Schwellendosis und Wirkungsdauer von Desoxycorticosteron-trimethylazetat und Desoxycorticosteron-azetat an der nebennierenlosen Ratte und am nebennierenlosen Hund

	Schwellendosis bei täglicher Applikation öliger Lösung		Wirkungsdauer			
			10 mg ölige Lösung 1 mal s.c.		10 mg Mikrokristall-suspension, 1mal s.c.	
	Ratte	Hund	Ratte	Hund	Ratte	Hund
Desoxycorticosteron-trimethylazetat . .	0,05 mg	0,3 mg	35 Tage	14–15 Tage	50 Tage	40 Tage
Desoxycorticosteron-azetat	0,1 mg	0,6 mg	12–15 Tage	8 Tage	20–25 Tage	18 Tage

erst vereinzelte klinische Erfahrungen[1] haben die tierexperimentellen Befunde im wesentlichen bestätigt.

F. GROSS und E. TSCHOPP

Aus den wissenschaftlichen Laboratorien der Ciba, Aktiengesellschaft, Basel, den 28. Dezember 1951.

Summary

Desoxycorticosterone-trimethylacetate, a new ester of desoxycorticosterone, shows the following special properties as compared with desoxycorticosterone-acetate: longer duration of action if applied in form of an oily solution, better efficiency if injected in form of a microcrystalline suspension, even if the crystals are of smaller size than those of a desoxycorticosterone-acetate suspension. There is some evidence that desoxycorticisterone-trimethylacetate might be more useful for therapeutic application than the acetate, especially in the form of microcrystalline suspensions, which are easy to handle and well tolerated in human beings.

[1] P. FORSHAM und T. FRAWLEY, J. clin. Endocrinol. *11*, 772 (1951).

PRO LABORATORIO

Manometric Measurement of Gas Evolution in High Temperature Reactions

The apparatus described was devised for the study of the kinetics of gas evolution from solid phase reactions in the temperature range of 150–500°C. It can, however, be equally well applied for the investigation of the thermal decomposition of solids or of reactions between solids and gases, and, in general, for all reactions accompanied by changes of pressure.

Apparatus for the measurement of gas evolution in high temperature reactions generally consists of a reaction chamber, connected to a vacuum pump, a manometer and a "cold limb" which contains the sample before the start of the reaction. The reaction chamber is evacuated and heated to the desired temperature and the sample introduced into the reaction chamber by some mechanical device, such as lowering it in a small bucket suspended by a thin wire[1], or by pushing it into the reaction space by means of an electromagnet[2]. The existence of a relatively large volume outside the reaction chamber and of a considerable temperature gradient cause an inaccuracy in the conversion of the pressure data to standard conditions.

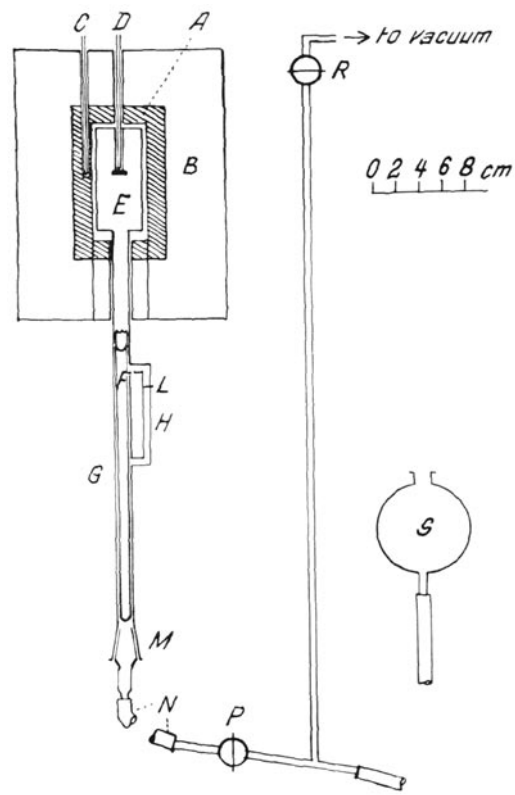

Fig. 1.—Scale Diagram of the Apparatus.
A, heating block; *B*, insulation; *C* and *D*, thermocouples; *E*, reaction chamber; *F*, floating sample holder; *G*, neck; *H*, side arm; *L*, reference mark; *M*, ground-glass joint; *N*, rubber vacuum tubing; *K*, measuring arm; *S*, levelling bulb; *P* and *R*, stopcocks.

