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File No.: T 0615/90 - 3.3.2
Application No.: 85 303 737.2
Publication No.: 0 167 265
Classification: A01N 43/22
Title of invention: Insect repellent composition and method of repelling insects

D E C I S I O N
of 16 October 1993

Applicant: Coulston International Corporation

Opponent:

Headword: Insect repellent/COULSTON

EPC: Art. 56

Keyword: "Inventive step (yes) - alternatives not foreshadowed by state of the art"

Headnote
Catchwords

Case Number: T 0615/90 - 3.3.2

DECISION
of the Technical Board of Appeal 3.3.2
of 16 October 1993

Appellant: Coulston International Corporation
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Representative: Geissler, Bernhard, Dr. jur., Dipl.-Phys.
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Decision under appeal: **Decision of the Examining Division of the
European Patent Office dated 28 February 1990
refusing European patent application
No. 85 303 737.2 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: P.A.M. Lançon
Members: A.J. Nuss
S.C. Perryman

Summary of Facts and Submissions

- I. European patent application No. 85 303 737.2 was filed on 28 May 1985 and published under No. 0 167 265.
- II. On 28 February 1990, the Examining Division issued a decision refusing the application under Article 97 (1) EPC for failure to comply with either Article 54 EPC or Article 56 EPC. The decision was based on six claims received on 16 May 1988.
- III. The ground for the refusal was that, in the opinion of the Examining Division, the article by K.H.Büchel headed "Insekten-Repellents" in the standard textbook "Chemie der Pflanzenschutz- und Schädlingsbekämpfungsmittel" - Band 1, 1970, Springer Verlag Berlin-Heidelberg-New York, pages 487 to 496, document (1), disclosed the applicability of bicyclic lactones such as iridomyrmecines as insect repellents and thus, implicitly disclosed or at least made obvious the claimed method of repelling insects from a situs by applying to said situs an effective amount of iridomyrmecines. It was also argued that US-A-2 459 684, document (4), described various (cyclic) lactones useful as insecticidal toxicants and repellents.
- IV. The Appellant lodged an appeal against this decision. Together with the statement setting out the grounds of appeal it was proposed as a subsidiary request to restrict the claimed subject-matter to a method of repelling insects of the group comprising mosquitoes, fleas and flies.
- V. In a communication pursuant to Article 110 (2) EPC, the Board informed the Appellant that the subject-matter according to the main request lacked novelty in the

light of the publication of Eisner et al. in Science, Vol. 146, 1964, pages 1318 to 1320, document (5), which disclosed the proven activity of iridomyrmecin as an insect repellent. Furthermore, it was pointed out that having regard to this prior art, the subject-matter of the subsidiary request appeared to be obvious to a person skilled in the art.

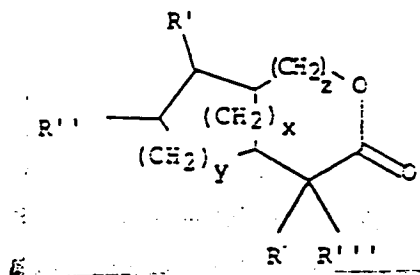
VI. In response to the communication of the Board, the Appellant filed a new set of claims limited to a method of repelling insects from a situs in which cyclohexyl lactones are applied to said situs and argued that these derivatives were purely synthetic and did not occur in nature whereas the naturally occurring methylcyclopentyl compounds were the only ones discussed in (5). In Tetrahedron, 1959, Vol. 6, pages 201 to 216, document (6), a scientific article referred to in the application, only the synthesis of these cyclohexyl lactones was described; it contained no biological data for the compounds thus prepared.

Moreover, it was to be noted that Büchel in his article "Insekten-Repellents" in (1) summarised the insect repellent technology and mentioned, in conjunction with defensive chemicals, iridomyrmecines, but did not mention the cyclohexyl derivative compounds synthesised by Korte according to (6) although he was, of course, fully aware of this publication because, the two scientists worked together at the time the article in (6) was written by Korte, i.e. one of the inventors in the present case. Furthermore, as pointed out on page 496 of this document, it was not considered to be possible in this field to make any conclusion from a chemical structure of one compound as to the insect repellent activity of a chemically different compound.

