

exts from seed meals may be expected to exhibit nonspecific absorption in the uv, it was considered likely that a correction would be necessary. Minima on either side of the λ_{\max} 283 peak occurred near 255 and 305 nm. To provide the desired correction, absorbances at 255 and 305 nm were averaged and subtracted from the absorbance at the maximum to give a net value. From our measurements a net absorbance of 1.000 was equiv to 65 $\mu\text{g}/\text{ml}$. Confidence in the uv absorption as a rapid means of quantitation was gained by comparison of the value (6.7%) obtained for *M. holtonii* with that calcd for *M. holtonii* when detd on the ion-exchange analyzer (6.2%).

Dopa was isolated from *M. deeringiana* by the patented process.⁴ The dopa used for reference and calibration measurements

was from Mann Research Laboratories. Uv measurements were made with a Beckman Model DK-2a recording spectrophotometer.

The names of the 135 families, 447 genera, and 724 species examined in the present work are available from the authors on request.

Acknowledgments.—We thank Mrs. Gertrude Rose for technical assistance and Mr. J. F. Cavins for estimation measurements of dopa with the amino acid analyzer.

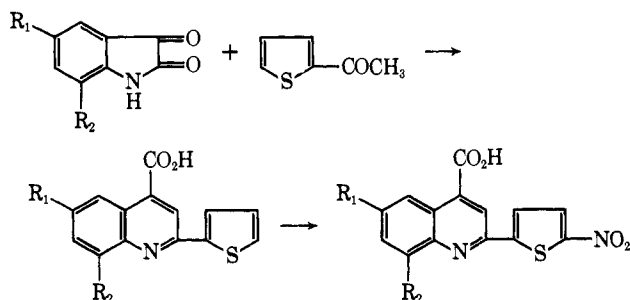
New Compounds

2-(5-Nitro-2-thienyl)cinchoninic Acids

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The antibacterial activities of 2-(5-nitro-2-furyl)cinchoninic acid and derivatives have been reported.¹ In a search for more potent antibacterial compounds, we have been preparing a series of their S analogs, 2-(5-nitro-2-thienyl)cinchoninic acids.



Preliminary *in vitro* tests of the compounds prepared, against *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Salmonella typhosa*, and *Staphylococcus album* did not show significant activity.

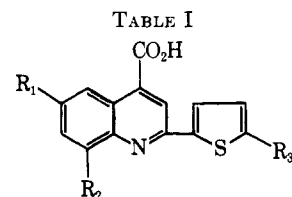
Experimental Section²

2-(2-Thienyl)cinchoninic Acids.—A mixture of 0.02-mole quantities of an appropriate isatin and 2-acetylthiophene in 15 ml of aq 20% KOH and 15 ml of EtOH was heated under reflux for 12 hr. The reaction mixt was cooled and acidified with dil HCl and the resulting yellow ppt was removed by filtration and crystd from AcOH (See Table I).

2-(5-Nitro-2-thienyl)cinchoninic Acids.—To a cold soln of 0.01 mole of 2-(2-thienyl)cinchoninic acid in 15 ml of concd H_2SO_4 , 3 ml of a mixt of concd H_2SO_4 and concd HNO_3 (1:1) was added with vigorous stirring. After 1 hr, 200 g of crushed ice was added to the reaction mixt and the resulting ppt was filtered and crystd from AcOH. The positions of the NO_2 groups were confirmed by nmr spectroscopy (DMSO). (See Table I.)

(1) Homer A. Burch, *J. Med. Chem.*, **12**, 535 (1969).

(2) Melting points were taken on a Kofler hot stage microscope and were uncorrected. The ir spectra were determined with a Leitz Model III spectrograph. Nmr spectra were obtained on a Varian A60A instrument.



