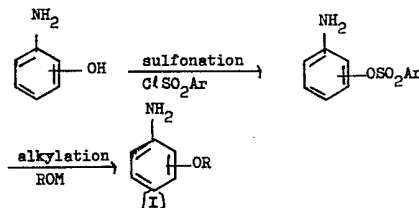


However, the steps of acetylation and hydrolysis are included in the process (1) and accordingly, the reaction steps are complicated and many steps are needed which increases the cost of the alkoxyaniline, and the process is therefore not satisfactory as an industrial process.

It has been proposed to use the other alkylating agents instead of the alkyl halide. In particular, it has been proposed to produce the alkoxyanilines by the process (2) which comprises converting the hydroxyl group (—OH) of hydroxyaniline to a sulfonic acid ester ($\text{—OSO}_2\text{Ar}$) with a sulfochloride (ArSO_2Cl) and using an alkali metal alcoholate (ROM) as the alkylating agent.

<Journal of the Pharmaceutical Society of Japan Vol 74 Pages 872 to 875 (1954) and Afinidad Organo de la Asocion de Quimicos Vol. 25 Pages 547 to 551 (1948)>

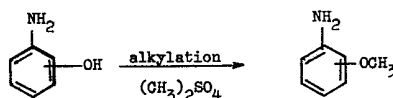
Process (2):



It has also been proposed to produce alkoxyanilines by the process (3) which comprises directly alkylating hydroxyaniline with a dialkyl sulfate as the alkylating agent.

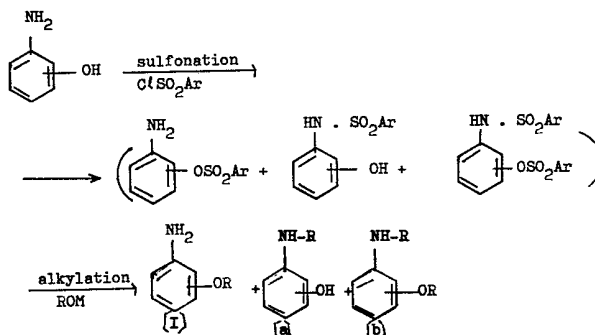
<Journal of Organic Chemistry Vol. 22, Pages 333 to 334 (1957)>.

Process (3):



However, the sulfochlorides used in the process (2) react with alcohols and phenols to produce sulfonic esters, and also react with ammonia, primary amines and secondary amines to produce sulfamides. Accordingly, in the case of a hydroxyaniline, having a hydroxyl group and an amino group, when the sulfochloride is used, the hydroxyl group of hydroxyaniline is converted to the sulfonic acid ester, and the amino group is converted to a sulfamide group at the same time, as shown in the following reaction formula (2'), whereby N-alkyl hydroxyaniline [a] and N-alkyl alkoxyaniline [b] are produced as the by-products.

Process (2'):



The sulfochlorides have a powerful smell, the alkali metal alcoholates used as the alkylating agents are expensive, the operations for the reaction and the post-treatment are complicated on an industrial scale and the cost is disadvantageously high. Moreover, two steps are needed in the process (2).

In the process (3), the dialkyl sulfate used as the alkylating agent acts as an alkylating agent for both the hydroxyl group and the amino group whereby the N-alkyl hydroxyaniline [a] and N-alkyl alkoxyaniline [b] are produced as by-products.

Only dimethyl sulfate and diethyl sulfate are easily available as the dialkyl sulfates. Accordingly, the alkylations by the dialkyl sulfates are limited to methylation and ethylation, and it is not easy to achieve alkylation with an alkyl group having 3 or more carbon atoms.

Generally, dialkyl sulfates have high toxicity. Though dimethyl sulfate is an active methylating agents, it has high toxicity, and it is not easy to use because poisoning is caused by breathing the vapor and absorption through the skin causes dermatitis and damage to the mucous membrane.

