

Development of Quality Control Procedures for a Production Plant to Manufacture Aliphatic Nitriles for use as a Lemon Bleach Fragrance

In this case study, you are asked to assume the role of a quality control manager in a chemical company that manufactures fragrance chemicals. Your R&D Department has synthesised a new aliphatic nitrile suitable for use as a fragrance in lemon bleach (see Lemon Bleach Scenario). Some background information on this aliphatic nitrile is described in the US patent number 4,579,680 by Charles Sell (*below*). Your Finance Department has determined the cost of manufacturing the aliphatic nitrile (see Money section) and your Marketing Department has developed a marketing strategy to commercialise it (see Marketing section). Your Production Department has built a new plant to manufacture the aliphatic nitrile and your role now is to outline a quality control procedure to ensure that the product satisfies customer requirements.

Obviously to do this exercise in detail you will need to be in the real life situation of being in charge of the actual manufacturing plant. However, this case study asks you to consider the broad issues that you will need to consider. What quality procedures would you want to implement? And, what criteria do you propose the company should control, and how?

Using your knowledge of quality assurance and control from the Quality section, prepare a 2 or 3 page outline quality control document for the production of the aliphatic nitriles. A few thoughts on some of the quality issues are provided below.

Quality Assurance:

Will you wish to implement ISO9000 quality assurance procedures? Consider the advantages and disadvantages. What will be your quality assurance policy? What items within the production of aliphatic nitriles (see patent for details) would you wish to measure and control? Will you set up process improvement teams? How might they work?

Statistical Process Control:

Will you use statistical process control techniques during the production of the aliphatic nitriles?

How accurate/precise would you wish the manufacturing process to be, consider the advantages and disadvantages of your decision? Will you use Shewhart or CuSum charts, and why, or why not? What will you need to measure to set up the charts? What will you measure to monitor the process in real time? How many samples will you take? And, how often? Consider the commercial consequences of your decisions.

United States Patent [19]

Sell

[11] Patent Number: **4,579,680**

[45] Date of Patent: **Apr. 1, 1986**

[54] **ALIPHATIC NITRILES**

[75] Inventor: **Charles S. Sell, Kent, England**

[73] Assignee: **Internationale Octrooi Maatschappij
"Octropa" B.V., Rotterdam,
Netherlands**

[21] Appl. No.: **671,015**

[22] Filed: **Nov. 13, 1984**

Related U.S. Application Data

[63] Continuation of Ser. No. 413,446, Aug. 31, 1982, abandoned.

[30] **Foreign Application Priority Data**

Sep. 3, 1981 [GB] United Kingdom 8126748

[51] Int. Cl.⁴ **A61K 7/46; C11B 9/00;
C11D 3/50**

[52] U.S. Cl. **252/522 R; 252/106;
252/174.11; 424/69; 424/70; 424/71; 558/435**

[58] Field of Search **252/522 R; 260/465.1**

[56] **References Cited**

U.S. PATENT DOCUMENTS

Re. 27,332 4/1972 Somerville et al. 252/522 R
2,912,455 11/1959 Smiley 260/465.8 R
3,531,510 9/1970 Blumenthal 252/522 R X
3,739,007 6/1973 Schwager et al. 260/464
3,899,398 8/1975 Cole et al. 203/49

4,193,934 3/1980 Bauer et al. 252/522 R X
4,277,377 7/1981 Webb et al. 252/522 R

OTHER PUBLICATIONS

Fischli, *Helvetica Chimica Acta.*, vol. 61, (1978), pp. 2560-2578.

Arctander, *Perfume and Flavor Chemicals*, (1969) vol. 1, Compound 1121; vol. 2, Compounds 2130, 2292, 2362 and 3010.

Beilsteins *Handbuch der Organischen Chemie*; vol. 2, 1942, second supplement; pp. 312, 315, 316, 323.

Beilsteins *Handbuch der Organischen Chemie*; vol. 2, 1960, third supplement; pp. 825, 826, 831, 832, 848, 853, 863, 864, 865, 979.

Croteau (editor); "Fragrance and Flavor Substances", (1980), pp. 123-128, article by Hagena et al.; D&PS. Verlag, 3017 Pattersen 1, W. Germany.

De Simone, "Perfumer & Flavorist," vol. 4, (1980), pp. 2, 3, 4, 6, 7 and 8.

Sell, et al: *Perfumer & Flavorist*, 7 (1983), 14-16.

Primary Examiner—Joseph Paul Brust

Attorney, Agent, or Firm—Cushman, Darby & Cushman

[57]

ABSTRACT

This invention provides perfume compositions containing certain substituted saturated aliphatic nitriles and some novel nitriles useful as perfumery components.

