FORM – 2

THE PATENTS ACT, 1970

(39 of 1970)
&
THE PATENTS RULES, 2003

COMPLETE

SPECIFICATION

(See section 10 and rule 13)

SYNTHESIS OF ANILOFOS

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THE FOLLOWING SPECIFICATION PARTICULARLY DESCRIBES THE INVENTION AND THE MANNER IN WHICH IT IS TO BE PERFORMED.

Field of the Disclosure

The present disclosure relates to a process for preparing an Anilofos and its analogues.

Background

Anilofos is chemically known as O, O- dimethyl-S-4-chloro isopropylbenzene carbamoyl -N- dimethyl phosphorothioate, a phosphorodithioate ester herbicide, mainly used in rice fields for controlling annual grass and sedge weeds. Anilofos is a pre-emergence and early post-emergence selective herbicide used for the control of annual grasses, sedges and some broad-leaved weeds in transplanted and direct seeded rice. Anilofos is absorbed by the weeds primarily through the roots and to some extent through newly emerging shoots and young leaves. The mechanism of action of Anilofos lies in acting on the meristematic tissues of weeds that severely affects the cell division and cell elongation.

Various conventional methods have been developed for the synthesis of Anilofos owing to its wide popularity. However, the previously described methods are associated with certain drawbacks such as poor stability and product purity. Further, most of the conventional methods employ huge quantities of expensive reagents that increase the expenditure associated with the processes along with jeopardizing the environmental sanctity.
Therefore, there is felt a need for simple and cost effective process for the preparation of Anilofos with high purity and stability.

Objects

Some of the objects of the present disclosure, which at least one embodiment is adapted to provide, are described herein below:

- It is an object of the present disclosure to provide a process for the preparing Anilofos and its analogues.

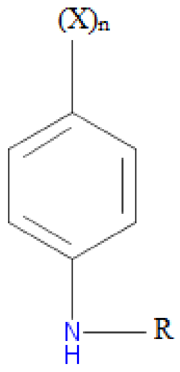
- It is another object of the present disclosure to provide a process for the preparation of anilofos and its analogues, which is rapid, stable, economic and environment friendly.
- It is still another object of the present disclosure to provide a process that gives high yield.
- It is yet another object of the present disclosure to provide a process that yields high purity product.

Other objects and advantages of the present disclosure will be more apparent from the following description which is not intended to limit the scope of the present disclosure.

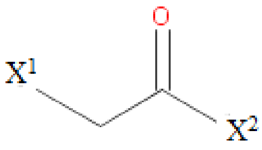
Summary:

The present disclosure provides a simple and economic process for preparing a compound (Anilofos) of Formula 1 and its analogues.

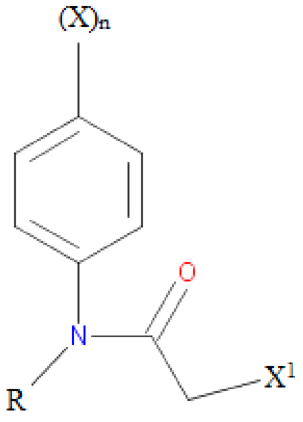
The process comprising the step of i) reacting a compound of Formula 2 and a compound of Formula 3 to obtain a compound of Formula 4;



Formula 2



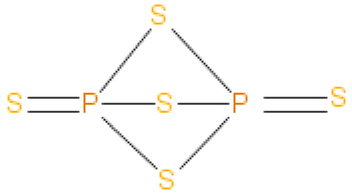
Formula 3



Formula 4

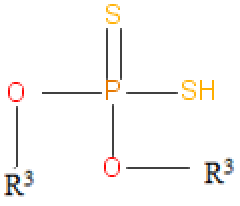
wherein, X^1 and X^2 are selected from the group that includes but is not limited to chlorine, bromine and iodine, preferably chlorine; X is selected from the group that includes but is not limited to chlorine, bromine and iodine, preferably chlorine; n is an integer in the range of 1-5, preferably 1; and R is selected from the group consisting of Hydrogen and branched or un-branched C_1-C_{10} alkyl groups,

ii) alkoxylating phosphorous pentasulfide (P_2S_5) with a compound of Formula 5 to obtain a compound of Formula 6;



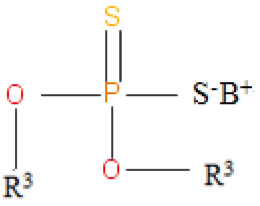
R^3OH

Formula 5



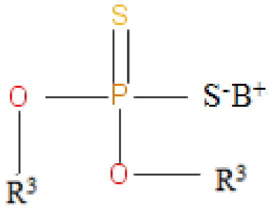
Formula 6

iii) reacting compound of Formula 6 with the base to obtain a compound of Formula 7 (alkoxylated phosphorous pentasulfide base); and

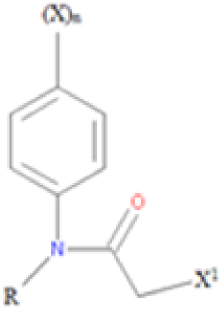


Formula 7

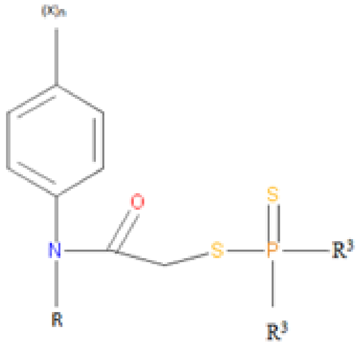
iv) reacting the compound of Formula 4 with alkoxylated phosphorous pentasulfide base of Formula 7 to obtain a compound of Formula 1.



Formula 7



Formula 4



Formula 1

Typically, R^3 is selected from the group that includes but is not limited to linear or branched C_1-C_5 alkyl groups.

Brief decription of drawings:

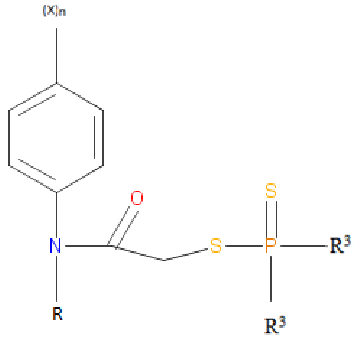
Figure 1 illustrates the schematic represnetation of reactions in accordance with the present disclosure.

