This final solution was analyzed for I and N, and thus the total antigen and total antibody content determined. Solutions in greater antigen excess were prepared by adding known amounts of BSA-5I to this solution.

Ultracentrifuge experiments were carried out in phosphate buffer, *p*H 7.6, $\mu = 0.1$, at 21 ± 1°. Several species of antigen-antibody complexes, as well as free antigen, appeared in the sedimentation diagrams, as was originally observed by Heidelberger and Pedersen[1] in similar systems. The faster-sedimenting complexes, present to a large extent in solutions in low antigen excess, were considerably diminished in solutions in high excess, and in the latter a single peak (*a* complex) became most prominent. The *a* complex appears to be the richest antigen-containing complex capable of being formed by the antibody in this system. Extrapolation of the sedimentation constants of the *a* complex to zero effective concentration yields the value $s^{w}_{20} = 8.7\ S$.

Electrophoresis experiments were performed in veronal buffer, *p*H 8.5, $\mu = 0.1$. Resolution of the free antigen, with its appropriate mobility, was readily achieved in both ascending and descending limbs, and the relative areas under the free antigen peak were accurately determined from the ascending pattern. The values so obtained agreed with the per cent. of free antigen evaluated from the ultracentrifuge diagrams. Resolution among the complexes was poor, but in solutions in which sufficiently large proportions of the *a* complex were present, a partial but definite separation of a faster-moving peak from the other complexes was observed. The relative area under this peak agreed with the per cent. of the *a* complex in the solution determined ultracentrifugally.

For several reasons which are too lengthy to be detailed here, it is unlikely that the *a* complex is the 3:1 antigen:antibody species. One reason is that such a complex, with $s^{w}_{20} = 8.7\ S$ and a molecular weight of 370,000, would be required to have a frictional ratio, f/f_0, of 2.1. This value suggests a molecular asymmetry that is larger than would be expected for a complex in which 3 antigen molecules were attached to a single antibody molecule. The *a* complex must therefore be either largely the 1:1 or 2:1 antigen:antibody species, or a mixture of about equal proportions of the two. However, 1:1 and 2:1 complexes should have observably different electrophoretic mobilities, and the fact that all of the *a* complex observed ultracentrifugally can be accounted for under a single peak electrophoretically makes it unlikely that the *a* complex is a mixture of the two species, and likely that it is rather largely one or the other.

The following considerations indicate that the *a* complex cannot be the 1:1 species. If the amount of free antigen in a given solution, determined electrophoretically, is subtracted from the total antigen present, the result is the total amount of antigen bound in all of the complexes in that solution. This, divided by the total antibody, and multiplied by the appropriate molecular weight factor, 2.3, gives $\overline{(AG/AB)}_{N,B}$, the *average* number of antigen molecules bound per antibody in *all* of the complexes in the solution. The results are presented in Table I. This average number rises well above unity as the antigen excess is increased. Solution II-2 contains about 33% of the complexes as the *a* complex, the other species in the solution being characterized by smaller antigen-antibody ratios. The *a* complex therefore cannot be the 1:1 species, since it must obviously be richer in antigen.

TABLE I

COMPOSITION OF ANTIGEN-ANTIBODY COMPLEXES

Solution	% Total antigen	% Free antigen	$\overline{(AG/AB)}_{N,B}$
I	34.7	8.6	0.92
II	35.8	12.4	0.82
I-1	50.0	28.1	1.01
I-2	62.2	42.6	1.19
II-2	68.1	50.9	1.24

We conclude that the major part of the *a* complex contains 2 antigen molecules and 1 antibody molecule, and that the antibody is therefore largely bivalent. Further studies with this and similar systems are in progress or are contemplated, and a detailed account of this investigation will be published shortly.

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(1) M. Heidelberger and K. O. Pedersen, *J. Exp. Med.* **65**, 393 (1937).

A NEW ROUTE TO HYDROPHENANTHRENE KETONES. THE SYNTHESIS OF THE C_{18} KETONE DERIVED FROM DEHYDROABIETIC ACID

Sir:

The presently available methods for the preparation of hydrophenanthrene ketones of type I are useful only in the special case where R′ = H,[1] while the synthesis of substances related to the resin acids from such intermediates would require that the R′ group be methyl. We now wish to report a simple general synthesis of these hydrophenanthrene ketones.

