trans-2-Aminoethyl 2-Acetoxycinnamates. Potential Analgetic Antiinflammatory Agents

ALEX GRINGAUZ

Brooklyn College of Pharmacy, Long Island University, Brooklyn, New York 11216

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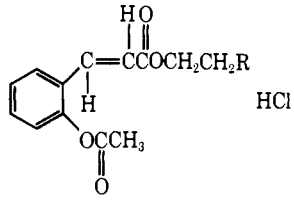
As part of a continuing study of compounds related to salicylic acid[1] a series of five 2-aminoethyl 2-acetoxycinnamates were prepared as HCl salts for biological evaluation. Oral administration to mice at a 200 mg/kg dose level failed to elicit any tetrabenazine antagonism nor other dose range activity. Compounds III and IV failed to show activity in the gastric acid secretion test carried out in the chronic gastric fistula rat at 50 mg/kg. An adjuvant arthritic screen exhibited no antiinflammatory activity.

Experimental Section

***trans*-2-Diethylaminoethyl 2-Acetoxycinnamate Hydrochloride** (I).—To a PhH solution of *o*-acetoxycoumaryl chloride prepared from 10.3 g (0.05 mole) of *o*-acetoxycoumaric acid[2] there was added 5.85 g (0.05 mole) of 2-diethylaminoethanol in PhH dropwise at room temp. The mixt was stirred several hours, and the ppt was collected. Several recrysts from EtOAc–*i*-PrOH afforded 60% of product, mp 127–129°. *Anal.* ($C_{17}H_{24}ClNO_4$) C, H. Ir spectra were as expected. The other compounds similarly prepared are given in Table I.

TABLE I



Compd	R	Mp, °C[a]	Formula	Anal.[b]
I	Diethylamino	127–129	$C_{17}H_{24}ClNO_4$	C, H
II	Piperidino	179–181	$C_{18}H_{24}ClNO_4$	C, H
III	*tert*-Butylamino	131–133	$C_{17}H_{24}ClNO_4$	C, H[c]
IV	Morpholino	194–196	$C_{17}H_{22}ClNO_5$	C, H
V	3-Aza[3.2.2]bicyclononyl	181–184	$C_{21}H_{29}ClNO_4$	C, H

[a] Determined on a Hoover Uni-Melt and uncorrected. Ir spectra were recorded on a Perkin-Elmer 337 (KBr). [b] Elemental analyses were performed by Dr. F. B. Strauss, Oxford, England, and were within 0.4% of calcd value. [c] Calcd: C, 59.73, H, 7.08; found: C, 60.41, H, 7.33.

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(1) (a) G. Cwalina and A. Gringauz, *J. Org. Chem.*, **26**, 3344 (1960). (b) A. Gringauz, *J. Med. Chem.*, **11**, 611 (1968). (c) A. Gringauz, *J. Pharm. Sci.*, **59**, 422 (1970). (d) A. Gringauz, *J. Med. Chem.*, **13**, 1250 (1970).

(2) T. S. Seshardi and P. S. Rao, *Proc. Indian Acad. Sci.*, **3A**, 293 (1936).

Derivatives of Fluorene. 34.[1] N^1-Acetyl-N^2-fluorenylasparagines[2]

MOSES J. NAMKUNG AND T. LLOYD FLETCHER*

Chemistry Research Laboratory, Department of Surgery, University of Washington, School of Medicine, Seattle, Washington 98105

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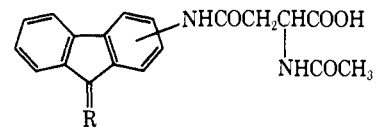
We have prepared all of the N^1-acetyl-N^2-(ring)-fluorenyl (and 9-oxofluorenyl)asparagines (see Table I). Thus far these compounds have been screened by the Cancer Chemotherapy National Service Center, National Cancer Institute, in BDF_1 mice with L1210 lymphoid leukemia; all were inactive.

TABLE I

N^1-ACETYL-N^2-FLUORENYLASPARAGINES



R	Ring position	L or DL	Yield, %	Mp, °C	Formula	Analyses
H_2	1	L	80	203–204	$C_{19}H_{18}N_2O_4$	C, H, N
H_2	2	L	98	207–209	$C_{19}H_{18}N_2O_4$	C, H, N
H_2	3	L	95	219–220	$C_{19}H_{18}N_2O_4$	C, H, N
H_2	4	L	89	250–251	$C_{19}H_{18}N_2O_4$	C, H, N
H_2	1	DL	98	227–228	$C_{19}H_{18}N_2O_4$	C, H, N
H_2	2	DL	99	198–200	$C_{19}H_{18}N_2O_4$	C, H, N
H_2	3	DL	96	211–212	$C_{19}H_{18}N_2O_4$	C, H, N
H_2	4	DL	96	221–222	$C_{19}H_{18}N_2O_4$	C, H, N
O	1	L	88	223–224	$C_{19}H_{16}N_2O_5$	N
O	2	L	85	245–246	$C_{19}H_{16}N_2O_5$	N
O	3	L	95	262–263	$C_{19}H_{16}N_2O_5$	N
O	4	L	93	277–278	$C_{19}H_{16}N_2O_5$	N

Experimental Section

N^1-Acetyl-N^2-fluorenyl-L(or DL)-asparagines.—To a soln of 1.8 g (0.01 mole) of each of the 4 fluorenamines in 200 ml of abs EtOH, 1.6 g (0.01 mole) of *N*-acetyl-L(or DL)-aspartic anhydride[3] was added, and the mixt was boiled for 15 min. It was then boiled down to 30 ml and allowed to cool to room temp. The white ppt was filtered and dried. One recrystn from EtOH gave an analytically pure sample of each compd.

N^1-Acetyl-^2N-(9-oxofluorenyl)-L-asparagine.—To a soln of 3 g (0.015 mole) of each of the four 9-oxofluorenamines in 30 ml of pyridine, 2.4 g (0.015 mole) of *N*-acetyl-L-aspartic anhydride was added, and the mixt was boiled for 3 min and cooled. Upon pouring into H_2O and acidifying with HCl, a yellow ppt appeared which was filtered, washed with H_2O, and dried.

(1) For paper 33 see T. L. Fletcher and M. J. Namkung, *J. Org. Chem.*, **35**, 4232 (1970).

(2) Supported in part by Grant No. CA-01744 from the National Cancer Institute and by Career Development Award 5-KO3-CA-14,991.

(3) C. C. Barker, *J. Chem. Soc.*, 453 (1953).