If, furthermore, a U-type manometer is used, there is also a correction for the change of volume caused by the displacement of the mercury. These disadvantages are avoided in the simple apparatus described in this paper. Here, the reaction chamber itself is used as the constant-volume part of a manometer in which the mercury is always kept on the same mark by a levelling bulb; the pressure changes are read in the second (evacuated) limb of the manometer and the sample is introduced into the reaction chamber by means of a floating sample holder by suitable manipulation of the mercury.

Description of the apparatus (see Fig. 1).

The furnace. The cylindrical heating block, *A* (length: 14 cm; diameter: 8 cm; wall: 15 mm) was made of steel,

[1] E. G. PROUT and F. C. TOMPKINS, Trans. Farad. Soc. *40*, 488 (1944).

[2] S. PATAI and E. HOFFMANN, J. Amer. Chem. Soc. *72*, 5098 (1950).

wrapped with two thin layers of mica and wound with 10 m flat Cr–Ni wire (resistance 10 Ω/m); its upper end was closed, while its lower end carried removable plugs so that the reaction chamber could be inserted. *A* was insulated with light magnesium oxide, *B*; a well carried the chromel-alumel thermocouple *C*, which was connected to the pyrometer. The temperature fluctuation of the heating block at 400°C was about 2°; in the reaction chamber, about 1°.

The reaction chamber, made of heavy-walled Pyrex glass (*E*) was 100 mm long and 40 mm in diameter. The well (40 mm deep), provided for the thermocouple, *D*, was joined to a glass button of 10 mm diameter, which served as a buffer for the sample holder *F*. The neck, *G*, of the reaction chamber was 385 mm long, terminating in a 14/35 standard ground glass joint, *M*. To eliminate differences in the capillary depression of the mercury, a side arm, *H*, made of the same glass tubing as the measuring arm of the manometer, *K*, was attached to *G*. It carried a reference mark, *L*. *H* was filled with closely fitting glass pieces above the mark *L*, so as to reduce still further the dead volume. The male part of *M* was connected to *K* by a piece of rubber vacuum tubing, just long enough to permit the opening of *M*. The measuring arm, *K*, was backed by a millimetre scale, and the levelling bulb, *S*, held in position by a ring with an attachment for fine adjustment. *K* was connected (above the stopcock, *R*) to the vacuum-system. The sample holder *F* was made of glass tubing, closed at both ends, with a recess at the upper end for the sample. The clearance between *F* and *G* was 0·5 mm.

Operation. *F* with the sample is introduced into *G*. When *M* is closed, *F* rests on the male part of *M*. The levelling bulb *S* is lowered about 80 cm below desk level and the whole apparatus evacuated; simultaneously the reaction chamber is heated to the desired temperature. Stopcock *P* is now closed and *S* raised until the mercury passes stopcock *R*, which is immediately closed[1].

The levelling bulb is then lowered to the level of *L*, *P* is opened so that the mercury flows into *G*, and *F* floats on top of the mercury and rises to the glass button of the well of the thermo-couple *D*[2]. The levelling bulb is now adjusted quickly so that the mercury in *H* stands exactly at *L*, and the position of the mercury in *K*, as well as the time, are noted. As the pressure in *E* rises, the mercury level in *H* falls; before each reading of *K*, it has to be adjusted again to *L*. No manipulation of *S* is necessary between readings up to a pressure change of 40–50 mm.

After completion of the reaction, *S* is again lowered to about 80 cm below desk level. In this position, gas samples can be withdrawn through *R*. Air is *slowly* admitted into the apparatus, *M* opened, the sample holder removed, weighed (if necessary) and cleaned. The apparatus is now ready for a second operation.

Calculation of results. In the apparatus used, the total dead volume (outside the heating block) was about 1·3 cm³ (less than 1·5% of the volume of the reaction chamber). The temperature gradient was confined to a volume of about 0·7 cm³ (the part of the clearance between *F* and *G*, passing through the isolation of the furnace).

[1] This is to ensure Toricellian vacuum above the mercury in the measuring arm. If the mercury is not absolutely clean and gas-free, it is preferable to leave *K* connected to the vacuum during the experiment.

[2] This should take place already when the mercury is still about 4·5 cm below mark *L*.

