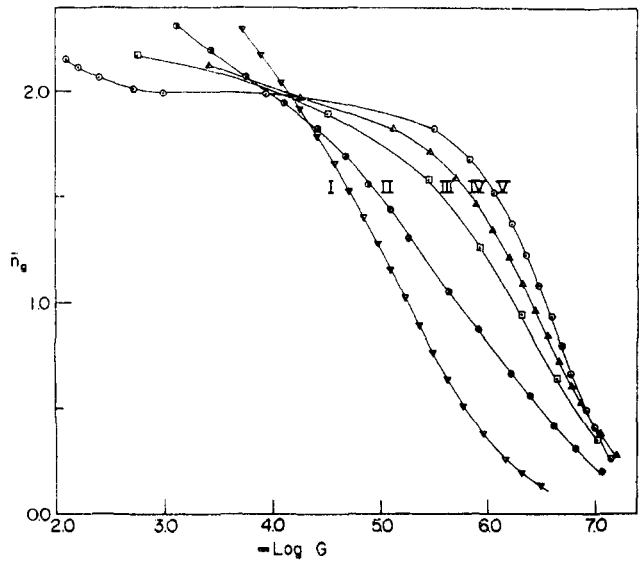


Fig. 1.—The effect of pyruvate on the complexing of glycinate by nickel(II): pyruvate concentration, I, 0.00 *M*; II, 0.05 *M*; III, 0.10 *M*; IV, 0.15 *M*; V, 0.15 *M*. The Ni(II) concentration is 0.050 *M* in all cases except for V where it is 0.020 *M*; 0.50 *M* KCl, 25°.

to ligand of 1:1 predominated or it was assumed that only such a Schiff base complex was present. Evidence of higher species however has been obtained for solution[3] and solid[5] phases.

It is valuable to consider the Schiff base complexes as "mixed" complexes since it does not matter in the mathematical treatment of the data, whether the carbonyl compound and the amine are independently coördinated to the metal ion or are combined as a Schiff base. Watters[9] has demonstrated that the pH method developed by Bjerrum[10] can be applied successfully to systems of "mixed" complexes when the two different ligands have sufficiently varying acid–base properties. In these laboratories we are currently studying Schiff base complexes and we wish to report the successful application of Watters' concept to pyruvate–glycinate "mixed" complexes.

The acid dissociation constant of pyruvic acid is 4.07×10^{-3} (0.50 *M* KCl, 25°) and for glycine K_{1a} and K_{2a} are 3.43×10^{-3} and 2.01×10^{-10}. Therefore, in solutions containing known total concentrations of a complexing metal ion, pyruvic acid and sodium glycinate and in which the equilibrium pH values are 4.3 or higher, the amount of complexed glycinate ion can be calculated using the results of pH measurements. For Ni(II) systems the experimental values of $\bar{n}_G$ (G_{comp}/Ni_t) are shown in Fig. 1.

For divalent metal ions of the first transition series the mass relationships are described by the equations

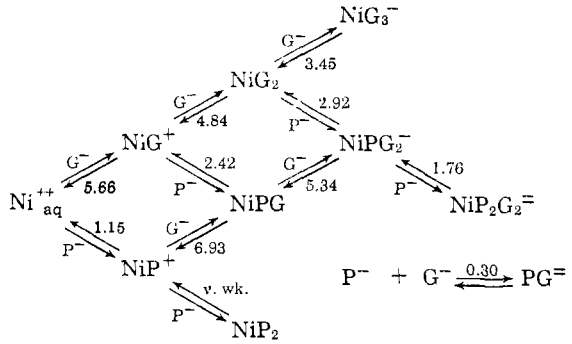
$$M_t = (M^{++}) + (MG^+) + (MG_2) + (MG_3^-) + (MP^+) + (MPG) + (MPG_2^-) + (MP_2G_2^=)$$

$$P_t = (P^-) + (MP^+) + (MPG) + (MPG_2^-) + 2(MP_2G_2^=) + (PG^=)$$

$$G_{comp} = (MG^+) + 2(MG_2) + 3(MG_3^-) + (MPG) + 2(MPG_2^-) + 2(MP_2G_2) + (PG^=)$$

where the quantities on the right-hand side represent the known total concentrations of M(II), pyruvate and glycinate and those on the left hand side represent the equilibrium concentrations of the various species. Terms in the concentration of MP_2 have been omitted (and accordingly those in MP_2G) because of the low stability of these species.

