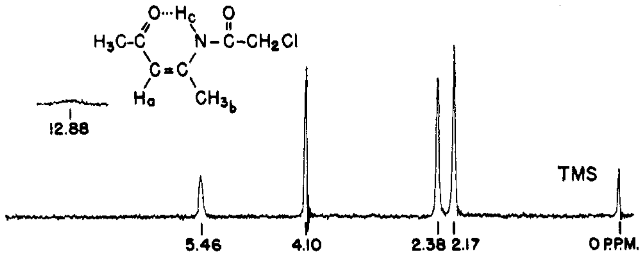
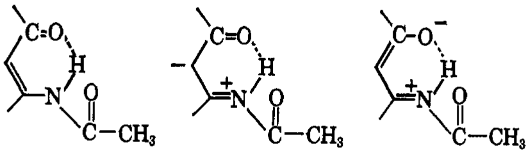


Figure 3.—The n.m.r. spectrum of 4-chloroacetylamino-3-penten-2-one in $CDCl_3$ at 60.00 Mc.

by the n.m.r. results.[42] Unfortunately, replacement (indirect) of the imido proton by a methyl group in the 4-acylamino-3-penten-2-ones for purposes of spectra comparison was not successful.[18] It has been noted[36] that the enolic proton in acetylacetone is shifted 0.9 p.p.m. downfield when benzene replaces carbon tetrachloride as the solvent. Thus the corresponding shift of only 0.16 p.p.m. observed for 4-acetylamino-3-methyl-3-penten-2-one (IIe) lends support to the vinylogous imide as the predominant tautomer for appropriate compounds in Tables III and IV. This conclusion is strongly reinforced by infrared and ultraviolet spectral measurements.[31] For example, the following absorption peaks observed for 4-acetylamino-3-penten-2-one (IIa) are quite comparable to those noted in the prior discussion of cyclic compounds—IIa: $\lambda_{\max}^{CH_3OH}$ 293 mμ (ε 17,000); $\nu_{\max}^{CCl_4}$ 1723, 1645, and 1597 cm.$^{-1}$ The absence of a distinct NH stretching band coupled with a normal ketone band at 1723 cm.$^{-1}$ in the infrared spectrum of IIa can only be interpreted satisfactorily on the basis of the chelated vinylogous imide structure.

From the above evidence, it is concluded that the introduction of an electron-withdrawing acyl group at the nitrogen atom of a vinylogous amide is not accompanied by a tautomeric shift; rather, a stable vinylogous imide results. This is in agreement with previous studies[36] which have shown simple vinylogous amides maintain their structural integrity with a variety of nitrogen substituents ranging from ethyl to β,β,β-trifluoroethyl. It seems likely from the infrared results that the presence of an additional carbonyl group decreases the contributions of such polar forms as the following structures to the resonance stabilization of the vinylogous imide.



Acknowledgment.—The author wishes to thank Dr. R. M. Silverstein of Stanford Research Institute and Mr. Eugene A. Pier of Varian Associates, Palo Alto, for obtaining the n.m.r. spectra. The technical assistance of Miss Martha McClelland and Mr. James Westgard as undergraduate research participants is gratefully acknowledged.

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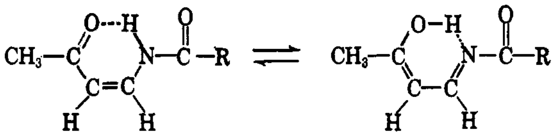
[42] Proton resonance data should suffice in the case of the 4-acylamino-3-buten-2-ones. Coupling between the NH and adjacent CH in the vinylo-



gous imide should occur, with a *trans* NH–CH spin–spin coupling of ~13.0 c.p.s.[24] Such compounds will be studied.

Equilibrium and Kinetic Studies of the Meerwein–Ponndorf–Verley–Oppenauer (MPVO) Reaction[1]

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Equilibrium constants have been measured in toluene at 45° for the Meerwein–Ponndorf–Verley–Oppenauer (MPVO) reduction of nine methyl ketones, $RCOCH_3$, with 9-fluorenol and aluminum *t*-butoxide. The equilibrium constants have been successfully correlated with substituent constants by the equation, $\log K = 0.456 + 1.13\sigma^* - 0.08156\#$, $R = 0.992$, $s = 0.082$. By the "swamping" technique, the reaction was found to be first order with respect to aluminum *t*-butoxide, 9-fluorenol, and $RCOCH_3$. Both the reaction between 9-fluorenol and aluminum *t*-butoxide and the hydride ion transfer are slow steps in the over-all reaction. Infrared spectra indicate the presence of a small amount of *t*-butyl alcohol in an equilibrated mixture of 9-fluorenol and aluminum *t*-butoxide. This supports the first step of the generally accepted mechanism.

Wilds[2] has reviewed the Meerwein-Ponndorf-Verley reduction of aldehydes and ketones and Djerassi[3] has reviewed the Oppenauer oxidation of primary and secondary alcohols. Each of these reactions is reversible and the mechanism is probably similar for both reactions.[3] The stoichiometry for either reaction is $RR'C{=}O + R''R'''CHOH \rightleftharpoons RR'CHOH + R''R'''C{=}O$, with an aluminum alkoxide as catalyst. If the primary interest is in the reduction of $RR'C{=}O$ to $RR'CHOH$, then this reaction is the Meerwein–Ponndorf–Verley reduction and is usually carried out with isopropyl alcohol as reducing agent and aluminum isopropoxide as catalyst. On the other hand, if the principal concern is in the oxidation of $R''R'''CHOH$ to $R''R'''C{=}O$, then the same reaction is referred to as the Oppenauer oxidation with, usually, acetone as oxidizing agent and aluminum *t*-butoxide as catalyst. Consequently, it may be more appropriate to refer to the over-all oxidation–reduction as the Meerwein–Ponndorf–Verley–Oppenauer (MPVO) reaction.