1 Claim, No Drawings

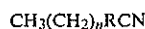
ALIPHATIC NITRILES

This is a continuation of application Ser. No. 413,446, filed Aug. 31, 1982, now abandoned.

This invention relates to substituted saturated aliphatic nitriles, more particularly to alpha- and beta-substituted nitriles which have been found to have value in perfume compositions.

Various substituted aliphatic nitriles have been known for some years, but hitherto their value as perfume components has not been appreciated. Our work has shown that certain of the alpha- and beta-substituted aliphatic nitriles, some of which are novel, have particular merit in perfumery compositions.

Accordingly, the present invention provides a perfume composition comprising perfume components and an organoleptically discernible amount of a nitrile of the formula:



in which

R = —CHCH₃— or —CHCH₃CH₂— and in which, when

R = —CHCH₃—, n is an integer from 5-9 and when

R = —CHCH₃CH₂—, n is an integer from 4-8.

In addition, this invention provides certain novel substituted nitriles of particular value in perfume formulations, having the formula:



in which n is 6, 7 or 8.

The nitriles useful in perfume compositions provided by this invention have, in addition to their useful odour characteristics, good stability when used in perfume formulations which are to be used or stored in an aggressive environment, such as in soaps, disinfectants, laundry powders and other compositions in which active chemicals are present or which have to withstand the effects of daylight or heat.

The nitriles useful according to this invention may be prepared by various processes, but a convenient process for the preparation of the alpha-substituted nitriles is as follows:

Procedure A

A solution of the required methyl alkyl ketone (50 m mol) and tosylmethylisocyanide (12 g, 60 m mol) in dry

diglyme (120 ml) was added over 15 minutes at 0° C. under nitrogen to a stirred solution of potassium t-butoxide (freshly prepared from potassium 4.3 g, 0.11 g atom) in dry t-butanol (100 ml) and diglyme (100 ml).

When the addition was complete, the mixture was allowed to warm to room temperature then stirred for 2 hours and left to stand overnight. The resultant solution was poured into water (400 ml) and extracted with light petroleum (3×100 ml, bp 40°-60° C.). The combined organic extracts were washed with water (2×500 ml), then brine (500 ml) and dried (MgSO₄). The solvent was removed under reduced pressure and the residue chromatographed using a column (3 cm diameter, 30 cm height) of silica gel with 5% ether in light petroleum (bp 40°-60° C.) as solvent. Those fractions containing the product were freed of solvent under reduced pressure and the residue distilled to give the desired 2-methyl substituted nitrile.

A convenient process for the preparation of the betanitriles is as follows:

Procedure B

The required methyl alkyl ketone (1 mol), cyanoacetic acid (93.5 g, 1.1 mol), ammonium acetate (13 g, 0.17 mol) and toluene (175 ml) were stirred under reflux (pot temperature 140°-160° C.) in a Dean-Stark apparatus until carbon dioxide ceased to be evolved (3-6 hours). The resultant mixture was cooled, washed with saturated aqueous sodium hydrogen carbonate (2×50 ml) and water (50 ml) then the solvent was removed under reduced pressure. The crude mixture of nitriles was then added to one quarter of its volume of 50% aqueous sodium hydroxide to which Tergitol* (3 drops) had been added. The resulting mixture was stirred under reflux for 1 hour then cooled. The organic layer was removed, washed with water (3×50 ml) and distilled. 5% Palladium on carbon (0.1% by weight relative to the nitrile mixture) was then added followed by ethyl acetate (2×weight of distillate) and the suspension stirred vigorously in an atmosphere of hydrogen until uptake of gas ceased. The catalyst was removed by filtration and the solvent by evaporation under reduced pressure. Fractional distillation of the residue afforded the desired 3-methyl substituted nitrile.

*Tergitol is a trade name for a surfactant (Union Carbide).