The step-wise equilibria and the logarithms of the stepwise constants which have been found to describe the Ni(II) system are[11]



These results show that each of the species NiPG, $NiPG_2$ and $NiP_2G_2^=$ has an appreciable stability and none can be safely ignored. It is interesting to note how the previous coordination of one of the moieties of the "mixed" species enhances the coördination of the other in spite of statistical and electrical effects which have been observed[9b] in mixed complexes to operate in the other direction. This large "rest effect"[10] suggests that Schiff base formation occurs in the "mixed" complexes. It is also interesting to note the relatively large value of the constant for the step $NiG_2 + P^- \rightarrow NiP_2^-$ compared to the analogous steps $NiG^+ + P^- \rightarrow NiGP$ and $NiPG_2^- + P^- \rightarrow NiP_2G_2^=$. While any conclusions at the present time are tentative, this result may indicate that the rate of establishment of the equilibrium

$$Ni(G')(P{=}G)^- \rightleftharpoons Ni(G'{=}P)/(G^-)$$

is rapid compared to the over-all formation or dissociation rates of the complex. Equilibration periods of the order of 5-30 minutes were observed in this study.

Transamination was also found to occur in the Ni(II)-pyruvate–glycinate system. Solutions after the last addition of sodium glycinate (pH ~ 9) were allowed to stand at room temperature for about 60 hours. After this time the complex was decomposed by adding EDTA which removed the stabilizing Ni(II) ions. Paper electrophoresis showed that appreciable amounts of alanine had been formed.

Ca(II), Mn(II) and Zn(II) ions also have been found to form complexes having the composition MPG and $MP_2G_2^=$ but these ions do not appear to form MPG_2^-.

These studies are being continued and will be reported in greater detail in future publications.

The author wishes to express his appreciation to the American Dental Association for its financial support of this work in its initial phase at the National Bureau of Standards.

(9) (a) J. I. Watters, *J. Am. Chem. Soc.*, **81**, 1560 (1959); (b) J. I. Watters and R. De Witt, *ibid.*, **82**, 1333 (1960).

(10) J. Bjerrum "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1941.

(11) Solutions were obtained using a high speed digital computer. Programs were written using the OMNITAB routine developed at the National Bureau of Standards by J. Hilsenrath and G. Ziegler.

DEPARTMENT OF CHEMISTRY
OHIO STATE UNIVERSITY
COLUMBUS, OHIO
D. L. LEUSSING

RECEIVED OCTOBER 27, 1962

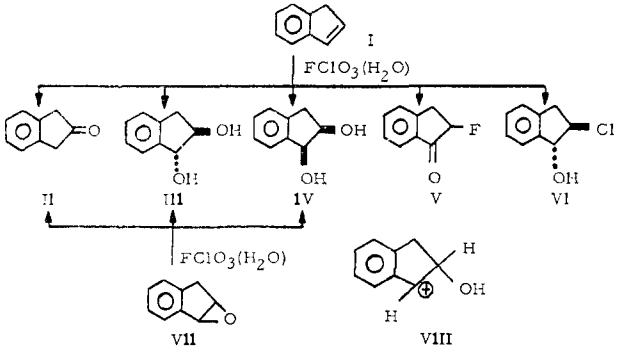
OXOFLUORINATION—A NEW BIDENT REACTION OF PERCHLORYL FLUORIDE

Sir:

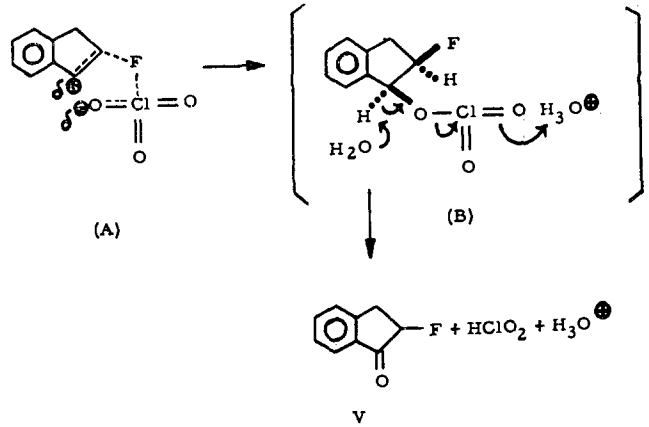
Perchloryl fluoride (PF) is a stable, tetrahedrally symmetrical molecule, which reacts as an ambident electrophile.[1] No isolated, or conjugated, carbon-

(1) A. S. Kende and P. MacGregor, *J. Am. Chem. Soc.*, **83**, 4197 (1961).

carbon double bond undergoes C-fluorination with PF, unless activated for electrophilic attack by substitution with nitrogen or oxygen functions.[2a] We have designed conditions,[2b] conducive to reaction of PF at a C=C bond *devoid* of heteroatom bearing activating substituents, by presenting the 2,3-double bond of indene (I) for *bident* attack by fluorine and oxygen of PF. A solution of I in dioxane-water[3] was kept saturated with PF at room temperature for 4 hours. Adsorption chromatography, fractional crystallization and



gas chromatography afforded five products: 2-indanone (II), *trans-* (III) and *cis*-1, 2-dihydroxyindan (IV), 2-fluoroindanone (V), m.p. 59–60° λ_{max}^{EtOH} 250 mμ (ε 12,700), 295 mμ (ε 2,700), $\lambda_{max}^{CH_2Cl_2}$ 5.78 6.21 μ (*Anal.* Found: C, 71.70; H, 4.88; F, 12.6); and *trans*-2-chloroindanol (VI). The proportion of II:III:IV:V:VI was 3:4:5:18:9. In an analogous reaction of 1,2-epoxyindan (VII) with PF, only products II, III and IV were obtained in an approximate proportion of 1:16:16. The analogy in products II, III, and IV formed by reaction of PF in aqueous dioxane with either I or VII, implicated a common intermediate carbonium ion, such as VIII. The following reaction scheme is proposed for the production of the fluoroketone V from I.



A transition state such as (A) would lead, by C—O bonding and F—Cl bond fission, to the intermediate *cis*-fluoro-chlorate (B), which would in turn undergo oxidation to the fluoroketone V by a concerted elimination of chlorous acid. Facile disproportionation of the latter would afford the products giving rise to the *trans*-chlorohydrin VI by reaction with I.[4] In our view, this scheme accounts uniquely for relative yields and specificities in orientation of functional groups in products V and VI, and for the stereochemistry of VI.