As stated above, it has been difficult to produce the alkoxyanilines selectively by directly reacting hydroxyaniline with an alkyl halide. Accordingly, various processes have been proposed, but these processes have not been satisfactory for use on an industrial scale.

The present invention provides a process for producing an alkoxyaniline having the formula



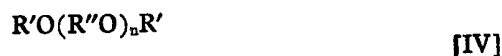
wherein R represents an alkyl group, by directly reacting a hydroxyaniline having the formula



with an alkyl halide having the formula



wherein R represents an alkyl group and X represents a halogen atom in the presence of an alkali metal alcoholate or hydroxide in a nonprotonic organic solvent selected from N-dimethyl acetamide, tetramethyl urea, hexamethylphosphoric triamide, dimethyl sulfoxide and N-methyl pyrrolidone or a polyalkyleneglycol alkyl ether having the formula



wherein R' represents an alkyl group having 1 to 4 carbon atoms and R'' represents an alkylene group having 2 to 3 carbon atoms and n is an integer of 1 to 3.

The hydroxyanilines having the formula [II] used as the starting material in the process of the invention, include *o*-hydroxyaniline, *m*-hydroxyaniline and *p*-hydroxyaniline.

The alkyl halides having the formula [III] include alkyl fluorides, alkyl chlorides, alkyl bromides and alkyl iodides having a straight chain or branched chain alkyl group such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-amyl, iso-amyl, n-hexyl and n-heptyl group.

The bases used in the process of the invention are alkali metal alcoholates or alkali metal hydroxides, for example sodium methylate, potassium methylate, sodium ethylate, potassium ethylate, sodium hydroxide and potassium hydroxide.

When an alkali metal hydroxide is used, it is preferable to add it in a form of powder or granules.

In the process of the invention, alkali metal carbonates or hydrogencarbonates are not used instead of alkali metal alcoholates and hydroxides, since they give reduced selectivity and yield.

The nonprotonic organic solvents which can be used in the process of the invention as the reaction solvent include N-dimethyl acetamide, tetramethyl urea, hexamethylphosphoric triamide $<[(\text{CH}_3)_3\text{N}]_3-\text{P}=\text{O}>$, dimethyl sulfoxide, and N-methyl 2-pyrrolidone.

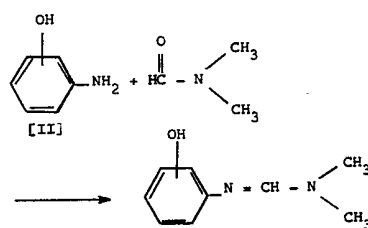
The polyalkyleneglycol alkyl ethers which may be used in the process of the invention include the compounds shown in Table 1.

TABLE 1

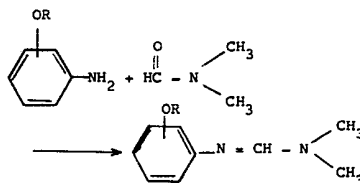
ethyleneglycol dimethyl ether	$\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_3$
ethyleneglycol diethyl ether	$\text{C}_2\text{H}_5\text{OCH}_2\text{CH}_2\text{OC}_2\text{H}_5$
diethyleneglycol dimethyl ether	$\text{CH}_3\text{O}-(\text{CH}_2\text{CH}_2\text{O})_2-\text{CH}_3$
diethyleneglycol dibutyl ether	$\text{C}_4\text{H}_9\text{O}-(\text{CH}_2\text{CH}_2\text{O})_2-\text{C}_4\text{H}_9$
triethyleneglycol dimethyl ether	$\text{CH}_3\text{O}-(\text{CH}_2\text{CH}_2\text{O})_3-\text{CH}_3$
triethyleneglycol diethyl ether	$\text{C}_2\text{H}_5\text{O}-(\text{CH}_2\text{CH}_2\text{O})_3-\text{C}_2\text{H}_5$
triethyleneglycol dibutyl ether	$\text{C}_4\text{H}_9\text{O}-(\text{CH}_2\text{CH}_2\text{O})_3-\text{C}_4\text{H}_9$
propyleneglycol dimethyl ether	$\text{CH}_3\text{O}-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}\text{CH}_2\text{O}-\text{CH}_3$
propyleneglycol diethyl ether	$\text{C}_2\text{H}_5\text{O}-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}\text{CH}_2\text{O}-\text{C}_2\text{H}_5$
dipropyleneglycol dimethyl ether	$\text{CH}_3\text{O}-(\overset{\text{CH}_3}{\underset{ }{\text{CH}}}\text{CH}_2\text{O})_2-\text{CH}_3$
dipropyleneglycol diethyl ether	$\text{C}_2\text{H}_5\text{O}-(\overset{\text{CH}_3}{\underset{ }{\text{CH}}}\text{CH}_2\text{O})_2-\text{C}_2\text{H}_5$

