PATENT SPECIFICATION

804,880

Date of Application and filing Complete Specification: May 29, 1956.
No. 2168/58.
Application made in United States of America on June 6, 1955.
(Divided out of No. 804,879).
Complete Specification Published: Nov. 26, 1958.

Index at acceptance:—Class 2(3), C2B43(C1: G1).
International Classification:—C07c.

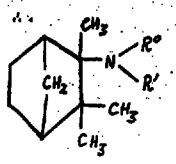
COMPLETE SPECIFICATION

Isocamphane Compounds and their preparation

We, MERCK & CO., INC., a corporation duly organised and existing under the laws of the State of New Jersey, United States of America, of Rahway, New Jersey, 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:—

This invention is concerned with novel isocamphane compounds.

In brief, this invention provides new N-substituted derivatives of 3-aminoisocamphane having the general formula:



where R^0 is an acyl radical derived from a C_{1-8} carboxylic acid and R^1 is a hydrogen atom or a C_{1-8} alkyl group. These compounds are used as starting materials in certain of the processes described and claimed in the specification of our copending application No. 16533/56 (Serial No. 804,879). In accordance with one embodiment of the present invention, 3-(N-formylamino) isocamphane is obtained by intimately contacting camphene with hydrogen cyanide and an acid.

The conversion of camphene to the 3-(N-formylamino)isocamphane is conveniently effected by intimately contacting camphene with hydrogen cyanide and sulphuric acid or a sulphonic acid in glacial acetic acid at low temperatures under essentially anhydrous conditions. Although higher temperatures can be used, it has been found that when this reaction is carried out at temperatures below about 20° C. maximum yields of the desired formamide compound are obtained under optimum conditions. Generally it is preferred to effect the reaction by mixing the reactants at temperatures between about 0° and 5° C., and then allowing the reaction mixture to warm up to about 20° C. to complete the reaction.

The preparation of the formamide compound can be carried out with hydrocyanic acid or a cyanide salt which will furnish the hydrocyanic acid *in situ* by reaction with the acid present. The hydrocyanic acid should be present in an amount equivalent to at least one mole per mole of camphene. However, it is preferable to have the equivalent of at least two moles of hydrocyanic acid present since with such an excess of this reactant maximum yields of the desired product are obtained under optimum conditions.

The sulphuric acid or sulphonic acid employed in the reaction should be essentially anhydrous since it is desirable to carry out the reaction under essentially anhydrous conditions. The acid should be present in an amount equivalent to at least one mole per mole of the camphene reacted. Preferably, an excess of the acid, for example, 2 to 3 moles per mole of camphene is used, since maximum yields of the formamide compound are thereby obtained. In addition to sulphuric acid, the sulphonic acids, i.e. acids having a $-HSO_3$ group, are suitable in this reaction. Examples of such sulphonic acids that might be mentioned are alkyl sulphonic acids such as methane sulphonic acid and ethane sulphonic acid, and aromatic sulphonic acids such as benzene sulphonic acids, toluene sulphonic acids, and naphthalene sulphonic acids.

Thus, the formamide compound is conveniently prepared by dissolving the camphene in glacial acetic acid, adding liquid hydrogen cyanide, cooling the resulting solution to a temperature of about 0° C., and then adding a mixture of sulphuric acid in acetic acid while maintaining the temperature of the reaction mixture between about 0° and 5° C. The resulting reaction mixture is then allowed to rise to about 20° at which point the reaction is essentially complete.

The desired 3-(N-formylamino) isocamphane is conveniently recovered from the reaction mixture by the addition of cold water and

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extraction of the formamide compound with a suitable solvent such as chloroform. The product is recovered from the chloroform solution by adding a dilute solution of an aqueous alkali such as sodium bicarbonate to the chloroform extract until the aqueous layer has a pH of about 7 to 8. The chloroform solution is then washed with water to remove the excess alkali and finally dried and evaporated to dryness under diminished pressure. The residue so obtained is dissolved in petroleum ether and then cooled to obtain 3-(formylamino)isocamphane in crystalline form.

