(8) A. V. J. Challoner, in "Non-Invasive Physiological Measurements, Vol. I," P. Rolfe, Ed., Academic, New York, N.Y., 1979, pp. 125–151.
(9) A. B. Hertzmann and W. C. Randall, *J. Appl. Physiol.*, **1**, 234 (1948).
(10) E. G. Cummings, *J. Invest. Dermatol.*, **53**, 64 (1969).
(11) P. Thune, *Acta Derm. Venerol.*, **51**, 261 (1971).
(12) C. Ramsay, *Br. J. Dermatol.*, **81**, 37 (1969).
(13) R. B. Stoughton, W. E. Clendenning, and D. Kruse, *J. Invest. Dermatol.*, **35**, 337 (1960).
(14) W. J. Albery and J. Hadgraft, *J. Pharm. Pharmacol.*, **31**, 140 (1979).
(15) R. B. Fountain, B. S. Baker, J. W. Hadgraft, and I. Sarkany, *Br. J. Dermatol.*, **81**, 202 (1969).
(16) R. H. Guy and H. I. Maibach, *Arch. Dermatol. Res.*, **273**, 91 (1982).

ACKNOWLEDGMENTS

Partial presentation of the work reported here was made at the 31st National Meeting of the APhA Academy of Pharmaceutical Sciences in Orlando, Florida, November 1981 and at the 43rd Annual Meeting of the Society for Investigative Dermatology in Washington, DC, May 1982.

The authors thank Medpacific, Inc. for the loan of the LDV apparatus and representatives of both Medpacific and Medasonics for their assistance and comments.

Stabilizing Effect of Fructose on Aqueous Solutions of Hydrocortisone

N. P. BANSAL, E. M. HOLLERAN, and C. I. JAROWSKI ˣ

Received July 1, 1982 from the *Department of Allied Health and Industrial Sciences, College of Pharmacy and Allied Health Professions and the School of Chemistry, St. John's University, Jamaica, NY 11439.* Accepted for publication August 26, 1982.

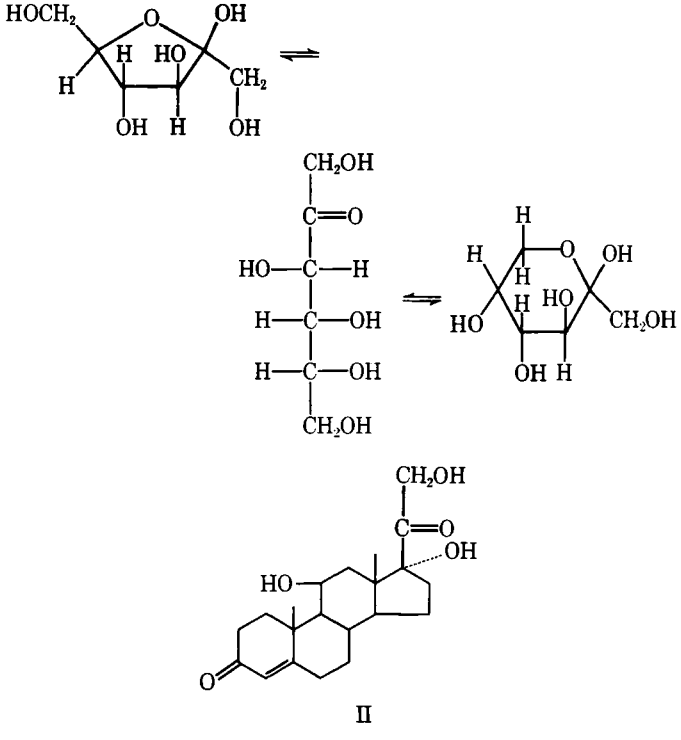
Abstract □ Accelerated stability studies (37°, 47°, and 57°) were conducted on buffered aqueous solutions (pH 7.4, 8.4, and 9.4) of hydrocortisone in the presence of various molar ratios of D-fructose. First-order degradation was observed. Significant improvement in hydrocortisone stability was seen in those solutions containing a 25 *M* excess of D-fructose. Hydrocortisone solutions containing dextrose, lactose, sucrose, sorbitol, propylene glycol, or glycerin in the same molar ratio were not stabilized.