Alkylation of the sodium derivative of Hagemann's ester[2] in a 3:1 mixture of benzene and dimethylformamide with the required β-phenethyl bromide gave, in 70% yield, the following 2-substituted-3-methyl-4-carbethoxy-Δ²-cyclohexenones: 2-[β-phenethyl], b.p. 178–182° (0.4 mm.), dinitrophenylhydrazone (orange needles) m.p. 132–133° ($C_{24}H_{26}N_4O_6$: C, 61.79; H, 5.62; found: C, 62.19; H, 5.68), semicarbazone m.p. 167–168° ($C_{19}H_{24}N_3O_3$: C, 66.66; H, 7.07; found: C, 66.96; H, 7.46); 2-[β-*m*-isopropylphenethyl], b.p. 190–194° (0.4 mm.), dinitrophenylhydrazone (orange-red needles) m.p. 103° ($C_{27}H_{32}N_4O_6$: C, 63.76; H, 6.34; found: C, 64.09; H, 6.34). These were decarbethoxylated

(1) *Inter alia*, R. Robinson and J. Walker, *J. Chem. Soc.*, 747 (1936), 183 (1938); W. E. Bachmann, S. Kushner and A. C. Stevenson, THIS JOURNAL, **64**, 974 (1942).

(2) C. T. Hagemann, *Ber.*, **26**, 876 (1893); *cf.* L. I. Smith and G. F. Rouault, THIS JOURNAL, **65**, 631 (1943).

