degree of protection even at concentrations 1000 times lower[82]. Some degree of antagonism against polysaccharides may also be seen in cultures of chicken leucocytes, where the enhancement of leucotaxis produced by bacterial endotoxins is reduced by aldosterone, although not to the same extent as it is by cortisol-like compounds[83]. Whether the stimulating effect of aldosterone on leucocyte agglutination and its inhibition by cortisol are of a specific nature, is however, doubtful[84].

The mechanism of action by which aldosterone may influence toxic reactions provoked by bacterial lipopolysaccharides is not elucidated so far, but it cannot be excluded that disturbances of cell permeability leading to altered distribution of sodium and potassium in the extra- and intracellular compartment of various tissues may be involved. In spite of the lack of a satisfactory explanation for this new effect of aldosterone, on the basis of the experimental data available to-day, it seems to be justified to try aldosterone in conditions of severe shock, especially if toxins are involved in the etiology and if the response to blood pressure elevating substances is reduced or abolished.

This brings us back to the introductory remark that the current characterisation of aldosterone, limiting its function to partial control of tubular cation exchange, needs reconsideration and that other aspects of its importance to the organism under physiological and pathological conditions are worth studying with greater intensity. This not only holds true for experimental but also for clinical medicine.

Zusammenfassung. Es wird eine Übersicht über die Wirkungen von Aldosteron unter physiologischen und verschiedenen experimentellen Bedingungen gegeben und gezeigt, dass das Hormon nicht nur die tubuläre Nierenfunktion, sondern auch extrarenale Vorgänge beeinflusst.

1. Aldosteron fördert die Rückresorption von Natrium in den distalen Tubuli der Niere sowie die Ausscheidung von Kalium und Wasserstoffionen, wobei eine gewisse Latenzzeit bis zum Eintreten eines signifikanten Effektes charakteristisch ist.

2. Am adrenalektomierten Tier gelingt es, durch einmalige Gabe hoher Dosen einen Zustand von schwerer Nebenniereninsuffizienz während mehrerer Tage zu unterdrücken.

3. Längerdauernde Anwendung hoher Dosen von Aldosteron führt beim Menschen oder beim Hund zu einem «escape»-Phänomen in bezug auf Natrium- und Wasserretention.

Zur Erzielung einer Blutdrucksteigerung an der Ratte sind unter gleichen Versuchsbedingungen relativ höhere Dosen von Aldosteron als von Cortexon notwendig.

4. An isolierten Geweben oder Organen (Erythrocyten, Harnblase, Froschherz, Kaninchenaorta) lassen sich erst mit relativ hohen Konzentrationen identische Effekte hervorrufen.

5. Aldosteron besitzt antitoxische Wirkungen gegenüber Polysacchariden bakteriellen Ursprungs, die mit Hilfe verschiedener Versuchsanordnungen nachweisbar sind und teilweise die für Cortisol oder Prednison bekannten ähnlichen Effekte übertreffen.

[83] B. SCHÄR, Personal communication.
[84] J. D. HARTMAN and W. F. GORDON, Amer. J. Physiol. *196*, 279 (1959).

Brèves communications – Kurze Mitteilungen – Brevi comunicazioni – Brief Reports

6-Azacytidine - A New Antimetabolite

In the course of a programme of study of antimetabolites of the principal components of the nucleic acids[1], we have now synthesised 6-azacytidine by the following procedure: 6-Azauridine[2] was converted into the tribenzoyl derivative (I), and this, on treatment with phosphorus pentasulphide in dry pyridine, directly afforded the 4-thioderivative (II), which on ammonolysis gave 6-azacytidine (III) m.p. 215°. The same product was obtained when the de-benzoylated thiocompound (IV) was ammonolysed.

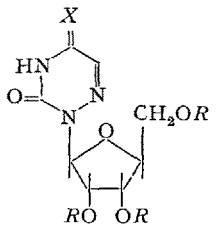
6-Azacytidine has been found to be an antimetabolite of the pyrimidine components of the nucleic acids. Its antibacterial activity against *E. coli* has been shown to be superior to that of 6-azauridine and it has also been found to inhibit the growth of some experimental tumours. The toxicity of 6-azacytidine, like that of 6-azauridine, is very low.

A more detailed account of these findings will be published in due course in Collection of Czech. Chem. Commun.

[1] F. ŠORM, A. JAKUBOVIČ, and L. ŠLECHTA, Exper. *12*, 271 (1956). – F. ŠORM and H. KEILOVÁ, Exper. *14*, 215 (1958). – J. ŠKODA and F. ŠORM, Coll. Czech. Chem. Commun. *21*, 1328 (1956). – J. ŠKODA, J. KÁRA, Z. ŠORMOVÁ, and F. ŠORM, Biochem. biophys. Acta *33*, 579 (1959). – J. GUT, J. MORÁVEK, C. PARKÁNYI, M. PRYSTAŠ, J. ŠKODA, and F. ŠORM, Coll. Czech. Chem. Commun. *24*, 3154 (1959).

[2] J. ŠKODA, V. F. HESS, and F. ŠORM, Exper. *13*, 150 (1957); Coll. Czech. Chem. Commun. *22*, 1330 (1957).

