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(19)

(54) PROCESS FOR THE PRODUCTION OF HALOACYLAMIDES

(71) We, MONSANTO COMPANY, a corporation organised under the laws of the State of Delaware, United States of America, of 800 North Lindbergh Boulevard, St. Louis, Missouri 63166, United States of America, 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 invention herein relates to the field of chemical processes for the production of haloacylamides, particularly haloacetanilides, useful in the agronomic arts, e.g., as pesticides and plant growth regulators.

Haloacylamides and haloacetanilides of the type described herein have been prepared by a variety of means known to the prior art. In one prior art process, N-substituted-2-haloacetanilides are prepared by reacting a primary or secondary amine with the acid chloride of haloacetic acid typically in the presence of caustic soda to neutralize the by-product hydrogen halide. A similar process is described wherein the intermediates and final products are characterized by a N-loweralkoxyethyl substituent wherein the ethyl radical may have one or two methyl groups attached thereto.

In yet another prior art process N-substituted-N-cycloalkenyl-2-haloacetamides are prepared by the haloacetylation of the corresponding N-substituted-cyclo-alkyl-imine in the presence of an acid acceptor.

Still another prior art process for producing 2-haloacetanilides is described and claimed in Monsanto Company's British Patent No. 1,149,843, the process comprises reacting the appropriate intermediate compound, an N-halomethyl-2-haloacetanilide, with the appropriate alcohol preferably in the presence of an acid binding agent. An analogous process wherein fluoroacylamino-trichloromethyl-chloromethane is reacted with a thio compound of the formula Me—S—R where Me is H or alkali metal; when the thio compound is used in the free form it is expedient to use an acid-binding agent; when the thio compounds are used in the form of their salts, it is not necessary to add an acid binding agent.

One prior document describes processes as useful in the preparation of 2-haloacetamides (also described as acylamines) examplified by N-chloroacetyl-N-substituted (hydrogen, lower alkyl, alkoxymethyl, allyloxymethyl or methoxyethyl)-aminoindanes.

As relevant to the present invention involving the alcoholysis of the N-haloalkyl-N-substituted 2-haloacylamide or 2-haloacetanilide intermediate, the prior art describes the preparation of the 2-haloacetanilide intermediate by the haloacetylation of the appropriate phenylazomethine.

In another process N-halo-N-substituted amides and imides are methylenated at the nitrogen-halogen bond using diazomethane to produce the corresponding N-halomethyl-N-substituted-amide or imide followed by condensation with nucleophiles. One species of this process involves the reaction of N-chloro-N-methyl-2-chloroacetamide with diazomethane to produce the corresponding N-chloromethyl-N-methyl-2-chloroacetamide, which can then be reacted with a nucleophile.

One of the above-mentioned pieces of prior art discloses N-chloromethyl and N-bromomethyl-N-substituted-cycloalkenyl-2-haloacetamides which are representative of this class of compounds which can serve as intermediates in the process of the present

invention. Still other known processes for producing some intermediates used in this invention involve the N-haloalkylation of the appropriate aniline followed by N-haloacylation. For example, N-2-chloroethyl or N-2-chloro-1-methylethyl 2-haloacetanilides may be prepared by reacting the corresponding aniline with 2-chloroethyl-*p*-toluenesulfonate and 2-chloro-1-methylethyl-*p*-toluenesulfonate, respectively, followed by chloroacetylation. Still another process for preparing the N-haloalkyl intermediate involves reacting the appropriate halo-alkane, e.g., 1-chloro-2-bromoethane, with the appropriate aniline followed by chloroacetylation.

In the process for producing N-substituted-2-haloacetanilides by alcoholysis of the corresponding N-haloalkyl-2-haloacetanilide intermediate compound, hydrogen halide is generated as a by-product which adversely affects not only the yield of desired product, but also adversely affects the natural environment. Hence, as indicated in some of the above-mentioned prior art, it is necessary that this alcoholysis be conducted in the presence of an acid-binding agent. Examples of acid-binding agents which have been used in the prior art include inorganic and organic bases such as the alkali metal and alkaline earth metal hydroxides and carbonates, e.g., sodium and potassium hydroxide and sodium carbonate, tertiary amines, e.g., trimethyl- and triethylamines, pyridine and pyridine bases, ammonia, quaternary ammonium hydroxides and alcoholates; metal alcoholates, e.g., sodium and potassium methylates and ethylates. Both the hydrogen halide and the acid-binding agent can promote adverse side reactions which are undesirable, hence, constitute a disadvantage in prior art processes.

A significant disadvantage commonly encountered in the above-mentioned prior art processes is that the acid-binding agent reacts with the by-product hydrogen halide to form insoluble precipitates which must be separated from the reaction mixture and disposed of. Separation of the desired product from waste by-products frequently requires and/or includes stripping of any solvent used, aqueous washing, steam stripping of hydrogen halide, dehydration, filtration and/or stabilization of product. Other purification procedures include fractional distillation at sub- or super atmospheric pressure, solvent extraction, film distillation and recrystallization. For example, it is disclosed in the prior art that in the production of N-(butoxymethyl)-2′-t-butyl-6′-methyl-2-chloroacetanilide (common name "terbuchlor"), the acid-binding agent, i.e., triethylamine, forms a voluminous precipitate of fine needles of triethylamine hydrochloride which must be removed by aqueous washing, solvent stripping and filtration.

As another example, when ammonia is used as the acid-binding agent in the production of 2′,6′-diethyl-N-(methoxymethyl)-2-chloroacetanilide (common name "alachlor" and active ingredient in the commercial herbicide Lasso, registered trademark of Monsanto Company), ammonium chloride is formed as a solid by-product in large quantity and must be disposed of.

