TABLE II.
Effects of Dietary Supplements on Concentration of Glycogen in Liver and Heart of Hyperthyroid Rats

Exp. No.	No. of rats	Avg daily gain, g	Avg liver wt, g	Avg liver glycogen, %	Heart % body wt	Heart glycogen %	Heart glycogen Mg per 100 g body wt	Diet used
8	7	.16	3.9	.6 (.01-3.1)	.62	—	—	Diet 1 + .13% thyroid.
	6	.42	4.9	.4 (.01-0.8)	.64	—	—	As above + 2 mg biotin + 5 mg folic acid/kg.
	8	1.9	7.5	.5 (.01-0.6)	.63	—	—	Diet 2 + .13% thyroid.
	6	2.4	7.1	5.7 (4.1-8.4)	.34	—	—	Diet 1
14	7	1.7	6.6	.2 (.02-0.8)	.61	.11	.49	Diet 2 + .13% thyroid.
	8	1.7	6.5	.04 (.01-0.1)	.76	.08	.51	As above + 5 mg folic acid/kg.
	6	2.2	7.8	.04 (.01-0.1)	.64	.05	.40	As above + 5 mg folic acid + 2 mg biotin/kg.
	10	3.1	6.4	1.9 (.06-4.6)	.33	.46	1.56	Diet 2
34	6	2.9	9.5	1.9 (1.2-3.4)	.55	.06	.33	Diet 2 + 10% liver meal* + .25% thyroid.
	6	2.6	9.4	1.7 (.2-2.3)	.57	.12	.65	Diet 2 + 10% liver meal† + .25% thyroid.
	5	2.9	7.0	2.1 (.2-7.5)	.61	.06	.50	Diet 2 + .25% thyroid.
	10	3.0	5.0	7.0 (3.0-9.8)	.37	.24	.93	Diet 2.
40	5	3.2	10.0	.9 (.04-1.7)	.50	.16	.78	Diet 5 + .4% thyroid.
	4	2.3	7.8	.2 (.01-0.6)	.64	.11	.52	Diet 4 + .4% thyroid.
	5	3.2	8.3	5.5 (2.3-7.9)	.32	.26	.76	Diet 4.
39	8	2.8	5.2	.07 (.05-0.1)	.52	.11	.67	Diet 3 + 30 γ B_{12}/kg + .25% thyroid.
	4	2.9	5.9	.07 (.04-0.1)	.60	.11	.67	Diet 3 + .25% thyroid.

* Dried water insoluble residue from the manufacture of the anti-P.A. factor.
† Viobin, defatted liver.

Received May 19, 1950. P.S.E.B.M., 1950, v74.

Progestational Activity of 1,2-*bis*-(p-Aminophenyl)-2-Methylpropanone-1 Dihydrochloride. (17999)

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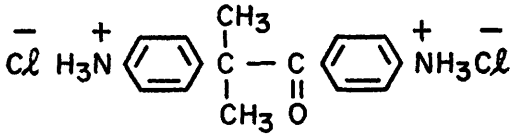
In the course of a comprehensive study of the relationship between chemical structure and biological activity in a series of substituted desoxybenzoins it was found that 1,2-bis-(p-aminophenyl)-2-methylpropanone-1 dihydrochloride exhibits progestational activity.



COMPOUND I.

The synthesis and properties of this compound have been previously described (Allen and Corwin) (1). We have employed a modification of the biological test for progesterone described by Clauberg(2). Juvenile female rabbits (New Zealand Whites) initially weighing between 600 and 800 g were utilized. Each test animal was pre-treated daily for 6

1. Allen and Corwin, *J.A.C.S.*, 1950, v72, 117.
2. Clauberg, C., *Zentralblatt f. Gynak*, 1930, v54, 2757

TABLE I.
Progestational Effect of 1,2-*bis*-(p-aminophenyl)-2-methylpropanone-1 Dihydrochloride.

Compound injected	Daily dose, mg	Vehicle and vol., cc	Uterine wt., mg	Body wt	Grade of response
I	166	H_2O/2	1828	1068	+2
I	166	"	1435	1109	+1
P	0.5	0.1 oil	2660	1152	+4
I	332	H_2O/4	1420	1265	+4
I	332	"	2900	1002	+3
I	166	H_2O/2	2010	1318	±
I	166	"	1420	1120	+1
I	332	oil/4	2014	1300	+2
I	332	"	2000	1140	+2
P	0.5	.1 oil	6660	1322	+4
P	0.5	"	4900	1000	+4
I	200	H_2O/2	2410	1331	+3
I	200	"	2100	1141	+4
I	400	"	4335	1110	+4
I	400	"	3780	982	+4
I	600	"	3115	1232	+3
I	600	"	2115	1249	+4
I	100	H_2O/2	4340	1700	+3
I	100	"	3930	1822	+3
I	200	H_2O/4	4590	1265	+4
I	200	"	4450	1650	+2
I	400	H_2O/8	3770	1834	+4
I	400	"	4370	1539	+4
I	600	H_2O/12	4250	1532	+4
I	600	"	5730	1314	+4
P	0.5	.5 oil	10140	1655	+4
P	0.5	"	8220	1734	+4
I	50	H_2O/1	2035	1150	±
I	50	"	1230	1162	±
I	100	H_2O/2	2030	1160	±
I	100	"	1830	1076	±
P	.25	.25/oil	3525	1008	+4
P	.25	"	2200	968	+4