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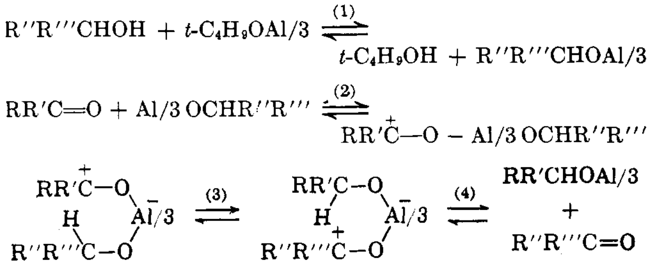
[1] Abstracted in part from the Ph.D. Dissertation of B. J. Yager, Texas A & M University, Aug. 1962.

[2] A. L. Wilds, *Org. Reactions*, **2**, 178 (1944).

[3] C. Djerassi, *ibid.*, **6**, 207 (1951).

The generally accepted mechanism[4,5] is shown below for the MPVO reduction of a ketone, RR′C=O, by means of a secondary alcohol, R″R‴CHOH, with aluminum *t*-butoxide as catalyst.



$$\mathrm{R''R'''CHOH} + t\text{-}\mathrm{C_4H_9OAl/3} \xrightleftharpoons{(1)} t\text{-}\mathrm{C_4H_9OH} + \mathrm{R''R'''CHOAl/3}$$

$$\mathrm{RR'C{=}O} + \mathrm{Al/3\,OCHR''R'''} \xrightleftharpoons{(2)} \mathrm{RR'\overset{+}{C}{-}O} - \mathrm{Al/3\,OCHR''R'''}$$

Step 3 of this mechanism, involving the transfer of a hydride ion, has been considered generally to be rate determining.[6]

Williams, Krieger, and Day[5] pointed out that the hydride ion might be transferred as in step 3 or by the attack of another molecule of the coordinated complex. Moulton, VanAtta, and Ruch[7] measured the rate of the MPVO reduction of benzophenone by aluminum isopropoxide in isopropyl alcohol and concluded that the reduction is first order in benzophenone and approximately 1.5 order in aluminum isopropoxide. They propose that the reaction may proceed by two simultaneous mechanisms, one being the mechanism shown above which involves a pseudo-cyclic transition state and 1 mole of aluminum isopropoxide, and a second mechanism which involves a noncyclic transition state and 2 moles of aluminum isopropoxide.

Shiner, Whittaker, and Fernandez[8] reported recently that, in a number of organic solvents, aluminum *t*-butoxide is dimeric while aluminum isopropoxide is tetrameric. At higher temperatures, either on melting or in solution, aluminum isopropoxide is converted into a cyclic trimer which only slowly reverts to the tetramer at lower temperatures. Shiner and Whittaker[6] studied the rate of reduction of acetophenone with aluminum isopropoxide in 50 mole % benzene and isopropyl alcohol solvent at 25° and found that the rate of α-phenylethanol formation is considerably slower than the rate of acetone formation. They concluded that the rate-determining step is alcoholysis of the mixed alkoxide and not hydride transfer.

The present study was undertaken to obtain further kinetic and equilibrium information on the MPVO reaction and to interpret these and other available data in view of the above ideas about the mechanism.

Results and Discussion

Equilibrium Studies.—The equilibrium constants for the MPVO reduction in toluene at 45° of nine methyl ketones, $\mathrm{RCOCH_3}$, with 9-fluorenol[9] and aluminum *t*-butoxide are listed in Table I, with alternate *K*-values being given in parentheses for four of the ketones. These alternate values were calculated from eq. 1, using the E_0-values (oxidation potentials) given

$$\log K = (2/0.0592)(E_0 \text{ for RCOR}' - 0.117) \qquad (1)$$

by Adkins, *et al.*,[10a] for the MPVO reduction of RCOR′ (−0.117 is the E_0-value in volts for 9-fluorenone). The *K*-values are in close agreement for ketones **2**, **4**, and **8**. The agreement is less satisfactory for acetone (**1**), but still corresponds to agreement of E_0-values within 5 mv. which does not exceed the accuracy of ±5 mv. claimed by Adkins, *et al.*

Table I

Equilibrium Constants and Substituent Constants for the MPVO Reduction in Toluene at 45° of Nine Methyl Ketones, $\mathrm{CH_3COR}$, with 9-Fluorenol and Aluminum *t*-Butoxide