In some instances, during or after the alcoholysis of the N-haloalkyl intermediate, the bulk of the generated hydrogen halide by-product can be removed by conventional distillation. However, the hydrogen halide itself is a gaseous pollutant in the environment. Moreover, in some cases distillation of the reactant alcohol and by-product hydrogen halide results in the production of an alkyl halide and water and water is detrimental to yield of product. Further, a certain percentage of the hydrogen halide remains in the reaction mixture and must be removed by an acid-binding agent, thus forming solid waste products as mentioned earlier. For example, in prior work on the alachlor process by another worker in the laboratories of the Applicant, efforts were made to remove by-product HCl with excess methanol by conventional vacuum distillation. However, these efforts involved prolonged exposure, i.e., ~2 hours, of the N-chloromethyl intermediate and final product (alachlor) to the adverse action of HCl, water and other by-products and resulted in greatly diminished yields of alachlor. It was then concluded that an acid-binding agent should be used during or after the distillation stage, hence encountering the attendant disadvantages mentioned above.

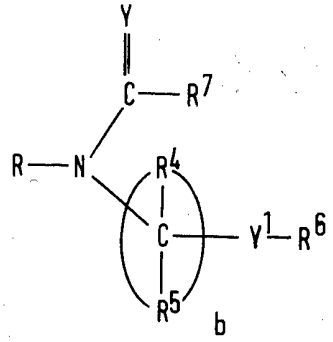
In view of energy conservation and environmental considerations bearing on the disposal of process wastes it has become exceedingly crucial to find new processes which eliminate or minimize the adverse impact of all kinds of wastes, i.e., solids, liquids and/or gases from chemical processing. In some instances deleterious by-products can be reprocessed for recycling of component parts. In other situations, by-products may be purified or converted to other useful products. However, each of the foregoing treatments require additional capital investment and reprocessing costs and energy consumption. Accordingly, it is much more desirable to avoid the creation of environmentally adverse products as far as possible.

Still another problem in connection with known prior art processes for the pro-

duction of 2-haloacetanilides is that they are batch processes with attendant disadvantages, particularly on a commercial scale.

Therefore, it is an object of this invention to provide an improved process for producing 2-haloacylamides or 2-haloacetanilides which overcomes or minimises disadvantages of prior art processes.

The present invention relates to a process, preferably continuous, for the preparation of N,N-disubstituted-haloacylamides, particularly compounds of Formula I

I 

wherein R is hydrogen, C_{1-18} alkyl, alkenyl, alkynyl, alkoxy, polyalkoxy, alkoxyalkyl, polyalkoxyalkyl, C_{5-7} cycloalkyl, cycloalkylalkyl, cycloalkenyl, C_{6-18} aryl, aralkyl, or alkaryl or said R members substituted with radicals which are nonreactive with hydrogen, under the conditions of this reaction e.g., alkyl, halogen, hydroxy, alkoxy, nitro or cyano;

R^4 and R^5 are independently hydrogen, fluorine, C_{1-6} alkyl, haloalkyl, alkoxy or alkoxyalkyl;

R^6 is hydrogen, C_{1-10} alkyl, alkenyl, alkynyl, alkoxyalkyl, oxoalkyl, C_{3-7} cycloalkyl, low cycloalkylalkyl or cycloalkenyl, C_{6-12} aryl or aralkyl; $-N(R^8)_2$ wherein R^8 is hydrogen, C_{1-6} alkyl, alkenyl, or alkynyl; or said R^6 members substituted with alkyl, alkylthio, halogen, hydroxy, alkoxy, nitro or cyano when these radicals are non-reactive with hydrogen under the reaction conditions;

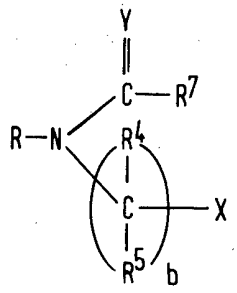
R^7 is C_{1-5} mono- or dihaloalkyl;

Y and Y^1 are oxygen or sulfur; and

b is an integer from 1—4 inclusive;

which comprises performing at least one sequence of reaction/separation operations comprising:

(A) reacting a compound of Formula II

II 

with a compound of Formula III

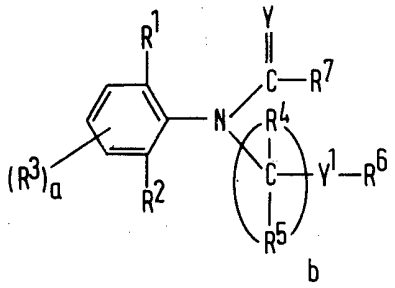
III R^6Y^1H

wherein R, R^4, R^5, R^6, R^7, Y, Y^1 and b are as defined above and X is halogen in the absence of added acid-binders and

(B) directing an effluent stream of the reaction mixture from Step (A) to a separation zone from which is removed a complex mixture of by-product HX with said compound of Formula III and a product stream comprising predominantly said compound of Formula I.

A subgenus of compounds of particular interest which may be prepared by the process of this invention includes haloacetanilides of Formula IV

IV



wherein R^1 and R^2 are independently hydrogen, halogen, C_{1-6} alkyl, haloalkyl, alkoxy or alkoxyalkyl;

R^3 is hydrogen, halogen, C_{1-6} alkyl, haloalkyl, alkoxy, alkoxyalkyl, alkylthio, CN, NO_2 or CF_3 or R^3 may be combined with R^1 or R^2 to form an alkylene chain of up to 4 carbon atoms;

R^4 and R^5 are independently hydrogen, fluorine, C_{1-6} alkyl, haloalkyl, alkoxy or alkoxyalkyl

R^6, R^7, Y, Y^1 and b are as defined above, and

a is zero or an integer from 1—3 inclusive.

Preferred haloacetanilides include those wherein R^1, R^2 and R^6 are C_{1-6} alkyl, R^4 and R^5 are hydrogen or C_{1-6} alkyl, R^7 is monohaloalkyl, Y and Y^1 are oxygen, a is zero and b is 1 or 2.

In the most preferred embodiment, the process of this invention is a process for the preparation and recovery of alachlor which comprises performing at least one sequence of reaction/separation operations comprising:

(A) reacting methanol with 2',6'-diethyl-N-(chloromethyl)-2-chloroacetanilide at a molar ratio of 2—100:1 at temperatures within the range of from 25°—65°C for a period of from 15—30 minutes in the absence of added acid binders, and

(B) directing an effluent stream of the reaction mixture from Step (A) to a separation zone from which is rapidly removed a complex mixture of HCl and methanol and a product stream comprising predominantly alachlor.