Detailed Description

Anilofos (S-[2-[(4-chlorophenyl) (1-methylethyl) amino]-2-oxoethyl] O, O-dimethyl phosphorodithioate) and its analogues are active chemicals of commercial grade herbicide. The previously suggested method provides less stable and low purity anilofos and its analogues. Further, the conventional methods are costly as it employs comparatively high quantities of expensive reagents that increase the cost of the process.

Accordingly, the process in accordance with the present disclosure provides a simple and cost effective for the preparation of anilofos and its analogues that have high purity and stability.

In accordance with the present disclosure there is provided a process for the preparation of a compound of Formula 1. The structure of the compound of Formula 1 is presented herein below.



Formula 1

X in the Formula 1 is selected from the group consisting of chlorine, bromine and iodine, preferably chlorine. n is an integer in the range of 1-2, preferably 1. R is selected from the group consisting of Hydrogen and branched or un-branched C_1-C_{10} alkyl groups. R^3 is independently selected from the group consisting of linear or branched C_1-C_5 alkyl groups.

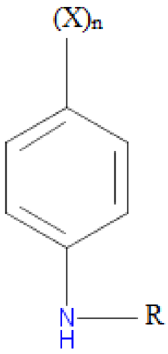
In one embodiment of the present disclosure, the compound of Formula 1 is Anilofos.
In the first step of the process of present disclosure, a compound of Formula 2 is reacted with a compound of Formula 3 to obtain a compound of Formula 4. The reaction is called amidization of the compound of Formula 2. The reaction is carried out at a temperature ranging from 30-80^{o}C.

The compound of Formula 2 used in the process of present disclosure includes but is not limited to 4-chloroisopropyl aniline, 4-bromoisopropyl aniline and 4-iodoisopropyl aniline. Preferably, 4-chloroisopropyl aniline (IPPCA) is employed as compound of Formula 2. The purity of Formula 2 used in the process of present disclosure ranges from 99.0 to 99.9%.

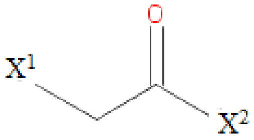
The compound of Formula 3 used in the process of present disclosure includes but is not limited to chloroacetyl chloride, bromoacetyl chloride, iodoacetyl chloride, bromoacetyl boomide, iodoacetyl iodide, bromoacetyl iodide and iodoacetyl bromide. Preferably chloroacetyl chloride is employed as compound of Formula 3. The purity of Formula 3 used in the process of present disclosure ranges from 99.0 to 99.9%.

The reaction scheme is represented in **Figure 1.**

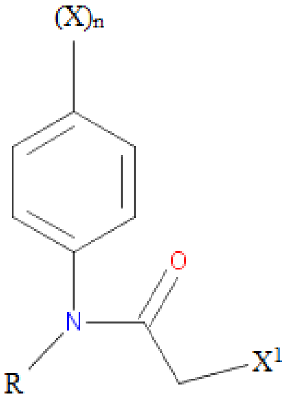
The structures of the compounds of Formula 2, 3 and 4 are presented herein below.



Formula 2



Formula 3



Formula 4

X^1 and X^2 are selected from the group that includes but is not limited to chlorine, bromine and iodine, preferably chlorine. X is selected from the group that includes but is not limited to chlorine, bromine and iodine, preferably chlorine. n is an integer in the range of 1-5, preferably 1. R is selected from the group consisting of Hydrogen and branched or un-branched C_1-C_{10} alkyl groups.

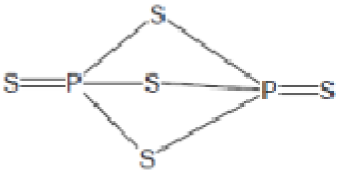
The compound of Formula 4 used in the process of present disclosure includes but is not limited to 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide, 2-bromo-N-(4-chlorophenyl)-N-isopropylacetamide, 2-iodo-N-(4-chlorophenyl)-N-isopropylacetamide, 2-bromo-N-(4-bromophenyl)-N-isopropylacetamide, 2-iodo-N-(4-iodophenyl)-N-isopropylacetamide, 2-bromo-N-(4-iodophenyl)-N-isopropylacetamide and 2-iodo-N-(4-bromophenyl)-N-isopropylacetamide.

The purity of compound of Formula 4 used in the process of present disclosure ranges from 97.0 to 99.0%.

In one embodiment of the present disclosure chloroacetyl chloride (Formula 3) is reacted with 4-chloroisopropyl aniline (Formula 2) at a temperature ranging from 30-80°C to obtain 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide of Formula 4.

In the second step of the process of present disclosure, Phosphorus pentasulfide (P_2S_5) is reacted with a compound of Formula 5 to undergo alkoxylation in the presence of at least one first reaction medium to obtain a compound of Formula 6. The reaction is carried out at a temperature ranging from 10-50°C. The reaction scheme is given in **Figure 1.**

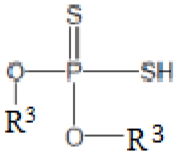
The structures of phosphorous pentasulfide, Formula 5 and Formula 6 are represented herein below:



Phosphorous pentasulfide

R^3OH

Formula 5



Formula 6

R^3 of Formula 5 and Formula 6 is selected from the group that includes but is not limited to linear or branched C_1-C_5 alkyl groups. The compound of Formula 5 of the present disclosure is selected from the group consisting of alcohols containing C_1-C_5 alkyl groups. In one embodiment alcohol (Formula 5) used in the process of present disclosure is methanol. The amount of alcohol used in the process of present disclosure ranging from 4 to 6 moles with respect to moles of P_2S_5.

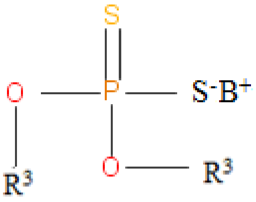
Alcohol (Formula 5) used in the step of alkoxylation is taken in an amount sufficient to react with P_2S_5. This prevents the formation of polysulfide impurities during the reaction which affects the final product yield and purity. In one embodiment, the quantity of the alcohol is more than that required to sufficiently react with P_2S_5. The molar ratio of P_2S_5 and the alcohol used in the process of present disclosure ranges from 1: 4 to 1: 6.

The first reaction medium of the present disclosure is selected from the group consisting of polar and non-polar solvents. The reaction medium includes but is not limited to dichloromethane (DCM), tetrahydrofuran (THF), ethyl acetate, dimethylformamide (DMF), acetone, acetonitrile, dimethyl sulfoxide (DMSO), ethanol, methanol, xylene, benzene, ethylbenzene, hexane, cyclohexane, toluene and mixtures thereof.