[3] Institute of Organic Chemistry, Academy of Science of the Ukrainian SSR, Kiev.



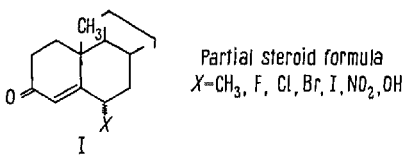
I (X = O; R = Benzoyl)
II (X = S; R = Benzoyl)
III (X = NH; R = H)
IV (X = S; R = H)

Zusammenfassung. 6-Azacytidin wurde synthetisiert; es erwies sich als Antimetabolit.

F. Šorm, J. Smrt, and V. Černeckij[3]
Department of Organic Synthesis, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science, Prague, November 3, 1960.

The Ultraviolet Light Absorption Spectra of Steroid C-6 Substituted-Δ^4-3-Ketones[1]

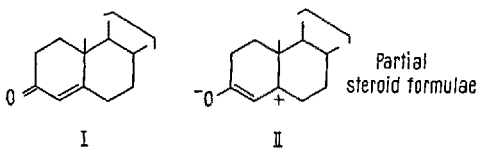
The basic structures under consideration are illustrated by formula I[2].



I

In the absence of extraneous factors (e.g. 11-keto substituents) a steroidal Δ^4-3-ketone, unsubstituted at C-2 or C-6, in alcohol solution exhibits maximum absorption in the ultraviolet at 240–242 mμ[3]. Substitution of electronegative groups at C-6 gives rise to either bathochromic or hypsochromic shifts in the absorption maximum. Before detailing the individual cases, the principal factors affecting the ultraviolet light absorption properties of C-6 substituted Δ^4-3-keto steroids will be discussed.

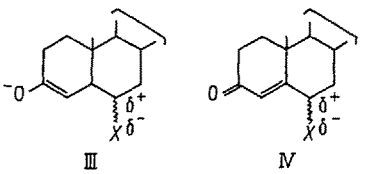
The excited state of Δ^4-3-keto steroids. The principal high intensity band of Δ^4-3-keto steroids observed in the 240 mμ region is the K band (N→V transition) and is attributed to the formation of the excited state (I→II) wherein the charged dipolar form dominates.



I II

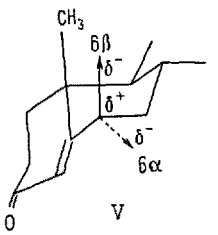
Possible factors affecting transition energy (ΔE) of C-6 substituted Δ^4-3-keto steroids. a) *Planarity.* For effective electronic transition between the ends of a dipole it is necessary that the chromophore, in this case the unexcited unsaturated ketone, be essentially uniplanar. Steric factors which result in distortion of the chromophore plane may affect the energy requirement necessary to reach the excited state. *A priori* it might have been anticipated that a bulky 6β-axial substituent would cause a distortion of the chromophore by virtue of the 1,3-diaxial non-bonded interactions between such a group and the C-10 methyl group. Anticipating the discussion which follows it may be noted that the effect on the ultraviolet maximum of this 1,3-diaxial interaction can only be minimal.

b) *Inductive effect.* The inductive effect of an electron-withdrawing group γ-substituted to an α,β-unsaturated ketone will oppose the polarization inherent in the excited state by charge repulsion between the C-5 and C-6 electron deficient centres (cf. III). Further, an electronegative γ substituent will, by placement of a partial positive charge on the γ-carbon atom (cf. IV) oppose the mobilization of the π-electrons necessary to reach the excited state.



III IV

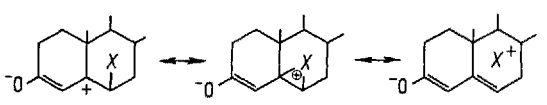
The geometry of the system is such that if the substituent at C-6 occupies the β-axial position its interaction with the dipole of the α,β-unsaturated ketone system, is of greater magnitude than that of an identical substituent in the α-equatorial position, cf. Figure V. Thus the inductive effect of a 6β substituent will be greater than that of the corresponding 6α substituent.



V

Although no such cases have been reported, one may predict that C-6 substitution of a Δ^4-3-ketone by a strong electron releasing group would result in a lowering of the excitation energy and a consequent bathochromic shift in the position of maximum absorption (K band) in the ultraviolet spectrum.

c) *Neighbouring group participation in the excited state.* If a substituent at C-6 is in such a position that it may with minimal movement interact with the unshared orbital of the excitation state C-5 carbonium ion and if the substituent is capable of accepting a positive charge, participation in the excited state is possible (Fig. VI).



VI

This will result in a lowering of the excitation energy due to an extension of the effective length of the conjugated

[1] This paper is considered to be Steroids CLXI in the series from these laboratories; part CLX, C. Casas Campillo and L. F. Bojalil, American Review of Respiratory Diseases, in press.
[2] For leading references to the preparation of compounds of this type cf. A. Bowers, E. Denot, M. B. Sanchez, L. M. Sanchez-Hidalgo, and H. J. Ringold, J. Amer. chem. Soc. *81*, 5233 (1959).
[3] For an excellent compendium and review of the ultraviolet absorption spectra of steroids, covering the literature into 1952, see L. Dorfman, Chem. Rev. *53*, 47 (1953).