In accordance with a further embodiment of this invention, the formamido compound is converted to 3-aminoisocamphane by reaction with a base. Thus, when an aqueous methanolic solution of the formamide compound and an alkali such as potassium hydroxide or sodium hydroxide is heated under reflux, 3-aminoisocamphane is produced. The product can be recovered from the reaction by evaporating the solvent, removing the 3-aminoisocamphane by steam distillation, extracting the product from the distillate by extraction with a water-immiscible solvent for the 3-aminoisocamphane and evaporating the solvent extract.

In accordance with a further embodiment of the invention, other N-acyl derivatives of 3-aminoisocamphane are produced by reacting 3-aminoisocamphane with an acylating agent derived from a C_{1-8} aliphatic carboxylic acid. The resulting acylamino compound can be reduced, in accordance with methods described and claimed in the specification of our copending application No. 16533/56 (Serial No. 804,879) to produce the corresponding 3-(N-lower alkyl amino) isocamphane or 3-(N,N-di-lower alkyl amino) isocamphane. For example, 3-(N-ethylamino) isocamphane is produced by reacting 3-aminoisocamphane with about one mole equivalent of acetyl chloride in the presence of a base to produce 3-(N-acetylamino)isocamphane, and reducing this compound with an aluminium hydride. Alternatively, the monoacetyl derivative may also be prepared by reacting the amino camphane with glacial acetic acid or preferably acetic anhydride in the presence of a small amount of sulphuric acid. In accordance with the above-described methods of the present invention, the N-acetyl, N-propionyl, N-butyryl, N-hexanoyl, N-octanoyl, N-isopropionyl, and N-isobutyryl derivatives of 3-aminoisocamphane are obtained.

The N-(C_{1-8} alkyl) derivatives of 3-aminoisocamphane, which are part of the invention claimed in the specification of our copending application No. 16533/56 (Serial No. 804,879) are converted to the 3-[N-(C_{1-8})carboxylic acyl)-N-(C_{1-8} alkyl)-amino] isocamphane by reacting the mono alkyl derivatives with an acylating agent derived from a lower aliphatic acid. Thus, the acid anhydride may be used in the presence of sulphuric acid. For example, 3-(N-acetyl-N-ethylamino) isocamphane is produced by reacting 3-(N-ethylamino) isocamphane with acetic anhydride in the presence of a small amount of sulphuric acid. The N-acetyl derivative on treatment with lithium aluminium hydride in accordance with the invention claimed in the specification of our copending application No. 16533/56 (Serial No. 804,879) is reduced to the diethyl derivative.

The following examples are given for the purpose of illustration:

EXAMPLE 1.

Preparation of 3-(N-formylamino) isocamphane

Into a three-necked flask which had been equipped with an agitator, thermometer, dropping funnel and reflux condenser through which water at 5—10° C. was circulated, 31.7 g. of *dl*-camphene was added and 58 cc. of glacial acetic acid. The mixture was stirred until all the solid had dissolved and then with stirring cooled to 10—12° C. At this point 20 cc. of liquid hydrogen cyanide was added while continuing the stirring. The solution was now cooled to 0° C. A slurry of white crystalline solid separated. With the maintenance of the reaction temperature at 0—2° C. by outside cooling, the addition of a solution of 63.5 cc. of conc. H_2SO_4 in 58 cc. of glacial acetic acid was begun. After the addition of about 1—2 cc. of the sulphuric acid solution, the reaction mixture became very fluid and most of the solid dissolved. The acid was added over a period of two hours, during which time the reaction took on a yellowish colour. After all the acid had been added, the yellow-orange reaction mixture was stirred for an additional hour at 0—2° C. The cooling bath was removed and the reaction temperature was allowed to rise to 22° C. in 2 hours. The viscous reaction mixture was put under vacuum (25—35 mm.) for 15—30 minutes with stirring in order to remove most of the excess of hydrogen cyanide.