The alkoxylated product (Formula 6 - dialkoxy thiophosporic acid) is obtained by the reaction between phosphorous pentasulfide and alcohol at a temperature ranging from 10-50°C upon removal of hydrogen sulfide.

In one embodiment of the present disclosure phosphorous pentasufide is reacted with methanol (Formula 5) at a temperature ranging from 10-50°C to obtain dimethoxy thiophosporic acid (Formula 6).

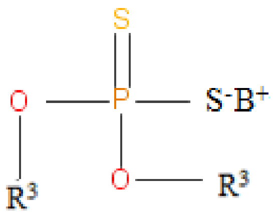
In third step of the process of present disclosure, the compound of Formula 6 obtained in second step of the present disclosure is treated with at least one aqueous base to provide a compound of Formula 7.



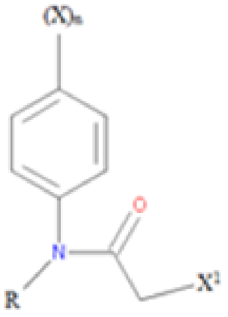
Formula 7

R^3 in Formula 6 and 7 of the present disclosure is selected from the group consisting of linear or branched C_1-C_5 alkyl groups, and B^+ is a cationic part of the base.
The base used in the process of the present disclosure includes but is not limited to ammonia, ammonium hydroxide, sodium hydroxide, and potassium hydroxide. B^+ in the compound of Formula 7 includes but is not limited to $NH_3^{+,}$ Na^+ and K^+.

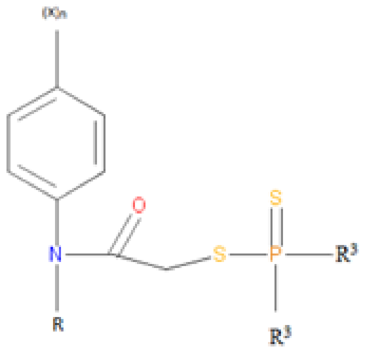
In the fourth step of the process of present disclosure, the compound of Formula 4 of the present disclosure is condensed with Formula 7 of the present disclosure in the presence of at least one second reaction medium to obtain a compound of Formula 1.



Formula 7



Formula 4



Formula 1

The second reaction medium of the present disclosure is selected from polar and non-polar solvents. The second reaction medium includes but is not limited to dichloromethane (DCM), tetrahydrofuran (THF), ethyl acetate, dimethylformamide (DMF), acetone, acetonitrile, dimethyl sulfoxide (DMSO), ethanol, methanol, xylene, benzene, ethylbenzene, hexane, cyclohexane, toluene and mixtures thereof. The first reaction medium and the second reaction medium of the present disclosure may or may not be the same. The step of condensation of the compound of Formula 4 is carried out at a temperature ranging from 20 to 50^{o}C.

The proportion of compound of Formula 4 and the compound of Formula 7 of the present disclosure ranging from 1:1 to 1:1.5. Significantly, the step of condensation is carried out in a shorter time span, as compared to previously known process.

Further, the product obtained in accordance with the process of the present disclosure has more than 85-90 % yields, with purity ranging from 95-99%.

According to the present disclosure, heat precipitation procedure is not carried out during the reaction procedure. Therefore, a potential danger of the decomposition of the product under heat is avoided and hence product yield and quality are improved. The preparation method of herbicide anilofos provided by the present disclosure has advantages of simple process to obtain high product yield with high purity. The process of the present disclosure is safe and hence environment friendly, therefore is suitable for industrial level production.

The present disclosure is further described in light of the following non-limiting examples which are set forth for illustration purpose only and not to be construed for limiting the scope of the disclosure.

Example 1:

Preparation of Formula 4 of the present invention disclosure:

170gm of 4-chloro-isopropyl aniline (IPPCA) was condensed with 124gm of chloroacetyl chloride at 74-75^{o}C in a suitable solvent media to obtain 243gm of 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide.

Preparation of Formula 7 of the present invention disclosure:

1 gm mole of P_2S_5 in 270 ml of xylene was reacted with 5.0 m/m methanol at 44-45^{o}C till total hydrogen sulfide evolved. The dissolved H_2S was vacuum pulled and the first reaction mixture comprising DMTA was neutralized to pH 9.5-10.5 by treating with 8 -10N NaOH to obtain 162-163 gm of sodium salt of DMTA in the form of a solution.

Reaction of Formula 4 and Formula 7:

1.0 gm mole of 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide was charged into a 4-neck RB flask containing 400 ml of n-Hexane with overhead stirring at 28-32^{o}C. Into this mass, 1.2 gram mole of freshly prepared Na-DMTA solution of 3.9N was added over 1 hour maintaining the temperature at 28-32^{o}C. The reaction was maintained at the same temperature under stirring for 15 hours, till anilide content in the reaction mass becomes less than 1.0%. The reaction progress was monitored by HPLC/GLC. The obtained reaction mass was white colored slurry into which 0.1 mole of 8-10N NaOH solution was added and upon addition the slurry was cooled to 25^{o}C and filtered to obtain the product. The filtered product (cake) was washed with water to make it free of alkalinity, followed by 100 ml of n-Hexane wash. The hexane wet cake was dried at 54-55°C under vacuum till constant weight. The yield obtained was 330 gm with 97% of purity.

Example 2:

The compound of Formula 4(2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide) and Formula 7(NH_4-DMTA) was prepared by the method as provided in example 1 except for preparation of Formula 7, ammonia was used as a base to obtain NH_4-DMTA.
1.0 gm mole of 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide was charged into a 4-neck RB flask containing 400 ml of n-Hexane with overhead stirring at 28-32°C. 1.2 gm mole of freshly prepared NH_4-DMTA solution of 3.8N was added in the reaction mixture over 1 hour maintaining temperature at 28-32°C. The stirring was carried out for 18 hours at the same temperature till anilide content in the reaction mass becomes less than 1.0%. The reaction progress was monitored by HPLC/GLC. The obtained reaction mass was a white colored slurry, into which 0.1 mole of 8-10N NaOH solution was added followed by cooling it to 25°C and filtration. The filtered cake was washed with water to make it free of alkalinity followed by 100ml of n-Hexane wash. The hexane wet cake was dried at 54-55°C under vacuum till constant weight. The yield obtained was 305 gm with 96.5% of purity.