If v_1 is the actual volume of the reaction chamber (total volume inside the heating block, less the volume occupied by the part of the sample holder which was inside the reaction chambet) at T_1 (absolute temperature), v_2 the volume in which the temperature falls from T_1 to room temperature T_2; and v_3 the volume which is at room temperature, a *virtual volume*, V, can be calculated for each reaction temperature according to the equation:

$$V = v_1 + v_2 \frac{2\,T_1}{T_1 + T_2} + v_3 \frac{T_1}{T_2}.$$

V would be the volume of the gas, if *all* parts of the apparatus were at the temperature T_1. Owing to the relative smallness of v_2 and v_3, changes in room temperature were neglected and T_2 was taken as 293° *K*. From V and the experimental values of pressure and temperature, all other data can easily be calculated.

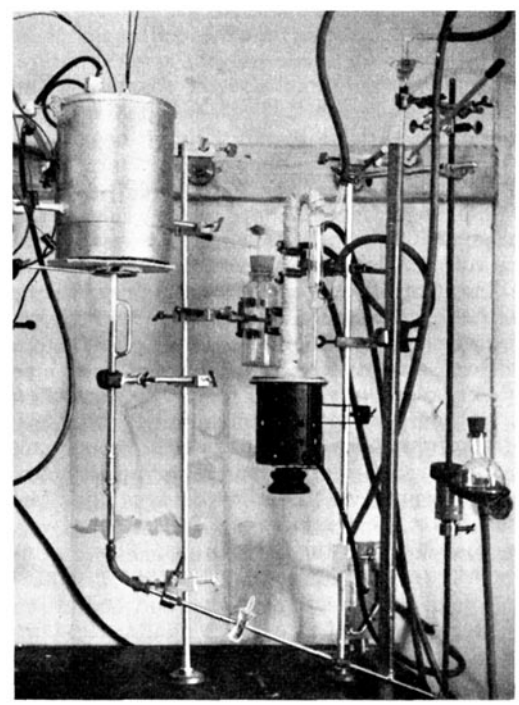

Fig. 2.—View of the apparatus.

Remarks. The apparatus described can be used up to a pressure of about 400 mm and by lengthening of the measuring arm *K*, up to 900 mm.

Magnifying glasses were used to facilitate the adjustment of the mercury level in *H* to *L*, and the reading of the pressure in *K*. Thus, the experimental error was limited to ± 0·25 mm.

By filling the side arm *H* above *L* not with glass pieces, but some specific adsorbent, one can adapt the apparatus to the study of reactions of the type

$$A_{(\text{solid})} + B_{(\text{gas})} = C_{(\text{gas})}.$$

For instance the reaction $C + O_2 = CO_2$, although not accompanied by any change of pressure, can be followed if the side arm *H* is filled with ascarite. In this case, the apparatus is filled with air or oxygen and the *fall* of the pressure measured as the carbon dioxide produced is absorbed by the ascarite.

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Department of Organic Chemistry, Hebrew University, Jerusalem, November 12, 1951.

Zusammenfassung

Ein Apparat für manometrische Messungen von Druckänderungen bei hohen Temperaturen unter konstanten Volumbedingungen wird beschrieben. Die Substanz wird in die Reaktionskammer mit Hilfe eines Schwimmers eingeführt, der durch Änderung eines Quecksilberniveaus betätigt wird. Während der Messung wird das Quecksilberniveau konstant gehalten, und die Druckänderung wird auf einem besonderen Messungsarm des Manometers abgelesen. Die Konstruktion des Apparates ist einfach, das tote Volumen wird auf Minimum gehalten, und die Berechnung der Resultate ist leicht.

PRO EXPERIMENTIS

Zur Technik der intravitalen Phasenmikroskopie

Die wesentlichen Vorteile des Phasenmikroskops können nur bei Untersuchungen *lebender* Zellen voll ausgenützt werden. Bisher beschränkte man sich weitgehend auf die Beobachtung von Einzellern, künstlich separierten Einzelzellen und kleinen Zellverbänden sowie von Zellkulturen und erzielte damit wesentliche neue Einblicke[1]. Es schien uns jedoch besonders verlockend, die Zellen in ihrem natürlichen Milieu in voller Abhängigkeit von Blutzufuhr, Nerveneinflüssen, Hormonen und Enzymen, also im Gewebsverband, zu untersuchen. Als besonders geeignetes Objekt wählten wir das Mesenterium der Ratte, doch setzt seine Verwendung zwei technische Spezialeinrichtungen voraus, über welche *ad usum alterorum* im folgenden berichtet werden soll.