This process is illustrated in Example 1 below.

In preferred embodiments the above reaction/separation process sequence is repeated a plurality of times to assure complete conversion of said compound of Formula II to said compound of Formula I. In the most preferred embodiment the process is efficiently carried out in two stages or reaction/separation sequences which comprise:

(A) reacting in a first reaction zone a compound of Formula II with a compound of Formula III;

(B) directing an effluent stream of the reaction mixture of Step (A) to a first separation zone from which is rapidly removed most of by-product HX as a complex with said compound of Formula III and a product stream comprising predominantly a compound of Formula I and unreacted compound of Formula II;

(C) directing said product stream from said first separation zone to a second reaction zone into which is also introduced an additional quantity of said compound of Formula III to react with said unreacted compound of Formula II;

(D) directing an effluent stream of the reaction mixture of Step (C) to a second separation zone from which is rapidly removed substantially all of the remaining by-product HX as a complex with said compound of Formula III and a product stream comprised of said compound of Formula I and trace impurities.

In one preferred embodiment Steps (B) and (D) are conducted at temperatures and pressures sufficient to separate a complex of the compound of Formula III and hydrogen halide from the effluent streams of Steps (A) and (C).

Significant features of the process of this invention include: (1) the elimination of an added base as used in the prior art as an acid-binding agent for liberated hydrogen halide; and concomitantly (2) elimination of recovery systems for the neutralization by-product of (1) hence, elimination from the environment of the by-product itself and (3) separation, preferably immediately and usually within ≤ 0.5 minute of equilibration of the reaction mixture, of by-product hydrogen halide as a complex with the compound of Formula III in the product separation operation(s) of the process.

In preferred embodiments of the invention, the molar ratio of the compound of Formula III relative to the compound of Formula II in Step A is greater than 1:1 and usually within the range of about 2—100:1 and, in the case of the alachlor process, within the range of about 2—10:1 and preferably of 4—5:1.

The reaction temperatures in Step (A) will depend upon the particular reactants and/or solvents or diluents involved. In general, these temperatures will be temperatures at which mixtures of the alcohols of Formula III and/or solvents or diluents form complexes, e.g., azeotropic mixtures, with by-product hydrogen halide without significant degradation of the reactant compound of Formula II or desired product of Formula I due to reaction with hydrogen halide. In general, a temperature within the range of from about −25° to 125°C or higher depending upon the melting/boiling points of the reactants is used.

In those embodiments of the invention involving a plurality of reaction/separation sequences, or stages, the hydrogen halide concentration is greatly reduced in successive reaction zones, hence the respective reaction temperatures are generally somewhat elevated over the temperatures used in Step (A) in order to drive the reaction of the unreacted compound of Formula II to completion with additional alcohol. Accordingly, temperatures in the second and any subsequent reaction zone are generally within the range of from about −25 to 175°C or higher if necessary.

Suitably the temperatures and pressures within the separation zone(s) are, respectively, within the ranges of from 50°C to 175°C and 1.0 to 300 mm Hg absolute, depending upon the boiling point of the particular compound of Formula III.

Example 1.

This Example describes the use of the process of this invention in the preparation of alachlor. This process is efficiently carried out in a reaction/separation sequence of two stages as follows:

Stage 1. Molten (45—55°C) 2′,6′-diethyl-N-chloromethyl-2-chloroacetanilide is fed to an in-line mixer at a rate of 102.8 lbs/hr (46.67 kg/hr) and mixed with substantially anhydrous methanol which is fed to said mixer at a rate of 60.0 lbs/hr (27.24 kg/hr). The mixture is pumped through a thermostatted pipe reactor maintained at 40—45°C of sufficient length to give a residence time of at least thirty (30) minutes. The reaction produces a yield of ~92% 2′,6′-diethyl-N-(methoxymethyl)-2-chloroacetanilide (alachlor) and hydrogen chloride based on the N-chloromethyl intermediate. The generated HCl is dissolved in excess methanol. The reactor effluent is directed to a falling film evaporator operated at 100°C and 30 mm Hg absolute. A complex is removed and fed to a methanol recovery system.

Stage 2. The product stream from the evaporator in Stage 1 comprising predominantly alachlor and unreacted 2′,6′-diethyl-N-(chloromethyl)-2-chloroacetanilide is fed to a second in-line mixer into which is also fed an additional quantity of methanol at a rate of 60 lbs/hr (27.24 kg/hr). The mixture is then fed to a second reaction zone also comprising a thermostatted pipe reactor maintained at 60—65°C to give a residence time of thirty (30) minutes. The effluent from this reactor is fed to a second falling film evaporator, operated at 100°C and 30 mm Hg absolute, from which is removed a complex of methanol and substantially all of the remaining HCl. The methanol/HCl complex from this second stage evaporator is mixed with the methanol/HCl complex from the evaporator in Stage 1 and fed to a methanol recovery system from which anhydrous methanol is recovered and recycled to Stage 1.

The product stream from the evaporator in Stage 2 comprises alachlor in essentially quantitative yield and greater than 95% purity together with minor amounts of impurities. This alachlor can be used effectively as a herbicide as produced.

As will be apparent from the foregoing Example, the reaction/separation process sequence of Stage 1 by itself produces alachlor of high yield. Hence, under optimum conditions of reactant purities and concentrations, temperatures and residence times in the reactor and separation zones, at least one reaction/separation process sequence corresponding to said Stage 1 operation would suffice to produce a commercial grade of alachlor or other compounds within the scope of the above Formula I.

Example 2.

This Example describes the preparation of 2-chloro-2',6'-diethyl-N-(ethoxymethyl) acetanilide.