	R in $\mathrm{RCOCH_3}$	$K^{45°}$	σ^{*a}	$E_s^{\circ b}$	$(n-3)^c$	6-Number $(6\#^d)$
1	$\mathrm{CH_3}$	3.74 (2.55)^e	0.000	0.00	0	0
2	$\mathrm{C_2H_5}$	1.64 (1.60)^e	−0.100	−0.38	−1	0
3	*n*-$\mathrm{C_3H_7}$	1.29	−0.115	−0.67	−1	3
4	*i*-$\mathrm{C_3H_7}$	1.71 (1.60)^e	−0.190	−1.08	−2	0
5	*n*-$\mathrm{C_4H_9}$	1.11	−0.130	−0.70	−1	3
6	*i*-$\mathrm{C_4H_9}$	0.712	−0.125	−1.24	−1	6
7	*s*-$\mathrm{C_4H_9}$	0.804	−0.210	−1.74	−2	3
8	*t*-$\mathrm{C_4H_9}$	1.48 (1.37)^e	−0.300	−2.46	−3	0
9	$\mathrm{ClCH_2}$	43.6	1.050	−0.55	−1	0

[a] See ref. 15a. [b] See ref. 15b and 18. [c] *n* is the number of α-hydrogens in R of $\mathrm{CH_3COR}$. [d] See ref. 19 and 20. [e] *K*-values in parentheses calculated by eq. 1 from E_0-values given in ref. 10a.

The equilibrium constant for the reaction, $\mathrm{RCOCH_3}$ + 9-fluorenol ⇌ $\mathrm{RCHOHCH_3}$ + 9-fluorenone, may or may not be the same as that for the MPVO reduction of $\mathrm{RCOCH_3}$ with 9-fluorenol and an excess of aluminum *t*-butoxide, depending on the extent to which the two alcohols are present as mixed alkoxides and to which the two ketones are coordinated with aluminum alkoxides. Data of Baker and Adkins[10b] show that the *K*-value for the MPVO reduction in toluene of benzophenone with 9-fluorenol and aluminum *t*-butoxide is independent of the concentrations of the reactants and catalyst (the ratio of catalyst concentration to reactant concentrations was varied from 0.7-fold to 10-fold). This fact, along with the fact that the *K*-values reported herein for the MPVO reduction of four ketones (**1**, **2**, **4**, and **8** in Table I) agree satisfactorily with values calculated from the polarographic data of Adkins, *et al.*,[10a] indicates that the *K*-value for the MPVO reduction is about the same as that for the equilibrium given above. Further support may be afforded by the results of kinetic studies reported herein which show that the concentration of product 9-fluorenone found *in situ* is the same as that found, under the same conditions, after hydrolysis with 75% aqueous isopropyl alcohol. This fact indicates either that essentially all of the 9-fluorenone is present

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[4] R. B. Woodward, N. L. Wendler, and F. J. Brutschy, *J. Am. Chem Soc.*, **67**, 1425 (1945); L. M. Jackman and J. A. Mills, *Nature*, **164**, 789 (1949); R. E. Lutz and J. S. Gillespie, Jr., *J. Am. Chem. Soc.*, **72**, 344 (1950); L. M. Jackman and A. K. Macbeth, *J. Chem. Soc.*, 3252 (1952); W. v. E. Doering and T. C. Aschner, *J. Am. Chem. Soc.*, **75**, 393 (1953); E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, p. 545; D. C. Bradley in Advances in Chemistry Series, No. 23, American Chemical Society, Washington, D. C., 1959, p. 10; M. S. Bains and D. C. Bradley, *Chem. Ind.* (London), 1032 (1961).

[5] E. D. Williams, K. A. Krieger, and A. R. Day, *J. Am. Chem. Soc.*, **75**, 2404 (1953).

[6] V. J. Shiner, Jr., and D. Whittaker, *ibid.*, **85**, 2337 (1963).

[7] W. N. Moulton, R. E. VanAtta, and R. R. Ruch, *J. Org. Chem.*, **26**, 290 (1961).

[8] V. J. Shiner, Jr., D. Whittaker, and V. P. Fernandez, *J. Am. Chem. Soc.*, **85**, 2318 (1963).

[9] R. H. Baker and H. Adkins, *ibid.*, **62**, 3305 (1940).

[10] (a) H. Adkins, R. M. Elofson, A. G. Rossow, and C. C. Robinson, *ibid.*, **71**, 3622 (1949); (b) R. H. Baker and H. Adkins, *ibid.*, **62**, 3305 (1940).

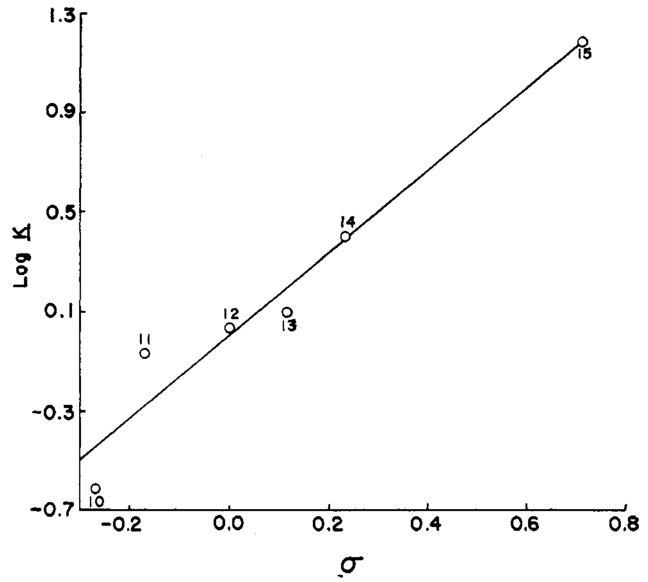

Figure 1.—Relationship between log K and σ for the MPVO reduction of six *meta-* or *para-*substituted acetophenones with 9-fluorenol and aluminum *t*-butoxide.

as such or that it and its coordinated complex with aluminum alkoxide absorb similarly at 381 mμ.

