Abstract: The present invention provides an improved process for preparation of (E)-α-[2-butyly-1-[(4-(methoxycarbonyl)phenyl)methyl]-1 H-imidazole-5-yl] methylene]-2-thiophene propanoic acid ethyl ester in high purity and in high yield. Thus, for example, 4-[2-butyly-5-formyl-1 H-imidazole-1-yl][methyl]benzoic acid methyl ester is reacted with ethyl 2-carboxy-3-(2-thienyl) propionate in the presence of piperidinium propionate in diisopropyl ether or a mixture of n-hexane and a solvent selected from toluene and cyclohexane, optionally purifying the crude compound to obtain (E)-α-[2-butyly-1-[(4-(methoxy carbonyl)phenyl)methyl]-1 H-imidazole-5-yl]methylen]-2-thiophene propanoic acid ethyl ester substantially free of 3-(2-thienyl) propanoic acid ethyl ester impurity.
**INTERNATIONAL SEARCH REPORT**

A. CLASSIFICATION OF SUBJECT MATTER

**IPC**: C07D 401/04 (2006.01)

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)

**IPC**: C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPOQUENET; CAS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tr>
<td>E,X</td>
<td>CN 101215284 A (ZHEJIANG HUAHAI PHARMACEUTICAL) 09 July 2008 (09.07.2008) Claims 1-4</td>
<td>1-5</td>
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<tr>
<td>E,X</td>
<td>WO 2008/078330 A1 (HETERO DRUGS LIMITED) 03 July 2008 (03.07.2008) page 4-5, reference example 2, claims 1, 5-10</td>
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☐ 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 23 March 2011 (23.03.2011)

Date of mailing of the international search report 06 April 2011 (06.04.2011)

Name and mailing address of the ISA/AT

**Austrian Patent Office**

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Form PCT/ISA/210 (second sheet) (January 2004)
Continuation of first sheet

Continuation No. III:

Observations where unity of invention is lacking

(Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

- A process for preparing (E)-a-[[2-butyl-1-[[4-(methoxycarbonyl)phenyl]methyl]-1H-imidazole-5-yl]methylene]-2-thiophene propanoic acid ethyl ester (Claims 1-5)
- A process for the purification of (E)-a-[[2-butyl-1-[[4-(methoxycarbonyl)phenyl]methyl]-1H-imidazole-5-yl]methylene]-2-thiophene propanoic acid ethyl ester (Claims 6-8)

The application does not relate to one invention or to a group of inventions so linked as to form a single general inventive concept. The following groups of inventions can be separated in the application.

Group I. of inventions relates to a process for preparing (E)-a-[[2-butyl-1-[[4-(methoxycarbonyl)phenyl]methyl]-1H-imidazole-5-yl]methylene]-2-thiophene propanoic acid ethyl ester.

Group II. of inventions relates to a process for the purification of (E)-a-[[2-butyl-1-[[4-(methoxycarbonyl)phenyl]methyl]-1H-imidazole-5-yl]methylene]-2-thiophene propanoic acid ethyl ester comprising 3-(2-thienyl)propanoic acid ethyl ester impurity in 10% or above. Claims 6-8 in their present forms relate to the production of (E)-a-[[2-butyl-1-[[4-(methoxycarbonyl)phenyl]methyl]-1H-imidazole-5-yl]methylene]-2-thiophene propanoic acid ethyl ester prepared by any known or (presently unknown) production method.

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos. 1-5
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