Example 3:

The compound of Formula 4(2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide) and Formula 7(Na-DMTA) was prepared by the method as provided in example 1
1.0 gm mole of 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide was charged into a 4-neck RB flask containing 200 ml of n-Hexane with overhead stirring at 28-32°C. Into this mass, 1.2 gm mole of freshly prepared Na-DMTA solution of 3.9N was added over 1 hour maintaining a temperature ranging from 28-32°C. The reaction was stirred at the same temperature for 12 hours, till anilide content in the reaction mass becomes less than 1.0 %. The reaction progress was monitored by HPLC/GLC. The obtained reaction mass was a white colored slurry into which 0.1mole of 8-10N NaOH

solution and 200ml of n-Hexane was added and then further cooled to 22-23°C followed by filtering the slurry. The filtered cake was washed with water to make it free of alkalinity followed by 100ml of n-Hexane wash. The hexane wet cake was dried at 54-55°C under vacuum till constant weight. The yield obtained was 320gm with 96.7% of purity.

Example 4:

The compound of Formula 4(2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide) and Formula 7(Na-DMTA) was prepared by the method as provided in **example** 1.
1.0 gm mole of 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide was charged into a 4-neck RB flask containing 100 ml of cyclohexane with overhead stirring at 28-35°C. 1.2 gm mole of freshly prepared Na-DMTA solution of 4.1N was added in the reaction mixture over 1 hour maintaining at a temperature ranging from 28-32°C. The stirring of the reaction was carried out at the same temperature for 18 hours, till anilide content in the reaction mass becomes less than 1.0 %. The reaction progress was monitored by HPLC/GLC. The obtained reaction mass was a white colored slurry into which 0.1 mole of 8-10N NaOH solution was added and then cooled to 18-20°C and filtered. The filtered cake was washed with water to make it free of alkalinity followed by 50ml of cyclohexane wash. The hexane wet cake was dried at 54-55°C under vacuum till constant weight. The yield obtained was 322 gm with 97% of purity.

Example 5:

The compound of Formula 4 i. e 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide and Formula 7(NH_4-DMTA) was prepared by the method as provided in example 3.
1.0 gram mole of 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide was charged into a 4-neck RB flask containing 100ml of cyclohexane with overhead stirring at 28-35°C to obtain a mass. 1.2gram mole of freshly prepared NH_4-DMTA solution of 3.8N was added in the obtained mass over 1 hour maintaining temperature at 28-32°C. The

stirring of the reaction was maintained at a temperature of 28-35^{o}C for 17 hours, till anilide content in the reaction mass becomes less than 1.0 %. The reaction was monitored by HPLC/GLC. The obtained reaction mass was a white colored slurry, into which 0.1 mole of 8-10N NH_4OH solution was added and then cooled to a temperature of 18-20^{o}C. After cooling, the slurry was filtered through Buchner funnel. The filtered cake was washed with water to make it free of alkalinity followed by 50 ml of cyclohexane wash. Cake was dried at 54-55^{o}C under vacuum till constant weight. The yield obtained was 215 gm with 96.6% of purity.

The examples 1-5 are summarized in the Table 1 as given below:

Example no	**Formula 4**	**Formula 7**	**Second reaction medium**	**Reaction time**	**Purity of the compound of Formula 1**
Example 1	2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide	Na-DMTA	n-Hexane	15 hours	97%
Example 2	2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide	NH4-DMTA	n-Hexane	18 hours	96.50%
Example 3	2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide	Na-DMTA	n-Hexane	12 hours	96.70%
Example 4	2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide	Na-DMTA	Cyclohexane	18 hours	97%
Example 5	2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide	NH4-DMTA	Cyclohexane	17 hours	96.60%

Technical advances

-The present disclosure provides simple and economic process for preparing anilofos and its analogues.

-Product obtained from the process of the present disclosure has yielded more than 90%.

-Product obtained from the process of the present disclosure has purity more than 95%.

-The present disclosure provides a stable process for preparing an anilofos and its analogues.

The exemplary embodiments herein quantify the benefits arising out of this disclosure and the various features and advantageous details thereof are explained with reference to the non-limiting embodiments in the description. Descriptions of well-known components and processing techniques are omitted so as to not unnecessarily obscure the embodiments herein. The examples used herein are intended merely to facilitate an understanding of ways in which the embodiments herein may be practiced and to further enable those of skill in the art to practice the embodiments herein. Accordingly, the examples should not be construed as limiting the scope of the embodiments herein.

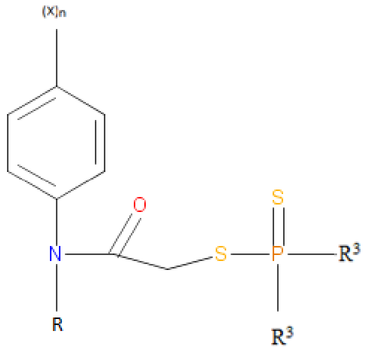
The foregoing description of the specific embodiments will so fully reveal the general nature of the embodiments herein that others can, by applying current knowledge, readily modify and/or adapt for various applications such specific embodiments without departing from the generic concept, and, therefore, such adaptations and modifications should and are intended to be comprehended within the meaning and range of equivalents of the disclosed embodiments. It is to be understood that the phraseology or terminology employed herein is for the purpose of description and not of limitation. Therefore, while the embodiments herein have been described in terms of preferred embodiments, those skilled in the art will recognize that the embodiments herein can be practiced with modification within the spirit and scope of the embodiments as described herein.

Any discussion of documents, acts, materials, devices, articles and the like that has been included in this specification is solely for the purpose of providing a context for the disclosure. It is not to be taken as an admission that any or all of these matters form a part of the prior art base or were common general knowledge in the field relevant to the disclosure as it existed anywhere before the priority date of this application.

While considerable emphasis has been placed herein on the particular features of this disclosure, it will be appreciated that various modifications can be made, and that many changes can be made in the preferred embodiments without departing from the principles of the disclosure. These and other modifications in the nature of the disclosure or the preferred embodiments will be apparent to those skilled in the art from the disclosure herein, whereby it is to be distinctly understood that the foregoing descriptive matter is to be interpreted merely as illustrative of the disclosure and not as a limitation.