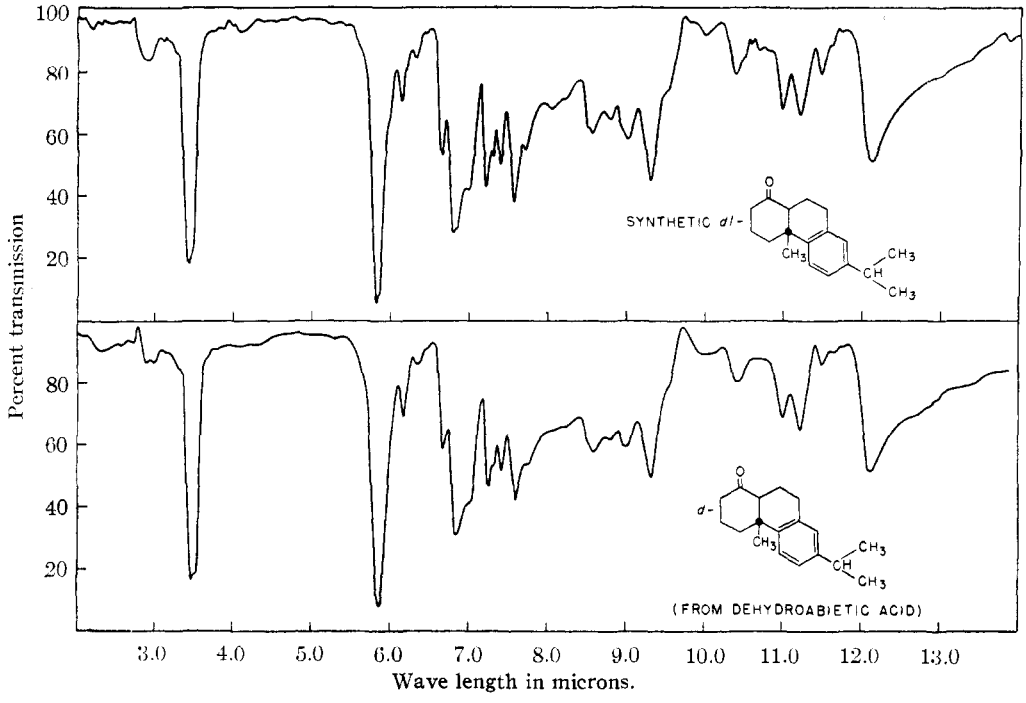


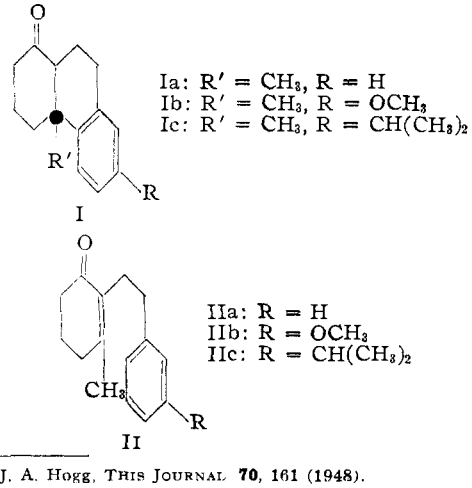
Fig. 1.—Infrared spectra in chloroform.

with alcoholic KOH under nitrogen in 80% yield to the following 2-[β-phenethyl]-3-methyl-Δ^2-cyclohexenones (II):

IIa (R = H), b.p. 140–143° (0.4 mm.), dinitrophenylhydrazone (red needles) m.p. 171–172° ($C_{21}H_{22}N_4O_4$: C, 63.94; H, 5.62; found: C, 64.22; H, 5.67), semicarbazone m.p. 185° ($C_{16}H_{21}N_3O$: C, 70.82; H, 7.80; found: 70.44; H, 7.81).

IIb (R = OCH_3), b.p. (bath temp.) 160–170° (0.5 mm.), dinitrophenylhydrazone (red prisms) m.p. 169–170° ($C_{22}H_{24}N_4O_5$: C, 62.25; H, 5.70; found: C, 62.25; H, 5.67), prepared from the corresponding Hagemann ester derivative described previously.[3]

IIc (R = $CH(CH_3)_2$), b.p. (bath temp.) 165–170° (0.6 mm.), dinitrophenylhydrazone (red platelets) m.p. 134° ($C_{24}H_{28}N_4O_4$: C, 66.04; H, 6.47; found: C, 66.21; H, 6.50), semicarbazone m.p. 142–143° ($C_{19}H_{27}N_3O$: C, 72.80; H, 8.68; found: 73.15; H, 8.76).



(3) J. A. Hogg, THIS JOURNAL **70**, 161 (1948).

Heating IIa with 85% phosphoric acid at 165–170° for 12 hours resulted in a 70% yield of 1-keto-12-methyl-1,2,3,4,9,10,11,12-octahydrophenanthrene (Ia), b.p. (bath temp.) 150–155° (0.5 mm.), dinitrophenylhydrazone (yellow needles) m.p. 193–195° (found: C, 64.01; H, 5.52), semicarbazone m.p. 227–228° (found: C, 71.13; H, 7.83). IIb on cyclization with phosphoric acid at 115–120° for 6 hours similarly produced Ib, b.p. (bath temp.) 165–170° (0.5 mm.), in 65% yield, dinitrophenylhydrazone (deep yellow prisms) m.p. 203° (found: C, 62.61; H, 5.78), semicarbazone m.p. 213–215° ($C_{17}H_{23}N_3O_2$: C, 67.75; H, 7.69; found: C, 67.87; H, 7.65). Cyclization of IIc was best effected by heating with a mixture of phosphoric acid (5 parts) and concd. sulfuric acid (1 part) at 120–125° for 12 hours when Ic, b.p. (bath temp.) 155–160° (0.3 mm.), was formed in 65% yield, dinitrophenylhydrazone (yellow needles) m.p. 189–190° (found: C, 66.41; H, 6.43), semicarbazone m.p. 225–226° (found: C, 73.23; H, 8.98).

Compounds IIa, IIb and IIc had the I.R. absorption of α,β-unsaturated ketones (6.0 and 6.1 μ), in contrast to Ia, Ib and Ic, which exhibited only saturated carbonyl absorption (5.85 μ). The tricyclic ketones have a *trans* decalone system as expected from their method of formation and demonstrated by the identity of the derivatives obtained before and after heating with alcoholic base.[4]

Dehydrogenation of the lithium aluminum hydride reduction product of Ia smoothly afforded phenanthrene, while dehydrogenation of the carbinol formed by the action of methyl lithium on Ic

(4) It is of considerable interest that on treatment with sulfuric acid the 4-carbethoxy derivative of IIb has been found to undergo *cyclodehydration* to a tetrahydrophenanthrene carboxylate rather than *cyclization* to a ketone.[5] This latter reaction has previously been attempted without success in related cases (see J. W. Cook and A. Cohen, *J. Chem. Soc.*, 1098 (1933); 1570 (1935)).

