(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
6 February 2014 (06.02.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/021707 A1

(51) International Patent Classification:
C07C 241/04 (2006.01) *C07C 243/16* (2006.01)

(21) International Application Number:
PCT/MY2013/000142

(22) International Filing Date:
31 July 2013 (31.07.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PI 2012003471 31 July 2012 (31.07.2012) MY

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

WO 2014/021707 A1

(54) Title: A PROCESS TO PRODUCE HYDRAZIDE DERIVATIVES

(57) Abstract: The present invention provides a process to produce hydrazide derivatives wherein the process includes steps of dissolving hydrazide in a solvent to form a mixture, stirring the mixture, adding a reactant, allowing reaction in the mixture to form hydrazide derivatives, allowing formation of solid precipitate and separating the solid precipitate from the mixture.

A PROCESS TO PRODUCE HYDRAZIDE DERIVATIVES

FIELD OF INVENTION

The present invention relates to a process to produce hydrazide derivatives.

BACKGROUND OF INVENTION

In recent years, emphasis on a variety of hyrazide derivatives has increased due to diverse applications in pharmaceutical products, detergent as well as in oil and gas industries. Toliwal *et al.* in 2009 reported that triazole derivatives obtainable from hydrazide exhibit corrosion inhibition, antibacterial and insecticidal activities. Most of corrosion inhibitors are generally toxic and generate health hazards. In 2008, Shanbhag and co-workers found that hydrazide derivatives with heterocyclic compounds are non-toxic as corrosion inhibitor.

Various ways have been employed in the past to synthesize hydrazide derivatives. US Patent No.5300688 and US Patent No.4985461 taught methods to produce hydrazide derivatives using volatile chemical compounds as starting sources. However, these methods disclosed a drawback which is not conducive for the environment. Efforts for a better and more eco-friendly way of producing hydrazide derivatives are being amplified, for example, using a source from vegetable oils.

Accordingly, a need still exists for a process to produce hydrazide derivatives from reaction of hydrazides of vegetable oils with acyl halides for a use as corrosion inhibitors and anti-friction.

SUMMARY OF INVENTION

The present invention relates to a process to produce hydrazide derivatives from reaction of hydrazides of vegetable oils with acyl halides, particularly for a use as corrosion inhibitors and anti-friction.

The present invention provides a process to produce hydrazide derivatives wherein the process includes steps of:

i) dissolving hydrazide in a solvent to form a mixture;
ii) stirring the mixture;
iii) adding a reactant into the mixture;
iv) allowing reaction in the mixture to form hydrazide derivatives;
v) allowing formation of solid precipitate containing hydrazide derivatives; and
vi) separating the solid precipitate from the mixture.

These and other objects of the present invention will become more readily apparent from the detailed description given hereafter. However, it should be understood that while embodiments and examples of the present invention have been illustrated and described, it is not intended that these embodiments and examples illustrate and describe all possible forms of the present invention. Rather, words used in the specification are words of description rather than limitation and various changes may be made without departing from the scope of the invention.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

It should be noted that the following detailed description is directed to a process for producing hydrazide derivatives. More particularly, an object of the present invention is to provide a process for producing hydrazide derivatives, for example, adipoyl di-fatty hydrazide, from reaction of hydrazides of vegetable oil and acyl halides in organic solvent.

Firstly hydrazide was dissolved in organic solvent medium. The organic solvent can be polar or non polar. Preferably, the organic solvent used in invention is chloroform in a ratio of 1:150 (w/v). Next, the mixture of hydrazide in the organic solvent is stirred at a temperature ranging from 20°C to 27°C and for a period from 1 hour to 3 hours. Then, following step was adding a reactant into the mixture to allow reaction forming hydrazide derivatives. The mixture is then stirred at a temperature ranging from 20°C to 27°C and for a period from 5 to 30 minutes to allow formation of solid precipitate containing hydrazide derivatives. Lastly, filtration was conducted to separate the solid precipitate from the mixture.

Hydrazides made from oil or fat can be employed in the disclosed process for producing the hydrazide derivatives. For example, hydrazide made from palm oil, palm olein, palm stearin, soybean oil, coconut oil, groundnut oil, safflower oil, linseed oil, corn oil, sunflower oil, olive oil, canola oil, cottonseed oil, rapeseed oil, tung oil, fish oil, lard, tallow and any derivatives thereof such as fatty acid methyl ester. Preferably, hydrazides were synthesized from refined, bleached and deodorized (RBD) palm olein and hydrazine monohydrate at pH 12 by way of enzymatic route as taught in the Malaysian patent application PI 2011005479.

In another embodiment, hydrazide used in the invention was produced by reacting refined bleached and deodorized palm olein with hydrazine monohydrate at pH 12 using an enzymatic route. Alternatively, hydrazide can be obtained from the market commercially.