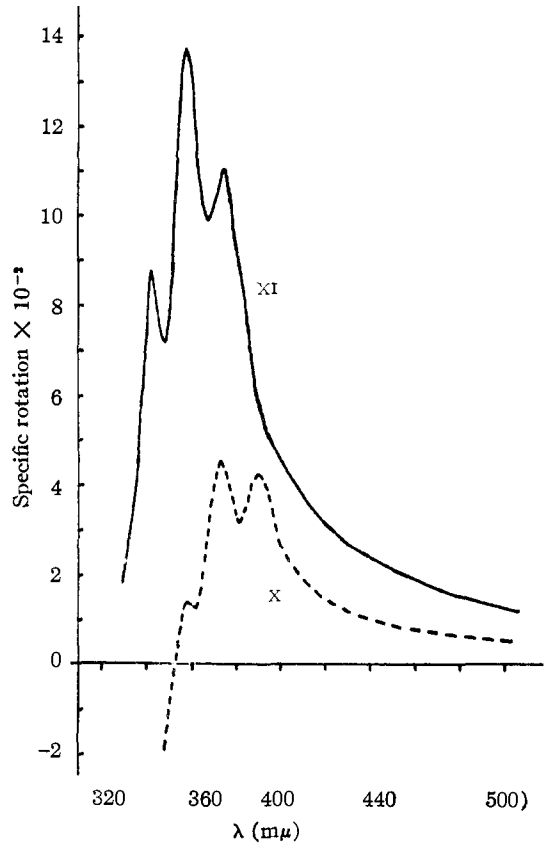
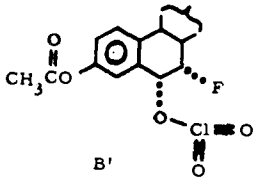


Fig. 1.—O.r.d. of 3-acetoxy-7α-fluoro-1,3,5(10)-estratriene-6,17-dione (X) and 3-acetoxy-1,3,5(10)-estratriene-6,17-dione XI) in dioxane (*C* = 0.10).

Generality of the new oxofluorination reaction of PF was demonstrated by subjecting 3-acetoxy-1,3,5-(10),6-estratetraene-17-one (IX) to reaction with PF in 99:1 dioxane–water, affording as the major product the fluoroketone X, m.p. 238–239°, $\lambda_{max}^{CHCl_3}$ 257 mμ (ε 11,300), 306 mμ (ε 2,500); $\lambda_{max}^{CH_2Cl_2}$ 5.68, 5.76, 5.91 μ (*Anal.* Found: C, 69.01; H, 6.39).[5] The n.m.r. spectrum at 60 Mc. of X, in chloroform-*d*, showed a doublet, centered at τ = 5.08, J_{HF} = 50 cps., representing H-7. The optical rotatory dispersion curve (Fig. 1) of X closely resembled that of XI, but showed a bathochromic shift of 16 mμ, and a negative contribution of fluorine to the Cotton effect; in view of the negative specific rotativity of fluorine,[6a] it is therefore positioned in a positive octant.[6b] These findings, together with the absence of J_{aa} = 8–12 cps. from the n.m.r. signal of H-7, indicating its gauche juxtaposition relative to H-8, permit the unequivocal formulation of X as



(2) (a) Relative reactivities of enol derivatives in C-fluorination with PF are consistent with the relative abilities of heteroatoms to donate electrons to the double bond, S. Nakanishi and E. V. Jensen, *J. Org. Chem.*, **27**, 702 (1962); (b) electrophilic reactions of PF (exclusive of aromatic C-perchlorylation with PF-aluminum halide complex, C. E. Inman, R. E. Oesterling and E. A. Tyczkowski, *J. Am. Chem. Soc.*, **80**, 5286 (1958)) on nucleophilic carbon result in C-fluorination. Electrophilic attack on I occurs at C-2, and would result in a transition state approximating a benzylic carbonium ion. These factors, together with the geometry of the reactants, gave promise of selective orientation in a reaction of PF and I.

(3) The initial 19:1 dioxane–water mixture was progressively diluted to 3:2. The final pH was 2.5.

(4) R. Weissgerber, *Ber.*, **44**, 1443 (1911).

(5) 3-Acetoxy-1,3,5(10)-estratriene-6,17-dione (XI) (U. S. Patent 2,-294,938) had $\lambda_{max}^{CHCl_3}$ 248 mμ (ε 10,800), 297 mμ (ε 2,200); $\lambda_{max}^{CH_2Cl_2}$ 5.68, 5.76, 5.93 μ.