Keyphrases □ Hydrocortisone—stability in aqueous buffers, stabilization by D-fructose □ Stability studies—hydrocortisone, stability in aqueous buffers, stabilization by D-fructose

A ketol side chain is present at the 17-position in the following therapeutically important glucocorticoids: cortisone, hydrocortisone, dexamethasone, prednisone, prednisolone, and 6-α-methylprednisolone. Removal of the ketol side chain results in a significant loss of therapeutic activity.

The reactivity of the ketol side chain of the adrenocorticosteroids is well documented. Base-catalyzed rearrangements and eliminations have been shown to occur under both aerobic and anaerobic conditions (1–5). Guttman and Meister (6) showed that at least three parallel first-order reactions were involved in the base-catalyzed degradation of prednisolone. Neutral and acidic degradation products were obtained. Caspi *et al.* (7) studied oxidative cleavage of the ketol side chain of cortisone with lead tetraacetate. Lewbart and Mattox (8) reported that trace amounts of copper in actinic glassware caused destruction of cortisone and related steroids.

Mauger *et al.* (9) followed the degradation of 21-hydrocortisone hemisuccinate at 70° in aqueous solutions buffered at pH 6.9, 7.2, and 7.6. The data obtained indicated that the overall kinetic pathway at each pH value could be interpreted as consecutive first-order reactions. The blue tetrazolium assay confirmed that the production of a species devoid of the ketol side chain at the 17-position occurred after the steroid alcohol was formed. The ketol group imparts reducing properties to the glucocorticoid molecules similar to those of fructose (Scheme I), which contains a similar ketol group. It was speculated that the presence of excess fructose in aqueous solutions of hydrocortisone (II) might retard the base-catalyzed degradation of the latter. The significance of the ketol group would be checked by using other polyols lacking this group.



II

EXPERIMENTAL

Materials—The following were obtained from commercial sources: hydrocortisone, USP (lot 15C-6126)[1], blue tetrazolium[1], tetramethylammonium hydroxide[1], D-fructose[2], dextrose USP[3], glacial acetic acid

[1] Sigma Chemical Co., St. Louis, Mo.
[2] Pfaltz and Bauer, Inc., Flushing, N.Y.
[3] Mallinckrodt Chemical Works, St. Louis, Mo.

0022-3549/83/0900-1079$01.00/0

Table I—Rate of Degradation of Hydrocortisone at pH 7.4 in the Presence of D-Fructose at 37, 47, and 57°

Time, hr	Percent Remaining, Molar Ratio of Hydrocortisone–Fructose 1:0	1:1	1:5	1:10	1:25
		37°			
0	100	100	100	100	100
4	98.9	98.8	99.3	99.7	100
24	95.1	95.2	95.7	95.9	99.1
72	91.3	91.9	92.0	93.5	96.6
144	82.3	82.9	84.2	87.7	90.1
264	69.2	71.0	73.5	77.1	95.8
408	57.9	59.9	63.5	68.6	79.4
528	47.5	49.5	52.3	61.3	72.0
648	42.2	44.6	47.4	55.3	66.8
		47°			
0	100	100	100	100	100
14	97.2	96.8	97.1	98.6	98.2
50	81.1	79.8	87.0	89.8	94.6
72	74.9	73.8	81.7	84.5	90.1
120	62.9	62.0	71.9	77.3	84.9
168	48.6	51.1	63.3	69.2	79.0
216	38.2	39.7	54.6	59.5	75.0
264	30.5	33.8	48.1	54.3	68.1
336	21.7	22.6	36.1	49.0	63.0
384	19.0	20.0	34.4	44.5	61.5
		57°			
0	100	100	100	100	100
1	97.3	97.3	98.6	99.2	99.8
4	92.3	92.0	91.3	96.2	95.6
9	87.1	88.6	89.1	94.0	95.1
24	75.9	79.0	84.1	90.6	94.0
48	58.2	63.5	74.2	80.7	87.0
72	45.8	49.8	63.9	75.4	81.8
120	28.4	32.9	48.0	62.1	72.5
150	20.2	23.4	38.1	54.5	67.6
180	10.8	14.6	33.0	46.6	63.3