For the above equilibrium, where the only structural variation is in the R-group, consideration of the reactant state ($RCOCH_3$) and of the product state ($RCHOHCH_3$) indicates that the equilibrium constant might be changed by polar, hyperconjugation, steric, and 6-number effects resulting from changing the structure of the R-group. For a series of *meta-* and *para-*substituted benzophenones, Brockman and Pearson[11] found quantitatively that the polarographic reduction of these benzophenones becomes easier as the substituent becomes more strongly electron withdrawing. A Hammett[12] ρ-value of 1.30 has been found[13] for the equilibrium constants for the MPVO reduction in toluene at 100° of benzophenone and seven *para-*substituted benzophenones. The positive sign of ρ shows that the equilibrium constant increases as the *para-*substituent becomes more strongly electron withdrawing. Further, we have used eq. 1 and data from ref. 10 to calculate the K-values shown in Table II for the MPVO reduction of acetophenone and five *meta-* or *para-*substituted acetophenones with 9-fluorenol. Linear regression analysis[14a] of log K on σ gives eq. 2 with a linear correlation coefficient, r, of 0.976 and a standard deviation from regression, s, of 0.143. The plot of log K *vs.* σ and the line of eq. 2 are shown in Figure 1.

$$\log K = 0.003 + 1.66\,\sigma \qquad (2)$$

Polar effects, measured by Taft's polar substituent constants,[15a] should also be important in the MPVO reduction of aliphatic ketones. Hyperconjugation effects[16] (as used in the present article, "hyperconjugation" has the meaning of "α-hydrogen bonding" as proposed by Kreevoy and Eyring[17]) might be significant since the hyperconjugative stabilization of the unsaturated reactant state ($RCOCH_3$) would be greater than that of the saturated product state ($RCHOHCH_3$). Steric effects, measured by Taft's steric substituent constants[15b] corrected[18] for hyperconjugation effects, must also be considered since, at the reaction site, the reactant state is trigonal while the product state is tetrahedral and more crowded. Newman[19] has shown that the 6-number of a substituent (*i.e.*, the number of atoms in the 6-position from the carbonyl oxygen atom as atom number one) makes a large contribution to the total steric effect of that substituent.

TABLE II

EQUILIBRIUM CONSTANTS AND SUBSTITUENT CONSTANTS FOR THE MPVO REDUCTION OF SIX ACETOPHENONES, $RC_6H_4COCH_3$, WITH 9-FLUORENOL AND ALUMINUM *t*-BUTOXIDE

	R in $RC_6H_4COCH_3$	K^a	σ^b
10	*p*-CH_3O	0.246	−0.268
11	*p*-CH_3	0.856	−0.170
12	H	1.08	0.000
13	*m*-CH_3O	1.26	0.115
14	*p*-Br	2.54	0.232
15	*m*-NO_2	15.2	0.710

[a] Calculated from eq. 1 and the data of ref. 10a. [b] See ref. 12.

For the nine methyl ketones, substituent constants for polar, steric, hyperconjugation, and 6-number effects[20] are recorded in the last four columns of Table I as σ^*, E_s^c, $(n - 3)$, and *6#*, respectively. The analysis of the multiple regression[14b] of log K on these four variables gives eq. 3 with a multiple correlation coefficient, R, of 0.995 and a standard deviation from regression, s, of 0.079. The numbers in parentheses below the four coefficients of eq. 3 are the per cent confidence levels of the corresponding variables as determined by Students t tests.[14c]

$$\log K = 0.542 + \underset{(100.0\%)}{1.12\sigma^*} - \underset{(78.5\%)}{0.0204E_s^c} + \underset{(80.4\%)}{0.188(n - 3)} - \underset{(99.4\%)}{0.104\mathit{6\#}} \qquad (3)$$

The least significant variable, E_s^c, was dropped and regression eq. 4 was obtained.

$$\log K = 0.482 + \underset{(100.0\%)}{1.12\sigma^*} + \underset{(30.9\%)}{0.0171(n - 3)} - \underset{(99.7\%)}{0.0832\mathit{6\#}} \qquad (4)$$
$$R = 0.992;\ s = 0.088$$

Similarly, the next least significant variable, $(n - 3)$, was eliminated and regression eq. 5 was obtained.

$$\log K = 0.456 + \underset{(100.0\%)}{1.13\sigma^*} - \underset{(99.9\%)}{0.0815\mathit{6\#}} \qquad (5)$$
$$R = 0.992;\ s = 0.082$$

The validity of eq. 5 is indicated by the values of R and s and by the per cent confidence levels of σ^* and *6#*. If the variable, *6#*, is arbitrarily eliminated,

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(11) R. W. Brockman and D. E. Pearson, *J. Am. Chem. Soc.*, **74**, 4128 (1952).

(12) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., Chapter 7.

(13) D. E. Pickart and C. K. Hancock, *J. Am. Chem. Soc.*, **77**, 4642 (1955).