After most of the cyanide had been removed, the reaction was quenched by the slow addition of 500 cc. of cold water. The temperature of the reaction was maintained at 18—20° C. by external cooling. The resulting milky solution was extracted with 2 × 100 cc. and 1 × 50 cc. of chloroform. Care must be exercised at this point, for the aqueous as well as the organic extracts contain hydrogen cyanide. The chloroform layer was washed with 2 × 100 cc. of water and then brought to a pH of 7—8 with a 10% solution of sodium bicarbonate, and finally washed with 150 cc. portions of water until the aqueous layer was free of cyanide.

After the final water wash, the chloroform layer was dried over 20 gm. of anhydrous sodium sulphate, filtered and concentrated on the steam bath in a vacuum of 25—35 mm. to dryness. When practically no more chloroform distilled, the yellow viscous residue was flushed with 100 cc. of *n*-heptane (Skelly-

solve C) at 25—35 mm. at 100° C. in order to remove the remaining chloroform. The residue was dissolved in 140 cc. *n*-heptane at 100° C. After all the residue had gone into solution, it was cooled slowly with agitation in order to allow slow crystallization. After 5 hours the temperature had fallen to 20—25° C. and a copious white precipitate had settled. The mixture was cooled with stirring to 5° C. for 8—10 hours, filtered and washed with cold *n*-heptane (3 × 10 cc.) and finally with 3 × 15 cc. of petroleum ether. The *dl*-3-(formylamino) isocamphane so obtained melted at 160—163° C.

Example 2

Preparation of 3-(N-formylamino) isocamphane

Into a 5-litre three-necked round-bottomed flask equipped with stirrer, dropping funnel and thermometer, was added 325 ml. of glacial acetic acid. Then, portionwise, a total of 133 g. of sodium cyanide (granular, 2.6 mole) was added with stirring while holding the temperature at 15° C. To the thick white slurry was added dropwise a previously prepared cold mixture of 325 ml. glacial acetic acid and 360 ml. conc. sulphuric acid. After addition of a few ml. at 15° C., the thick slurry thinned slowly and the remainder of the mixture of sulphuric and glacial acetic acids was added at 0—2° C. A total of about 2 hours was required for the addition. After addition, stirring was continued for 15 minutes. Then dropwise, over an hour, a solution of 178 g. (1.3 mole) of *dl*-camphene in 50 ml. of glacial acetic acid was added while keeping the temperature at about 0° C. (±3°).

Stirring was continued for two hours at 0° C. during which time a slight pinkish-yellow colour developed in the reaction mixture. The cooling bath was removed and the temperature allowed to rise to 15—20° C. in about 2—3 hours. The ice bath was then replaced and while holding the temperature at about 20° C., the mixture was gradually diluted with 3 litres of water while stirring vigorously. After an hour or two of good agitation at room temperature, the oily product was extracted with 2 × 500 ml. and 1 × 200 ml. of chloroform and the combined extracts washed with 2 × 500 ml. of water. The chloroform extract was then rendered neutral by stirring with 500 ml. of water and gradually adding solid sodium bicarbonate to the mixture until the aqueous phase had a pH of about 7; required, approximately 88 g. of $NaHCO_3$. After separation the chloroform layer was washed with 2 × 500 ml. of water, dried over calcium chloride, and after filtration the solvent was removed *in vacuo* on the steam bath. A solid somewhat sticky residue of 231.2 g. was obtained. After removal of last traces of chloroform by repeated swishing with petroleum ether, the cake was finally refluxed with about 500 ml. petroleum ether (b. 30—60° C.) until a thick crystalline slurry was obtained. After refrigeration for a day, the white crystalline mass was filtered by suction, washed with petroleum ether (2 × 125 ml.), then *n*-heptane (2 × 125 ml.) and again with petroleum ether (2 × 125 ml.). After air drying at room temperature to constant weight, 180.6 g. of the *dl*.3-(N-formylamino) isocamphane melting at 160—165° C. was obtained.