WE CLAIM:

1. A process for preparing a compound of Formula 1,



wherein,

X is selected from the group consisting of chlorine, bromine and iodine,

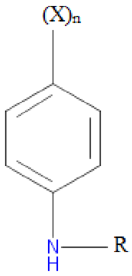
n is an integer in the range of 1 to 2,

R is selected from the group consisting of hydrogen and branched or un-branched C_1-C_{10} alkyl groups, and

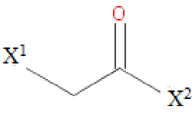
R^3 is selected from the group consisting of linear or branched C_1-C_5 alkyl groups,

said process comprising the following steps:

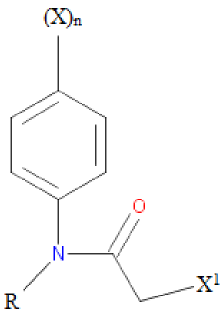
i. amidizing a compound of Formula 2, by reacting said compound of Formula 2 and a compound of Formula 3 to obtain a compound of Formula 4;



Formula 2



Formula 3



Formula 4

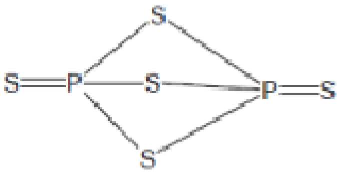
wherein,

X, X^1 and X^2 are independently selected from the group consisting of chlorine, bromine and iodine;

n is an integer in the range of 1 to 2; and

R is selected from the group consisting of hydrogen and branched or un-branched C_1-C_{10} alkyl groups,

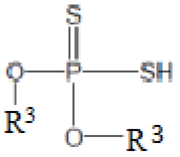
ii. alkoxylating phosphorous pentasulfide (P_2S_5) by reacting phosphorous pentasulfide and a compound of Formula 5 in the presence of at least one first reaction medium to obtain a compound of Formula 6;



Phosphorous pentasulfide

R^3OH

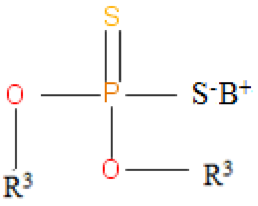
Formula 5



Formula 6

wherein, R^3 is selected from the group consisting of linear or branched C_1-C_5 alkyl groups,

iii. basifying the compound of Formula 6 by adding at least one base to obtain a compound of Formula 7; and



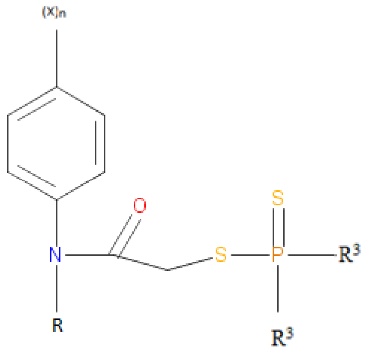
Formula 7

wherein, R^3 is selected from the group consisting of linear or branched C_1-C_5 alkyl groups, and

B^+ is a cationic part of the base,

iv. condensing the compound of Formula 7 and the compound of Formula 4 in the presence of at least one second reaction medium to obtain a compound of Formula 1.

2. The process as claimed in claim 1 wherein the compound of Formula 1 is represented by



wherein,

X is chlorine,

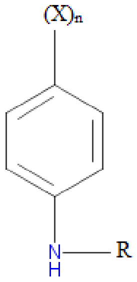
n is an integer 1,

R is selected from the group consisting of hydrogen and branched or un-branched C_1-C_3 alkyl groups, and

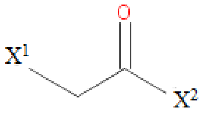
R^3 is selected from the group consisting of linear or branched C_1-C_3 alkyl groups,

and said process comprising the following steps:

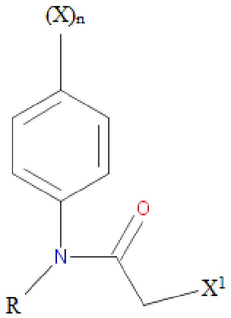
i. amidizing a compound of Formula 2, by reacting said compound of Formula 2 and a compound of Formula 3 to obtain a compound of Formula 4;



Formula 2



Formula 3



Formula 4

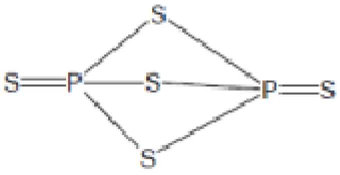
wherein,

X, X^1 and X^2 are chlorine,

n is an integer, and

R is selected from the group consisting of hydrogen and branched or un-branched C_1-C_3 alkyl groups,

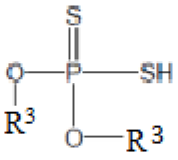
ii. alkoxylating phosphorous pentasulfide (P_2S_5) by reacting phosphorous pentasulfide and a compound of Formula 5 in the presence of at least one first reaction medium to obtain a compound of Formula 6;



Phosphorous pentasulfide

R^3OH

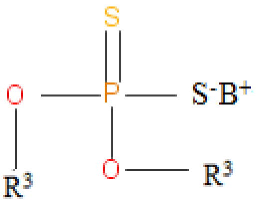
Formula 5



Formula 6

wherein, R^3 is selected from the group consisting of linear or branched C_1-C_3 alkyl groups,

iii. basifying the compound of Formula 6 by adding a base selected from the group consisting of sodium hydroxide and ammonium hydroxide to obtain a compound of Formula 7; and



Formula 7

wherein, R^3 is selected from the group consisting of linear or branched C_1-C_3 alkyl groups, and

B^+ is selected from the group consisting of Na^+ and $NH4^+$,

iv. condensing the compound of Formula 7 and the compound of Formula 4 in the presence of at least one second reaction medium to obtain a compound of Formula 1.

3. The process as claimed in claim 1, wherein the step of amidizing is carried out at a temperature ranging from 30 to 80 °C.

4. The process as claimed in claim 1, wherein the step of alkoxylating is carried out at a temperature ranging from 10 to 50 ^{o}C.

5. The process as claimed in claim 1, wherein the base is selected from the group consisting of ammonia, ammonium hydroxide, sodium hydroxide and potassium hydroxide; the cation B^{+} is selected from the group consisting of NH4^{+}, Na^{+} and K$^{+;}$ and the base is in the form of an aqueous solution.