Table II—Rate of Degradation of Hydrocortisone at pH 8.4 in the Presence of D-Fructose at 37, 47, and 57°

Time, hr	Percent Remaining, Molar Ratio of Hydrocortisone–Fructose 1:0	1:1	1:5	1:10	1:25
		37°			
0	100	100	100	100	100
4	89.0	89.0	95.4	95.4	98.6
24	77.1	82.7	89.7	93.2	91.5
72	61.6	62.5	67.0	74.9	78.4
144	42.1	41.4	44.5	60.9	65.2
264	19.9	20.2	22.6	34.2	40.3
408	7.7	7.6	9.7	16.3	23.5
528	3.9	3.8	5.3	11.3	17.3
		47°			
0	100	100	100	100	100
2	95.3	95.6	95.9	95.6	98.4
14	82.0	83.0	88.0	90.0	94.8
50	63.8	63.9	66.0	73.2	82.8
72	51.3	53.2	56.1	63.5	74.5
120	35.3	35.2	42.9	51.3	64.6
168	23.9	24.2	29.8	38.3	51.6
216	15.9	16.2	21.7	28.8	43.0
264	10.6	11.3	15.7	22.4	36.2
336	5.8	6.5	9.2	14.7	25.6
384	3.6	4.1	6.6	11.8	23.1
		57°			
0	100	100	100	100	100
1	98.8	98.7	98.8	99.6	99.7
4	91.1	91.1	98.1	96.5	98.1
9	81.8	85.0	95.8	94.5	96.6
24	51.8	60.0	80.8	92.3	95.0
48	24.5	37.1	65.7	84.2	91.2
72	16.9	30.4	52.8	77.5	90.1
120	14.9	21.3	34.4	62.4	84.2
150	14.5	17.9	27.0	56.3	82.2
180	13.8	14.3	19.4	54.3	81.8

(reagent grade)[4], phosphoric acid (reagent grade)[4], hydrochloric acid (reagent grade)[4], monobasic potassium phosphate (reagent grade)[5], boric acid USP[5], potassium chloride (reagent grade)[6], sodium hydroxide (reagent grade)[6], citric acid USP[7], sorbitol USP[7], lactose USP[3], sucrose (reagent grade)[8], chloroform NF[9], absolute ethanol, (reagent grade)[9], glycerol (reagent grade)[10], propylene glycol (reagent grade)[10], and nitrogen, extra dry[10].

Equipment—The following pieces of equipment were used: a double beam spectrophotometer[11], a precision temperature-controlled oven[12], and a pH meter[13].

Preparation of the Buffer Solutions—The pH 7.4 buffer was prepared by dissolving monobasic potassium phosphate, (6.8045 g), and sodium hydroxide (1.564 g) in sufficient distilled water to make 1 liter. The buffer solution at pH 8.4 was prepared by dissolving boric acid (3.0915 g), potassium chloride (3.7277 g), and sodium hydroxide (0.344 g) in sufficient distilled water to make 1 liter. The pH 9.4 buffer solution contained similar quantities of boric acid and potassium chloride plus 1.284 g of sodium hydroxide.

Preparation of Hydrocortisone Solutions with and without D-Fructose—Stock solutions of hydrocortisone in absolute ethanol (5 mg/ml) and D-fructose in each of the buffer solutions (24.85 mg/ml, 0.14 *M*) were prepared. Control solutions were prepared by diluting 10 ml of the glucocorticoid stock solution (50 mg, 0.14 mmole) with the appropriate buffer solution to 100 ml. Blank solutions were also prepared by diluting the stock solutions of D-fructose (1, 5, 10, or 25 ml) to 100 ml with the appropriate buffer solution. Hydrocortisone–D-fructose solutions (molar ratios: 1:1, 1:5, 1:10, and 1:25) were prepared by adding various volumes of the D-fructose stock solutions to 10 ml of the hydrocortisone stock solution and diluting to 100 ml with the appropriate buffer. The solutions were analyzed in duplicate and placed in ovens set at 37, 47, and 57 ± 1°.