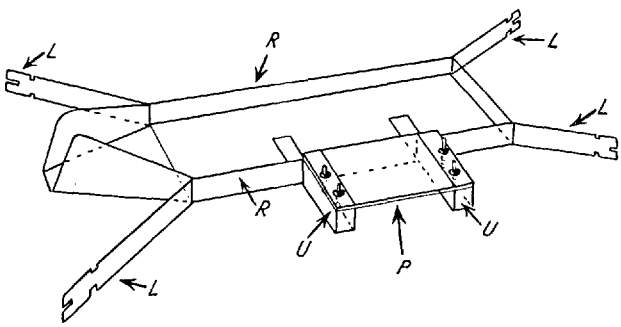

Abb. 1.

Wird das Mesenterium der narkotisierten, in Rückenlage befestigten Ratte mitsamt den dazugehörigen Darmschlingen aus einem seitlichen Operationsschnitt herausgezogen, so muß es auf einer gegenüber der Auflagefläche des Versuchstieres erhöhten Plattform ausgelegt werden, da sonst die Gefäße zu stark stranguliert werden. In Abbildung 1 ist ein einfaches Aufspanngerät für derartige Versuche wiedergegeben. Es läßt sich aus dünnen Plastikplatten aussägen und mit Hilfe von Eisessig zusammenfügen. Die erhöhten seitlichen Ränder (R) verhindern die Beschmutzung des Mikroskops durch abtropfendes Blut und Spülflüssigkeit. Die abstehenden Leisten (L) dienen zur Fixierung der Extremitäten. Seitlich ist die erhabene Beobachtungsplattform (P) angebracht, deren Höhe durch anschraubbare Unterlageblöcke (U) von unterschiedlicher Höhe variabel ist. Nach Ausspannen des Tieres und Ausbreiten des Mesenteriums auf der Plattform kommen die Unterlageblöcke (U) zwischen die Klemmen des Kreuztisches zu liegen, das Tier selbst ist vom Beobachter abgewendet (siehe Abb. 2). Zur Untersuchung mit Ölimmersion wird ein Deckglas mit geschützten Rändern auf das Mesenterium gelegt, eventuell nach Beifügen von physiologischer Kochsalzlösung.

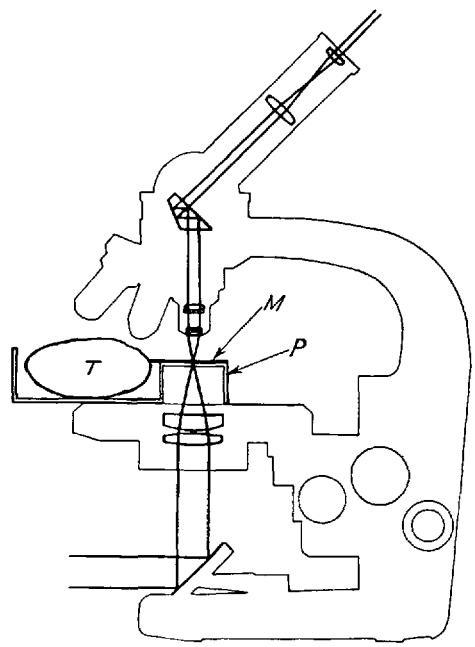

Abb. 2.

Die relative Dicke des Objektes verlangt ein Objektiv mit relativ großem Arbeitsabstand. Wir verwenden mit Vorteil das Ph HI 85 von WILD, welches überdies ganz ausgezeichnete Kontraste liefert.

Ein weiteres Problem stellt die Beleuchtung dar, denn die üblichen Phasenkondensatoren arbeiten mit Kondensorfrontlinsen-Objektiv-Abständen von wenigen Millimetern, während die vorliegende Versuchsanordnung zwangsläufig viel größere Abstände voraussetzt. Ohne korrekte Köhlersche Beleuchtungsanordnung läßt sich jedoch keine erfolgreiche phasenoptische Beobachtung durchführen. Auf unsere Anregung hat die Firma WILD (Heerbrugg) einen Spezialkondensor mit hohem optischem Schnittpunkt ausgearbeitet, der besonders auch für Arbeiten mit Zellkulturen geeignet sein dürfte. Abbildung 2 zeigt den Strahlengang bei aufgesetzter Beobachtungsplattform (P). T = Versuchstier im Querschnitt, M = Mesenterium. An Stelle des Blendenrevolvers sind Hülsenblenden gewählt worden, welche auch den Phasenobjektiven anderer Fabrikate angepaßt werden können. Die Lichtausbeute des Lichtkondensors ist ausgezeichnet; wir arbeiten mit den selben photographischen Belichtungszeiten wie mit den üblichen Phasenkondensoren. – Die beschriebene Versuchsanordnung erlaubt auch die kinematographische Verfolgung schnell ablaufender Vor-

[1] Rev. hématol. *5*, 696 (1950).