(6) (a) W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne and C. Djerassi, *J. Am. Chem. Soc.*, **83**, 4013 (1961); (b) C. S. Barnes and C. Djerassi, *ibid.*, **84**, 1962 (1962)[1]

3 - acetoxy - 7α - fluoro - 1,3,5(10) - estratriene - 6,17-dione. The orientation and configuration of the substituents at C-6 and C-7 of X point to the intermediate B′ in the formation of X by bident α-attack of PF on IX.[7a,c]

(7) (a) Supported by American Cancer Society Grant P-265A; (b) Postdoctoral Fellow; (c) presented in part at the 2nd International Symposium on Fluorine Chemistry, Estes Park, Colorado, 1962.

ROSWELL PARK MEMORIAL INSTITUTE M. NEEMAN
BUFFALO 3, NEW YORK YOSHIO OSAWA[7a,b]

RECEIVED OCTOBER 16, 1962

SYNTHESIS OF CYCLOPROPENONES BY A MODIFIED FAVORSKII REACTION

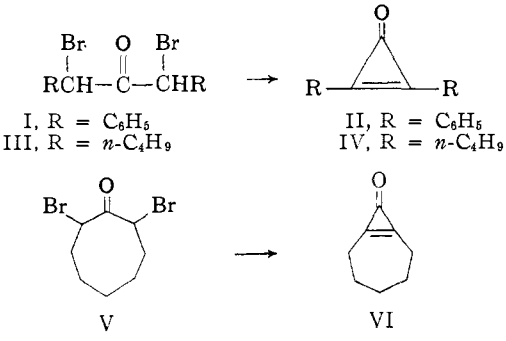
Sir:

The Favorskii reaction of α-haloketones with base has been shown to proceed through an intermediate with the symmetry of a cyclopropanone in at least some cases.[1,2,3] We wish to report[4] that under some conditions a cyclopropanone can be intercepted, when the starting material is a dibromo ketone, by dehydrobromination to the very stable cyclopropenone system. This is much more convenient than the types of syntheses reported previously[5,6,7] for cyclopropenones.

Treatment of α,α′-dibromodibenzyl ketone (I) (either the pure isomer, m.p. 112–114°,[8] or the mixture of *d,l*- and *meso*-compounds, m.p. 79–85°) with excess 20% triethylamine in methylene chloride at room temperature for 30 min. affords 50–60% yields of diphenylcyclopropenone (II),[5,6] best isolated by silica gel chromatography. The reaction also can be applied to the synthesis of cyclopropenones bearing only aliphatic substituents. Thus α,α′-dibromodi-*n*-amyl ketone (III) b.p. 101–106° (0.7 mm.), ($C_{11}H_{20}OBr_2$: C, 40.26; H, 6.14; Br, 48.72. Found: C, 40.46; H, 6.41; Br, 48.42; n.m.r. shows that this is a mixture of the *meso* and *d,l* compounds, with triplets at 5.45 and at 5.60 τ in addition to the other expected peaks), was treated with a 40:1 mixture of chloroform and triethylamine at reflux for 48 hr. A 12% yield of dibutylcyclopropenone (IV) was obtained, b.p. 95–97° (0.3 mm.) ($C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.72; H, 11.27). In the infrared the compound has the expected absorption at 1850 and 1660 cm.$^{-1}$; in the n.m.r. the methylenes attached to the cyclopropene ring are found as a triplet at 7.6 τ, with the remaining protons as a multiplet at 8.6 τ (methylenes) and a triplet at 9.15 τ (methyls).