Preparation of Hydrocortisone Solutions with Various Polyols—The following polyols were added to hydrocortisone solutions

Table III—Rate of Degradation of Hydrocortisone at pH 9.4 in the Presence of D-Fructose at 37, 47, and 57°

Time hr	Percent Remaining, Molar Ratio of Hydrocortisone–Fructose 1:0	1:1	1:5	1:10	1:25
		37°			
0	100	100	100	100	100
4	96.6	97.3	98.5	98.7	99.6
24	87.0	89.7	94.4	96.7	96.2
72	71.6	73.8	80.9	87.4	93.0
144	52.3	54.1	68.4	75.3	86.2
264	28.8	31.7	47.3	58.8	77.4
408	15.0	17.1	32.4	43.9	67.9
528	8.5	9.1	22.3	33.8	62.9
648	4.1	4.5	16.7	26.9	51.7
		47°			
0	100	100	100	100	100
2	94.7	94.9	96.6	98.2	98.9
14	83.6	84.7	91.2	95.8	96.1
50	50.1	51.7	65.3	78.0	90.3
72	35.1	36.7	55.1	66.4	87.0
120	21.7	23.1	37.4	53.9	79.6
168	10.9	11.9	25.4	39.8	68.6
216	6.3	6.6	18.2	31.2	64.5
264	0	0	12.1	24.1	61.5
		57°			
0	100	100	100	100	100
1	97.6	97.3	98.2	99.1	99.4
4	86.9	88.7	87.1	93.4	94.3
10	63.0	64.9	75.8	78.7	89.0
24	40.7	40.8	47.9	51.3	64.5
48	19.7	19.7	25.1	26.1	28.9
72	18.1	18.7	19.5	23.7	28.9
120	15.7	15.7	19.5	22.5	27.5

[4] J. T. Baker Chemical Co., Phillipsburg, N.J.
[5] Merck & Co., Inc., Rahway, N.J.
[6] Fisher Scientific Co., Fair Lawn, N.J.
[7] Pfizer, Inc., New York, N.Y.
[8] Mann Research Labs., New York, N.Y.
[9] New York Laboratory Supply Co., New York, N.Y.
[10] Union Carbide Inc., New York, N.Y.
[11] Coleman-Hitachi, model No. 124, Coleman Instruments Division, Maywood, N.J.
[12] Precision Temperature Controlled Oven, model No. 18, New York Laboratory Supply Co., New York, N.Y.
[13] Will Scientific Co., Inc., New York, N.Y.

Table IV—Rate of Degradation of Hydrocortisone at pH 7.4 in the Presence of Various Polyols at 37° [a]

Time, hr	Percent Remaining						
	Control	Dextrose	Lactose	Sucrose	Sorbitol	Propylene Glycol	Glycerin
				1:10			
0	100	100	100	100	100	100	100
4	98.5	99.5	98.9	99.5	98.6	98.7	99.4
24	93.7	95.4	95.1	94.4	93.2	93.9	95.0
72	89.2	89.6	88.9	90.7	88.7	89.3	90.5
144	81.0	82.8	81.6	82.7	82.1	82.5	82.6
264	70.0	72.0	70.9	71.1	71.2	70.8	70.6
408	58.2	58.9	58.8	60.2	58.5	58.2	59.5
552	45.7	47.8	45.7	45.7	45.9	47.8	47.6
696	33.5	35.9	36.1	35.4	33.9	36.4	37.3
864	21.3	22.9	22.7	21.8	22.4	23.8	23.7
				1:25			
0	100	100	100	100	100	100	100
4	98.5	99.6	99.0	99.2	98.9	98.3	99.4
24	93.7	94.6	95.0	93.5	93.0	93.6	94.8
72	89.2	89.7	89.3	88.3	88.4	88.8	89.0
144	81.0	82.9	81.9	82.8	81.5	82.3	82.4
264	70.0	73.2	71.1	72.2	72.8	71.6	72.0
408	58.2	60.5	59.4	58.2	59.8	58.9	59.5
552	45.7	48.5	47.9	48.7	48.6	49.2	48.7
696	33.5	36.1	35.5	35.7	34.8	35.0	35.5
864	21.3	23.7	24.8	23.6	25.6	24.0	25.3