In the process of the invention, it is not suitable to use an organic solvent other than those mentioned above. For example, when dimethyl formamide is used as the solvent, the side-reactions of dimethyl formamide with the hydroxyaniline [II] and the resulting alkoxyaniline [I] are caused as in the reaction formulae (4) and (5) to form the by-products of formamidines.

Process (4):



Process (5):



In an alcohol such as methanol or ethanol, the reaction will take place but the selectivity is poor and the yield is also low.

On the other hand, in a ketone such as acetone or methylethyl ketone, the desired alkoxyaniline is not obtained because of side reactions.

In a nitrile such as acetonitrile or butyronitrile, the selectivity is high but the reaction velocity is too low and the yield of the alkoxyaniline is low.

In a nonpolar solvent such as benzene, toluene, xylene or hexane or a nonprotonic organic solvent of a cyclic ether such as tetrahydrofuran or dioxane, the yield of the alkoxyaniline [I] is not satisfactory because of a low reaction velocity.

The reaction of the invention is normally performed by stirring the hydroxyaniline [II] and the alkyl halide [III] in the presence of the specific base in the specific nonprotonic organic solvent or the specific polyalkyleneglycol alkyl ether with heating.

Usually the reaction is performed under atmospheric pressure, but it can be performed under high pressure in an autoclave.

The reaction temperature is usually 50 to 200° C, preferably 70 to 100° C. When the reaction temperature is too high, the selectivity is low.

The ratio of the hydroxyaniline to the alkyl halide can be the stoichiometric mole ratio for the reaction. However, it is preferable to use an excess of the alkyl halide in a range of 1.0 to 2.5 mole per 1 mole of the hydroxyaniline. It is preferable to use 1.0 to 2.0 moles of the specific base per 1 mole of the hydroxyaniline.

After the reaction, the resulting alkoxyaniline can be easily separated from the reaction mixture by distilling under reduced pressure. The nonprotonic organic solvent or the polyalkyleneglycol alkyl ether used in the reaction, can be easily recovered by distilling under a reduced pressure.

The characteristics and advantages of the process of the invention are as follows:
1) It is possible to produce the alkoxy aniline selectively by directly reacting the hydroxyaniline with the alkyl halide which has been considered to be difficult.

2) It is possible to prevent any substantial formation of by-products of N-alkyl hydroxyaniline and N-alkyl alkoxyaniline, whereby the alkoxyaniline can be obtained in high conversion, high selectivity and high yield.

The invention will be further illustrated by the following Examples and references.

EXAMPLE 1.

In a 500 ml autoclave made of glass, 150 ml of N-dimethyl acetamide, 15.2 g (0.3 mole) of methyl chloride, 8.8 g (0.22 mole) of sodium hydroxide and 21.8 g (0.2 mole) of *o*-hydroxyaniline were charged, and the reaction was carried out at 80° C for 5 hours with stirring. During the reaction, the pressure in the autoclave was kept at 6.3 kg/cm².