The reactant used in the invention is preferably, but not limiting to, acid chloride or acid dichloride. Typically, the acid chloride or acid dichloride used in this invention includes adipoyl dichloride, terephthaloyl dichloride, hexanoyl chloride and octanoyl chloride. Reaction is carried out at room temperature and mole ratio of hydrazide of vegetable oil to acid chloride is preferably 1:1 or hydrazide of vegetable oil to acid dichloride is 1:0.5.

The following examples further illustrate but by no means limit the scope of present invention:

Example 1: RBD palm olein

100 g of RBD palm olein was discharged into 2-L jacketed glass reactor (equipped with a circulating water bath to control temperature, a chiller and condenser to prevent solvent evaporation and a thermocouple to monitor temperature of the reaction) containing 400 mL of n-hexane. Accordingly, 122.5 g of hydrazine monohydrate at pH 12 was added into the reactor. The temperature of the mixture was set at 40°C. Once the temperature of the mixture reached the set temperature, the desired amount of enzyme (Lipozyme RMIM) was added into the reaction mixture. The stirring speed was set at 400 rpm and the reaction was run for 20 hours. After 20 hours of reaction, a white milky paste was discharged from the reactor. A 1-L beaker containing the discharged product was heated at 60 to 80°C in the presence of ethanol to separate the product from the enzyme. A hot liquid mixture was left to cool for at least three hours at ambient temperature at 28°C for crystallization process. Finally, a white paste product was formed. Before drying under vacuum, about 300 to 400 mL of ethanol was added into the white paste product to ease filtration process. After drying, a white-solid hydrazide is obtained. The conversion of fatty acid to fatty hydrazide is 99%.

Example 2: Soya bean oil

100 g of soya bean oil was discharged into 2-L jacketed glass reactor (equipped with a circulating water bath to control temperature, a chiller and condenser to prevent solvent evaporation and a thermocouple to monitor temperature of the reaction) containing 400 mL of n-hexane. Accordingly, 112.3 g of hydrazine monohydrate was added into the reactor. The temperature of the mixture was set at 40°C. Once the temperature of the mixture reached the set temperature, the desired amount of enzyme (Lipozyme RMIM) was added into the reaction mixture. The stirring speed was set at 400 rpm and the reaction was run for 20 hours. After 20 hours of reaction, a white milky paste was discharged from the reactor. A 1-L beaker containing the discharged product was heated at 60 to 80°C in the presence of ethanol to separate the product from the enzyme. A hot liquid mixture was left to cool for at least three hours at ambient temperature (28°C) for crystallization process. Finally, a white paste product was formed. Before drying under

vacuum, about 300 to 400 mL of ethanol was added into the white paste product to ease filtration process. After drying, a white-solid hydrazide is obtained. The conversion of fatty acid to fatty hydrazide is 97%.

Example 3: Adipoyl dichloride

Hydrazide of RBD palm olein (0.56 g, 2.0 mmol) was charged into 250 ml reaction vessel and chloroform (84 ml) was charged into the same vessel. The hydrazide of vegetable oil was dissolved in chloroform or hexane, and the mixture was stirred throughout the reaction. The reaction temperature was kept at room temperature (25°C). Adipoyl dichloride (0.15 ml, 1.0 mmol) was added into the reaction mixture. The reaction mixture was stirred for 30 minutes at room temperature. After 30 minutes, some precipitates formed were filtered off. The collected weight of the precipitates was 0.72 g and percentage of yield was 63%. The product was an off-white solid at room temperature.

Example 4: Terephthaloyl dichloride

Hydrazide of RBD palm olein (0.56 g, 2.0 mmol) was charged into 250 ml reaction vessel and chloroform (84 ml) was charged into the same vessel. The hydrazide of vegetable oil was dissolved in chloroform or hexane, and the mixture was stirred throughout the reaction. The reaction temperature was kept at room temperature (25°C). Terephthaloyl dichloride (0.20 g, 1.0 mmol) was added into the reaction mixture. The reaction mixture was stirred for 30 minutes at room temperature. After 30 minutes, some precipitates formed were filtered off. The collected weight of the precipitates was 0.70 g and percentage of yield was 53%. The product was an off-white solid at room temperature.

Example 5: Hexanoyl chloride

Hydrazide of RBD palm olein (0.56 g, 2.0 mmol) was charged into 250 ml reaction vessel and chloroform (84 ml) was charged into the same vessel. The hydrazide of vegetable oil was dissolved in chloroform or hexane, and the mixture was stirred throughout the reaction. The reaction temperature was kept at room temperature (25°C). Hexanoyl chloride (0.28 ml, 2.0 mmol) was added into the reaction mixture. The reaction mixture

was stirred for 30 minutes at room temperature. After 30 minutes, some precipitates formed were filtered off. The collected weight of the precipitates was 0.49 g and percentage of yield was 36%. The product was an off-white solid at room temperature.

