

trans-2-Aminoethyl 2-Acetoxy-cinnamates.
Potential Analgetic Antiinflammatory Agents

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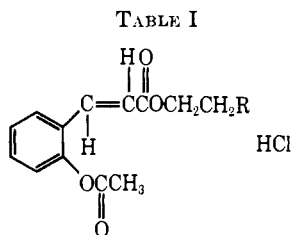
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As part of a continuing study of compounds related to salicylic acid¹ a series of five 2-aminoethyl 2-acetoxy-cinnamates were prepared as HCl salts for biological evaluation. Oral administration to mice at a 200 mg/kg dose level failed to elicit any 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-Acetoxy-cinnamate Hydrochloride (I).—To a PhH solution of *o*-acetoxy-coumaril chloride prepared from 10.3 g (0.05 mole) of *o*-acetoxy-coumaric acid² 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 recryst from EtOAc-*i*-PrOH afforded 60% of product, mp 127–129°. *Anal.* (C₁₇H₂₄NClO₄) C, H. Ir spectra were as expected. The other compounds similarly prepared are given in Table I.



Compd	R	Mp, °C ^a	Formula	Anal. ^b
I	Diethylamino	127–129	C ₁₇ H ₂₄ NClO ₄	C, H
II	Piperidino	179–181	C ₁₈ H ₂₄ NClO ₄	C, H
III	<i>tert</i> -Butylamino	131–133	C ₁₇ H ₂₄ NClO ₄	C, H ^c
IV	Morpholino	194–196	C ₁₇ H ₂₃ NClO ₅	C, H
V	3-Aza[3.2.2]bicyclononyl	181–184	C ₂₁ H ₂₈ NClO 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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Derivatives of Fluorene. 34.¹
N¹-Acetyl-N²-fluorenylasparagines²

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We have prepared all of the N¹-acetyl-N²-(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 BDF₁ mice with L1210 lymphoid leukemia; all were inactive.

TABLE I
 N¹-ACETYL-N²-FLUORENYLASPARAGINES

R	Ring position	L or DL	Yield, %	Mp, °C	Formula	Analyses
H ₂	1	L	80	203–204	C ₁₉ H ₁₈ N ₂ O ₄	C, H, N
H ₂	2	L	98	207–209	C ₁₉ H ₁₈ N ₂ O ₄	C, H, N
H ₂	3	L	95	219–220	C ₁₉ H ₁₈ N ₂ O ₄	C, H, N
H ₂	4	L	89	250–251	C ₁₉ H ₁₈ N ₂ O ₄	C, H, N
H ₂	1	DL	98	227–228	C ₁₉ H ₁₈ N ₂ O ₄	C, H, N
H ₂	2	DL	99	198–200	C ₁₉ H ₁₈ N ₂ O ₄	C, H, N
H ₂	3	DL	96	211–212	C ₁₉ H ₁₈ N ₂ O ₄	C, H, N
H ₂	4	DL	96	221–222	C ₁₉ H ₁₈ N ₂ O ₄	C, H, N
O	1	L	88	223–224	C ₁₉ H ₁₆ N ₂ O ₅	N
O	2	L	85	245–246	C ₁₉ H ₁₆ N ₂ O ₅	N
O	3	L	95	262–263	C ₁₉ H ₁₆ N ₂ O ₅	N
O	4	L	93	277–278	C ₁₉ H ₁₆ N ₂ O ₅	N

Experimental Section

N¹-Acetyl-N²-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 anhydride³ 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.

N¹-Acetyl-N²-(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 H₂O and acidifying with HCl, a yellow ppt appeared which was filtered, washed with H₂O, 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-K03-CA-14,991.

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