The combined petroleum ether and *n*-heptane washed were concentrated under diminished pressure and the residual oil dissolved in a minimum amount of hot petroleum ether (about 75 ml.). The resulting solution was placed in the refrigerator for two days. The precipitated *dl*-3-(N-formylamino) isocamphane was then recovered by filtration and washed with petroleum ether and *n*-heptane as described above. Obtained 12.6 g. of product having a melting point of 158—164° C.

The *dl*-3-(N-formylamino) isocamphane (193 g.) was dissolved in 1.9 litres *n*-heptane by heating on steam bath. After clarifying the solution by filtration, the clear filtrate was allowed to stand at room temperature until crystallization was complete. The crystalline product is filtered by suction, washed with a little cold *n*-heptane and air dried. The *dl*-3-(N-formylamino) isocamphane melted at 169—174° C.

Example 3

Preparation of 3-aminoisocamphane

dl-3-(N-formylamino) isocamphane (21.75 g.) was dissolved in a mixture containing 70 g. sodium hydroxide, 70 cc. water and 210 cc. methanol, and the resulting solution refluxed for about 16 hours. After removal of the bulk of methanol (*in vacuo* at about 50° C.), the alkaline liquor is steam-stripped until no more oil is collected. The distillate is saturated with sodium chloride and the amine extracted with ether. After drying (Na_2SO_4) and removal of the ether, the oily residue crystallizes to obtain the *dl*-3-aminoisocamphane as a waxy solid melting at 172—174° C. with softening at 171° C.

After subliming the product under diminished pressure the *dl*-3-aminoisocamphane melted at 173—175° C.

The amine is slightly soluble in water; the pH of the solution is about 10.5. For further identification it was converted to the hydrochloride which is obtained in quantitative yield and in a crystalline form by neutralizing the base with HCl and concentrating the solution.

Anal. Calcd. for $C_{10}H_{19}N.HCl$ (189.73): C, 63.30; H, 10.63; N, 7.38; Cl, 18.69.

Found: C, 63.59; H, 10.79; N, 7.06; Cl, 18.83.

The hydrochloride is quite soluble in water; it does not melt below 300° C.

The phosphate was obtained in a similar way.

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Anal. Calcd. for $C_{10}H_{19}N.H_3PO_4$ (404.53): C, 47.80; H, 8.83; N, 5.58; P, 12.30.

Found: C, 47.84; H, 8.69; N, 6.70; P, 11.94.

The phosphate is a white crystalline salt, soluble in water, but insoluble in ethanol. It melts at 281—283° C. with effervescence.

EXAMPLE 4

Preparation of 3-acetamido isocamphane

To 30 grams of *dl*-3-aminoisocamphane (m.p. 174°) was gradually added 120 ml. acetic anhydride with external cooling. After adding about one ml. of conc. sulphuric acid with good agitation a clear solution was obtained, which was allowed to age at room temperature for about 15 hours. The reaction mixture was then added slowly to 600 ml. of water with cooling and vigorous stirring. The white amorphous precipitate which formed gradually became crystalline with stirring. It was filtered by suction, well washed with water and air dried. The *dl*-3-acetamido-isocamphane melted at 132—134° C.

Crystallization from hot Skellysolve (b. 95° C.—100°; 18 ml./g.) raised the m.p. to 133—135.5° C.

Anal. Calcd. for $C_{12}H_{21}NO$ (195.3): C, 73.77; H, 10.83; N, 7.18.

Found: C, 73.48; H, 10.58; N, 7.18.