(regenerated from its semicarbazone) gave a 60% yield of retene, m.p. 99.5–100.5° (picrate m.p. 125.5–126.5°), undepressed with an authentic sample prepared from dehydroabietic acid.[5]

The structural identity of the synthetic *dl*-1-keto-7-isopropyl-12-methyl-1,2,3,4,9,10,11,12-octahydrophenanthrene (Ic) with the C_{18} *d*-ketone recently obtained from dehydroabietic acid[6] is confirmed by comparison of their infrared spectra (Fig. 1).

The extension of this work to the stereospecific synthesis of the resin acids is being actively pursued.

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RECEIVED JUNE 15, 1951

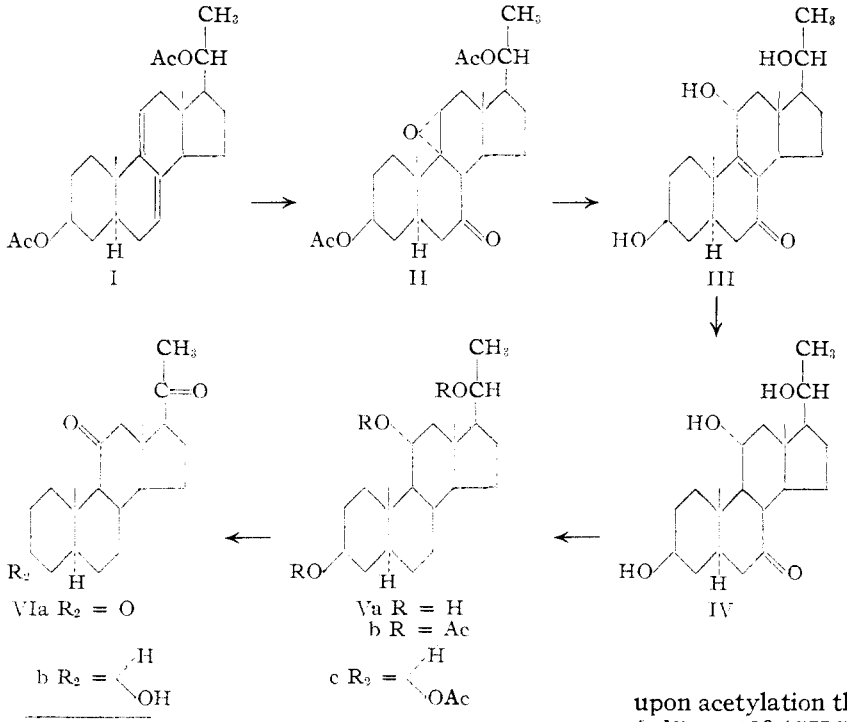
(5) L. Ruzicka and H. Waldmann, *Helv. Chim. Acta*, **16**, 842 (1933).
(6) A. Brossi, H. Gutmann and O. Jeger, *ibid.*, **33**, 1730 (1950).
(7) National Institutes of Health Predoctoral Fellow, Harvard University, 1950–1951.

STEROIDS. XXIV.[1] INTRODUCTION OF THE 11-KETO AND 11α-HYDROXY GROUPS INTO RING C UNSUBSTITUTED STEROIDS

Sir:

The conversion of Δ^5-3β-hydroxy steroids to a number of $\Delta^{7,9(11)}$-dienes of the pregnane and sapogenin series with both the *allo* and *normal* configuration at C-5 has recently been reported from this Laboratory.[1–4] In two Communications[5,6] to the Editor, there is described the transformation of such $\Delta^{7,9(11)}$-dienes to 11-ketosteroids by way of Δ^8-unsaturated and thence saturated 7,11-diones. We should like to record herewith an alternate procedure for the synthesis of 11-oxygenated steroids from ring C unsubstituted steroids via $\Delta^{7,9(11)}$-dienes, which does not involve the above mentioned[5,6] intermediates. In addition to its versatility, the presently described method exhibits the attractive feature of representing a novel and convenient synthesis for the hitherto unknown 11α-hydroxyallopregnanes and sapogenins.[6a]