[a] Molecular ratios of hydrocortisone–polyol are 1:10 and 1:25.

buffered at pH 7.4 (molar ratios of hydrocortisone–polyol, 1:10 and 1:25): dextrose, sucrose, lactose, sorbitol, glycerin, and propylene glycol. The stability of these solutions was only studied at 37 ± 1°.

Assay Procedure for Hydrocortisone—At various time intervals, 10 ml of the sample was extracted with three 20-ml portions of chloroform. The chloroform extracts were passed through a glass wool pledget previously rinse with chloroform. The combined extracts were diluted to 100 ml and then evaporated to dryness in a stream of nitrogen at room temperature. The residue was dissolved in 20 ml of absolute ethanol and treated with 1 ml of blue tetrazolium solution (1% in absolute ethanol) plus 1 ml of tetramethylammonium hydroxide (1 ml of a 10% aqueous solution diluted to 10 ml with absolute ethanol). The color was allowed to develop in the dark for exactly 45 min. Color development was then quenched by the addition of 1 ml of glacial acetic acid. The absorbance was determined at 525 nm. A standard solution of hydrocortisone in absolute ethanol was carried through the identical procedure and was used as a color reference in calculating the concentration of steroid in the sample. Blank solutions were also subjected to the same procedure. The results are summarized in Tables I–IV.

RESULTS AND DISCUSSION

The stability data for the solutions of II plus I are summarized in Tables I–III. It is evident that an increase in the concentration of I results in an improvement in the stability of II. This relationship holds for the three pH values and three temperatures studied. The importance of the ketol group in I is also evident after inspection of the data in Table IV. None of the polyols at ratios of 1:10 or 1:25 showed any stabilization of II as compared with the control.

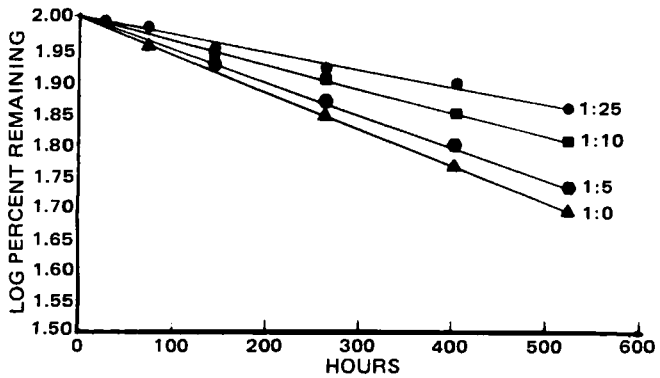


Figure 1—*Influence of molar concentrations of D-fructose on the stability of aqueous solutions of hydrocortisone (50 mg%) buffered at pH 7.4 and stored at 37° plotted in first-order fashion.*

The rate constants, *y*-intercepts, and correlation coefficients summarized in Table V were derived from first-order plots of the data shown in Tables I–III. Selected solutions buffered at pH 7.4 were plotted in first-order fashion (Fig. 1) to illustrate the linearity of the data.

A possible explanation for the stabilization observed is the complex formation between II and I. Such complexes could resist oxidative destruction more effectively than solutions of II alone. An alternative mechanism is that fructose competes with II for the oxygen present in the system and thus acts as an antioxidant. Failure of the other polyols to exert a protective effect could be attributed to the greater reaction speed of I as compared with the polyols studied. Thus, Singh *et al.* (10) reported that the order of the oxidative reaction speed catalyzed by bi-

Table V—Rate Constant (*k*), *y*-Intercept, and Correlation Coefficient (*r*) Values Derived from First-Order Plots of the Data in Tables I–III [a]