(14) G. W. Snedecor, "Statistical Methods," 5th Ed., The Iowa State College Press, Ames, Iowa, 1956: (a) Chapter 6; (b) Chapter 14; (c) pp. 46, 418, and 441.

(15) R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956: (a) p. 619; (b) p. 598.

(16) R. S. Mulliken, C. A. Rieke, and W. G. Brown, *J. Am. Chem. Soc.*, **63**, 41 (1941).

(17) M. M. Kreevoy and H. Eyring, *ibid.*, **79**, 5121 (1957).

(18) C. K. Hancock, E. A. Meyers, and B. J. Yager, *ibid.*, **83**, 4211 (1961).

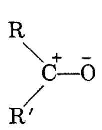
(19) M. S. Newman, *ibid.*, **72**, 4783 (1950).

(20) C. K. Hancock, B. J. Yager, C. P. Falls, and J. O. Schreck, *ibid.*, **85**, 1297 (1963).

$$\log K = 0.321 + 1.25\sigma^* \quad (100.0\%) \qquad (6)$$
$$r = 0.940;\ s = 0.198$$

linear regression analysis[14a] of log K on σ^* gives eq. 6. The decrease in the correlation coefficient and the increase in the standard deviation both further indicate that the 6-number effect makes a small but statistically significant contribution to the value of log K. The close prediction of log K values by eq. 5 is shown graphically in Figure 2.

The ρ^*-value of 1.13 in eq. 5 compares favorably with the ρ-value of 1.30 reported by Pickart and Hancock.[18] The positive sign indicates that the reactant ketone is stabilized by electron-donating groups more than the product secondary alcohol. This stabilization can be attributed to contributing structures of the type of I and II as proposed by Felton and Orr[21] to explain the decrease in the infrared absorption frequencies of carbonyl groups when electron-donating groups are present. Conversely, electron-withdrawing groups decrease the ability of the ketone to assume these structures and destabilize the ketone. In the saturated alcohol, the polar effects are negligible and its stability is not appreciably affected by varied electron density.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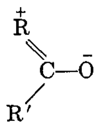

II

The low significance of both hyperconjugative resonance and steric (E_s^c) effects may be attributed to the series studied. The ketones all have one methyl group next to the carbonyl group. The methyl group has a low steric requirement ($E_s^c = 0.00$) and three α-hydrogens. There were always at least three hydrogens available for hyperconjugative resonance and one side of the carbonyl carbon was not sterically hindered. Steric effects as measured by E_s^c can be important in the MPVO reduction of ketones as shown by the following study. An attempt was made to prepared di-*t*-butylcarbinol from di-*t*-butyl ketone by MPVO reduction. The solution was refluxed for several days, but no reaction occurred. The alcohol was prepared by another method,[22] and an attempt was made to oxidize it with 9-fluorenone and aluminum *t*-butoxide at 45°. Again, no reaction took place over a period of 2 weeks as evidenced by the constant concentration of 9-fluorenone. The failure of this alcohol and ketone to react is almost certainly due to the large *t*-butyl groups which cover the "backside" of the carbonyl and carbinol carbon atoms. Thus, steric effects can be very important but, when one of the groups attached to the carbonyl group is a methyl group, these steric effects become negligible.

The steric effect of the atoms in the 6-position is somewhat different. While E_s^c measures the ability of a group to "cover" the atom to which it is attached, the 6-number measures the interaction between the carbonyl oxygen atom and the atoms in the 6-position from the carbonyl oxygen as atom number one. Examination of molecular models show that there is greater interaction of the 6-atoms with the carbinol oxygen than with the carbonyl oxygen. This is due to the change in geometry in going from the trigonal ketone to the tetrahedral alcohol. It appears from eq. 5 that this type of interaction is more important in this reaction series than are steric effects as measured by E_s^c.

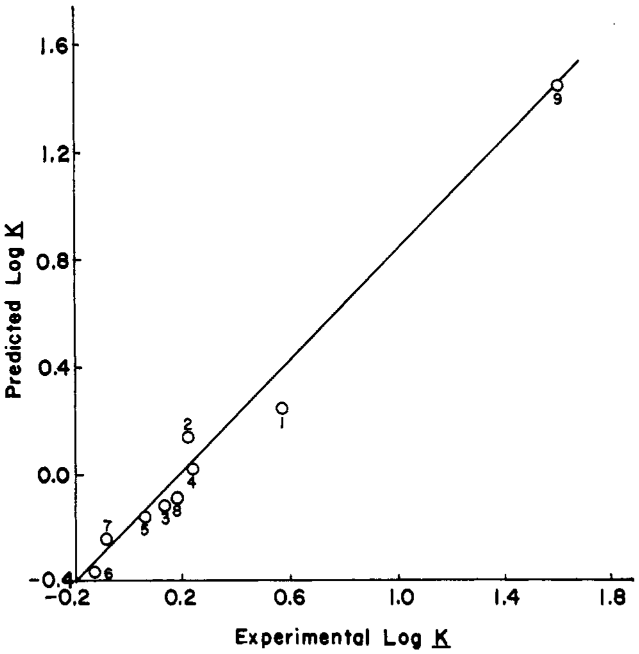
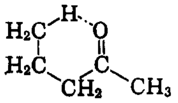
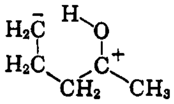


Figure 2.—Relationship between experimental log K values and log K values calculated from eq. 5 for the MPVO reduction of nine methyl ketones with 9-fluorenol and aluminum *t*-butoxide.