After the reaction, the autoclave was cooled and the reaction mixture was filtered. A part of the filtrate was sampled and the components in the reaction mixture were measured by gas chromatography analysis.

The filtrate was concentrated under a reduced pressure to distil off N-dimethyl acetamide and the residue was fractionally distilled to obtain 22.0 g of *o*-methoxyaniline having a boiling point of 115 to 117° C/19 mmHg. (yield: 89.5%).

According to the gas chromatography analysis, the ratio of *o*-methoxyaniline: N-methyl-*o*-hydroxyaniline: N-methyl-*o*-methoxyaniline in the reaction mixture was 94.2 : 0 : 5.8.

EXAMPLE 2.

In a 500 ml autoclave made of glass, 150 ml of ethyleneglycol dimethyl ether, 15.1 g (0.3 mole) of methyl chloride, 42.4 g (0.22 mole) of sodium methylate in 28% methanol solution and 21.8 g (0.2 mole) of *o*-hydroxyaniline were charged and the reaction was carried out at 80° C for 6 hours with stirring. During the reaction, the pressure in the autoclave was kept at 3 kg/cm.

After the reaction, the autoclave was cooled and the reaction mixture was filtered. A part of the filtrate was sampled and the components in the reaction mixture were measured by gas chromatography analysis.

The filtrate was concentrated under a reduced pressure to distil off ethyleneglycol dimethyl ether and the residue was fractionally distilled to obtain 16.6 g of *o*-methoxyaniline having a boiling point of 118 to 120° C/25 mmHg. (yield: 67.8%).

According to the gas chromatography analysis, the ratio of *o*-methoxyaniline: N-methyl-*o*-hydroxyaniline: N-methyl-*o*-methoxyaniline in the reaction mixture was 96.6 : 0 : 3.4.

EXAMPLE 3.

In accordance with the process of Example 1, 150 ml of dimethyl sulfoxide, 19.4 g (0.3 mole) of ethyl chloride, 8.8 g (0.22 mole) of sodium hydroxide and 21.8

g (0.22 mole) of *p*-hydroxyaniline were charged in an autoclave and the reaction was carried out at 80° C for 5 hours with stirring to obtain 24.7 g of *p*-ethoxyaniline having a boiling point of 123.5 to 124.5° C/10 mmHg. (yield: 90.1%).

5 According to a gas chromatography analysis, the ratio of *p*-ethoxyaniline: N-ethyl-*p*-hydroxyaniline: N-ethyl-*p*-ethoxyaniline in the reaction mixture was 94.7 : 0 : 5.3. 5

EXAMPLE 4.

10 In accordance with the process of Example 2, 150 ml of diethyleneglycol dimethyl ether, 19.3 g (0.3 mole) of ethyl chloride, 42.2 g (0.22 mole) of sodium methylate in 28% methanol solution and 21.8 g (0.2 mole) of *p*-hydroxyaniline were charged in an autoclave and the reaction was carried out at 80° C for 6 hours with stirring to obtain 19.7 g of *p*-ethoxyaniline having a boiling point of 135 to 136° C/24 mmHg. (yield: 72.1%). 10

15 According to a gas chromatography analysis, the ratio of *p*-ethoxyaniline: N-ethyl-*p*-hydroxyaniline: N-ethyl-*p*-ethoxyaniline in the reaction mixture was 95.9 : 0 : 4.1. 15

EXAMPLE 5.

20 In a 300 ml four necked flask equipped with a stirrer, a thermometer and a condenser, 150 ml of N-dimethyl acetamide, 39.3 g (0.5 mole) of iso-propyl chloride, 16.0 g (0.4 mole) of sodium hydroxide and 21.8 g (0.2 mole) of *m*-hydroxyaniline were charged and the reaction was carried out at 85° C for 5 hours with stirring. 20

After the reaction, the reaction mixture was filtered. A part of the filtrate was sampled and the components in the reaction mixture were measured by gas chromatography analysis.