First-order Parameters	Molar Ratio of Hydrocortisone–Fructose				
	1:0	1:1	1:5	1:10	1:25
		pH 7.4			
k_{37}	1.35[a]	1.26	1.16	0.91	0.62
y-intercept	1.998	1.998	1.998	1.997	2.001
r	0.998	0.998	0.998	0.999	0.995
k_{47}	4.51	4.28	2.88	2.17	1.34
y-intercept	2.011	2.006	2.004	2.000	2.000
r	0.998	0.997	0.996	0.993	0.992
k_{57}	11.4	10.0	6.03	4.05	2.50
y-intercept	2.000	2.000	1.988	1.996	1.994
r	0.989	0.993	0.996	0.997	0.995
		pH 8.4			
k_{37}	6.06	6.13	5.62	4.40	3.41
y-intercept	1.978	1.987	2.000	2.014	2.002
r	0.999	0.999	0.999	0.996	0.997
k_{47}	8.45	8.15	6.98	5.57	3.89
y-intercept	1.987	1.982	1.986	1.988	2.000
r	0.999	0.999	0.999	0.999	0.998
k_{57}	11.9	10.9	9.03	3.57	1.15
y-intercept	1.882	1.934	2.005	1.996	1.992
r	0.827	0.946	0.999	0.991	0.965
		pH 9.4			
k_{37}	4.70	4.58	2.79	2.04	0.96
y-intercept	2.002	2.011	2.000	2.002	2.000
r	0.995	0.996	0.999	0.999	0.992
k_{47}	15.4	15.3	7.97	5.39	1.93
y-intercept	2.040	2.050	1.990	2.000	2.000
r	0.958	0.952	0.999	0.999	0.987
k_{57}	18.0	16.8	15.3	14.2	12.7
y-intercept	1.890	1.890	1.910	1.930	1.950
r	0.867	0.827	0.812	0.821	0.808

[a] All values for *k* must be multiplied by 10^{-3}. Units: hr^{-1}.

valent copper is fructose > glucose > galactose. Joslyn and Miller (11) reported that I was more effective than sucrose and dextrose in stabilizing ascorbic acid solutions against oxidative degradation. These authors concluded that no simple rate law governed the oxidation of ascorbic acid in the presence of sugars. They also observed that the temperature coefficients of the oxidation in the presence or absence of the sugars were similar. This observation would seem to indicate that complex formation was not occurring since the temperature coefficients would be expected to differ. Ashida (12) also reported that methylene blue was more easily reduced by a ketose such as fructose than by an aldose such as glucose.

The data and speculations serve as a stimulus for additional research to establish a mechanism for the stabilization observed. It will be of interest to learn if the redox potential of I is similar to that for II. Such similarity is anticipated because of the structural relationship between the portions of the two molecules where oxidation reactions have been shown to occur. The redox potentials of the other polyols are anticipated to differ significantly.

REFERENCES

(1) L. Velluz, A. Petit, M. Pesez, and R. Berret, *Bull Soc. Chim. France*, **1947**, 123.

(2) P. T. Herzig and M. Ehrenstein, *J. Org. Chem.*, **16**, 1050 (1951).

(3) H. L. Mason, C. S. Myers, and E. C. Kendall, *J. Biol. Chem.*, **116**, 267 (1936).

(4) H. L. Mason, *Proc. Staff Meetings Mayo Clinic*, **13**, 235 (1938).

(5) N. L. Wendler and R. P. Graber, *Chem. Ind. (London)*, **1956**, 549.

(6) D. E. Guttman and P. D. Meister, *J. Am. Pharm. Assoc., Sci. Ed.*, **47**, 773 (1958).

(7) E. Caspi, W. Schmid, and T. A. Wittstruck, *Tetrahedron*, **16**, 271 (1961).

(8) M. L. Lewbart and V. R. Mattox, *J. Org. Chem.*, **21**, 2001 (1963).

(9) J. W. Mauger, A. N. Paruta, and R. J. Gerraughty, *J. Pharm. Sci.*, **58**, 574 (1969).

(10) M.Pd. Singh, B. Krishna, and S. Ghosh, *Z. Phyzik. Chem. (Leipzig)*, **205**, 285 (1956).