It has been suggested that there can be weak intramolecular hydrogen bonding between the hydrogen atoms in the 6-position and the carbonyl oxygen of aliphatic acids.[23,24] If such effects were present in this reaction series, they would stabilize the reactant ketone by contributing structures such as III and IV. Such structures should cause a marked decrease in the infrared absorption frequency of the carbonyl group of ketones with several hydrogen atoms in the 6-position. However, examination of the carbonyl absorption frequencies[25,26] of several methyl ketones in both vapor phase and solution shows that the number of atoms in the 6-position has no apparent effect on the absorption frequency. This is particularly evident in the case of methyl isobutyl ketone which has six hydrogens in the 6-position, but has a slightly higher absorption frequency than does acetone. Thus, it appears that 6-number effects are steric rather than polar in nature.


III


IV

Kinetic Studies.—A complete kinetic study was not undertaken, but some problems suggested by the proposed mechanism were studied. An unsuccessful attempt was made to find a kinetic equation to fit the kinetic data. The reaction of equal concentrations of 9-fluorenol and ketone with an excess of aluminum *t*-

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[21] D. G. I. Felton and S. F. D. Orr, *J. Chem. Soc.*, 2170 (1955).

[22] J. B. Conant and A. H. Blatt, *J. Am. Chem. Soc.*, **51**, 1227 (1929).

[23] J. F. J. Dippy, *Chem. Rev.*, **25**, 151 (1939).

[24] A. L. Henne and C. J. Fox, *J. Am. Chem. Soc.*, **75**, 5750 (1953).

[25] L. J. Bellamy and R. L. Williams, *J. Chem. Soc.*, 4294 (1957).

[26] N. Fuson, M. Josien, and E. M. Shelton, *J. Am. Chem. Soc.*, **76**, 2526 (1954).

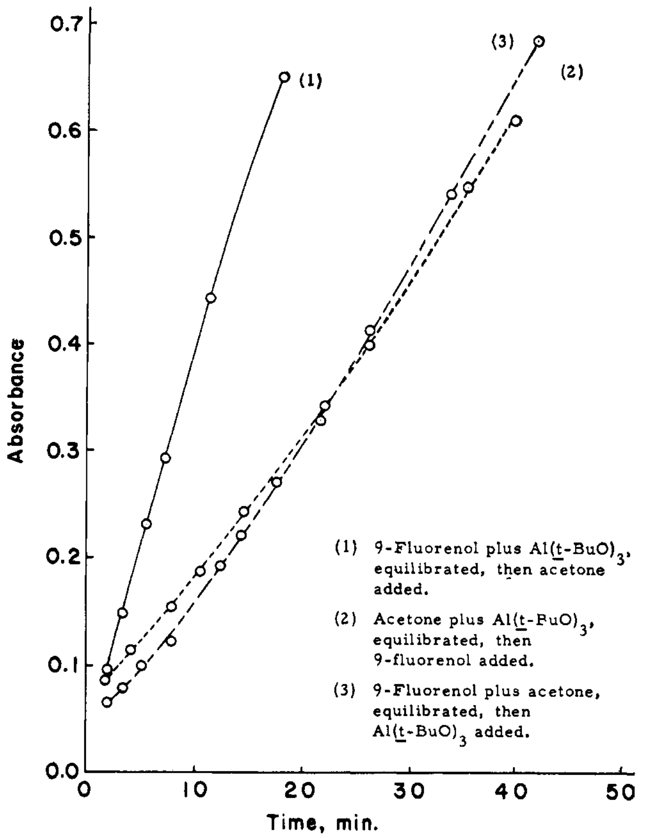

Figure 3.—Effect on the reaction rate of the order of mixing the reactants in the MPVO reduction of acetone with 9-fluorenol and aluminum *t*-butoxide.

butoxide followed neither the reversible second-order[27a] nor the regular second-order equation.[27b] The unintegrated rate expression of eq. 7 was used instead. The

$$\frac{dx}{dt} = k[A - x]^{n}A[B - x]^{n}B[C - x]^{n}C \qquad (7)$$

initial rate of reaction was determined from a plot of absorbance *vs.* time. The slope of this line, d*x*/d*t*, is directly proportional to the rate of reaction as the absorbance is a measure of the concentration of product, 9-fluorenone. This method for comparing rates of reaction was used to determine the effect of different order of mixing of reactants, the kinetic order of the reactants, and the effect of varied electron density on the reaction rate. The effect of the order of mixing of reactants was determined by measuring the rates of reaction when (1) 9-fluorenol and aluminum *t*-butoxide were mixed, then acetone added; (2) acetone and aluminum *t*-butoxide were mixed, then 9-fluorenol added; and (3) 9-fluorenol and acetone were mixed, then aluminum *t*-butoxide added. In each case, the mixture of the first two reactants was allowed to stand overnight before the third reactant was added.

It was found that the rate of reaction was significantly increased when the alcohol and catalyst were allowed to equilibrate before the ketone was added. There was no difference in the rate of reaction in cases 2 and 3. Figure 3 shows these results graphically. This is evidence in support of the first step of the proposed mechanism, the reaction of aluminum *t*-butoxide with the alcohol. This is evidently a slow step as found by Shiner and Whittaker,[6] and, by allowing this reaction to take place first, the over-all reaction rate was increased.