25 The filtrate was concentrated under a reduced pressure to distill off N-dimethyl acetamide and the residue was fractionally distilled to obtain 28.9 g of *m*-iso-propoxyaniline having the boiling point of 136 to 138° C/25 mmHg. (yield: 93.4%). 25

30 According to the gas chromatography analysis, the ratio of *m*-iso-propoxyaniline: N-iso-propyl-*m*-hydroxyaniline: N-iso-propyl-*m*-isopropoxyaniline in the reaction mixture was 98.0 : 0 : 2.0. 30

EXAMPLE 6.

35 In a 300 ml four necked flask equipped with a stirrer, a thermometer and a condenser, 150 ml of diethyleneglycol dimethyl ether, 39.3 g (0.5 mole) of iso-propyl chloride, 77.1 g (0.4 mole) of sodium methylate in 28% methanol solution and 21.8 g (0.2 mole) of *m*-hydroxyaniline were charged and the reaction was carried out at 85° C for 8 hours with stirring. 35

After the reaction, the reaction mixture was filtered. A part of the filtrate was sampled and the components in the reaction mixture were measured by gas chromatography analysis.

40 The filtrate was concentrated under a reduced pressure to distil off diethylene-glycol dimethyl ether and the residue was fractionally distilled to obtain 21.6 g of *m*-iso-propoxyaniline having a boiling point of 137 to 138° C/23 mmHg. (yield: 71.5%). 40

45 According to the gas chromatography analysis, the ratio of *m*-iso-propoxyaniline: N-iso-propyl-*m*-hydroxyaniline: N-iso-propyl-*m*-isopropoxyaniline in the reaction mixture was 96.0 : 0 : 4.0. 45

EXAMPLE 7.

50 In accordance with the process of Example 5, 0.5 mole of isopropyl halide was reacted with 0.2 mole of *m*-hydroxyaniline in the presence of 0.4 mole of each base in 150 ml of each solvent. The results are shown in Table 2. 50

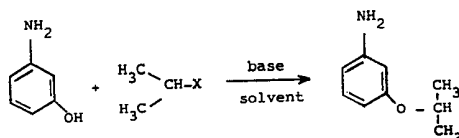


TABLE 2

Test No.	X	Base	Solvent	Ratio of components in reaction mixture			Yield (%)
				O	N	ON	
1	Br	NaOH	DMAC	55.0	0	45.0	52.5
2	Cl	CH ₃ ONa	DMAC	98.1	0	1.9	85.0
3	Cl	KOH	DMAC	97.9	0	2.1	93.2
4	Cl	NaOH	TMU	96.1	0	3.9	84.8
5	Cl	NaOH	MPD	94.3	0	5.7	82.4
6	Cl	NaOH	DMSO	94.6	0	5.4	85.5
7	Cl	C ₂ H ₅ ONa	HMPA	89.3	0	2.2	84.3
8	Br	NaOH	EGDM	90.3	5.8	3.9	60.9
9	Cl	CH ₃ ONa	DEGDM	96.0	0	4.0	71.5
10	Cl	KOH	„	92.1	1.4	6.5	59.1
11	Cl	NaOH	EGDM	93.3	1.0	5.7	58.0
12	Cl	NaOH	DEGDM	93.2	1.1	5.7	60.7
13	Cl	NaOH	TEGDM	94.0	0.3	5.7	65.2
14	Cl	C ₂ H ₅ ONa	DEGDM	97.2	0	2.8	70.7
Reference:							
1	Cl	NaOH	H ₂ O	61.0	26.0	13.0	16.8
2	Cl	NaOH	CH ₃ OH	75.6	11.5	12.8	36.1
3	Cl	NaOH	MIBK	none of the desired product was obtained because of side reactions			
4	Cl	NaOH	AcNi	97.6	0	2.4	15.0
5	Cl	CH ₃ ONa	Ben	93.4	0	6.6	10.9
6	Cl	NaOH	Dio	98.2	0	1.8	6.4