Performic acid oxidation of $\Delta^{7,9(11)}$-allopregnadiene-3β,20β-diol diacetate (I)[1] readily led to 9α,11α-oxidoallopregnane-3β,20β-diol-7-one diacetate (II) (m.p. 260–262° (all m.p.s are uncorrected), $[\alpha]^{20}D$ −55° ($CHCl_3$), no ultraviolet maximum, $\lambda_{max.}^{nujol}$ 1736 cm.$^{-1}$ (acetate) and 1718 cm.$^{-1}$ (7-ketone), no free hydroxyl band; found: C, 68.95; H, 8.39). Alkaline hydrolysis was accompanied by isomerization and afforded in high yield Δ^8-allopregnene-3β,11α,20β-triol-7-one (III) (m.p. 250–252°, $[\alpha]^{20}D$ −25° (EtOH), $\lambda_{max.}^{EtOH}$ 254 mμ, log ε 4. 11, $\lambda_{max.}^{nujol}$ 1662 cm.$^{-1}$, found: C, 72.52; H, 8.97; triacetate, m.p. 203–205°; found: C, 68.21; H, 8.06). Catalytic hydrogenation (palladized charcoal in ethanol solution) of III produced 78% of allopregnane-3β,11α,20β-triol-7-one (IV) (m.p. 246–248°, $[\alpha]^{20}D$ −112° (EtOH), no ultraviolet maximum, $\lambda_{max.}^{nujol}$ 1718 cm.$^{-1}$; found: C, 71.58; H, 10.01). Wolff–Kishner reduction gave allopregnane-3β,11α,20β-triol(Va) (m.p. 253–255°, $[\alpha]^{20}D$ −28° (EtOH), no carbonyl band in infrared; found: C, 74.63; H, 10.83), which formed a triacetate (Vb) (m.p. 162–164°, $[\alpha]^{20}D$ −16° ($CHCl_3$), $\lambda_{max.}^{CS_2}$ 1736 cm.$^{-1}$ (acetate), no free hydroxyl band; found: C, 70.47; H, 9.26). Chromium trioxide oxidation of the triol Va led to the known[7] allopregnane-3,11,20-trione (VIa) (m.p. 211–213°, $[\alpha]^{20}D$ +129° (EtOH); found: C, 76.19; H, 9.39), which on Raney nickel reduction smoothly yielded allopregnane-11,20-dione-3β-ol (VIb) (m.p. 192–194°, $[\alpha]^{20}D$ +99° ($CHCl_3$); found: C, 75.44; H, 9.55) and upon acetylation the acetate (VIc)[8] (m.p. 143–144°, $[\alpha]^{20}D$ +89° ($CHCl_3$), $\lambda_{max.}^{CS_2}$ 1736 and 1710 cm.$^{-1}$, no



(1) Paper XXIII, J. Romo, G. Rosenkranz and C. Djerassi, THIS JOURNAL, in press.
(2) R. Yashin, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, (1951) in press.
(3) G. Rosenkranz, J. Romo, E. Batres and C. Djerassi, *J. Org. Chem.*, **16**, 298 (1951).
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(6a) W. T. Long, T. W. Marshall, and T. F. Gallagher, *J. Biol. Chem.*, **165**, 197 (1946), have prepared 11a-hydroxy compounds in the bile acid series.
(7) M. Steiger and T. Reichstein, *Helv. Chim. Acta*, **21**, 161 (1938), prepared the trione VIa by degradation of corticosterone and reported m.p. 212–216°, $[\alpha]^{20}D$ +133° (EtOH). A mixed melting point determination, kindly performed by Prof. T. Reichstein, further confirmed the identity of the two specimens.
(8) Ref. 5 records m.p. 141–143°, $[\alpha]D$ +88°.