Candidat's answer

Response to communication

Amendments and basis thereof

Amended claims 1-11 are filed herewith, to replace all claims previously on file.
Claim 1 has been amended to specify that R is alkyl having 3 to 6 carbon atoms. Support for the amendment is found in e.g. paragraph [0009] stating that the group R is preferably an alkyl group preferably of 3 to 6 carbon atoms.

Claim 1 has been further amended to specify that Y is aryl. This amendment finds basis in paragraph [0009], where it is stated that the properties of the compounds can be tailored with different combinations of X, R and Y. It is stated that very good results are obtained if Y is aryl.

Amended claim 2 corresponds to previous claim 3.

Amended claims 3-6 correspond to previous claims 5-8, respectively.

Amended claim 7 is based on previous claim 9 with the amendments of R being specified to be alkyl having 3 to 6 carbon atoms and Y being aryl. Support for these amendments can be found e.g. in paragraph [0009] where alkyl with 3 to 6 carbon atoms is stated as preferred group R and for group Y, aryl is stated as giving very good results.

Claims 8 corresponds to previous claim 10.

Claims 9-11 find support in paragraph [0013]. It is stated that to optimize effectiveness of treatment, an additional proton pump inhibitor may be added andor one or more antibiotics effective against Helicobacter pylori, such as amoxicillin, clarithromycin and/or metronidazole. Such compounds are added in the same tablet as the compound of the invention.

The presently amended claims are clearly derivable from the application as filed as set out above. The requirements of Art. 123(2) EPC are therefore satisfied.
The amended claims are also in line with Art. 84 EPC.

Unity (Art. 82 EPC)

Claim 9 corresponding to amended claim 7 was objected to under Art. 82 EPC. The amended claim 7 satisfies the requirements of Art. 82. EPC since the compound claimed in claim 7 is an intermediate of the compound claimed in claim 1. Therefore, the claims share a common inventive concept.

The intermediate (claim 7) and final products (claim 1) share the same essential structural element, the intermediate incorporating an essential structural element into the final product. Also, the final product is directly manufactured from the intermediate in a single step (see paragraph [0009]).

I refer to the Guidelines C-III 7.3.

Novelty

Document 1 (D1) discloses a belliake compound nitrogen-3-phenyl-4-dodecyl-belliake (NPDB) as being useful as proton pump inhibitor. Medical use in treatment of peptic ulcers in particular when combined with antibiotics is also disclosed. Tests with therapeutic efficacy of various combinations of NPDB with antibiotics are shown. Document D1 fails to disclose a compound of formula (1) where R is alkyl having 3 to 6 carbon atoms, the R group of NPDB being dodecyl. Claim 1 is therefore novel over D1.

Document 1 also fails to disclose any compound of formula (C). Claim 7 is therefore novel over D1.

D1 further fails to disclose a process for making a compound of formula (1). Claim 8 is therefore novel over D1.

Document 2 (D2) discloses compounds of formula (1). X can be NH, S or O. R and Y groups can be same or different and can be chosen from: alkyl, hydroxyalkyl, nitro, amino, aryl or halogen.

D2 fails to specifically disclose a compound of formula (1) where Y is aryl and R is alkyl having 3 to 6 carbon atoms. Thus the particular combination in claim 1, being a selection from two lists is novel, rendering claim 1 novel over D2. The same argument applies to claim 7 which is thus also novel over D2.

D2 also fails to disclose a process for making a compound as specified in claim 1 for the same reasons as shown above. Thus, claim 8 is novel over D2.

The dependent claims 2, 5, 6 and 9-11 are novel by containing all the features of claim 1 and are therefore novel by virtue of their dependency (Guidelines C-IV 11.12).

The claims 3 and 4 directed to first and second medical uses are novel by virtue of being uses of a novel product (Guidelines C-IV 11.12).

In summary, amended claims 1-11 are novel over both D1 and D2.

Inventive step

Claim 1 is directed to novel compounds of formula (I) where

X is NH, O or S
R is alkyl having 3 to 6 carbon atoms and
Y is aryl.

Said compounds are useful as proton pump inhibitors.

The closest prior art is document 2 (D2), since it also relates to compounds of formula (1) useful as proton pump inhibitors.

Document 1 (D1) relates to one special proton pump inhibitor compound only and is therefore somewhat less relevant. D1 also does not relate to the field of novel compounds (rather the properties of existing ones) which also makes is less relevant.

The technical difference between the invention according to the amended claim 1 and the disclosure of D2 is that D2 does not specifically disclose the combination of Y being aryl and R being alkyl having 3 to 6 carbon atoms.

The technical effect conferred by this difference is that compound having good properties both with respect to proton pump inhibition factor (ppif) and Pylori decrease factor (pdf) are provided.
This effect is clearly shown by examples 5, 8, 10, 11, 14 and 17 in comparison to examples 1-4, 6-7, 12-13, 15-16 of the application. It can be noted that the double efficacy is obtained in all cases where X, R and Y are as claimed in amended claim 1, but not in any other combinations of X, R and Y.

Thus, starting from the closest prior art according to D2, the objective technical problem underlying the present invention according to claim 1 was to provide a substance having good efficacy with regard to both ppif and pdf.

The above objective problem is solved by the novel compounds as set out in claim 1. As already indicated in detail above, the example provide experimental evidence for achieving good combined efficacy over the whole range of the claims.

D2 provides no suggestion that the good combined efficacy can be achieved by the combination of X, R and Y as defined in claim 1.