The kinetic orders of 9-fluorenol, ketone, and aluminum *t*-butoxide were determined by the initial rate method.[27c] The concentration of one of the reactants, A, was varied in the range of 0.003 to 0.0003 *M* while the concentrations of the other two reactants were held constant at 0.03 *M*. The initial rate of reaction was determined from a plot of absorbance *vs.* time for the three concentrations. Three determinations were made of each reaction rate. The kinetic order (n_A) of reactant A was found from the rates of reaction at two different concentrations of A, A_1 and A_2, by use of eq. 8.

$$n_A = \frac{\log (dA/dt)_1 - \log (dA/dt)_2}{\log A_1 - \log A_2} \qquad (8)$$

Table III shows the results of this investigation. In all cases, the reactants were found to be first order within experimental error. A study of the effect of change in electron density at the reaction site was undertaken to determine whether step 2 or 3 of the proposed mechanism is the rate-controlling step. In step 2, the ketone coordinates with the aluminum alkoxide. This step should be hindered by electron-withdrawing groups, since the coordination is between the aluminum, a Lewis acid, and the electron-rich oxygen. Electron-withdrawing groups would decrease the electron density of the oxygen and decrease the tendency to coordinate. In step 3, the transfer of the hydride ion, the converse is true. Electron-withdrawing groups would increase the positive nature of the carbonyl carbon and increase the probability of hydride-ion transfer. If no effect on the rate of reaction were noted when electron-withdrawing groups were attached to the carbonyl group, this would indicate that either the proposed mechanism is wrong or that step 4 is the rate-controlling step. The latter does not appear likely as parallel reaction rates were obtained from measurements made *in situ* and measurements made on samples withdrawn from the reaction mixture and hydrolyzed. Hydrolysis should break up any complex present and free the ketone so that a faster rate of appearance of ketone would be noted in these measurements than those made *in situ*.

TABLE III

KINETIC ORDERS, n_A, OF ACETONE, 9-FLUORENOL, AND ALUMINUM *t*-BUTOXIDE IN THE MPVO REDUCTION OF ACETONE

Reactant, A	Concn., *M*	d*A*/d*t*	n_A
Acetone	0.0033	0.0031	
Acetone	0.0016	0.0014	1.08
Acetone	0.00033	0.00031	1.00
9-Fluorenol	0.0033	0.0017	
9-Fluorenol	0.0016	0.00077	1.08
9-Fluorenol	0.00033	0.00019	0.95
Aluminum *t*-butoxide	0.0033	0.019	
Aluminum *t*-butoxide	0.0025	0.015	0.86
Aluminum *t*-butoxide	0.0016	0.008	1.20

Reaction rates were obtained for acetone, methyl ethyl ketone, and chloroacetone. All were at the same concentration (0.03 *M*) and were treated with 9-fluorenol and aluminum *t*-butoxide from the same stock solutions. The alcohol and catalyst were allowed to react before the ketone was added so that the effect of step 1

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(27) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953: (a) p. 175; (b) p. 14; (c) p. 44.

would be made negligible. The substituents, CH_3–CH_2– and Cl–CH_2–, were chosen to vary the electron density markedly but to have similar steric requirements. Figure 4 shows graphically the results of this study. The CH_3CH_2– group, $\sigma^* = -0.100$, slowed the reaction rate slightly. The $ClCH_2$– group, $\sigma^* = +1.050$, markedly increased the reaction rate. This is good evidence that the transfer of the hydride ion is the rate-determining step in the MPVO reaction.

A spectral study was made in the infrared region on carbon tetrachloride solutions of mixtures of the reactants. A weak new absorption band was observed at about 1150 cm.$^{-1}$ for a mixture of aluminum *t*-butoxide and 9-fluorenol. This is the region for the hydroxyl group deformation vibrations of tertiary alcohols.[28] This evidence is further support of step 1 of the proposed mechanism. No other changes in the infrared spectra of the mixtures were found.

Experimental

Materials.—The ketones and alcohols used in this study were purchased from commercial sources or prepared by standard methods. The liquid compounds were purified by distillation through a 1.5 × 46 cm. spinning-band column or a 1.5 × 50 cm. column filled with 0.32-cm. glass helices. 9-Fluorenone was purified by recrystallization from benzene–petroleum ether (b.p. 30–60°) mixture. After recrystallization from benzene and drying at 100° under 5-mm. pressure, 9-fluorenol melted at 155–156°.[9] Reagent grade toluene was further purified by refluxing over sodium and distilling through a 3 × 80 cm. column filled with 0.32-cm. glass helices. Aluminum *t*-butoxide was purchased commercially and was purified by dissolving in toluene and filtering through a fine-porosity, sintered-glass filter. The concentration of aluminum *t*-butoxide was determined by analysis[29] for Al_2O_3 and then the stock solution was diluted to the desired concentrations. Reagent grade carbon tetrachloride was used in the infrared spectral studies.