No.	R ₁	R ₂	R ₃	Yield, %	Mp, °C dec	Formula ^a
1	H	H	H	80	210 ^b	C ₁₄ H ₉ NO ₂ S
2	H	H	NO ₂	63	280	C ₁₄ H ₈ N ₂ O ₄ S
3	F	H	H	79	250	C ₁₄ H ₈ FN ₂ O ₂ S
4	F	H	NO ₂	84	299	C ₁₄ H ₇ FN ₂ O ₄ S
5	Cl	H	H	73	261	C ₁₄ H ₈ ClNO ₂ S
6	Cl	H	NO ₂	85	293	C ₁₄ H ₇ ClN ₂ O ₄ S
7	Br	H	H	95	250	C ₁₄ H ₈ BrNO ₂ S
8	Br	H	NO ₂	74	262	C ₁₄ H ₇ BrN ₂ O ₄ S
9	CH ₃	H	H	90	222	C ₁₅ H ₁₁ NO ₂ S
10	CH ₃	H	NO ₂	78	308	C ₁₅ H ₁₀ N ₂ O ₄ S
11	H	CH ₃	H	82	242	C ₁₅ H ₁₁ NO ₂ S
12	H	CH ₃	NO ₂	91	282	C ₁₅ H ₁₀ N ₂ O ₄ S

^a All compds were analyzed for C, H, and the anal. results were satisfactory. All compds were subjected to nmr and ir spectroscopy. The spectroscopic data were as expected. ^b Lit. [P. Schaefer, K. S. Kulkarni, R. Costin, J. Higgins, and L. M. Honig, *J. Heterocycl. Chem.*, **7**, 607 (1970)] gives mp 209–211°.

Acknowledgments—The authors gratefully acknowledge the constant encouragement of Professor A. Zargari of Tehran University.

Analogues of Albizziin

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Received October 22, 1970

The experimental and clinical use of asparaginase as antitumor agent¹ has led to a renewed interest in the synthesis of analogs of asparagine. Albizziin, L-2-amino-3-ureidopropionic acid,² contains an NH group

(1) J. D. Broome, *Trans. N. Y. Acad. Sci.*, **30**, 690 (1968).

(2) A. Kjaer, P. O. Larsen, and R. Gmelin, *Experientia*, **15**, 253 (1959); *Chem. Abstr.*, **54**, 17263f (1960).

in place of the 4-CH₂ group of glutamine and is thus a potential antagonist of this amino acid. However, there is also a structural resemblance to the lower homolog asparagine, and several *N'*-(substituted)ureidoalanine derivatives were synthesized for study in microbial and tissue culture systems.

Experimental Section³

L-2-*p*-Toluenesulfonamido-3-[*N'*-(substituted)ureido]propionic Acids (Table I).—All of these derivatives were prepd in a similar

TABLE I
RNHCONHCH₂CHCO₂H

R group	Mp, °C	Yield, %	Empirical formula ^a
Et	180–181 ^b	47	C ₁₃ H ₁₉ N ₃ O ₅ S
<i>n</i> -Pr	142–143 ^c	25	C ₁₄ H ₂₁ N ₃ O ₅ S
<i>n</i> -Bu	130–131 ^d	42	C ₁₅ H ₂₃ N ₃ O ₅ S
Allyl	141–142 ^d	76	C ₁₄ H ₁₉ N ₃ O ₅ S
Cyclohexyl	143–144 ^d	67	C ₁₇ H ₂₅ N ₃ O ₅ S
Ph	177–178 ^d	90	C ₁₇ H ₁₉ N ₃ O ₅ S
2-ClC ₆ H ₄	183–184 ^b	75	C ₁₇ H ₁₈ ClN ₃ O ₅ S
3-ClC ₆ H ₄	189–190 ^c	75	C ₁₇ H ₁₈ ClN ₃ O ₅ S
4-ClC ₆ H ₄	199–200 ^c	94	C ₁₇ H ₁₈ ClN ₃ O ₅ S
3,4-Cl ₂ C ₆ H ₃	211–212 ^b	69	C ₁₇ H ₁₇ Cl ₂ N ₃ O ₅ S
2,5-Cl ₂ C ₆ H ₃	189–190 ^c	64	C ₁₇ H ₁₇ Cl ₂ N ₃ O ₅ S
Naphthyl	191–192 ^b	66	C ₂₁ H ₂₁ N ₃ O ₅ S

^a For analyses indicated by symbols, the analytical results were within ±0.4% of the calcd values. All compds were analyzed for C, H, N. ^b From 95% EtOH. ^c From EtOAc. ^d From EtOAc-hexane.

fashion by conversion of *N*²-*p*-tolylsulfonfyl-L-asparagine⁴ to 3-amino-2-*p*-toluenesulfonamido-L-propionic acid by the method of Rudinger, *et al.*,⁵ and finally condensation with the appropriate isocyanate. A soln of 0.009 mole of the isocyanate in 20 ml of CHCl₃ was added with stirring over a 2-hr period to 0.009 mole of 3-amino-2-*p*-toluenesulfonamido-L-propionic acid in 15 ml of 1 *N* NaOH, and the reaction mixt was allowed to stir an additional 16 hr at room temp. The aq phase was sepd, taken to pH 1 with HCl, and satd with NaCl. After refrigeration, the solid which formed was filtered, washed with cold H₂O, air-dried, and crystd from the solvent indicated in Table I.