EXAMPLE 5

Preparation of 3-(N-ethyl-N-acetylamino) isocamphane

A solution of 4.0 g. of once crystallized *dl*-3-acetamido isocamphane in 90 ml. of anhydrous ether, was added over a period of 25 minutes with stirring to a solution of 1.75 g. (0.046 mole) of lithium aluminium hydride in 100 ml. of absolute ether. After refluxing for 3 hours, the mixture was slightly cooled and with vigorous stirring 8.3 ml. water was added very cautiously. The white granular precipitate was filtered and washed with ether. The ether extracts were washed with 2 × 50 ml. water then dried over anhydrous sodium sulphate. After concentrating the ether extract to a small volume, ethereal HCl was added with cooling to a pH of about 3. The resulting white precipitate was filtered by suction, washed with ether (until free of HCl), then air dried. The *dl*-3-(N-ethylamino) isocamphane hydrochloride melted at 248° C. Crystallization from boiling isopropanol (225 ml.) gave pure *dl*-3-(N-ethylamine) isocamphane hydrochloride, melting at 260—1° C. with decomposition. This preparation is described in Example 3 of specification No. 16533/56 (Serial No. 804,879).

The N-ethyl compound so obtained is treated with acetic anhydride in the presence of a small amount of sulphuric acid as described in Example 4, the acylated derivative, viz. 3-(N-ethyl-N-acetyl-amino)-isocamphane, is obtained.

EXAMPLE 6

Preparation of 3-(N-butyrylamino) isocamphane

n-Butyryl chloride (16 ml.) was added in portions with ice cooling to 8.0 g. of *dl*-3-aminoisocamphane, followed by the gradual addition of 80 ml. of 20% sodium hydroxide solution. The mixture was vigorously agitated until reaction had ceased and then diluted with 150 ml. water. After extraction of the reaction mixture with 3 × 80 ml. of benzene, the combined extracts were washed with 2.5*N* NaOH (75 ml.), water (2 × 100 ml.), 2.5*N* HCl (75 ml.), and again with 3 × 100 ml. of water. After drying the extract and removing the solvent, *dl*-3-(N-butyrylamino) isocamphane, melting point 75—76.5° C. was obtained.

Anal. Calcd. for $C_{14}H_{25}NO$ (223.35): C, 75.28; H, 11.28; N, 6.27.

Found: C, 75.49; H, 11.01; N, 6.33.

EXAMPLE 7

Preparation of 3-(N-3,3-dimethylbutyryl-amino) isocamphane

To 6.0 g. of *dl*-3-aminoisocamphane cooled in ice water was added a total of 12.0 ml. *t*-butylacetyl-chloride in 3 ml. portions with swirling over a period of about 10 minutes. To the thick slurry was then gradually added a total of 60 ml. of 20% NaOH with good agitation. After shaking for 2—3 hours, the reaction mixture was diluted with 200 ml. water and extracted with 3 × 60 ml. benzene. The benzene extracts were washed with 2.5*N* NaOH (50 ml.), water (2 × 80 ml.), 2.5*N* NCl (50 ml.), and finally with 4 × 70 ml. water. After drying over magnesium sulphate and removing the solvent, the crystalline *dl*-3-(N-3,3-dimethylbutyrylamino) isocamphane melting at 106—8° C. was obtained.

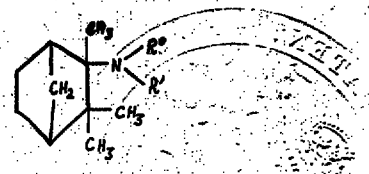
Crystallization from hot Skellysolve C. (b.p. 95—100° C.) gave pure product, melting at 107—108.5° C.

Anal. Calcd. for $C_{16}H_{29}NO$ (251.40): C, 76.44; H, 11.63; N, 5.57.

Found: C, 76.13; H, 11.48; N, 5.59.

WHAT WE CLAIM IS:—

1. An isocamphane compound having the general formula:



in which R^0 is an acyl radical derived from a C_{1-6} carboxylic acid and R^1 is a hydrogen atom or a C_{1-6} alkyl group.

2. 3-(N-formylamino)-isocamphane.

3. 3-(N-acetylamino)-isocamphane.

4. 3-(N-ethyl-N-acetyl-amino)-isocamphane.

5. 3-(N-butyrylamino)-isocamphane.

6. 3-(N-3,3-dimethylbutyrylamino)-isocamphane.

Anal. Calcd. for $C_{10}H_{19}N.H_3PO_4$ (404.53): C, 47.80; H, 8.83; N, 5.58; P, 12.30.