Note:

DMAC: N-dimethyl acetamide;
 TMU: tetramethyl urea;
 MPD: N-methyl-2-pyrrolidone;
 DMSO: dimethylsulfoxide;
 HMPA: hexamethylphosphoric triamide;

Note: (continued)

EGDM: ethyleneglycol dimethyl ether;
 DEGDM: diethyleneglycol dimethyl ether;
 TEGDM: triethyleneglycol dimethylether;
 MIBK: methylisobutyl ketone;
 AcNi: acetonitrile;
 Ben: benzene;
 Dio: dioxane.

In the column of the ratio of components in the reaction mixture, the symbols are as follows.

O: *m*-isopropoxyaniline;
 N: N-isopropyl-*m*-hydroxyaniline;
 ON: N-isopropyl-*m*-isopropoxyaniline.

EXAMPLE 8.

In a 300 ml four necked flask equipped with a stirrer, a thermometer and a condenser, 150 ml of N-dimethyl acetamide, 27.8 g (0.3 mole) of n-butyl chloride, 8.8 g (0.22 mole) of sodium hydroxide and 21.8 g (0.2 mole) of *p*-hydroxyaniline were charged and the reaction was carried out at 80° C for 5 hours with stirring.

After the reaction, the reaction mixture was filtered. A part of the filtrate was sampled and the components in the reaction mixture were measured by gas chromatography analysis.

The filtrate was concentrated under a reduced pressure to distill off N-dimethyl acetamide and the residue was fractionally distilled to obtain 30.7 g of *p*-n-butoxyaniline having a boiling point of 155 to 157° C/23 mmHg. (yield: 93.0%).

According to the gas chromatography analysis, a ratio of *p*-n-butoxyaniline: N-n-aniline: N-n-butyl-*p*-hydroxyaniline: N-n-butyl-*p*-butoxyaniline in the reaction mixture 98.1 : 0 : 1.9.

EXAMPLE 9.

In a 300 ml four necked flask equipped with a stirrer, a thermometer and a condenser, 150 ml of diethyleneglycol diethyl ether, 27.6 g (0.3 mole) of n-butyl chloride, 21.8 g (0.22 mole) of sodium methylate in 28% methanol solution and 21.8 g (0.2 mole) of *p*-hydroxyaniline were charged and the reaction of the mixture was carried out at 90° C for 5 hours with stirring.

After the reaction, the reaction mixture was filtered. A part of the filtrate was sampled and the components in the reaction mixture were measured by gas chromatography analysis.

The filtrate was concentrated under a reduced pressure to distill off diethyleneglycol diethyl ether and the residue was fractionally distilled to obtain 24.3 g of *p*-n-butoxyaniline having a boiling point of 143 to 145° C/10 mmHg. (yield: 73.6%).

According to the gas chromatography analysis, the ratio of *p*-n-butoxyaniline: N-n-butyl-*p*-hydroxyaniline: N-n-butyl-*p*-butoxyaniline in the reaction mixture was 97.3 : 0 : 2.7.

EXAMPLE 10.

In accordance with the process of Example 8, 0.3 mole of n-butyl halide was reacted with 0.2 mole of *p*-hydroxyaniline in the presence of 0.22 mole of sodium hydroxide in 150 ml of various nonprotonic organic solvents. The results are shown in Table 3.

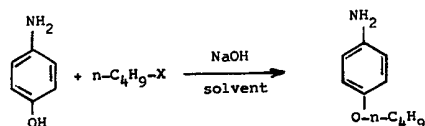


TABLE 3

Test No.	X	Solvent	Ratio of components in reaction mixture			Yield (%)
			O	N	ON	
1	Br	DMAC	57.5	0	42.5	54.0
2	Cl	TMU	96.7	0	3.3	82.1
3	Cl	MPD	94.4	0	5.6	80.9
4	Cl	DMSO	94.5	0	5.5	86.1
5	Cl	HMPA	90.6	0	2.5	85.6

Note: DMAC, TUM, MPD, DMSO and HMPA are shown in Table 2 of Example 7.