About 5.5 g (0.02 mole) of 2-chloro-2',6'-diethyl-N-(chloromethyl) acetanilide was dissolved in 25 ml of ethanol and allowed to stand in a 45°C bath for 30 minutes. Excess ethanol was removed rapidly on a rotary vacuum evaporator at 50°C and 10 mm Hg. Twenty-five (25) ml of fresh ethanol was added to the residual oil and the mixture held at 65°C for 30 minutes. Again excess ethanol was removed using a rotary evaporator. About 5.80 g. of a pale amber oil was obtained which assayed (by gas chromatography) 92.8% of the desired product and 1.7% 2-chloro-2',6'-diethylacetanilide (by-product). Yield of product was 94.5%.

Example 3.

Following the same procedure, operating conditions and quantities of reactants described in Example 2, but substituted isopropanol for ethanol, 5.92 gms of product, a light amber oil assaying 90.2% 2',6'-diethyl-N-(isopropoxymethyl)-2-chloroacetanilide (89.4% yield) and 1.8% of the secondary amide by-product, 2',6'-diethyl-2-chloroacetanilide was obtained.

Example 4.

Following the same procedure described in Examples 2 and 3, but substituting 1-propanol as the reactant alcohol, 5.66 gms of lemon-yellow oil was recovered which assayed 92.8% (87.9% yield) of 2',6'-diethyl-N-(n-propoxymethyl)-2-chloroacetanilide and 1.2% of the corresponding secondary amide by-product.

Example 5.

The same procedure described in Examples 2—4 was used in this example, but using isobutanol as the reactant alcohol, 6.20 gm of an oil product was recovered which assayed 96.4% (97% yield) of 2',6'-diethyl-N-(isobutoxymethyl)-2-chloroacetanilide and 3% of the corresponding secondary amide by-product.

Example 6.

Repeating the process of Examples 2—5, but using 2-chloro-ethanol as reactant alcohol, 6.96 gms of light-amber oil was recovered which assayed 86.0% (94.0% yield) of 2',6'-diethyl-N-(chloroethoxymethyl)-2-chloroacetanilide.

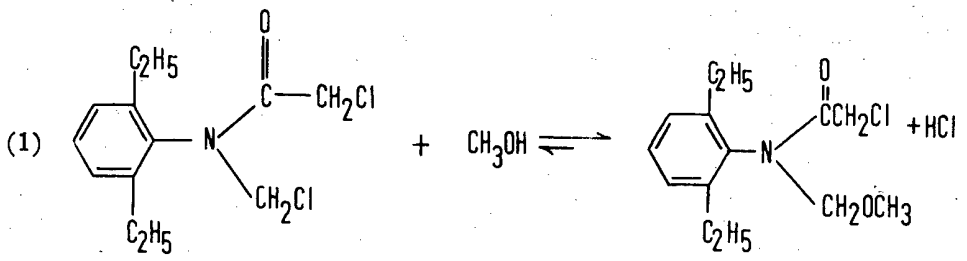
Example 7.

Following the same procedure described in Examples 2—6, but substituting n-butanol as the reactant alcohol, 6.18 gms of pale lemon-yellow oil was recovered which assayed 98.8% (99% yield) of 2',6'-diethyl-N-(n-butoxymethyl)-2-chloroacetanilide (i.e., butachlor) and 1% of the corresponding secondary amine by-product.

In the above Examples, NMR analysis indicated that the respective products were consistent with chemical structure thereof.

In further elaboration of the advantages provided by the present invention and the unobvious nature thereof, the following discussion and additional experimental data in Examples 8—12 is presented.

The reaction between compounds like those identified by Formula II and Formula III above is a reversible second-order reaction. Equation 1 below, exemplified by the reaction in Example 1, illustrates the reaction:



(a) (b) (c) (d)

Because the reaction is reversible, an equilibrium condition is established; this equilibrium is affected by and directly related to various factors, e.g., alcohol concentration and/or by-product hydrogen halide concentration. For example, in Equation (1) as alcohol (b) concentration, hence reactants ratio, (b):(a), increases (to a given practical maximum) the equation is shifted to the right because of additional conversion of starting material (a) thus producing more product (c) and hydrogen halide by-product (d).

Another way to shift the equilibrium of Equation (1) to the right is to remove the hydrogen halide (d), which can be done by adding an acid-binder, e.g., tertiary amines such triethylamine, as in the above prior art.

However, the use of acid-binding materials introduces other disadvantages as described above.

One prior art document suggests that when the thio compound starting material is in the form of an alkali metal salt the acid-binding material is unnecessary; the apparent reason for this is that said salts themselves provide the basic medium, favorable to the particular reaction described in that patent. In contrast, when the starting thio compound is used in the free form, it is necessary to use an acid-binder to bind the hydrogen chloride by-product.

As mentioned earlier efforts in the laboratories of the Applicant to perform the process of the prior art by reacting N-halomethyl-2-chloroacetanilide with methanol to obtain the preferred product alachlor with the significant difference of carrying out the process without an acid-binding agent to remove by-product hydrogen halide, resulted in greatly diminished yields of alachlor.

In order to obtain comparative results the Applicants conducted the processes described in Examples 8—12 below. In each of these Examples, the N-chloro-methyl-2-chloroacetanilide starting material was prepared by the reaction of the corresponding substituted N-methyleneaniline and haloacetyl halide.

Example 8 (Comparative).

This Example describes the preparation of 2-chloro-2′,6′-diethyl-N-(methoxymethyl) acetanilide (alachlor) as taught in the prior art.

One-hundred g of 2-chloro-2′,6′-diethyl-N-(chloromethyl) acetanilide assaying 96.0% (0.350 mole) dissolved in about 70 g of benzene was added to 65.8 g (2.054 moles) of methanol. On addition an exothermic reaction occurred. The reaction mixture was refluxed (at 63°C) and an excess (about 63.3 g) of triethylamine was added dropwise over 1½ hours. During this addition the temperature rose to about 70°C where it was maintained for about ten minutes after completion of the triethylamine addition. After cooling to 30°C, the reaction mixture was washed with two 170 ml portions of water. The product, in a heavy, oily layer was stripped of solvent and dehydrated by vacuum distillation to a terminal pot temperature of about 70°C at 1 mm hg. The residual amber oil weighed 96.15 g and assayed 90.4% product and 4.9% 2-chloro-2′,6′-diethylacetanilide (by-product) by gas chromatography. There was no unreacted starting material in the product. The yield of product was 92.0%.