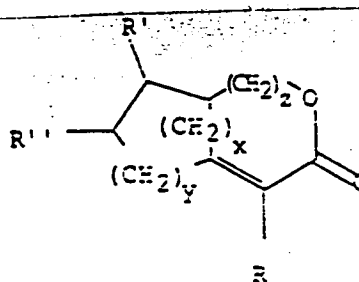
VII. The Appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of Claims 1 to 7 received on 6 September 1993.

VIII. Claim 1 according to this request reads as follows:

1. A method of repelling insects from a situs comprising applying to said situs an effective amount to repel said insects of a composition comprising a compound of the formula:



or the corresponding unsaturated compound thereof having the formula:



wherein R, R', R'' each are either methyl or hydrogen, and R''' is either hydrogen or methyl:

wherein y is 2 and x is 0 or y is 1 and x is 1 and z is 0 or 1.

Reasons for the Decision

1. The appeal is admissible.
2. There are no formal objections to the present claims under Articles 123 (2) EPC and 84 EPC.
 - 2.1 Claims 1, 2, 3 and 5 are based on Claims 6, 7, 5, 3 and 1 as originally filed in connection with table I on originally filed page 8; Claim 4 is based on page 17, first paragraph as originally filed and Claims 6 and 7 are based on pages 8 and 9 as originally filed.
 - 2.2 On the basis of a proper interpretation, it is clear that present Claim 1 although relating to a method of repelling insects, in reality defines the use of a compound of the class of bicyclic lactones, in other words, a physical entity to achieve an effect, namely repellency and does not define such a use to produce a product. Such a method claim is therefore not a process claim within the meaning of Article 64(2) EPC (cf. G2/88 OJ EPO 1990, 93, point 5.1 of the reasons for the decision).
3. Accordingly, the application concerns the use of a compound of bicyclic lactones in a method of repelling insects from a situs.
 - 3.1 The closest state of the art is the article in document (1) which is also concerned with compounds having insect repellent activity. In connection with repellents on the basis of natural ethereal oils (in the historical section of this article), reference is made to natural combat substances which are secreted by insects to fight off their natural enemies and parasites. It is furthermore indicated there that

besides other scientists Eisner *et al*, i.e. the authors of document (5), have isolated and identified a plurality of such substances from insects or ants. In a heterogeneous list of chemical compounds bicyclic lactones such as iridomyrmecines are mentioned together with aromatic and unsaturated aliphatic aldehydes, acids (formic acid and methacrylic acid), nitriles, esters and quinones. To summarise, it is then pointed out that there might be incentives from the field of natural combat substances for the synthesis of new repellents (cf. page 488 and page 489, first paragraph). The following chapter relates to a plurality of commercially available synthetic repellents applied to the skin of humans. Certain properties such as water solubility and skin irritation of several known repellents (i.e. dimethylphthalate, Rutgers 621, Indalone and the 622-mixture) are then described. In addition, the chemical structure, the use for certain groups of insects and physico chemical properties as well as results of oral LD₅₀ rat toxicological tests of further known repellents are indicated in tabular form. The table comprises inter alia bis-(2-ethylhexyl) fumarate as space repellent and hexachlorophene undecanoate as systemic repellent. A reference to lactones cannot be found in this chapter. It is then concluded that repellents are very important for hygienical reasons and that for the discovery of new repellents there is a need to develop more accurate test methods in order to detect more efficiently the repellent effect on insects. An interesting field of investigation is seen in the search for repellents having oral or systemic effects as well as in the new field of "space-repellents". It is then pointed out that until now nothing is known about the relationship between chemical structure and repellent activity (cf. pages 489 to 496).