The following table sets out the physical and the organoleptic properties of the nitriles useful in this invention:

TABLE

Sample	Series	Carbon Chain Length	Name	Structure
1	α-methyl	8	2-methyloctanonitrile	CH ₃ (CH ₂) ₅ CHCH ₃ CH
2	α-methyl	9	2-methylnonanonitrile	CH ₃ (CH ₂) ₆ CHCH ₃ CN
3	α-methyl	10	2-methyldecanonitrile	CH ₃ (CH ₂) ₇ CHCH ₃ CN
4	α-methyl	11	2-methylundecanonitrile	CH ₃ (CH ₂) ₈ CHCH ₃ CN
5	α-methyl	12	2-methyldodecanonitrile	CH ₃ (CH ₂) ₉ CHCH ₃ CN
6	β-methyl	8	3-methyloctanonitrile	CH ₃ (CH ₂) ₄ CHCH ₃ CH ₂ CN
7	β-methyl	9	3-methylnonanonitrile	CH ₃ (CH ₂) ₅ CHCH ₃ CH ₂ CN
8	β-methyl	10	3-methyldecanonitrile	CH ₃ (CH ₂) ₆ CHCH ₃ CH ₂ CN
9	β-methyl	11	3-methylundecanonitrile	CH ₃ (CH ₂) ₇ CHCH ₃ CH ₂ CN
10	β-methyl	12	3-methyldodecanonitrile	CH ₃ (CH ₂) ₈ CHCH ₃ CH ₂ CN
Sample	Preparation	Boiling Point (lit. bp)		Odour Description
1	Procedure A, 76% yield from 2-octanone	78-80° C. at 8 m bar (85 at 10 mm Hg)		Floral, jasmnic character with some celery aspects and a hint of coconut/lactone - very diffusive.
2	Procedure A, 69% yield	72-73° C. at 3 m bar		Soft, floral, lactonic,

TABLE-continued

3	from 2-nonanone Procedure A, 77% yield from 2-decanone	(100 at 10 mm Hg) 85-87° C. at 3 m bar (115 at 10 mm Hg)	jasmine/peachy character. A fine, light, jasmine/floral character with a soft peach quality.
4	Procedure A, 74% yield from 2-undecanone	84° C. at 1 m bar (133 at 12 mm Hg)	Fresh, floral with some lilac character - tenacious.
5	Procedure A, 59% yield from 2-dodecanone	125-127° C. at 7 m bar (146 at 10 mm Hg)	Soft, floral with a green jasminic type odour - very persistent.
6	Procedure B, 59% yield from 2-heptanone	66-68° C. at 4 m bar (207-8 at 760 mm Hg)	An unusual floral type consisting of a distinct fatty jasminic character combined with an agrumen quality.
7	Procedure B, 16% yield from 2-octanone	93° C. at 8 m bar (95-6 at 2-3 mm Hg)	Fresh, jasminic floral type with a slightly green quality.
8	Procedure B, 49% yield from 2-nonanone	72-74° C. at 0.7 m bar	Soft, citrus floral - reminiscent of jasmine.
9	Procedure B, 35% yield from 2-decanone	99-100° C. at 3 m bar	Light, fresh, green, floral suggesting lilac, with slight citrus undertones.
10	Procedure B, 26% yield from 2-undecanone	95-97° C. at 0.7 m bar	Distinct orange character which is suffused by a light green sea-fresh quality.

25

The following are two examples of perfume compositions comprising the nitriles of this invention:

Sample	Base Peak	M1	M2	M3	M4	M5
8 C ₁₀	41	43:85	57:84	68:66	55:50	96:46
9 C ₁₁	41	57:85	43:84	68:56	55:50	69:43
10 C ₁₂	41	57:92	43:90	55:54	68:53	70:48

30

Formula 1

Phenylethyl Alcohol	30.5
Terpineol	6.0
Paratertiary butyl cyclohexyl acetate high cis (PPL)	15.0
Benzyl Salicylate	14.8
Cinnamic Alcohol	10.0
Sandalone (PPL)	5.0
Galaxolide (IFF)	3.0
Hexyl Cinnamic Aldehyde	10.0
Coumarin	2.0
Rose Base AB 380 (PPL)	2.0
Isoeugenol	0.1
Vetivert Brazilian	0.1
Nitrile No 3	1.5

Formula 1 in the absence of nitrile 3 has a floral, woody bouquet suitable for a toilet soap. The addition of 1.5% of nitrile 3 enhances the overall freshness, giving a light floral, fruity effect. Using the above formulation but substituting nitrile 9 in place of nitrile 3, a perfume is created having an added fresh lightness with an enhanced floral, fruity and citrus character.

The three novel nitriles provided by this invention are those numbered 8, 9 and 10 in the samples list and their mass spectral data are as follows.

45

in which
R = —CHCH₃— or —CHCH₃CH₂— and in which,
when

R = —CHCH₃—, n is an integer from 5-9 and when
R = —CHCH₃CH₂—, n is an integer from 4-8,

the amount of the nitrile not exceeding 95% by weight of the perfume composition and the nitrile being characterized by its stability in the use or storage of said composition.

* * * * *

55

60

65