

t-butyl oxalate¹ and *t*-butyl fluoroacetate² in the presence of potassium *t*-butoxide, and characterised as dinitrophenylhydrazones, of m.p. 137–138°. Anal. Calc. for C₁₈H₂₃N₄O₈F: C, 48.7; H, 5.6; N, 12.7. Found: C, 48.5; H, 5.4; N, 12.1.

By catalytic pyrolysis of this ester using the general method of BRESLOW *et al.*³, a mixture of oxalic acid and oxalofluoroacetic acid was obtained; the latter gave an intense violet color reaction with alcoholic ferric chloride solution. Also, by this method, oxalofluoroacetic acid could not be prepared in pure form.

Both the sodium enolate of diethyl oxalofluoroacetate and the free ester, when injected intraperitoneally into rats, proved to be practically non-toxic. Doses as large as 350 mg/kg were without effect, whilst LD₅₀ of sodium fluoroacetate for rats is about 2–4 mg/kg⁴.

On the other hand, the (water-soluble) sodium enolate, in concentrations as low as 20–40 µg/ml, inhibited the growth of *Escherichia coli* and *Aerobacter aerogenes* in synthetic media containing ammonium phosphate as sole source of nitrogen.

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Résumé

Les esters éthyliques et tertibutyliques ont été synthétisés à partir des esters correspondants de l'acide oxalique et fluoroacétique par une condensation de Claisen Wislicenus.

En injection intrapéritonéale effectuée sur des souris et des rats, ces esters se sont montrés pratiquement non toxiques. En revanche, ils exercent (sous forme d'énolates sodiques hydro-solubles) une action inhibitrice prononcée sur la croissance de l'*Escherichia coli* et *Aerobacter aerogenes* dans des milieux de cultures synthétiques.

¹ H. J. BACKER and J. D. H. HOMAN, Rec. Trav. Chim. 58, 1048 (1939).

² I. BLANK and J. MAGER, unpublished results.

³ D. S. BRESLOW, W. BAUMGARTEN, and C. R. HAUSER, J. Amer. Chem. Soc. 66, 1286 (1945).

⁴ E. R. KALMBACH, Science 102, 232 (1945).

Stimulation of the Hypophysis by Administering Epinephrine in Adrenalectomized Rats

According to SAYERS the secretion of ACTH from the hypophysis in stress is regulated by the level of corticoids in the blood. During stress, the rate of utilization of cortical hormone is increased and consequently the titer of blood corticoids diminished. SAYERS considers that the hypophysis is stimulated by epinephrine in that same way¹.

In our experiment, the variations of the corticoids level in blood have been excluded by adrenalectomy and the ACTH contents in the hypophysis has been determined after an intravenous injection of epinephrine.

A total of 21 female albino rats, weighing 130 to 140 g, were adrenalectomized. 48 h after adrenalectomy, 11 of the rats were treated with 0.3 ml 0.9% NaCl intravenously. To the second group of 10 rats were administered 30 µg epinephrine per 100 g body weight, dissolved in the same volume of saline. The animals were killed exactly 5 min after the injection, and the adeno-

hypophysis was ground in a 0.9% NaCl solution made acid to 0.1 M with HCl for extracting of ACTH by the method of RICHARDS and SAYERS¹. Each milliliter of extracting medium contained two hypophysis. After being diluted 1:80 half a milliliter of the extracting material was tested by the adrenal ascorbic acid depletion method². The contents of ACTH in the extract was determined on 24 hypophysectomized rats.

The contents of ACTH in the hypophysis of the adrenalectomized animals treated by epinephrine was 120 µg per pituitary and in the control group 72 µg.

ACTH contents of hypophysis in adrenalectomized rats treated with epinephrine

	No. of animals	Average weight of rats gm	Average value of adrenal ascorbic acid depletion ² mg/100 gm	Average ACTH per pituitary µg
Saline control	11	135 ± 2.4 ¹	87 ± 14.0	72
Epinephrine	10	136 ± 2.2	105 ± 8.2	120

¹ St. error of the mean. ² 12 animals in each assay.

The results of this experiment indicate a sudden increase of the ACTH production in the hypophysis of adrenalectomized rats after the injection of epinephrine. The epinephrine has been shown by SAYERS³ to increase the concentration of ACTH in the peripheral blood of adrenalectomized rats. Therefore we have determined the contents of ACTH in the blood of two animals only for each group. In agreement with SAYERS, it has been found that the epinephrine increases the contents of ACTH in the blood in adrenalectomized rats.

From our experiment it can be concluded that it is possible to stimulate the production of ACTH in the hypophysis of adrenalectomized rats by epinephrine. According to our results, the mechanism of the regulation of ACTH secretion proposed by SAYERS appears not to be the only one. The direct action of epinephrine on the formation and discharge of ACTH from the hypophysis must be considered as a possibility.

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Zusammenfassung

Der ACTH-Gehalt der Hypophyse von nebennierenlosen Ratten, behandelt mit Adrenalin, wurde mit dem Ascorbinsäure-Verlust-Test der Nebennieren hypophysectomierter Ratten bestimmt. 5 min nach der intravenösen Adrenalin-Injektion hatten die Hypophysen der behandelten Tiere einen viel grösseren ACTH-Gehalt als die entsprechenden Kontrolltiere. Bei einigen Tieren wurde auch der ACTH-Gehalt des Blutes bestimmt. Auch im Blute der mit Adrenalin behandelten Tiere war der ACTH-Gehalt erhöht. Diese Versuche sprechen für die Möglichkeit einer direkten Wirkung des Adrenalins auf die Bildung und Ausschüttung von ACTH aus der Hypophyse.

¹ J. B. RICHARDS and G. SAYERS, Proc. Soc. Exper. Biol. Med. 77, 87 (1951).

² M. A. SAYERS, G. SAYERS, and L. A. WOODBURY, Endocrinology 42, 379 (1948).

³ G. SAYERS, Fourth Conference on the Adrenal Cortex, Macy Foundation, New York, Nov. 13–15, 1952; ref. H. SELYE and A. HORAVA, 2nd Ann. Report Stress, Acta Inc., Montreal 1952, p. 112.

¹ G. SAYERS, Phys. Rev. 30, 241 (1950).