* I = 1,2-*bis*-(p-aminophenyl)-2-methylpropanone-1 dihydrochloride.
P = Crystalline progesterone.

days with 10 μg of estradiol benzoate administered subcutaneously in 0.5 cc corn oil. For the ensuing 5 days either Compound I or progesterone was administered subcutaneously in the dosage and form indicated in Table I. Twenty-four hours after the last injection the animals were autopsied, their terminal body weight and uterine weight recorded, and the uterus prepared for histological grading of the progestational response as described by Hisaw and Leonard(3).

The data indicate that of 24 rabbits given a daily dose of 100 mg or more, all but 2 showed a decisive progestational response to Compound I. The grade of response varied considerably but such variability is characteristic of the progestational response in the young rabbit(2). In 2 rabbits treated with 50 mg daily only a doubtful response was elicited and a similarly marginal effect was seen in 2 rabbits receiving 100 mg daily. By comparison with the potency of progesterone under similar experimental conditions, it may be crudely estimated that Compound I is about 0.5 to 0.25% as active as progesterone.

From the observations on uterine weight it is apparent that Compound I brings about less increment in uterine weight than progesterone even in instances in which the progesta-

3. Hisaw, F. L. and Leonard, S. L., *Am. J. Phys.*, 1930, v92, 574.

tional effect upon the endometrium is maximal.

The progestational property of progesterone has been considered highly specific in that it is known to be possessed by only few closely related steroids and has not been previously demonstrated in non-steroidal compounds. Desoxycorticosterone and 17-hydroxy-11-dehydrocorticosterone (Cpd. E. of Kendall) are known to possess limited degrees of progestational activity(4). Conversely, progesterone has a limited corticoid effect(4). In view of the progestational activity of Compound I, the potential corticoid activity of this and related substances adds interest to the further biological characterization of this series of compounds. We shall subsequently report on the chemistry and physiological activities of other substituted desoxybenzoins.

4. Selye, H., Encyclopedia of Endocrinology, Section I, Steroids, I-IV; Richardson, Bond and Wright Co., Montreal, Canada, 1943.

Received May 19, 1950. P.S.E.B.M., 1950, v74.

Effects of Radioactive Iodine on Free Sarcoma 37 Cells in the Peritoneal Fluid of the Mouse.* (18000)

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In producing biological effects on living tissue cells, the gamma rays of radioactive isotopes expend their energy by ejection of high speed electrons. Consequently, it was presumed that the action of beta particles on cell complexes would be based on similar mechanism. However, it is known that beta particles do not penetrate significantly in the body or organ surface exposed to irradiation (Dobson and Lawrence)(1). Moreover it is difficult to distinguish the primary effect of beta particles on tumor cells from the secondary effect induced by the irradiated layer of malignant tissue in tumor stroma, blood vessels and deeper portions of the tumor. It seems reasonable to study the primary effect of beta particles on tumor cells, by introducing radioisotopes in body fluids containing free tumor cells. Thus, Evans and Quimby(2) injected radioactive sodium subcutaneously into leukemic mice and recorded the effects on blood counts. We have found that it is convenient to induce and to observe primary changes in tumor cells by injecting a radioactive isotope intraperitoneally into mice bearing viable free tumor cells in their peritoneal fluid. The viability of such cells has been demonstrated by several authors: by Graham(3) in human patients, by Warren and Gates(4) in rats and by several German authors(5) in mice. Recent experiments (Goldie and Felix)(6) have shown that it is possible to grow in the peritoneal fluid free tumor cells (sarcoma 37 cells in CFW mice, thymoma cells in dba mice) in serial intraperitoneal transfers. At each transfer the multiplication of tumor cells can be estimated quantitatively by counting cells and their mitoses first in the inoculated fluid and later on in specimens of peritoneal fluid from inoculated mice. This method was applied in the experiments reported below recording the changes in number and characteristics of free sarcoma 37 cells after intraperitoneal injection of radioactive iodine.

* This work was carried out under Contract AT-(40-1)-269 with the Division of Biology and Medicine, U. S. Atomic Energy Commission.

1. Dobson, R. L., and Lawrence, J. H., *Ann. Rev. Physiol.*, 1948, v10, 479.

2. Evans, T. C. and Quimby, E. H., *Am. J. Roentgenol. and Radium Ther.*, 1946, v55, 55.

3. Graham, G. S., *Am. J. Path.*, 1933, v9, 701.

4. Warren, Sh. and Gates, O., *Am. J. Cancer*, 1936, v27, 485.

5. Seeger, P. G., *Arch. Exp. Zellforsch.*, 1937, v20, 280.

6. Goldie, H. and Felix, M., to be published.