Example 9 (Comparative)

This Example describes the preparation of alachlor as taught in the prior art but without the use of an acid-binding agent.

One-hundred g of 2-chloro-2′,6′-diethyl-N-(chloromethyl) acetanilide assaying 96.0% (0.350 mole) dissolved in about 70 g. of benzene was added to 66.0 g. of methanol (2.059 moles). On addition, an exothermic reaction occurred and the reaction mixture was further heated to reflux (at 63°C) for one hour. No acid-binding agent was added. After refluxing, excess methanol and solvent were removed by vacuum

distillation to a final pot temperature of 70°C at 1 mm Hg. About 96.83 g. of a pale lemon-yellow oil was obtained which contained (by gas chromatographic analysis) 83.7% product, 7.5% by-product 2-chloro-2',6'-diethyl acetanilide and 5.5% unreacted starting material. The yield of product was 85.8%.

As will be noted, omission of an acid-binding agent in this Example resulted in a reduction in yield of 6.2%. In this process, the reaction was not shifted completely to the right. As a result, the by-product HCl reduced conversions and the unreacted starting material was found as a contaminant in the product.

Example 10 (Comparative)

This Example describes the preparation of alachlor as taught in the prior art but without the use of an acid-binding agent and under optimized temperature conditions.

One-hundred g. of 2-chloro-2',6'-diethyl-N-(chloromethyl) acetanilide assaying 96.0% (0.350 mole) dissolved in about 70 g. of benzene was added to 66 g. (2.059 moles) of methanol. An exothermic reaction occurred which raised the reaction mixture temperature to 45°C where it was maintained for one hour. No acid-binding agent was added. Excess methanol and solvent were stripped off under vacuum distillation to a final pot temperature of about 80°C at 1 mm Hg. About 96.20 g. of oil was recovered which assayed (by gas chromatography) 85.8% product, 6.2% by-product, 2-chloro-2',6'-diethyl acetanilide and about 4.6% unreacted starting material. The yield of product was 87.4%.

By optimizing reaction conditions in the absence of an acid-binding agent, an increase in product quality (2.7%) and yield (1.6%) was realized, but the basic problem, i.e., incomplete reaction, has still not been solved.

Example 11.

This Example describes the preparation of alachlor by the process of the present invention according to the embodiment using a single stage reactor; the starting materials used herein were the same as those used in Examples 8—10.

Ten g. of 2-chloro-2',6'-diethyl-N-(chloromethyl) acetanilide assaying 96.0% (0.035 mole) was added to about 6.0 g. (0.1873 mole) of methanol. An exothermic reaction occurred raising the reaction mixture temperature to about 45°C where it was maintained for thirty minutes. Excess methanol was removed rapidly on a vacuum rotary evaporator to a final pot temperature of 70°C at 1 mm Hg. About 9.80 g. of pale lemon-yellow oil was recovered assaying 91.0% product, 1.7% by-product 2-chloro-2',6'-diethylacetanilide, and 2.4% unreacted starting material by gas chromatography. The yield of product was 94.4%.

Thus, using only a single stage, the quality and yield of the desired product is substantially improved over that of the prior art despite the fact that the reaction was not complete (2.4% starting material in product). Comparison with Examples 8, 9 and 10 shows an obvious improvement, although no acid-binding agent was used.

Example 12.

This Example describes the preparation of alachlor in the absence of an added acid-binding agent according to the preferred process of the present invention using a multiple stage reactor.

Ten g. of 2-chloro-2',6'-diethyl-N-(chloromethyl) acetanilide assaying 96.0% (.0350 mole) was dissolved in 6.0 g. (0.1873 mole) of methanol. An exothermic reaction occurred raising the temperature to 45°C where it was maintained for one-half hour. Excess methanol was removed rapidly on a rotary vacuum evaporator to a final pot temperature of 45°C at 1 mm Hg. A second addition of fresh methanol, 6.0 g (0.1873 mole) was added, the reaction mixture warmed to 65°C and held for one-half hour. Excess methanol was removed as before and about 9.80 g. of pale lemon-yellow oil was recovered assaying 95.8% product, 1.4% 2-chloro-2',6'-diethylacetanilide and no unreacted starting material. The yield of product was 99.4%.

A summary of the comparative results of the processes described in Examples 8—12 is shown in the following table. In this table, the "Starting Material" is unreacted 2',6'-diethyl-N-(chloromethyl)-2-chloroacetanilide and the "By-Product" refers to 2',6'-diethyl-2-chloroacetanilide, the major acetanilide by-product in the processes of each of these examples. It will be understood that minor amounts of acetanilide and other by-products are produced in addition to the large quantities of hydrogen halide generated and, in the case of Example 8, triethylamine hydrochloride neutralization by-product produced. Product yield percentages herein are based on the 2',6'-diethyl-N-(chloromethyl)-2-chloroacetanilide starting material.

TABLE

Example No.	Process Type	Alachlor Yield (%)	Product Analysis (%)		
			Alachlor	By-Product	Starting Material
8	prior art; base added	92.0	90.5	4.9	0
9	Ditto, except base omitted	85.8	83.7	7.5	5.5
10	Same as Ex. 9 with optimized conditions	87.4	85.8	6.2	4.6
11	Present process, 1-stage	94.4	91.0	1.7	2.4
12	Ditto, plural stages	99.4	95.8	1.4	0

An analysis of the data in the above table will show as the salient features and distinct advantages of the process of this invention, i.e., Examples 11 and 12, vis-a-vis the process of the prior art exemplified in Examples 8—10; (1) substantial increases in yield of alachlor; (2) improvement in alachlor purity; (3) markedly decreased yields by-product; (4) increased conversion of starting material when operating without added base; and (5) absence of solid neutralization product which is present in large quantities in the base-added process of Example 8 — representing the best previously known technology for producing alachlor. These technical advantages are additive to the economical and ecological advantages mentioned earlier.