6. The process as claimed in claim 1, wherein the compound of Formula 1 is anilofos, the compound of Formula 2 is 4-chloroisopropyl aniline (IPPCA), the compound of Formula 3 is chloroacetyl chloride, the compound of Formula 4 is 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide, the compound of Formula 5 is methanol, the compound of Formula 6 is dimethoxy thiophosphric acid (DMTA) and the compound of Formula 7 is sodium salt of dimethoxy thiophosphric acid (DMTA).

7. The process as claimed in claim 1, wherein the first reaction medium and the second reaction medium are independently selected from the group consisting of dichloromethane (DCM), tetrahydrofuran (THF), ethyl acetate, dimethylformamide (DMF), acetone, acetonitrile, dimethyl sulfoxide (DMSO), ethanol, methanol, xylene, benzene, ethylbenzene, hexane, cyclohexane, toluene and mixtures thereof.

8. The process as claimed in claim 1, wherein the molar ratio of the compound of Formula 2 to the compound of Formula 3 ranges from 1:1 to 1:1.2.

9. The process as claimed in claim 1, wherein the molar ratio of P_2S_5 and the compound of Formula 5 ranges from 1: 4 to 1: 6.

10. The process as claimed in claim 1, wherein the molar ratio of the compound of Formula 4 to the compound of Formula 7 ranges from 1:1 to 1:1.5.

11. The process as claimed in claim 1, wherein the yield of the compound of Formula 1 is at least 90% and the purity is greater than 96%.

Dated this 23rd day of September, 2014

MOHAN DEWAN
OF R. K. DEWAN & CO.
APPLICANTS' PATENT ATTORNEY

ABSTRACT

The present disclosure relates to a simple and cost effective process for preparing a anilofos and its analogues.

NAME : GHARDA CHEMICALS LIMITED ONE SHEET
NO. : 3091/MUM/2013

COMPLETE SPECIFICATION

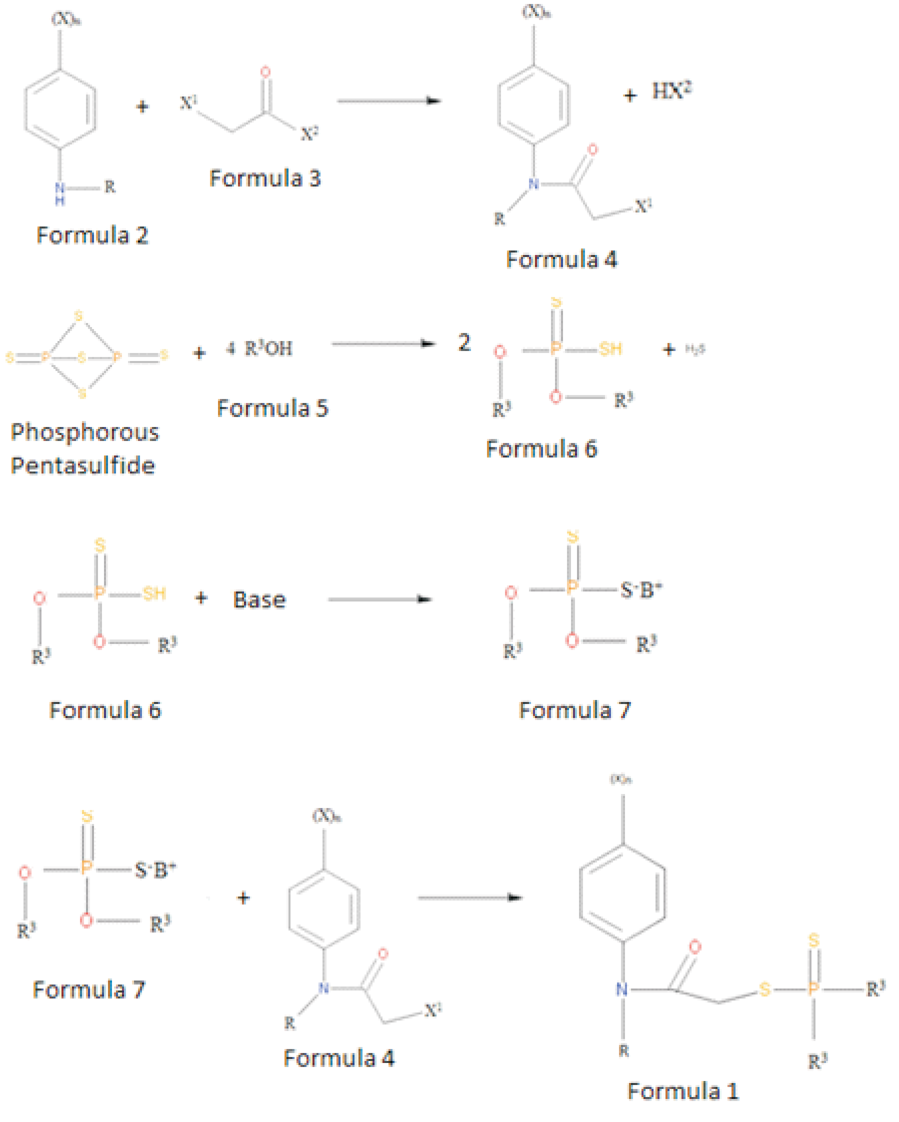


FIGURE 1

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Field of the Disclosure

The present disclosure relates to a method for the preparation of Anilofos.

Background

Anilofos is a pre-emergence and early post-emergence selective herbicide used for the control of annual grasses, sedges and some broad-leaved weeds in transplanted and direct seeded rice. Anilofos is absorbed by the weeds primarily through the roots and to some extent through newly emerging shoots and young leaves. The mechanism of action of Anilofos lies in acting on the meristematic tissues of weeds that severely affects the cell division and cell elongation.

Various methods have been developed for the synthesis of Anilofos owing to its wide popularity. However, the prior art methods are often associated with certain drawbacks such as poor stability and product purity. Further, most of the conventional methods employ huge quantities of expensive reagents that increase the expenditure associated with the processes along with jeopardizing the environmental sanctity.

The inventors of the present disclosure, therefore, envisage a process for the preparation of Anilofos that overcomes most of the disadvantages associated with the prior art processes.

Objects

Some of the objects of the present disclosure, which at least in one embodiment is adapted to provide, are described herein below:

It is an object of the present disclosure to provide a process for the preparation of Anilofos.

It is another object of the present disclosure to provide a process for the preparation of Anilofos, which is rapid, stable, economic and environment friendly.