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Preparation of 3-(N-ethyl-N-acetylamino) isocamphane

A solution of 4.0 g. of once crystallized *dl*-3-acetamido isocamphane in 90 ml. of anhydrous ether, was added over a period of 25 minutes with stirring to a solution of 1.75 g. (0.046 mole) of lithium aluminium hydride in 100 ml. of absolute ether. After refluxing for 3 hours, the mixture was slightly cooled and with vigorous stirring 8.3 ml. water was added very cautiously. The white granular precipitate was filtered and washed with ether. The ether extracts were washed with 2 × 50 ml. water then dried over anhydrous sodium sulphate. After concentrating the ether extract to a small volume, ethereal HCl was added with cooling to a pH of about 3. The resulting white precipitate was filtered by suction, washed with ether (until free of HCl), then air dried. The *dl*-3-(N-ethylamino) isocamphane hydrochloride melted at 248° C. Crystallization from boiling isopropanol (225 ml.) gave pure *dl*-3-(N-ethylamine) isocamphane hydrochloride, melting at 260—1° C. with decomposition. This preparation is described in Example 3 of specification No. 16533/56 (Serial No. 804,879).

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EXAMPLE 6

Preparation of 3-(N-butyrylamino) isocamphane

n-Butyryl chloride (16 ml.) was added in portions with ice cooling to 8.0 g. of *dl*-3-aminoisocamphane, followed by the gradual addition of 80 ml. of 20% sodium hydroxide solution. The mixture was vigorously agitated until reaction had ceased and then diluted with 150 ml. water. After extraction of the reaction mixture with 3 × 80 ml. of benzene, the combined extracts were washed with 2.5*N* NaOH (75 ml.), water (2 × 100 ml.), 2.5*N* HCl (75 ml.), and again with 3 × 100 ml. of water. After drying the extract and removing the solvent, *dl*-3-(N-butyrylamino) isocamphane, melting point 75—76.5° C. was obtained.

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EXAMPLE 7

Preparation of 3-(N-3,3-dimethylbutyryl-amino) isocamphane

To 6.0 g. of *dl*-3-aminoisocamphane cooled in ice water was added a total of 12.0 ml. *t*-butylacetyl-chloride in 3 ml. portions with swirling over a period of about 10 minutes. To the thick slurry was then gradually added a total of 60 ml. of 20% NaOH with good agitation. After shaking for 2—3 hours, the reaction mixture was diluted with 200 ml. water and extracted with 3 × 60 ml. benzene. The benzene extracts were washed with 2.5*N* NaOH (50 ml.), water (2 × 80 ml.), 2.5*N* NCl (50 ml.), and finally with 4 × 70 ml. water. After drying over magnesium sulphate and removing the solvent, the crystalline *dl*-3-(N-3,3-dimethylbutyrylamino) isocamphane melting at 106—8° C. was obtained.

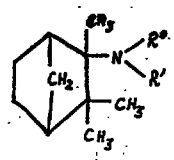
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2. 3-(N-formylamino)-isocamphane.

3. 3-(N-acetylamino)-isocamphane.

4. 3-(N-ethyl-N-acetyl-amino)-isocamphane.

5. 3-(N-butyrylamino)-isocamphane.

6. 3-(N-3,3-dimethylbutyrylamino)-isocamphane.

* C L M S *

7. The process that comprises bringing camphene into intimate contact with hydrogen cyanide in the presence of sulphuric acid or a sulphonic acid to produce 3-(N-formylamino)-isocamphane.

8. A process as claimed in Claim 7, in which the hydrogen cyanide is formed *in situ* by reaction of a cyanide salt with the acid.

9. A process as claimed in Claim 7 or 8, in which the reaction is carried out in an essentially anhydrous medium comprising glacial acetic acid.

10. A process as claimed in any one of Claims 7—9, in which at least two moles of hydrogen cyanide are present to every mole of camphene.