- 3.2 In relation to the above prior art (1), the problem to be solved by the present European application is to provide further compounds to be used in a method for repelling insects.
- 3.3 The solution consists in applying to a situs a composition comprising a compound of the group of cyclohexyl lactones specified in Claim 1 (see point VIII above). Having regard to the data provided in the application for the claimed compounds (see CIC-20; CIC-21; CIC-22 and CIC-23 on pages 22/23), which demonstrate repellency activity for the tested compounds, the Board is satisfied that the above stated problem has indeed been solved.
4. Since the claimed subject-matter does no longer relate to cyclopentyl lactones such as the iridomyrmecines and neither documents (1), (4) and (5) nor any other prior art considered during examination procedure, or forming part of the European search report, discloses the use of the specific group of cyclohexyl lactones in a method of repelling insects as currently claimed, novelty can accordingly be recognised.
5. It remains to consider whether or not the claims satisfy the requirements of Article 56 EPC in respect of inventive step.
- 5.1 Document (6), referred to in the description of the application and published some eleven years before the closest prior art according to (1), is the only document which describes the aspects of laboratory synthesis of both iridomyrmecines and bicyclic lactones comprising a cyclohexyl ring or cycloheptyl ring, i.e. compounds falling partly within the generic formula of present claim 1 (cf. page 201, formula "II", formula III and page 202). It is therefore necessary to assess the

actual meaning of the quite general hint in (1), namely that there might be incentives from the field of natural combat substances for the synthesis of new repellents, in the light of what was already known from (6). This document is an article published in "Tetrahedron", a journal specifically addressed to the chemist working in the field of organic synthesis. It is indicated that in order to apply the alpha-acyl-lacton rearrangement developed by Korte - one of the inventors in the present case - to bicyclic lactones, there was a need to synthesize compounds comprising cyclopentyl, cyclohexyl and cycloheptyl ring systems (cf. page 201 first paragraph including formulas I to IVa). It is furthermore pointed out by cross-reference to other secondary literature from the field of natural substances that the isolation of isomeric iridomyrmecines from ants, a combat substance known to have both insecticide and antibiotic effects, brought an interesting aspect to the laboratory synthesis of such bicyclic lactones (cf. page 201, last paragraph). Apart from this purely incidental reference to effects caused by substances naturally produced by ants and which are in no way correlated to (insect) repellent activities, document (6) is totally silent in respect of potential practical uses of the other synthetically prepared bicyclic substances. The rest of the document is concerned with the discussion of reaction mechanisms, steric arrangements of substituents and experimental data related to the laboratory synthesis in practice. From this document, it is therefore not possible to make any structurally related activity predictions regarding synthetically prepared substances except for those comprising a cyclopentyl ring.

- 5.2 Accordingly, although document (1) mentions the possibility of using bicyclic lactones as repellents, this teaching is clearly limited to naturally occurring

substances such as iridomyrmecines, i.e. cyclopentanoid monoterpenes produced by certain insects or plants. Therefore, the Board can agree with the Appellant that although the author of (1) was aware of document (6), i.e. prior art relating to the laboratory synthesis of a plurality of gamma and delta bicyclic lactones and in which iridomyrmecine is merely described as an insecticide and antibiotic, the intention cannot have been in (1) to include in the list of synthetic repellents other bicyclic lactones than those described there as natural combat (defensive) substances. There is further support for this view in that apart from the fact that (1) also emphasizes the absence of any relationship between structural elements of a compound and its repellent activity, neither the group of natural substances other than the iridomyrmecines nor the commercially available large group of chemically very different synthetic repellents mentioned in this prior art show the slightest connection between repellent activity and the cyclic structure. Accordingly, document (1) contains no information which might lead the skilled person towards the compounds used in method as now claimed.