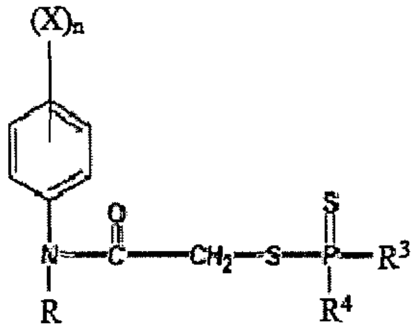
It is still another object of the present disclosure to provide a high yielding process for the preparation of Anilofos.

It is yet another object of the present disclosure to provide Anilofos with high purity.

Other objects and advantages of the present disclosure will be more apparent from the following description which is not intended to limit the scope of the present disclosure.

Detailed Description

The present disclosure provides a process for the preparation of a compound of Formula 1 that includes but is not limited to, initially, condensing a compound of Formula 2 with compound of Formula 3 to obtain a compound of Formula 4. The step of reacting is carried out at a temperature ranging between 30 and 70 °C.



Formula 1

The structure of the compound of Formula 1 is presented hereinabove wherein:

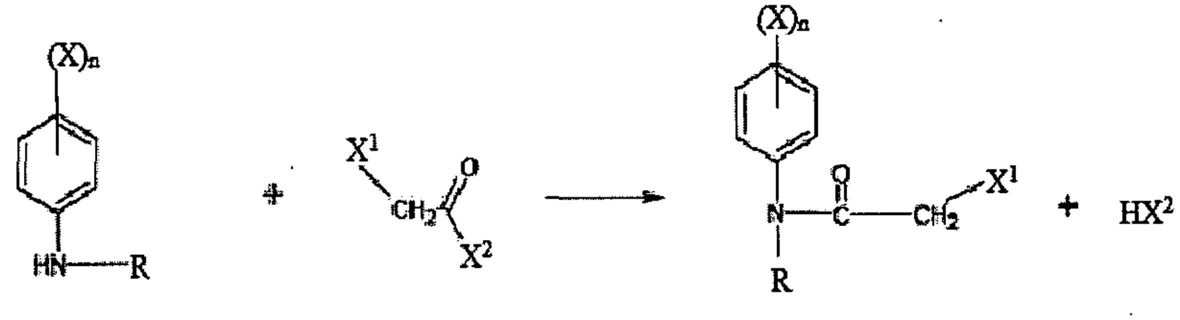
- X is selected from the group that includes but is not limited to Cl, Br and I;

- n is an integer in the range of 1-5;

- R is selected from the group that includes but is not limited to H and branched or unbranched C_1-C_{10} alkyl groups; and

- R^3 and R^4 are independently selected from the group that includes but is not limited to linear or branched C_1-C_5 alkyl groups.

In one embodiment, the compound of Formula 1 is Anilofos.



Formula 2 Formula 3 Formula 4

The structures of the compounds of Formula 2, 3 and 4 are presented hereinabove, wherein:

- X^1 and X^2 are independently selected from the group that includes but is not limited to Cl, Br and I;

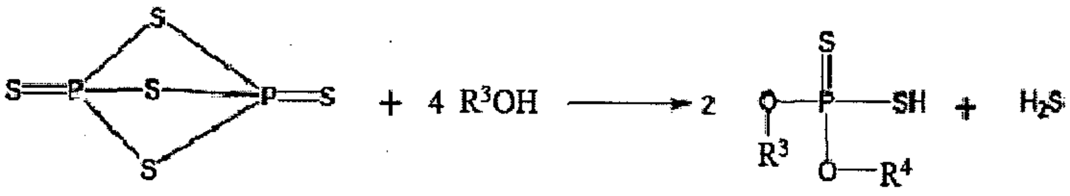
- X is selected from the group that includes but is not limited to Cl, Br and I;

- n is an integer in the range of 1-5; and

- R is selected from the group that includes but is not limited to H and branched or un-branched C_1-C_{10} alkyl groups.

In one embodiment, the compound of Formula 2 is 4-chloroisopropyl aniline (IPPCA). In another embodiment, the compound of Formula 3 is chloroacetyl chloride and yet another embodiment, the compound of Formula 4 is 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide.

Next, phosphorus pentasulfide (P_2S_5) is reacted with at least one alcohol, R^3OH, (represented by Formula 5) at a temperature ranging between 10.0 °C and 50.0 °C in the presence of at least one first reaction medium to provide a first reaction mixture comprising an acid, represented by Formula 6.



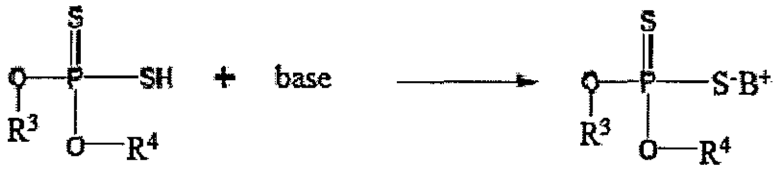
Formula 5

Formula 6

R^3 and R^4 are independently selected from the group that includes but is not limited to linear or branched C_1-C_5 alkyl groups. In one embodiment, the alcohol, represented by

Formula 5, is methanol. In another embodiment, the acid, represented by Formula 6, is dimethoxy thiophosporic acid (DMTA). The alcohol used in the present step is taken in an amount sufficient to react with P_2S_5. This prevents the formation of polysulfide impurities during the reaction which affects the final product yield and purity. In one embodiment, the quantity of the alcohol is more than that required to sufficiently react with P_2S_5. Typically, P_2S_5 and the alcohol are taken in a ratio ranging between 1.0: 4.0 and 1.0: 6.0. The first reaction medium of the present disclosure may be a polar or a non-polar solvent and includes but is not limited to dichloromethane (DCM), tetrahydrofuran (THF), ethyl acetate, dimethylformamide (DMF), acetone, acetonitrile, dimethyl sulfoxide (DMSO), ethanol, methanol, xylene, benzene, ethylbenzene, hexane, cyclohexane and toluene.