(11) M. A. Joslyn and J. Miller, *Food Res.*, **14**, 340 (1949).

(12) K. Ashida, *Mem. Inst. Sci. Ind. Res., Osaka Univ.*, **10**, 205 (1953).

Cinchophen Analogues as Potential CNS Agents

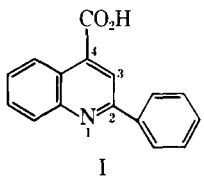
A. KAR

Received October 20, 1981, from the *Department of Pharmaceutical Chemistry, University of Nigeria, Nsukka, Nigeria.* Accepted for publication June 1, 1982.

Abstract □ Several amides of cinchophen were prepared and evaluated as CNS agents. Compounds III, VII, XII, XIII, and XIV exhibited analgesic activity while I, III, and XIV acted as CNS depressants.

Keyphrases □ Cinchophen—amide analogue synthesis, evaluation of CNS activity in mice □ Analgesics—potential, amide analogues of cinchophen, evaluation of CNS activity in mice □ Central nervous system agents—amide analogues of cinchophen, evaluation of CNS activity in mice

Cinchophen (I) was formerly used for the treatment of gout (1, 2); however, it was withdrawn from the market because of its toxic effects (3–5). It was concluded that the quinoline ring, a carboxylic acid group in the C-3 or C-4 position, and an aryl residue at C-2 were essential for the physiological action of cinchophen (6). Many structural modifications of cinchophen have been reported [*i.e.*, neocinchophen, 2-phenyl-3-hydroxycinchonic acid, hexophan, and 2-phenyl-4-hydroxyacetyl-6-methoxyquinoline (1)]. Reversal of the phenyl and carboxyl groups afforded an inactive compound (I).



I

In this study 16 amides of I were synthesized and evaluated as CNS agents. Cinchophen has been synthesized either by the condensation of acetophenone with isatic acid in alcoholic potassium hydroxide solution (7) or by heating pyruvic acid with either aniline and benzaldehyde or with benzylidene aniline in absolute ethanol (8). In the present study, I was prepared by the condensation of pyruvic acid with aniline and benzaldehyde (9, 10). The desired amides were subsequently synthesized by treating the corresponding acid chloride with the appropriate amine.

EXPERIMENTAL

Synthesis—The amides II–XVII were prepared (11) by vigorously shaking for 30 min at room temperature a mixture of the appropriate amine (0.002 mole), a 10–15% molar excess of the acid chloride of cinchophen, and 10 ml of 10% aqueous sodium hydroxide solution. The resulting solid material was removed by filtration and purified, as indicated in Table I.

Analysis and Spectral Data—Melting points were determined in open capillary tubes in an electrothermal apparatus and are uncorrected. NMR[1] spectra were obtained in deuterated acetone using tetramethylsilane as the internal standard. The mass spectra[2] of the various compounds were determined. Microanalyses were within ±0.3% of the theoretical values (Table I).

Pharmacological Evaluation—The hot plate method was employed to evaluate the analgesic activity of the amides in mice. The CNS-depressant activity was studied *in vivo* by noting the effect of the amides on spontaneous motor activity, ptosis, and pentobarbital-induced hypnosis. Swiss albino mice of both sexes, weighing 20–30 g, were used; solutions of normal saline or 3% (w/v) aqueous polysorbate 80 were given to the untreated and vehicle controls, respectively. Cinchophen (50 or 100 mg/kg), pentobarbital sodium (40 mg/kg), and morphine hydrochloride (4 mg/kg) were used as reference drugs to evaluate the activity of the amides.

Analgesic Activity—Analgesic activity was measured by the hot plate method at 53 ± 2°. The normal reaction time (pain threshold) for each mouse was determined by placing the mouse on the hot plate and noting the amount of time (≤5 sec) required for the mouse to leave the hot plate platform. The pain threshold was measured 30 min postinjection and at hourly intervals for 4 hr.

[1] Perkin-Elmer R-32 spectrometer.
[2] VG-Micromass 16F (with a VG system 2000 computer).

0022-3549/83/0900-1082$01.00/0