D2 does not contain the slightest hint, let alone a concrete disclosure that such compounds would have the good combined effect. The pdf parameter is not even mentioned in D2.

The same argument applies to D1, since this document only mentions the pdf aspect in context of a combination of NPDB with antibiotics. D1 is silent of the concept of a compound of formula (1) having pdf activity by itself.
Thus, even if the teachings of D1 and D2 were combined, the skilled person would still not arrive at the invention of claim 1.

The results showing that the good combined ppif and pdf efficace from a substance of formula (1) as claimed in claim 1 can be obtained are therefore an unexpected technical effect. For the above reasons it is submitted that the solution to the objective technical problem underlying the present invention of claim 1 is not obvious to the skilled person.

Consequently, the invention according to claim 1 involves inventive step.
It follows that claim 7 is also inventive, being directed to a novel intermediate of a novel and inventive compound.

It also follows that claim 8 is inventive, being a process for making a novel and inventive compound.

It furthermore follows that claims 3 and 4 directed to medical uses of a novel and inventive compound are inventive.

It also follows that the dependent claims 2, 5-6 and 9-11 are inventive. (I refer to Guidelines C-IV 11.12).

Concluding remarks

In view of the above, the amended claims 1-11 are novel, inventive and are industrially applicable; hence comply with the requirements for patentability as set out in Art. 52 EPC.

Grant of a European patent is hereby requested.

In case the Examining division nevertheless intends to refuse the present application, Oral proceedings pursuant to Art. 116 EPC are hereby requested.

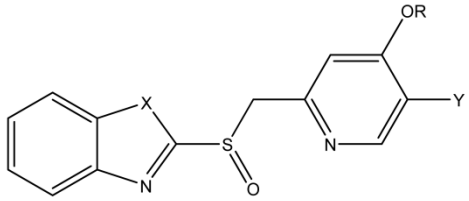
/SIGNATURE/

Mr. Attorney

Professional representative

Claims

1. Compound of formula (1)



in which X is chosen from NH, O and S
R is alkyl having 3 to 6 carbon atoms
Y is aryl.

2. *Compound according to claim 1 in which the aryl group is chosen from phenyl, xylyl and tolyl.*

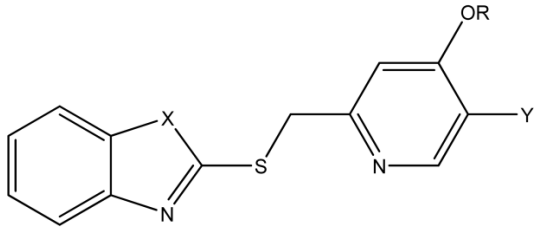
3. *Compound according to claim 1 for use in medicine.*

4. *Compound according to claim 1 for use in the treatment of peptic ulcers.*

5. *Composition comprising the compound of claims 1 to 2 and a pharmaceutically acceptable excipient.*

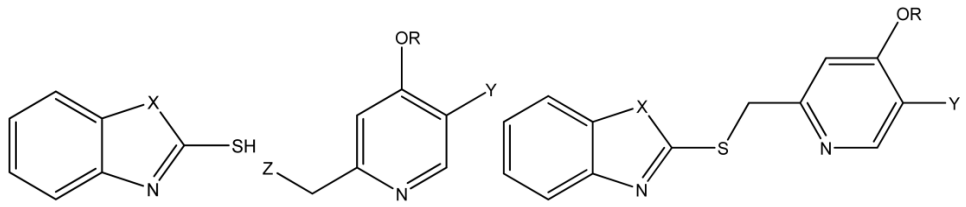
6. *Tablet comprising the composition of claim* 5.

7. *Compound of formula (C):*



in which *X is chosen from NH, O and S*
R is alkyl having 3 to 6 carbon atoms
Y is aryl.

8. *Process for making the compound of claim 1 comprising the steps of: (1) reacting compound A with compound B at a temperature of -78 to 0°C in the presence of a base having a pKa of greater than 13 such as n-butyl lithium, potassium t-butoxide, lithium diisopropylamide, lithium diethylamide and sodium hydride in a solvent selected from ethoxyethane, tetrahydrofuran and dimethyl formamide, forming compound C; and (2) oxidising compound C with an oxidising agent selected from t-butyl hydroperoxide, peracetic acid, m-chloroperbenzoic acid and pyridinium chlorochromate, using dichloromethane, chloroform or toluene as a solvent, the compounds A, B and C being as defined below:*



(A) (B) (C)

and where Z is a leaving group chosen from Br, I, tosylate and mesylate.

9. Tablet according to claim 6, further comprising an additional proton pump inhibitor.

10. Tablet according to claim 6 or 9, further comprising an antibiotic active against Helicobacter pylori.

11. Tablet according to claim 10, wherein the antibiotic is amoxicillin, clarithromycin, metronidazole, or a combination thereof.

EXAMINATION COMMITTEE I

Candidate No.

Paper B (Chemistry) 2011 - Marking Sheet

Category		Maximum possible	Marks awarded	
			Marker	Marker
Claims	Compound / medical uses	25	25	25
	Intermediate compound	10	10	10
Arguments	Amendments	12	8	10
	Novelty	18	15	15
	Inventive Step	30	24	24
	Unity	5	5	5
Total		**100**	**87**	**89**

Examination Committee I agrees on 88 marks and recommends the following grade to the Examination Board:

- [x] PASS (50-100)
- [ ] COMPENSABLE FAIL (45-49)
- [ ] FAIL (0-44)

30 June 2011

Chairman of Examination Committee I