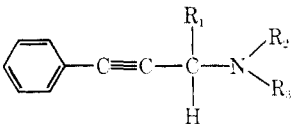
TABLE I



Compd	R_1	R_2	R_3	Mp (HCl), °C dec[a]	Yield, %	Formula	Anal[b]	Method	pK_a
I	H	H	H	216–217	51.6	$C_9H_{10}NCl$	C, H, N[c]	A	8.42
II	H	H	Me	165–166	58	$C_{10}H_{12}NCl$	C, H, N	A	8.10
III	H	H	Et	180–180.5	57	$C_{11}H_{14}NCl$	C, H, N[d]	A	8.30
IV	H	Me	Me	162–163	35.6	$C_{11}H_{14}NCl$	C, H, N	B	7.27
V	H	Et	Et	137–138	39	$C_{13}H_{18}NCl$	C, H, N	B[e,f]	8.46
VI[g]	Me	H	H	178–178.5	60	$C_{10}H_{12}NCl$	C, H, N	A[h]	7.93
VII	Me	H	Me	152.5–153	65	$C_{11}H_{14}NCl$	C, H, N	A[h]	8.21
VIII	Me	H	Et	178.5–179	60	$C_{12}H_{16}NCl$	C, H, N	A[h]	8.67
IX	Me	Me	Me	205–205.5	66	$C_{12}H_{16}NCl$	C, H, N[i]	A[h,j]	7.55
X	Me	Et	Et	134–135	55	$C_{14}H_{20}NCl$	C, H, N[k]	A[h,l]	7.57

[a] Melting points (uncorr) were taken in open capillary tubes. [b] Microanalyses were performed by Dr. C. Daessle, Organic Microanalysis, Montreal. [c] N: calcd, 8.36; found, 7.72. [d] C: calcd, 67.5; found, 68.4. [e] Water bath, 90 min. [f] Reagent II, Et_2N (Experimental Section). [g] Compounds VI–X were not resolved. [h] Reagent I, 1-phenyl-3-bromo-1-butyne (Experimental Section). [i] C: Calcd 68.7, found 69.14. [j] Five min. [k] C: Calcd 70.7, found 70.25. [l] Three days, room temperature.

ser for 30 hr. Work-up in the usual manner gave 31.7 g of the free base. Treatment of the base with HCl gas in Et_2O gave a solid which was recrystd (Me_2CO).

Antifungal Activity and Geometric Isomerism. Anilides of *o*-Coumarinic Acid

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The report by Schultz[1] that anilides of *o*-coumaric acid possessed some antifungal properties prompted the preparation of several cis analogs, anilides of *o*-coumarinic acid, for biological evaluation. Screening against *Trychophyton mentagrophytes*, *T. rubrum*, and *Candida albicans* by known methods,[2] however, showed these compounds to be inactive.

Experimental Section[3]

***o*-Hydroxy-*cis*-cinnamanilide.**—To a PhH solution of *o*-acetoxycoumarinyl chloride, prepared from 10.3 g (0.05 mole) of *o*-acetoxycoumarinic acid,[4] there was added 9.3 g (0.1 mole) of $C_6H_5NH_2$ at room temperature. After allowing the mixture to evaporate to dryness it was treated with 5% HCl. The solid obtained was then treated with 0.1 *N* NaOH for 30 min at 40–45°. Filtration and rapid acidification of the cooled filtrate (HCl) gave 5.9 g (49%) of product. Purification was effected by solution in cold EtOH and precipitation with crushed ice. Several repetitions gave mp 114–115° (trans isomer, mp 186–187°[1]). *Anal.* ($C_{15}H_{13}NO_2$) C, H.

A 1-g sample was refluxed in 95% EtOH for 1 hr. The product obtained after recrystallizing twice (EtOH 50%), melted at 186–188° (reported[1] mp 186–188°). A mixture melting point with an authentic sample of 2-hydroxycinnamanilide gave no depression; the ir spectra were identical.[5]

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(1) H. W. Schultz, *J. Pharm. Sci.*, **52**, 503 (1963).

(2) A. M. Kligman and E. J. Rosenweig, *J. Invest. Dermatol.*, **10**, 51 (1948).

(3) Melting points were determined on a Thomas-Hoover Uni-Melt and are uncorrected. Ir spectra were recorded on a Perkin-Elmer 337 (KBr); uv spectra on a Hitachi-Coleman 124 (95% EtOH). Elemental analyses were performed by F. B. Strauss, Oxford, England.

(4) R. Stoermer and B. Ladewig, *Ber.*, **44**, 651 (1911).

(5) The 2′-methyl- and 3′-methyl-*o*-hydroxy-*cis*-cinnamanilides were also prepared. However, repeated purifications failed to give samples of analytical purity. Recrystallizations from hot polar solvents invariably led to partial or total isomerization to the trans isomer. Uv spectra on all three compounds were as expected.

Potential Antidiabetics. VI. 3-Methyl-4-arylhydrazono-2-isoxazolin-5-ones and 3-Methyl-4-arylazo-5-(methyl/phenyl)isoxazoles

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In view of the weak hypoglycemic[1-5] and chemotherapeutic[6] properties of some pyrazoles, the synthesis of 3-methyl-4-arylhydrazono-2-isoxazolin-5-ones (I), 3,5-dimethyl-4-arylazoisoxazoles (IIa), and 3-methyl-5-phenyl-4-arylazoisoxazoles (IIb) containing both isoxazolyl and either arylhydrazono or arylazo grouping was undertaken.

Oral administration at various doses (12.5 to 100 mg/kg) in fasted male guinea pigs for 18 hr prior to and during testing, of 3-methyl-4-arylhydrazono-2-isoxazolin-5-ones (I) and 3,5-dimethyl-4-arylazoisoxazoles

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(2) H. G. Garg and P. P. Singh, *ibid.*, **11**, 1103 (1968).

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(5) W. E. Dulin and G. C. Gerritsen, *Proc. Soc. Exp. Biol. Med.*, **113** 683 (1963).

(6) R. G. Micetich, *J. Med. Chem.*, **12**, 611 (1969).