Equilibrium Constants.—All glassware was flushed with dry nitrogen to exclude atmospheric moisture. A toluene solution (50 ml.) was prepared which was approximately 0.025 *M* in each of the following: CH_3COR, 9-fluorenol, CH_3CHOHR, and 9-fluorenone. The total molarity of ketone (CH_3COR plus 9-fluorenone) was identical with the total molarity of secondary alcohol (CH_3CHOHR plus 9-fluorenol). A 25-ml. portion of this solution was transferred to a 50-ml. flask and a 5-ml. portion of 0.25 *M* aluminum *t*-butoxide in toluene was added. Four 5-ml. aliquots were withdrawn and sealed in constricted test tubes. These sealed tubes were placed in a bath maintained at 45.00 ± 0.02°. At various intervals, the tubes were removed and opened. The contents were transferred to a 50-ml. volumetric flask and diluted to the mark with 75% aqueous isopropyl alcohol. The mixture was shaken thoroughly, allowed to stand for 24 hr., and centrifuged, and then the absorbance of the clear solution at 381 mμ was measured, using a Beckman Model B spectrophotometer. Equilibrium was considered to be established when the same absorbance was recorded for successive samples. Since the initial concentrations of the reactants and products were known and the equilibrium concentration of 9-fluorenone was known from the absorbance at 381 mμ (toluene solutions of 9-fluorenone follow Beer's law closely at 381 mμ with ϵ 246 l. mole $^{-1}$ cm.$^{-1}$), thee quilibrium concentrations of 9-fluorenol, CH_3COR, and CH_3CHOHR could be calculated. Equilibrium constants for the reduction of CH_3COR were determined in triplicate and the average values are recorded in Table I. The average deviation from the mean of triplicate values did not exceed 5%.

The above procedure was modified for the reduction of chloroacetone. Since the corresponding alcohol, 1-chloro-2-propanol, is difficult to purify, a toluene solution of only chloroacetone and 9-fluorenol was mixed with the aluminum *t*-butoxide solution.

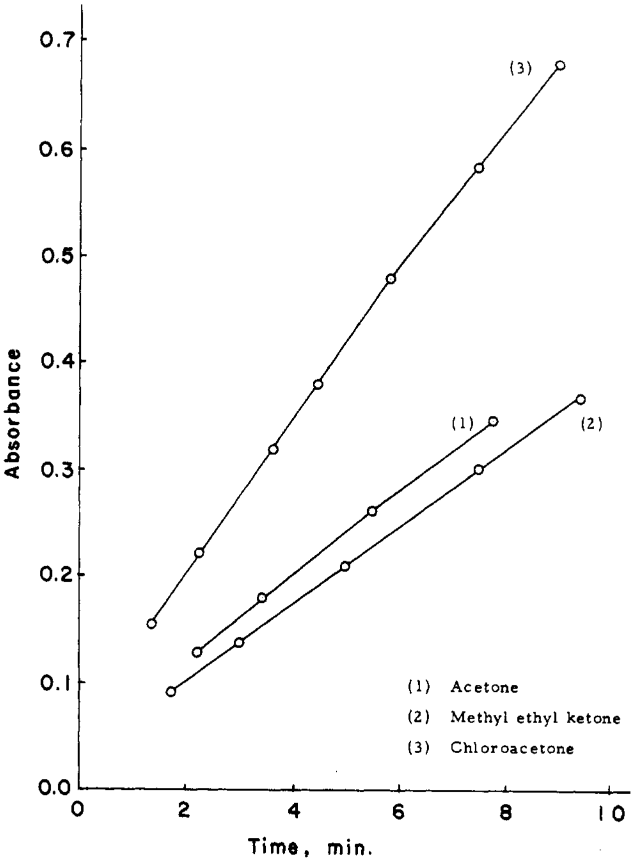

Figure 4.—Relative polar effect of the R-group on the rate of MPVO reduction of three methyl ketones, $RCOCH_3$, with 9-fluorenol and aluminum *t*-butoxide.

Kinetic Study.—Approximately 0.1 *M* stock solutions (250 ml.) of 9-fluorenol, $RCOCH_3$, and aluminum *t*-butoxide in toluene were prepared. Desired concentrations of each of the reactants were prepared by dilution of the stock solutions. The reactant solutions along with a 100-ml. flask were thermostated in a bath at 45.00 ± 0.02°. A 25-ml. aliquot of each of the reactants was transferred to the 100-ml. flask. (The order of addition of the reactants and the time between additions depended upon the problem being investigated, as described in the discussion.) The timer was started when one-half of the final aliquot was added. The mixture was shaken thoroughly and a 5-ml. portion was transferred to a 1-cm. spectrophotometer cell in the cell compartment of a Beckman Model B spectrophotometer. The cell compartment was equipped with thermospacers and was maintained at 45.00 ± 0.02° by circulating water from a constant-temperature bath. Absorbance readings at 381 mμ were taken at frequent intervals to measure the rate of appearance of 9-fluorenone. Kinetic runs were made in triplicate and generally the results were consistent within 5%. The results are shown in Table III and in Figures 3 and 4.

Infrared Spectra.—A Beckman IR-5 spectrophotometer was used. Infrared spectra were observed for carbon tetrachloride solutions of (1) 9-fluorenol, (2) acetone, (3) aluminum *t*-butoxide, (4) a mixture of 1 and 3, (5) a mixture of 2 and 3, and (6) a mixture of 1, 2, and 3.

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[28] L. J. Bellamy, "The Infrared Spectra of Complex Molecules", 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 108.

[29] T. Dupuis and C. Duval, *Anal. Chim. Acta*, **3**, 191 (1949).