In practicing the present invention, no solvent is required; however, in many cases a solvent or diluent may be used to moderate the reaction and/or aid in the solution, dispersion and/or recovery of reactants, by-products and products. Suitable solvents or diluents include those which are inert under the required conditions of reaction, such as petroleum ether, CCl_4, aliphatic and aromatic hydrocarbons, e.g., hexane, benzene, toluene and xylenes, and halogenated hydrocarbons, e.g., monochlorobenzene.

An advantage of the process according to this invention is that the reactant of Formula III may be readily separated from its complex with by-product hydrogen halide, purified and recycled to one or more reaction stages of the process. In like manner, the hydrogen halide itself may be readily recovered for use in many useful commercial operations, e.g., pickling of metals, oxychlorinations and electrolysis to elemental chlorine and hydrogen, or otherwise disposed of without detriment to the environment.

In one suitable raw material recovery/recycle system, exemplified with respect to the methanol/HCl complex formed in the alachlor process described in the above Examples 1, 11 and 12, the methanol/HCl complex from the separation stage(s) is fed to a distillation system from which purified methanol is obtained.

With further respect to the present process, while the use of technical grade reactants, i.e., the compounds of Formulae II and III, is suitable, it will be appreciated that the higher the purity of these reactants, the higher the quality of compounds of Formula I will be produced. Although in some instances the Formula III compounds, e.g., methanol, containing minor amounts of water can be used, it is much more preferable to use anhydrous compounds, because water may cause hydrolysis of the Formula II reactants resulting in deteriorated product of Formula I. However, it will be understood that in the special case where R^6 is hydrogen water itself can be used as the compound of Formula III to produce some compounds of Formula I by hydrolysis of the N-haloalkyl intermediate. For example, it has been disclosed in the prior art that 2'-tert-butyl-6'-ethyl-N-(chloromethyl)-2-chloroacetanilide is hydro-

lyzed with water in the presence of an acid binding agent to produce the corresponding N-hydroxymethyl compound which is useful as a herbicide. Accordingly, it will be appreciated that in some embodiments of the present process the presence of some water may be detrimental to product yield but not in other embodiments, depending upon the reactivity of water with other reactants and final products as will be understood by those skilled in the art. In like manner, since hydrogen halide adversely impacts on product quality, it is preferred to use reactants substantially free of hydrogen halides such as HCl.

Representative compounds produced according to the process of this invention include those in which the groups of the above formulae have the following identities:

R — hydrogen, C_{1-18} alkyls, e.g., methyl, ethyl, propyls, butyls, pentyls, hexyls, heptyls, octyls, nonyls, decyls, undecyls, dodecyls, pentadecyls and octadecyls; alkenyls, e.g., vinyl, allyl, crotyl, methallyl, butenyls, pentyls, hexenyls, heptenyls, octenyls, nonenyls and decenyls; alkynyls, e.g., ethynyl, propynyls, butynyls, pentynyls and hexynyls; the alkoxy, polyalkoxy, alkoxyalkyl and polyalkoxyalkyl analogs of the foregoing alkyl groups; cycloalkyls and cycloalkylalkyls having up to 7 cyclic carbons, e.g., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclopropylmethyl, cyclobutylmethyl and cyclopentylmethyl; cycloalkenyls and cycloalkadienyls having up to 7 cyclic carbons, e.g., cyclopentenes, cyclohexenes and cycloheptenes having mono- and di-unsaturation; C_{6-18} aryl and aralkyl and alkaryl groups, e.g., phenyl, tolyls, xylyls, benzyl and naphthyl, and said R members substituted with radicals which are non-reactive with hydrogen under the reaction conditions, e.g., alkyls, alkoxys, halogen, nitro or cyano; when the substituent is a halogen atom, it must not be on the α-carbon atom in which position it is reactive with hydrogen.

R^1, R^2, R^4 and R^5 — hydrogen, fluorine, the C_{1-6} alkyls of R, haloalkyls, e.g., chloromethyl, chloroethyl, bromomethyl, bromoethyl, iodomethyl, iodoethyl, trifluoromethyl, chloropropyl, bromopropyl, iodopropyl, chlorobutyl, iodobutyl and di- and trihalo analogs thereof; alkoxys, e.g., methoxy, ethoxy, propoxys, butoxys, pentoxys and hexoxys and corresponding polyalkoxys and alkoxyalkyls, e.g., methoxymethoxy, methoxyethoxy, ethoxymethoxy, ethoxyethoxy, methoxymethyl, methoxyethyl, ethoxymethyl, ethoxyethyl, propoxymethyl, isopropoxymethyl, butoxymethyl, isobutoxymethyl, tert-butoxymethyl, pentoxymethyl and hexoxymethyl.

R^1 and R^2 may also be chlorine, bromine or iodine.

R_3 may be hydrogen, the halo, alkyl, haloalkyl, alkoxy and alkoxyalkyl groups of R^1, R^2, R^4 and R^5, methylthio, ethylthio, propylthio, CN, NO_2, CF_3 or R^3 may be combined with R^1 or R^2 to form an alkylene chain of up to 4 carbon atoms, thus forming acylated 5-amino-tetralins and acylated 4-aminoindanes.

R_6 may be hydrogen, the C_{1-10} alkyl, alkenyl, alkynyl, and alkoxyalkyl groups of R; oxoalkyl groups corresponding to the above alkyl groups, e.g., 2-oxobutyl, 3-oxopentyl and 4-oxohexyl, the C_{3-7} cycloalkyl, cycloalkenyl and lower cycloalkylalkyl groups of R; the C_{6-12} aryl and aralkyl groups of R; amino and mono- and di-substituted amino containing the above C_{1-6} alkyl, alkenyl or alkynyl groups; and the above R^6 members which may be substituted with substituents such as alkyl, halogen, hydroxy, alkoxy, nitro, cyano or alkylthio, when these radicals are non-reactive with hydrogen under the reaction conditions.