11. A process as claimed in any one of Claims 7—10, carried out by mixing the reactants at 0—5° C. and allowing the mixture to warm up to about 20° C. to complete the reaction.

12. A process as claimed in Claim 7, substantially as described in Example 1 or 2 hereinbefore.

13. The process that comprises reacting 3-(N-formylamino)-isocamphane with a base to produce 3-aminoisocamphane.

14. A process as claimed in Claim 13 carried out by refluxing an aqueous methanolic solution of 3-(N-formylamino)-isocamphane and sodium hydroxide or potassium hydroxide.

15. A process as claimed in Claim 13, substantially as described in Example 3 hereinbefore.

16. A process as claimed in any one of Claims 13—15 in which the 3-(N-formylamino)-isocamphane has been prepared by a process as claimed in any one of Claims 7—12.

17. The process that comprises reacting 3-aminoisocamphane with an acylating agent derived from a C_{1-8} carboxylic acid to produce a compound as claimed in Claim 1 in which R^1 is a hydrogen atom.

18. A process as claimed in Claim 17, in which the acylating agent is derived from acetic acid.

19. A process as claimed in Claim 17, in which the acylating agent is derived from butyric acid.

20. A process as claimed in Claim 17, in which the acylating agent is derived from *t*-butylacetic acid.

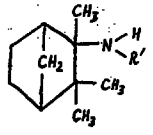
21. A process as claimed in any one of Claims 17—20, in which the acylating agent is an acid chloride.

22. A process as claimed in any one of Claims 17—20, in which the acylating agent is the acid itself or its anhydride, and the acylation is carried out in the presence of sulphuric acid.

23. A process as claimed in Claim 17, substantially as described in any one of Examples 4, 6 and 7 hereinbefore.

24. A process as claimed in any one of Claims 17—23 in which the starting material has been prepared by a process according to any one of Claims 13—16.

25. The process that comprises reacting a compound having the general formula



in which R^1 is a C_{1-8} alkyl group, with an acylating agent derived from a C_{1-8} carboxylic acid to produce a compound as claimed in Claim 1 in which R^1 is a C_{1-8} alkyl group.

26. A process as claimed in Claim 25 involving the acetylation of 3-(N-ethylamino)-isocamphane to produce 3-(N-ethyl-N-acetylamino) isocamphane.

27. A process as claimed in Claim 25 or 26 in which the acylating agent is an acid chloride.

28. A process as claimed in Claim 25 or 26, in which the acylating agent is the acid anhydride, and the acylation is carried out in the presence of sulphuric acid.

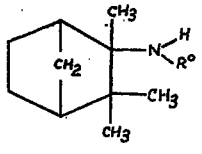
29. A process as claimed in Claim 25 substantially as described in Example 5 hereinbefore.

30. A process as claimed in any one of Claims 25—29, in which the starting material has been prepared by a process described and claimed in the specification of our copending application No. 16533/56 (Serial No. 804,879).

31. 3-(N-formylamino)-isocamphane when prepared by a process as claimed in any one of Claims 7—12 or an obvious chemical equivalent of such a process.

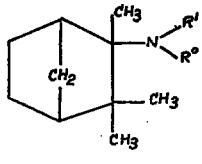
32. 3-aminoisocamphane when prepared by a process as claimed in any one of Claims 13—16 or an obvious chemical equivalent of such a process.

33. A compound having the general formula



in which R^0 is an acyl group derived from a C_{1-8} carboxylic acid, when prepared by a process as claimed in any one of Claims 17—24 or an obvious chemical equivalent of such a process.

34. A compound having the general formula



* C L M S *

in which R^0 is an acyl group derived from a C_{1-8} carboxylic acid and R^1 is a C_{1-8} alkyl group, when prepared by a process as claimed in any one of Claims 25—30 or an obvious chemical equivalent of such a process.

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Leamington Spa: Printed for Her Majesty's Stationery Office, by the Courier Press.—1958.
Published at The Patent Office, 25, Southampton Buildings, London, W.C.2, from which copies may be obtained.

* C L M S *

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