890 cm.$^{-1}$, which was identical with VIb, the 3-hydroxyetiolactone prepared from the synthetic etiolactone (V).

The isolation and characterization of 5α-(4,5)-dihydroaldosterone (Ia) and 3βOH,5α-(4,5)-tetrahydroaldosterone (IIa) indicates that the ring A reduced products with A/B *trans* (5α) in configuration are favored.

RESEARCH INSTITUTE FOR MEDICINE AND CHEMISTRY
CAMBRIDGE 42, MASS., AND
MASSACHUSETTS GENERAL HOSPITAL
BOSTON, MASS.
M. M. PECHET
R. H. HESSE
H. KOHLER

RECEIVED AUGUST 4, 1960

THE KETO-ENOL EQUILIBRIUM OF ETHYL ACETOACETATE UNDER HIGH PRESSURE

Sir:

It has been demonstrated in recent years that studies of the effect of pressure on reaction rates in the liquid phase often permit certain conclusions to be drawn regarding the mechanism involved.[1] For instance, reactions are accelerated if they proceed through a transition state that has a greater separation of charge than the reactant(s) and *vice versa*, since the intense electric field of an ion causes local compression of solvent molecules.[2] In the expression $d \ln k/dp = -\Delta V^*/RT$, the volume of activation is negative in such cases. On the other hand, a reaction is decelerated (ΔV^* is positive) if the formation of the transition state depends on homopolar bond breaking and *vice versa*,[3] since the sum of the van der Waals radii of the fragments exceeds that of the reactant.

It appeared that another feature often of interest in mechanistic studies, *i.e.*, formation of a cyclic transition state, could be subject to a pressure effect.[4] A comparison of the densities of straight chain hydrocarbons shows that the molar volume of n-C_mH_{2m+2} exceeds that of n-$C_{m-6}H_{2m-10}$ by 96 ± 1 ml./mole (m ranging from 11 to 17). This difference is a measure of the volume of hexamethylene, $—(CH_2)_6—$. This value is 12 ml./mole *smaller* than the molar volume of cyclohexane (108 ml./mole). Parachor data[5] on ring structures similarly suggest that ring structures have greater volume requirements than straight chains. Presumably the core of such doughnut-like molecules is too small to be accessible to other molecules.

In this work, the keto-enol equilibrium was studied as an example. If the process of forming a cyclic structure such as the enol form of ethyl acetoacetate[6] does not contribute to the change in molar volume, the equilibrium constant (K keto/enol) should decrease as the pressure is increased, since the molar volume of the group $—C(OH){=}CH—$ is smaller than that of the group $—COCH_2—$ by about 4.0 ml./mole (estimated from the densities of unsaturated alcohols and isomeric carbonyl compounds); if the internal H-bond is taken into account, this difference would undoubtedly be somewhat greater. If the ring formation has the positive volume requirement described above, the molar volume of the enol form should be *larger* than that of the keto form by about 5 ml./mole. The effect of pressure on this equilibrium was studied by Kabachnik, Yakushkima and Kislyakova,[7] who reported no significant change in K for the pure substance. Since the rate of interconversion is extremely variable (depending on traces of impurities[6]) it appeared desirable to repeat this work. The new data (Table I) show that K in the pure liquid increases with pressure; the molar volume of the enol form exceeds that of the keto form by 1.0–1.5 ml./mole. This would suggest that it may be possible to recognize reactions involving a cyclic transition state by a retarding effect of pressure. An experimental program to test this statement is about to start in this laboratory.

TABLE I

p(atm.)[a]	% enol[b]	K keto/enol	ΔV (ml./mole)[c]
1	7.7	12.0	−1.5
1350	7.2	13.0	−1.0
2500	7.0	13.2	−1.3
3700	6.4	14.6	

[a] The apparatus will be described at a later date. [b] At 25°. Samples of the ester were withdrawn without releasing the pressure, collected in a quartz vessel and analyzed at once in the usual way (K. H. Meyer and P. Kappelmeyer, *Ber.*, **44**, 2718 (1911)) Care was taken to insure the system was at equilibrium and that interconversion during analysis was negligible. [c] Calculated from $(\ln K_p - \ln K_1) = -\Delta V/RT$.

Acknowledgment.—This work was done at the Rohm and Haas Research Laboratories. The author had the benefit of many helpful discussions with Mr. O. H. Loeffler and Drs. C. Huggett and B. Iwanciow.

---

(1) For an excellent review, see S. D. Hamann, "Physico-Chemical Effects of Pressure," Academic Press, Inc., New York, N. Y., 1957.

(2) H. G. David and S. D. Hamann, *Trans. Far. Soc.*, **50**, 1188 (1952).

(3) A. E. Nicholson and R. G. W. Norrish, *Disc. Far. Soc.*, 97 (1956).

(4) C. Walling and J. Peisach have considered this possibility recently in the dimerization of isoprene to cyclic products (THIS JOURNAL **80**, 5819 (1958)).

(5) S. Sugden, "The Parachor and Valency," Geo. Rutledge & Sons, Ltd., London, 1929.

(6) G. W. Wheland, Ch. XIV, "Advanced Organic Chemistry," 2nd Edition, John Wiley & Sons, Inc., New York, N. Y., 1949.

(7) M. I. Kabachnik, S. E. Yakushkima and N. V. Kislyakova, *Doklady Akad. Nauk., S.S.S.R.*, **96**, 1169 (1954); *cf. C.A.*, **49**, 8815 (1955). The authors stated that the system was allowed 4 hours to reach equilibrium; in this work it was found that at least 20 hours was necessary.

STATE UNIVERSITY OF NEW YORK
LONG ISLAND CENTER
OYSTER BAY, NEW YORK
WILLIAM J. LE NOBLE

RECEIVED AUGUST 23, 1960

THE STEREOCHEMISTRY OF JACOBINE

Sir.

Recent investigations[1] have shown all previous structures proposed for jacobine, jaconecic acid and *iso*jaconecic acid to be incorrect. The structures of these compounds are correctly represented by I, II and III, respectively. We wish now to present evidence which permits assignment of stereochemistry to the above compounds, as shown in Ia, IIa and IIIa.

---

(1) R. B. Bradbury and S. Masamune, THIS JOURNAL, **81**, 5201 (1959), and also see T. A. Geissman, *Aust. J. Chem.*, **12**, 247 (1959).