R^7 is C_{1-5} haloalkyl, preferably C_{1-2} monohaloalkyls, such as chloromethyl, chloroethyl, bromomethyl, bromoethyl, iodomethyl, iodoethyl, fluoromethyl and fluoroethyl or dihaloalkyls such as 1,1-dichloromethyl, 1,1-dibromomethyl and 1,1-diodomethyl.

X is halo, especially chlorine or bromine.

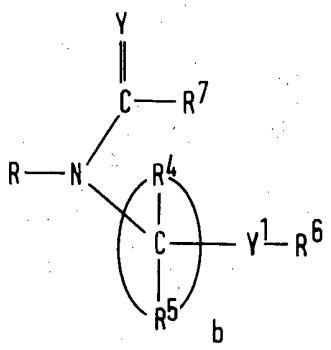
The process of the present invention is particularly amenable to use in the preparation of the above defined N-substituted-2-haloacetanilides wherein R^1, R^2 and R^6 are C_{1-6} alkyl, R^7 is monohalomethyl, Y and Y^1 are oxygen, a is zero and b is 1 or 2, preferably 1.

Compounds of Formula I prepared according to this invention are known compounds. Hence, the inventors herein lay no claim to the compounds, per se, of Formula I.

It will be appreciated by those skilled in this art that the preferred 2-haloacetanilides are a subgenus of N,N-disubstituted-2-haloacylamides.

WHAT WE CLAIM IS:—

1. A process for the production and recovery of compounds of Formula I

I 

wherein R is hydrogen, C_{1-18} alkyl, alkenyl, alkynyl, alkoxy, polyalkoxy, alkoxyalkyl, polyalkoxyalkyl, C_{5-7} cycloalkyl, cycloalkylalkyl, cycloalkenyl, C_{6-18} aryl, aralkyl ,or alkaryl or said R members substituted with radicals which are nonreactive with hydrogen under the reaction conditions;

R^4 and R^5 are independently hydrogen, fluorine, C_{1-6} alkyl, haloalkyl, alkoxy or alkoxyalkyl;

R^6 is hydrogen, C_{1-10} alkyl, alkenyl, alkynyl, alkoxyalkyl, oxoalkyl, C_{3-7} cycloalkyl, lower cycloalkylalkyl or cycloalkenyl, C_{6-12} aryl or aralkyl, $-N(R^8)_2$ wherein R^8 is hydrogen, C_{1-6} alkyl, alkenyl, or alkynyl; or said R^6 members substituted with alkyl, alkylthio, halogen, hydroxy, alkoxy, nitro or cyano when these radicals are non-reactive with hydrogen under the reaction conditions;

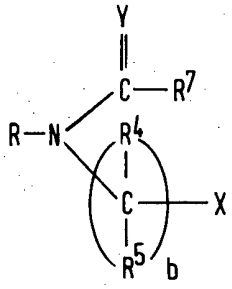
R^7 is C_{1-5} mono- or dihaloalkyl;

Y and Y^1 are oxygen or sulfur and

b is an integer from 1—4 inclusive;

which comprises performing at least one sequence of reaction/separation operations comprising:

(A) reacting a compound of Formula II

II 

with a compound of Formula III

III R^6Y^1H

wherein R, R^4, R^5, R^6, R^7, Y, Y^1 and b are as defined above and X is halogen in the absence of added acid-binders, and

(B) directing an effluent stream of the reaction mixture from Step (A) to a separation zone from which is rapidly removed a complex mixture of by-product HX with said compound of Formula III and a product stream comprising predominantly said compound of Formula I.

2. A process according to Claim 1 wherein said reaction/separation process sequence is repeated a plurality of times to assure complete conversion of said compound of Formula II to said compound of Formula I.

3. A process according to Claim 2 in which said reaction/separation process is carried out in a sequence of two stages which comprises:

(A) reacting in a first reaction zone a compound of Formula II with a compound of Formula III;

(B) directing an effluent stream of the reaction mixture of Step (A) to a first separation zone from which is rapidly removed most of by-product HX as a complex with said compound of Formula III and a product stream comprising predominantly a compound of Formula I and unreacted compound of Formula II;

(C) directing said product stream from said first separation zone to a second reaction zone into which is also introduced an additional quantity of said compound of Formula III to react with said unreacted compound of Formula II;

(D) directing an effluent stream of the reaction mixture of Step (C) to a second separation zone from which is rapidly removed substantially all of the remaining by-product HX as a complex with said compound of Formula III and a product stream comprised of said compound of Formula I and trace impurities.

4. A process according to Claim 3 wherein Step (A) is conducted at a temperature within the range of from about −25 to 125°C.

5. A process according to Claim 3 wherein Step (C) is conducted at temperatures within the range of from about −25 to 175°C.

6. A process according to Claim 3 wherein Steps (B) and (D) are conducted at temperatures and pressures sufficient to separate a complex of the compound of Formula III and hydrogen halide from the effluent streams of Steps (A) and (C).

7. A process according to Claim 3 wherein the compound of Formula III is used in an amount corresponding to a molar ratio of >1:1 relative to the compound of Formula II.

8. A process according to Claim 7 wherein said molar ratio is within the range of about 2—100:1.

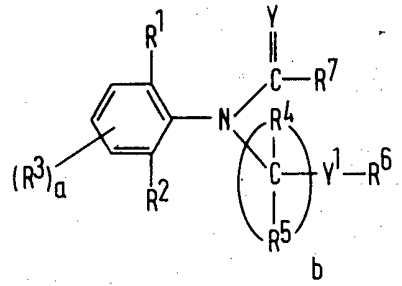
9. A process according to Claim 3 wherein said complex of HX with compound of Formula III from Step (D) is fed to a recovery system from which said compound of Formula III is removed from said hydrogen halide, purified and recycled to Steps (A) and/or (C).

10. A process according to Claim 3 wherein temperatures in Steps (B) and (D) are within the range of 50°C to 175°C and pressures are within the range of 1.0 to 300 mm Hg absolute.