Example 6: Octanoyl chloride

Hydrazide of vegetable oil RBD palm olein (0.56 g, 2.0 mmol) was charged into 250 ml reaction vessel and chloroform (84 ml) was charged into the same vessel. The hydrazide of vegetable oil was dissolved in chloroform or hexane, and the mixture was stirred throughout the reaction. The reaction temperature was kept at room temperature (25°C). Octanoyl chloride (0.35 ml, 2.0 mmol) was added into the reaction mixture. The reaction mixture was stirred for 30 minutes at room temperature. After 30 minutes, some precipitates formed were filtered off. The collected weight of the precipitates was 0.58 g and percentage of yield was 65%. The product was an off-white solid at room temperature.

While embodiments and examples of the present invention have been illustrated and described, it is not intended that these embodiments and examples illustrate and describe all possible forms of the present invention. Rather, words used in the specification are words of description rather than limitation and various changes may be made without departing from the scope of the invention.

CLAIMS

1. A process to produce hydrazide derivatives wherein the process includes steps of:
   i) dissolving hydrazide in a solvent to form a mixture;
   ii) stirring the mixture;
   iii) adding a reactant into the mixture;
   iv) allowing reaction in the mixture to form hydrazide derivatives;
   v) allowing formation of solid precipitate containing hydrazide derivatives; and
   vi) separating the solid precipitate from the mixture.

2. A process as claimed in claim 1 wherein the hydrazide in step (i) is obtained from palm oil, palm olein, palm stearin, soybean oil, coconut oil, groundnut oil, safflower oil, linseed oil, corn oil, sunflower oil, olive oil, canola oil, cottonseed oil, rapeseed oil, tung oil, fish oil, lard, tallow, or any of the combination thereof.

3. A process as claimed in claim 1 wherein the solvent in step (i) is an organic solvent.

4. A process as claimed in claim 3 wherein the organic solvent includes chloroform or hexane.

5. A process as claimed in claim 1 wherein step (i) is conducted at a ratio of 1:150 (w/v).

6. A process as claimed in claim 1 wherein step (ii) is conducted at a temperature ranging from 20°C to 27°C and for a period from 1 hour to 3 hours.

7. A process as claimed in claim 1 wherein the reactant in step (iii) is an acyl halide.

8. A process as claimed in claim 7 wherein the acyl halide includes acid chloride or acid dichloride.

9. A process as claimed in claim 8 wherein the acid chloride or acid dichloride includes adipoyl dichloride, terephthaloyl dichloride, hexanoyl chloride or octanoyl chloride.

10. A process as claimed in claim 1 wherein step (iii) is conducted at a mole ratio of 1:1 of hydrazide and acid chloride or at a mole ratio of 1:0.5 of hydrazide and acid dichloride.

11. A process as claimed in claim 1 wherein step (v) is conducted at a temperature ranging from 20°C to 27°C and for a period from 5 to 30 minutes.

12. A process as claimed in claim 1 wherein step (vi) is conducted using filtration.

13. A hydrazide derivative product as claimed in claims 1-12.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/MY2013/000142

A. CLASSIFICATION OF SUBJECT MATTER

C07C 241/04(2006.01)i, C07C 243/16(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07C 241/04; A01N 9/22; A61K 31/40; C07C 243/16

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: Fatty hydrazide, Acylation, Palm oil

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SONNTAG, NORMAN O. V., Reactions of fatty acid chlorides: II. Synthesis of monohydrazides or dihydrazides by acylation of hydrazine hydrate with saturated fatty acid chlorides, The Journal of The American Oil Chemists' Society, 1968, Vol. 45, pp. 571-574 See abstract; experimental procedures; tables I-IV.	1,3-13
Y		2
X	MOHAMAD, S. et al.,Enzymatic synthesis of fatty hydrazides from palm oils, J. Oleo. Sci., 2008, vol.57(5), pp.263-267 See abstract; page 264, lines 12-30; table 1.	13
Y		2
A	EMAD A. JAFFAR AL-MULLA et al., Synthesis, Characterization and Optimum Reaction Conditions of Fatty Hydrazide from Triacylglycerides, Res. J. Applied Sci., 2008, Vol. 3(8), pp. 545-549 See abstract; Fig. 1, 4-7.	1-13
A	US 04229463 A (KATHAWALA, FAIZULLA G.) 21 October 1980 See the whole document.	1-13

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 December 2013 (13.12.2013)	**13 December 2013 (13.12.2013)**

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/MY2013/000142

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 04229463 A	21/10/1980	JP 1474579 C	18/01/1989
		JP 54109930 A	29/08/1979
		JP 63-023987 B	18/05/1988
		US 04185118 A	22/01/1980
		US 04194002 A	18/03/1980
		US 04201785 A	06/05/1980
		US 04229463 A	21/10/1980
		US 04248893 A	03/02/1981
		US 04384124 A	17/05/1983
		US 04448785 A	15/05/1984