- 5.3 Document (5) which was published some twenty years before the priority date of the present application and forms part of the disclosure of (1) by way of reference, relates exclusively to cyclopentanoid monoterpenes isolated from insects and plants (cf. in particular page 1319, Figure 1). This document gives a clear teaching to investigate the whole group of so-called secondary plant substances and in particular the cyclopentanoid monoterpenes, with respect to their insect repellent activity (cf. page 1319, left column). However, in the absence of any pointer to bicyclic lactones not closely related to the said cyclopentanoid monoterpenes and in the light of the technical

background discussed above under point 5.1, this prior art does not contain any technical information extending beyond the disclosure of document (1).

As a consequence, even when taking into account the teaching of (5), the skilled person could at the most come to the conclusion that some naturally occurring cyclopentanoid monoterpene based substances were useful as insecticides, antibiotics or repellents. Accordingly, the Board can only conclude that there is no combination of the discussed documents which would have led the skilled person to assume that compounds falling under formula II of (6) show very similar biological effects as some structurally different products naturally produced by insects or plants.

5.4 In their reasoning the Examining Division made also reference to document (4). This document, however, relates to lactones formed from half esters of cis-3,6-endomethylene -delta⁴- tetrahydrophthalic acid. It is indicated there that these ester lactones supply excellent softening action in vinyl resins and give good plasticity values in butadiene-acrylonitrile rubbers. Without giving any further reference to concrete examples of lactone compounds it is then stated that various lactones are useful as insecticidal toxicants and repellents (cf. column 1, lines 1 to 50). Taking again into account the already discussed lack of correlation between the structure and the repellent activity of a chemical compound, and the fact that the lactones described in (4) show a skeletal structure which is far remote from the generic formula according to present claim 1, this document does not contain any information either which might lead the skilled person towards the present invention.

5.5 The other prior art documents cited during the examination procedure and in the European search report are even less relevant. Document (2), i.e. DE-B-1 007 555 (cf. column 1, lines 1 to 35), and chemical abstracts, vol. 48, no. 2, 25th January 1954, no. 896 c, disclose iridomyrmecin in connection with its insecticidal and antibacterial properties. The same reasoning as set out under point 5.1 above must therefore also apply here. Document (3), US-A-3 923 997 relates to anti-mating compositions for dogs and other domestic animals based on gamma-n-alkyl-gamma-butyrolactone and/or delta-n-alkyl-delta-valerolactone. Although it is stated that the compositions may also serve generally as a repellent for animals, there is no disclosure in this prior art as to a potential effect on other animals than dogs or cats (cf. column 1, lines 1 to 65 and column 3, lines 13 to 22 as well as examples 1 to 16). Thus, not only is there no teaching in (3) to use the anti-mating compositions also as insect repellents but the lactones actually used in these compositions are also not comparable with the bicyclic lactones of the present application. Finally, it is to be noted that document US-A-2 991 220 describes synergistic interactions of combinations of insect repellents on the basis of di-n-butyl succinate and other n-propyl and n-butyl diesters of maleic, fumaric and succinic acids with certain insecticides (cf. column 1, lines 1 to 65; Table 1 and Claim 1). In view of this obligatory use of a specific group of repellent active compounds in combination with compounds having insecticide properties and in the absence of any reference to lactones as such, there is clearly no link to the group of specific bicyclic lactones used according to the method of the present invention.

6. It is accordingly the Board's view that the subject-matter of Claim 1 would not be obvious from any citation taken singly or in combination. Thus, the required inventive step is acknowledged and the requirements of Article 56 EPC are satisfied. Claim 1 and dependent Claims 2 to 7 are therefore allowable having regard to Article 52 (1) EPC.

7. In view of the substantial limitation of the scope of Claim 1 at the appeal stage, the description does not fit with the present claims. The grant of the patent is thus subject to properly adapting the description to the claims.

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the Examining Division with the order to grant a patent on the basis of Claims 1 to 7 received on 6 September 1993 and a correctly adapted description.

The Registrar:

The Chairman:

P. Martorana

P.A.M. Lançon