11. A process according to any of Claims 2 to 10 wherein R^6 is hydrogen, C_{1-10} alkyl, alkenyl, alkynyl, alkoxyalkyl, oxoalkyl, C_{3-7} cycloalkyl, lower cycloalkylalkyl or cycloalkenyl, C_{6-12} aryl or aralkyl, $-N(R^8)_2$ wherein R^8 is hydrogen, C_{1-6} alkyl, alkenyl, or alkynyl; or said R^6 members substituted with alkyl, halogen, hydroxy, alkoxy, nitro or cyano, when these radicals are non-reactive with hydrogen under the reaction conditions.

12. A process according to Claim 1 wherein said compounds of Formula I are haloacetanilides of the Formula IV

IV



wherein R^1 and R^2 are independently hydrogen, halogen, C_{1-6} alkyl, haloalkyl, alkoxy or alkoxyalkyl;

R^3 is hydrogen, halogen, C_{1-6} alkyl, haloalkyl, alkoxy, alkoxyalkyl, alkylthio, CN, NO_2 or CF_3 or R^3 may be combined with R^1 or R^2 to form an alkylene chain of up to 4 carbon atoms;

R^4 and R^5 are independently hydrogen, fluorine, C_{1-6} alkyl, haloalkyl, alkoxy or alkoxyalkyl;
R^6, R^7, Y, Y^1 and b are as defined in Claim 1, and
a is zero or an integer from 1—3 inclusive.

13. A process according to Claim 12 wherein in said haloacetanilides

R^1, R^2 and R^6 are C_{1-6} alkyl,
R^4 and R^5 are hydrogen or C_{1-6} alkyl,
R^7 is C_{1-2} monohaloalkyl,
Y and Y^1 are oxygen,
a is zero and
b is 1.

14. A process according to Claim 13 wherein in said haloacetanilides

R^1 and R^2 are ethyl,
R^4 and R^5 are hydrogen,
R^6 is C_{1-6} alkyl and
R^7 is 2-chloromethyl.

15. A process according to Claim 12 wherein in said haloacetanilides

R^1, R^2 and R^6 are C_{1-6} alkyl,
R^4 and R^5 are hydrogen or C_{1-6} alkyl,
R^7 is C_{1-2} monohaloalkyl,
Y and Y^1 are oxygen,
a is zero and
b is 2.

16. A process according to Claim 14 wherein R^6 is methyl.
17. A process according to Claim 14 wherein R^6 is ethyl.
18. A process according to Claim 14 wherein R^6 is a propyl isomer.
19. A process according to Claim 14 wherein R^6 is a butyl isomer.
20. A process according to Claim 19 wherein said butyl isomer is n-butyl.
21. A process for the preparation and recovery of alachlor which comprises performing at least one sequence of reaction/separation operations comprising:

(A) reacting methanol with 2',6'-diethyl-N-chloromethyl)-2-chloroacetanilide at a molar ratio of 2—100:1 at temperatures within the range of from 25°—65°C for a period of from 15—30 minutes in the absence of added acid binders, and
(B) directing an effluent stream of the reaction mixture from Step (A) to a separation zone from which is rapidly removed a complex mixture of HCl and methanol and a product stream comprising predominantly alachlor.

22. A process according to Claim 21 wherein said reaction/separation sequence is repeated a plurality of times to assure substantially complete conversion of 2',6'-diethyl-N-(chloromethyl)-2-chloroacetanilide to alachlor.

23. A process according to Claim 22 which comprises:

(A) reacting in a first reaction zone maintained at 25—65°C methanol with 2',6'-diethyl-N-(chloromethyl)-2-chloroacetanilide at a molar feed ratio of 2—10:1 in the absence of added acid binders for a period of from 15 to 30 minutes;
(B) directing an effluent stream of the reaction mixture of Step (A) to a flash distillation zone maintained at temperatures and pressures within the ranges of 50—100°C and 30—300 mm Hg absolute from which is removed a complex mixture of methanol and most of by-product HCl and a product stream comprising predominantly alachlor and unreacted 2',6'-diethyl-N-(chloromethyl)-2-chloroacetanilide;
(C) directing said product stream from said first separation zone to a second reaction zone maintained at 25—65°C into which is also introduced an

additional quantity of methanol to react with said unreacted 2',6'-diethyl-N-(chloromethyl)-2-chloroacetanilide in an amount corresponding to the amount used in first reaction zone for a period of from 15 to 30 minutes;

(D) directing an effluent stream of the reaction mixture of Step (C) to a second flash distillation zone maintained at temperatures and pressures within the ranges of 50—100°C and 30—300 mm Hg absolute from which is removed a complex mixture comprising methanol and substantially all of the remaining by-product HCl and a product stream comprised of alachlor and trace impurities.

24. A process according to Claim 23 wherein said complex of methanol and HCl from Steps (B) and (D) are combined and fed to a methanol recovery system from which HCl is removed and recovered methanol is purified and recycled to Steps (A) and/or (C).

25. A process according to Claim 24 wherein the residence time of said reaction mixture in said flash distillation zones of Steps (B) and (D) is <0.5 minute.

26. A process according to any of Claims 1 to 20 wherein the rapid removal of by-product HX with said compound of Formula III is achieved by use of a rotary vacuum evaporator.

27. A process according to any of Claims 1 to 20 wherein the rapid removal of by-product HX with said compound of Formula III is achieved by using of a falling film evaporator.

28. A process according to any of Claims 21 to 25 wherein said separation zone or said flash distillation zone or zones comprises a rotary vacuum evaporator.

29. A process according to any of Claims 21 to 25 wherein said separation zone or said flash distillation zone or zones comprises a falling film evaporator.

30. A process for the production of alachlor substantially as hereinbefore described with reference to Example 1.

31. A process for the production of a 2',6'-diethyl-N-(alkoxymethyl) acetanilide substantially as hereinbefore described with reference to any of Examples 2 to 7, 11 and 12.

32. A compound of Formula I that has been produced according to any of Claims 1 to 20, 26 and 27.

32. Alachlor that has been produced by a process according to any of Claims 21 to 25 and 28 to 30.

33. A 2',6'-diethyl-N-(alkoxymethyl) acetanilide that has been produced by a process according to Claim 31.

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