L-2-Amino-3-[*N'*-(substituted)ureido]propionic Acids (Table II).—Using comparable synthetic procedures for each compd,⁶ 0.002 mole of the toluenesulfonamido derivatives previously described were dissolved in 30 ml of liquid NH₃, and approximately 0.3 g of Na was added in small pieces with stirring. The addition of Na was regulated by the disappearance of the blue color, and the reaction was considered complete when the blue color persisted for about 3 min. The excess Na was decompd by the addition of NH₄OAc, and NH₃ was allowed to evap at room temp. The residue was dissolved in a few milliliters of H₂O,

TABLE II
RNHCONHCH₂CHCO₂H
|
NH₂

R group ^a	Mp, °C	Yield, %	Empirical formula ^b
<i>n</i> -Bu	238–239	41	C ₈ H ₁₇ N ₃ O ₃
Allyl	232–233	18	C ₇ H ₁₃ N ₃ O ₃
Cyclohexyl hydrate	203–204	29	C ₁₀ H ₂₁ N ₃ O ₄
Ph	222–223	45	C ₁₀ H ₁₃ N ₃ O ₃

^a Na-liquid NH₃ cleavage of the protective *p*-toluenesulfonamido group also hydrogenolyzed the Cl substituents on the benzene ring. ^b See Table I, footnote *a*.

acidified to pH 3 with dil HCl, and placed in a refrigerator. The crystals which formed were recrystd from EtOH-H₂O and dried over CaCl₂ *in vacuo*.

Acknowledgments.—The authors are indebted to the Robert A. Welch Foundation and to the Samuel Roberts Noble Foundation for support of this study.

Conversion of Ergosterol into the Estrogen Neoergosterol by Direct Peroxide Cleavage

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Received November 20, 1970

Ergosterol and its irradiation product (vitamin D) have been shown to have marked estrogenic activity.² Neoergosterol was reported to demonstrate still greater estrogenic activity by the same workers.² Neoergosterol has been prepared by the irradiation of ergosterol in the presence of a sensitizing dye followed by a pyrolytic reaction.³ We have now shown that by application of a new type of peroxide-induced C-C cleavage reaction,⁴ neoergosterol can be prepared in a simple one-step reaction from ergosterol.

Experimental Section

Neoergosterol.—Ergosterol (1.50 g) and an equimolar amt of di-*tert*-butyl peroxide (0.530 g) were dissolved in 15 ml of H₂SO₄-washed and redistd decane. The soln was refluxed for 1 hr (174°). Crystals pptd on standing overnight and were found to be unreacted ergosterol (8%). The filtered reaction mixt was coned to a thick syrup under reduced pressure. The product was chromatographed over silica gel employing the following solvents in the order listed: hexane; 95:5 hexane-PhH; 50:50 hexane-PhH; PhH; Et₂O; and EtOH. The Et₂O eluate crystd and was recrystd twice from 95% EtOH to give (14%) neoergosterol: mp 150–151°, [α]_D²⁵ -12.1° (c 0.33, CHCl₃); lit.⁵ mp 151–152°, [α]_D²⁵ -12° (CHCl₃). Ir and uv spectra were as expected.

(3) Melting points were determined on a Thomas-Hoover apparatus; microanalyses were carried out by Mrs. Delaney Blocker, Chemistry Department, North Texas State University, Denton, Texas.

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(5) J. Rudinger, K. Poduška, and M. Zaoral, *ibid.*, **25**, 2022 (1960).

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(2) J. W. Cook, E. C. Dodds, C. L. Hewett, and W. Lawson, *Proc. Roy. Soc., Ser. B.*, **114**, 272 (1934).

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(4) W. H. Schuller and R. V. Lawrence, *Chem. Ind. N. Z.*, **6**, 203 (1970).

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