Journal of Steroid Biochemistry, 1970, Vol. 1. pp. 259–260. Pergamon Press. Printed in Great Britain

SHORT COMMUNICATION

A SIMPLE SYNTHESIS OF 18-HYDROXYDEOXYCORTICOSTERONE

M.P. LI, C. P. LANTOS*, H. TRAIKOV, M. K. BIRMINGHAM
Allan Memorial Institute of Psychiatry and Department of Investigative Medicine

and

T. H. CHAN
Department of Chemistry, McGill University, Montreal 110, Quebec, Canada

(*Received* 15 *December* 1969)

SUMMARY

A relatively simple synthesis of 18-hydroxydeoxycorticosterone via 18-hydroxyprogesterone is described.

18-HYDROXYDEOXYCORTICOSTERONE (I, 20, 21-dihydroxy-18, 20-epoxy-4-pregnen-3-one) is a major secretory product of the rat adrenal[1, 2] and is formed by the human adrenal as well[3, 4]. In the adrenalectomized rat it has an antidiuretic action exceeding that of deoxycorticosterone[5] and sodium-retaining properties[5–7]. Recent evidence suggests that it may be a hypertensive agent as well[5, 8, 9]. However, direct assessment of its hypertensive potential has so far not been possible because of the inavailability of the compound in quantities large enough for biological assay.

18-Hydroxydeoxycorticosterone (I) has been prepared by Pappo[10] via a fifteen-step synthesis starting from conessine. We wish to report here a simple synthesis of I starting from 18-hydroxyprogesterone (III, 20-hydroxy-18, 20-epoxy-4-pregnen-3-one). By following the procedure of Jeger *et al.*[11], crystalline 18-hydroxyprogesterone (m.p. 160–165°, IR identical with authentic sample [12]) could be obtained from the photolysis of 3,3-ethylenedioxy-21-acetoxy-5-pregnen-20-one (II) followed by acid hydrolysis. On treatment with phosphorus oxychloride in pyridine at room temperature for six hours under dry nitrogen, III was converted to the enolether (IV) which, however, could not be isolated. The reaction was followed by TLC from the disappearance of III and the formation of a less polar compound which could be hydrolysed back to III. Hydroxylation of IV *in situ* was accomplished by adding at 0° osmium tetroxide in pyridine to the reaction mixture. The mixture was stirred at room temperature for five hours and was treated with aqueous sodium bisulfite solution. After two hours at room temperature, the mixture was extracted with benzene and the extracts were washed with cold water and dried over anhydrous sodium sulfate. The filtrate was evaporated to dryness to yield colorless residue containing 18-hydroxydeoxycorticosterone. It could be purified by paper chromatography and its identity was established by comparison with the authentic compound (I) on

*Present address: Instituto De Biologia y Medicina Experimental, Buenos Aires, Argentina.

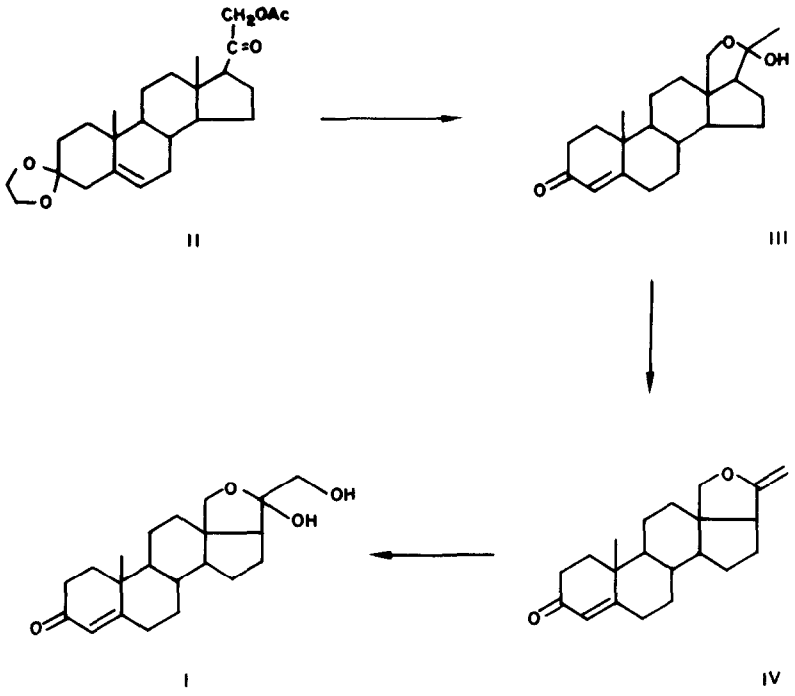

Fig. 1. Synthesis of 18-hydroxydeoxycorticosterone via 18-hydroxyprogesterone.

TLC, paper chromatography and spectroscopic evidences. The overall yield in the conversion of III to I was about 20%.

We are investigating the biological properties of 18-hydroxydeoxycorticosterone.

ACKNOWLEDGEMENTS

Financial support by the Medical and National Research Councils of Canada and the 33rd Degree Scottish Rite is gratefully acknowledged. The authors thank Prof. J. Hora of the Czechoslovak Academy of Science for the authentic sample of 18-hydroxyprogesterone. We also thank Drs. J. S. L. Browne, R. A. Cleghorn and G. Just for their interest in this work.

REFERENCES

1. M. K. Birmingham and P. J. Ward: *J. biol. Chem.* **236** (1961) 1661.
2. F. G. Peron: *Endocrinology* **69** (1961) 39.
3. A. F. de Nicola and M. K. Birmingham: *J. clin. Endocr.* **28** (1968) 1380.
4. A. F. de Nicola, H. Traikov, M. K. Birmingham, J. D. Palmer and D. W. Ruddick: *J. clin. Endocr.* **30** (1970) 402.
5. M. K. Birmingham, M. Macdonald and J. G. Rochefort: *Functions of Adrenal Cortex* (Edited by K. V. McKerns). Appleton-Century-Crofts, New York, Vol. II (1968), p. 647.
6. C. M. Kagawa and R. Pappo: *Proc. Soc. exp. Biol. Med.* **109** (1962) 982.
7. P. J. Ward and M. K. Birmingham: *Biochem. J.* **76** (1960) 269.
8. M. K. Birmingham, G. Rochefort and H. Traikov: *Endocrinology* **76** (1965) 819.
9. A. F. de Nicola, J. T. Oliver and M. K. Birmingham: *Endocrinology* **83** (1968) 141.
10. R. Pappo: *J. Am. chem. Soc.* **81** (1959) 1010.
11. H. Wehrli, M. Cereghetti, K. Schaffner and O. Jeger: *Helv. chim. Acta* **43** (1960) 367.
12. L. Labler and F. Sorm: *Chem. Ind.* (1959) 598.