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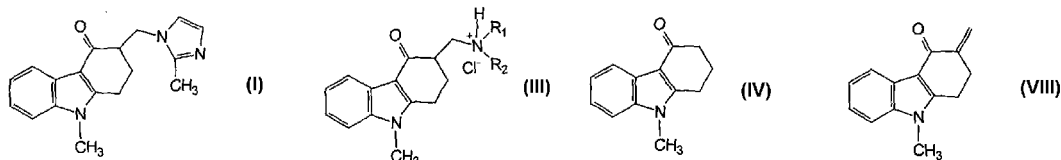
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- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
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- Declarations under Rule 4.17:**
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
 - of inventorship (Rule 4.17(iv))
- Published:**
- with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: A ONE-POT PROCESS FOR THE PREPARATION OF ANTIEMETIC AGENT, 1,2,3,9-TETRAHYDRO-9-METHYL-3-[(2-METHYL)-1H-IMIDAZOLE-1-YL]METHYL]-4H-CARBAZOL-4-O



(57) Abstract: A one-pot industrial process for preparing 1,2,3,9-tetrahydro-9-methyl-3-[(2-methyl-1H-imidazole-1-yl)methyl]-4H-carbazol-4-one of Formula-(I) from 1,2,3,9-tetrahydro-9-methyl-4H-carbazol-4-one of Formula-(IV) involves reaction of Formula (IV) with HNR_1R_2 salt and paraformaldehyde, where R_1, R_2 are independently alkyl groups or together forms a cyclic alkyl group, in a solvent system of acetic acid and hydrocarbon solvent to form a crude mixture of intermediate compounds of Formula (III) and (VIII), which is converted to ondansetron (Formula (I)) without isolation by reaction with 2methylimidazole in a suitable solvent system in the same pot.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IN04/00336

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : C07D 233/56, 403/06; A61K 31/415 US CL : 514/397; 548/311.4 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) U.S. : 514/397; 548/311.4 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) Please See Continuation Sheet		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	U.S. 2004/0181076 A1 (HESOUN, et al.), 16 September 2004 (16.09.2004), at page 4, 1st column, line 1 to page 5, 2nd column, line 40 (process of preparing ondansetron by combining a carbazolone derivative with an dialkyl amine salt and paraformaldehyde, in acetic acid solvent, then adding 2-methyl-imidazole); also page 5, 2nd column, lines 42-45 ("one pot" process as preferred embodiment).	1 - 6, 11 - 16, 19 - 29
A	U.S. 2002/0107275 A1 (LIDOR-HADAS, et al.), 8 August 2002 (08.08.2002), at page 2, lines 25 - 69 and page 3, lines 1 - 13; also page 3, 2nd column, lines 12 - 55 (Ondansetron Form B) and page 3, line 57 to page 4, line 28 (method of preparing Ondansetron Form B).	1 - 6, 11 - 16, 19 - 29
A	U.S. 4,695,578 (COATES, et al.), 22 September 1987 (22.09.1987), at col. 6, line 26 to col. 7, line 30 ("General Process A"); see also col. 7, line 31 to col. 8, line 19 ("General Process B") and col. 8, line 20 to col. 9, line 2 ("General Process C").	1 - 6, 11 - 16, 19 - 29
A	U.S. 2004/0198794 A1 (WESTHEIM, et al.), 7 October 2004 (07.10.2004), at page 3, line 30 to page 4, line 37.	1 - 6, 11 - 16, 19 - 29
A	U.S. 5,478,949 (BOD, et al.), 26 December 1995 (26.12.1995), at col. 3, lines 8 - 51; col. 6 at lines 34 - 54;	1 - 6, 11 - 16, 19 - 29
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> 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 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 06 September 2005 (06.09.2005)		Date of mailing of the international search report 29 SEP 2005
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-8300		Authorized officer <i>Mania J. Watson</i> Anthony J. Paviglianiti Telephone No. (571) 272-3107

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IN04/00336

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Please See Continuation Sheet

3. Claims Nos.: 7, 17 and 18
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box 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:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
 2. As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
 3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

 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.:
- Remark on Protest**
- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
 - The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
 - No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

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Continuation of Box II Reason 2:

Claims 7, 17 and 18 were not examined because they are improper multiply dependent claims under PCT Rule 6.4(a). Specifically, **Claim 7** is dependent upon "The process in claim 2 to 6...", **Claim 17** is dependent upon "The process as claimed in claim 11 to 16." and **Claim 18** is dependent upon "The process in claim 1 or any preceding claim...", which do not conform with the rule that any dependent claim that refers to more than one other claim shall refer to such claim *in the alternative* only.

Claim 18 also is not in conformity with the rule that a multiply-dependent claim may not serve as the basis for another multiply-dependent claim, as it depends on "any preceding claim," [thereby including **Claim 7** and **Claim 17**, which are multiply dependent claims].

Continuation of B. FIELDS SEARCHED Item 3:

CAS Online - STN search of ondansetron and methods of preparing; American Chemical Society journals - search terms: ondansetron, ZOFRAN, imidazole, 5-HT3