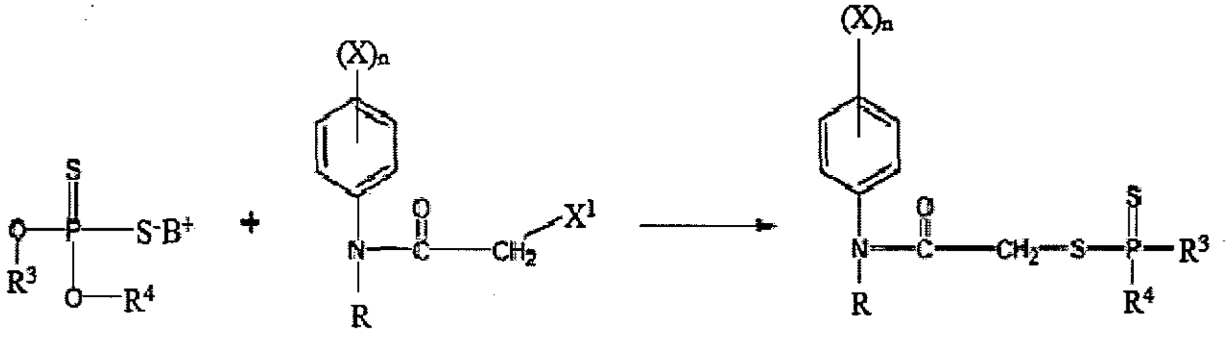
The first reaction mixture comprising the acid, represented by Formula 6, is then treated with at least one aqueous base to provide a second reaction mixture comprising a salt of the acid (compound of Formula 7).



Formula 6 **Formula 7**

wherein B^+ is a cationic part of the base. The base of the present disclosure includes but is not limited to ammonia, ammonium hydroxide, sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, lithium hydroxide, rubidium hydroxide, caesium hydroxide, francium hydroxide, beryllium hydroxide, strontium hydroxide, barium hydroxide and radium hydroxide. Therefore, B in the compound of Formula 7 is selected from the group that includes but is not limited to NH_3, Li, Na, K, Rb, Cs, Fr, Be, Mg, Ca, Sr, Ba and Ra. The second reaction mixture, typically existing in two phases, is subjected to layer separation, after which the separated aqueous layer comprising the salt of the acid (compound of Formula 7) is used further in the process.

The separated aqueous layer of the second reaction mixture comprising the salt of the acid (compound of Formula 7) is co-condensed with the compound of Formula 4 in the presence of water and optionally, at least one second reaction medium to provide the compound of Formula 1.



Formula 7

Formula 4

Formula 1

In one embodiment the step of co-condensation is carried out in the presence of both water and the second reaction medium. In another embodiment, the step of co-condensation is carried out only in the presence of water. The second reaction medium of the present disclosure may be a polar or a non-polar solvent and includes but is not limited to dichloromethane (DCM), tetrahydrofuran (THF), ethyl acetate, dimethylformamide (DMF), acetone, acetonitrile, dimethyl sulfoxide (DMSO), ethanol, methanol, xylene, benzene, ethylbenzene, hexane, cyclohexane and toluene. The first and the second reaction medium of the present disclosure may or may not be the same. The step of condensation with the compound of Formula 4 is carried out at a temperature ranging between 20 and 50 °C. In one embodiment, the separated aqueous layer comprising the salt of the acid (compound of Formula 7) is added in the compound of Formula 4. In another embodiment, the compound of Formula 4 is added to the separated aqueous layer the salt of the acid (compound of Formula 7). Typically, the compound of Formula 4 and the salt of the acid (compound of Formula 7) are taken in an amount ranging between 1:1 and 1:1.5. Significantly, the step of co-condensation is carried out in a shorter time span, as compared to the prior art process. Further, the product obtained in accordance with the process of the present disclosure has more than 90 % yield, with purity greater than 96%. Even further, the reaction conversion is greater than 99%.

The present disclosure is further described in light of the following non-limiting examples which are set forth for illustration purpose only and not to be construed for limiting the scope of the disclosure.

Example 1: Preparation of Anilofos according to the process of the present disclosure

170 g of 4-chloro-isopropyl aniline (IPPCA) was condensed with 124.0 g of chloroacetyl chloride at 30-75 °C to obtain 243.0 g of 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide.

1.0 gram mole of P_2S_5 in 270 ml of xylene was reacted with 5.0 m/m methanol at 20-40 °C till total hydrogen sulfide evolved. The dissolved H_2S was vacuum pulled and the first reaction mixture comprising DMTA was neutralized to 9.0-10.0 pH by treating with 8.0-10.0 N NaOH to obtain 162-163 g of sodium salt of DMTA in the form of a solution. The sodium salt of DMTA was then condensed with 208.0 g of 2-chloro-N-(4-chlorophenyl)-N-isopropylacetamide at 28-32 °C in the presence of 200 ml of hexane to obtain 280.0 g of Anilofos (96-98 % purity).

The embodiments herein and the various features and advantageous details thereof are explained with reference to the non-limiting embodiments in the description. Descriptions of well-known components and processing techniques are omitted so as to not unnecessarily obscure the embodiments herein. The examples used herein are intended merely to facilitate an understanding of ways in which the embodiments herein may be practiced and to further enable those of skill in the art to practice the embodiments herein. Accordingly, the examples should not be construed as limiting the scope of the embodiments herein.

The foregoing description of the specific embodiments will so fully reveal the general nature of the embodiments herein that others can, by applying current knowledge, readily modify and/or adapt for various applications such specific embodiments without departing from the generic concept, and, therefore, such adaptations and modifications should and are intended to be comprehended within the meaning and range of equivalents of the disclosed embodiments. It is to be understood that the phraseology or terminology employed herein is for the purpose of description and not of limitation. Therefore, while the embodiments herein have been described in terms of preferred embodiments, those skilled in the art will recognize that the embodiments herein can be practiced with modification within the spirit and scope of the embodiments as described herein.

Any discussion of documents, acts, materials, devices, articles and the like that has been included in this specification is solely for the purpose of providing a context for the disclosure. It is not to be taken as an admission that any or all of these matters form a part of the prior art base or were common general knowledge in the field relevant to the disclosure as it existed anywhere before the priority date of this application.

While considerable emphasis has been placed herein on the particular features of this disclosure, it will be appreciated that various modifications can be made, and that many changes can be made in the preferred embodiments without departing from the principles of the disclosure. These and other modifications in the nature of the disclosure or the preferred embodiments will be apparent to those skilled in the art from the disclosure herein, whereby it is to be distinctly understood that the foregoing descriptive matter is to be interpreted merely as illustrative of the disclosure and not as a limitation.

Dated this 27th day of September, 2013

Dr. Mohan Dewan

Of R. K. Dewan & Co.

Applicants' Patent Attorney