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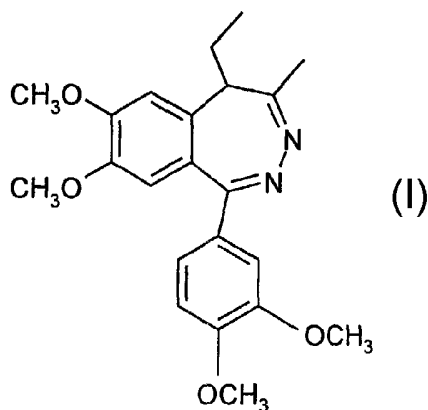
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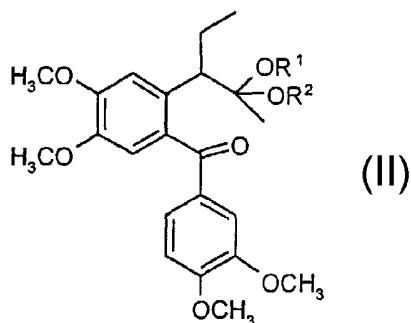
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(54) Title: PROCESS FOR THE PREPARATION OF TOFISOPAM AND NEW INTERMEDIATES



(57) Abstract: The invention relates to a new process for the preparation of 1-(3,4-dimethoxy-phenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine of Formula (I) which comprises reacting a compound of general Formula (II) (wherein R<sup>1</sup> and R<sup>2</sup> independently each stands for C<sub>1-4</sub>-alkyl or together form C<sub>2-6</sub>-alkylene) with hydrazine or a hydrate or salt thereof formed with an inorganic or organic acid. 1-(3,4-dimethoxy-phenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine of the Formula I is a known anxiolytic agent. The invention also relates to new intermediates and a process for the preparation thereof.



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## INTERNATIONAL SEARCH REPORT

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## A. CLASSIFICATION OF SUBJECT MATTER

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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)

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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 practical, search terms used)

WPI Data, CHEM ABS Data, EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GATTA F ET AL: "Derivatives of 2,3-Benzodiazepine" FARMACO, EDIZIONE SCIENTIFICA, SOCIETA CHIMICA ITALIANA, PAVIA, IT, vol. 40, 1985, pages 942-955, XP009011786 ISSN: 0430-0920 cited in the application Scheme 2, compounds VI-VII-II, page 949 compound VIIc, page 951 compound IIC, table VI compound VIIc5, table VII compound IIC5 page 943 -page 944	1-35
X	DE 21 22 070 A (E G Y T GYOGYSZERVEGYESZETI GYAR) 8 June 1972 (1972-06-08) page 5, line 29 - line 5; claim 1; example 1	1-35

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

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on on patent family members

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
DE 2122070	A	08-06-1972	AT 310171 B	25-09-1973
			AT 311982 B	10-12-1973
			BE 769080 A1	03-11-1971
			DE 2122070 A1	08-06-1972
			ES 392378 A1	16-09-1973
			FR 2112485 A1	16-06-1972
			GB 1334271 A	17-10-1973
			HK 27776 A	21-05-1976
			NL 7108994 A	09-05-1972
			PH 9942 A	14-06-1976
			PL 71111 B1	30-04-1974
			SE 368206 B	24-06-1974
			US RE30014 E	29-05-1979
			YU 112271 A1	29-02-1984
			ZA 7102798 A	23-02-1972

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