EXAMPLE 11.

In accordance with the process of Example 9, 0.3 mole of n-butyl halide was reacted with 0.2 mole of *p*-hydroxyaniline in the presence of a 28% methanol solution of 0.22 mole of sodium methylate in 150 ml of various polyalkyleneglycol alkyl ethers. The results are shown in Table 4.

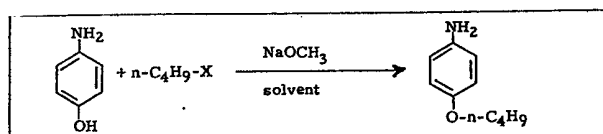


TABLE 4

Test No.	X	Solvent	Ratio of components in reaction mixture			Yield (%)
			O	N	ON	
1	Br	EGDM	93.5	2.5	4.0	60.5
2	Cl	„	96.6	0	3.4	68.3
3	Cl	DEGDM	96.9	0	3.1	71.8
4	Cl	TEGDM	97.0	0	3.0	71.5
5	Cl	DEGDP	96.8	0	3.2	73.6

Note:

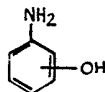
EGDM, DEGDM and TEGDM are shown in Table 2 of Example 7.

DEGDP: diethyleneglycol dipropyl ether.

As is clear from the examples and the references, in accordance with the process of the invention, the alkoxyanilines are obtained in high selectivity and high efficiency and high yield under without substantial formation of by-products of N-alkyl hydroxyaniline and N-alkyl alkoxyaniline.

5 WHAT WE CLAIM IS:—

1. A process for producing an alkoxyaniline which comprises reacting a hydroxy-
aniline having the formula



with an alkyl halide having the formula



wherein R represents an alkyl group and X represents a halogen atom, in the presence of an alkali metal alcoholate or hydroxide in a nonprotonic organic solvent selected from N-dimethyl acetamide, tetramethyl urea, hexamethylphosphoric triamide, dimethyl sulfoxide and N-methyl pyrrolidone or a polyalkyleneglycol alkyl ether having the formula



wherein R' represents an alkyl group having 1 to 4 carbon atoms and R'' represents an alkylene group having 2 to 3 carbon atoms and n is an integer from 1 to 3.

2. A process according to claim 1 wherein said alkali metal alcoholate or hydroxide is sodium or potassium methylate, ethylate or hydroxide.

3. A process according to claim 1 or claim 2 wherein the reaction is carried out in the presence of an alcoholic solution of an alkali metal alcoholate.

4. A process according to claim 1 or claim 2 wherein the reaction is carried out in the presence of an alkali metal hydroxide in the form of a powder or granules.

5. A process according to any preceding claim wherein said alkyl halide is an alkyl fluoride, chloride, bromide or iodide having an alkyl group selected from the group consisting of methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-amyl, iso-amyl, n-hexyl and n-heptyl groups.

6. A process according to any preceding claim wherein the reaction is carried out at 50 to 200° C under at least atmospheric pressure.

7. A process according to claim 6 wherein the reaction temperature is in the range from 70 to 100° C.

8. A process according to any preceding claim wherein the amount of the alkyl halide is 1.0 and 2.5 moles per 1.0 mole of the hydroxyaniline and the amount of the alkali metal alcoholate or hydroxide is 1 to 2.0 moles per 1.0 mole of the hydroxyaniline.

9. A process according to any preceding claim wherein the reaction is carried out in a solvent selected from the polyalkyleneglycol alkyl ethers in Table 1 herein.

10. A process according to claim 1 substantially as herein described with reference to the Examples.

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