The reaction can be extended to prepare other dialkylcyclopropenones. Interestingly, it also can be applied to dibromocycloöctanone. When 2,8-dibromocyclooctanone[9] (V) was heated under N_2 at 90° in a closed system with a 50% excess of 5% triethylamine in chloroform a 50% yield of cycloheptenocyclopropenone (VI) was obtained, m.p. 52–53° ($C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.85; H, 8.15). The material sublimes at 45° (1.5 mm.). In the infrared the compound shows the expected strong bands at 1840 and 1640 cm.$^{-1}$, and the n.m.r. spectrum confirms the structure. A four-proton triplet at 7.45 τ is assigned to the methylene groups attached to the ring, while a six-proton multiplet at 8.22 τ is found for the remaining protons. With refluxing aqueous KOH solution this compound affords cycloheptene-1-carboxylic acid, identical with an authentic sample.[9] It is hoped that VI may serve as a source of gas-phase cycloheptyne; in common with other cyclopropenones[5,6,7] VI loses carbon monoxide on pyrolysis, although in the case of VI rather high temperatures (250°) are required. Among other products, a 16% yield of tris-cycloheptenobenzene can be isolated from this pyrolysis, m.p. 184–185° ($C_{21}H_{30}$: C, 89.47; H, 10.48; mol. wt., 282. Found: C, 89.29: H, 10.71: mol. wt., 279, CCl_4 vapor pressure). In the ultraviolet the benzene has λ_{max} 274 mμ (ε = 262) while the n.m.r. spectrum shows the expected multiplets centered at 7.30 and 8.45 τ in a ratio of 2:3.

So far we have failed to prepare either unsubstituted cyclopropenone or cyclohexenocyclopropenone by application of our reaction conditions to appropriate haloketones. However, in both of these cases the difficulty might well lie with instability of the desired products rather than any failing of the synthetic method. Accordingly, our procedure promises to be of general use in the preparation of cyclopropenones.



DEPARTMENT OF CHEMISTRY RONALD BRESLOW
COLUMBIA UNIVERSITY JUDD POSNER
NEW YORK, N. Y. ADOLF KREBS

RECEIVED NOVEMBER 17, 1962

THE CHEMISTRY OF BLUENSOMYCIN. II. THE STRUCTURE OF BLUENSOMYCIN

Sir:

A previous communication[1] gave the structure of bluensidine, one of the two products obtained by methanolysis of the antibiotic bluensomycin. The identity of the second fragment is now described, and a structure for bluensomycin is proposed.

This second fragment (I) (colorless prisms from methanol–ether, m.p. 108–111°, $[\alpha]^{25}D$ −147° (*c*,1, water), $C_{14}H_{26}O_5N$,[2] one C-CH_3, one N-CH_3 (pK_a' 7.87) and one O-CH_3 group) appeared to be the methyl glycoside of an aminodisaccharide. Acetylation (pyridine–acetic anhydride) gave colorless prismatic needles (II), m.p. 195.5–197°, $[\alpha]^{25}D$ −124° (*c*, 1, $CHCl_3$). Analysis of this neutral product indicated $C_{12}H_{15}O_4(OCOCH_3)_4(N<^{CH_3}_{COCH_3})(OCH_3)$. A close similarity was found to exist between the properties of II and those reported for methyl pentaacetyldihydrostreptobiosaminide, obtained by several laboratories from the methanolysis of dihydrostreptomycin.[3–6] Since

(1) B. Bannister and A. D. Argoudelis, *J. Am. Chem. Soc.*, **85**, 119 (1963)

(2) Analytical values for all the compounds described in this paper were consistent with the indicated formulas.

(1) *Cf.* A. Kende, *Organic Reactions*, **11**, 261 (1960).

(2) G. Stork and I. Borowitz, *J. Am. Chem. Soc.*, **82**, 4307 (1960); H. House and W. F. Gilmore, *ibid.*, **83**, 3972, 3980 (1961).

(3) A. W. Fort, *ibid.*, **84**, 2620, 2625 (1962).

(4) Reported in part at the 17th National Organic Symposium, Bloomington, 1961. Support of this work by the National Science Foundation, the Petroleum Research Foundation, and the Sloan Foundation is gratefully acknowledged.

(5) R. Breslow, R. Haynie and J. Mirra, *J. Am. Chem. Soc.*, **81**, 247 (1959).

(6) M. Volpin, Yu. Koreshkov and D. Kursanov, *Izvest. Akad. Nauk*, SSSR, 560 (1959).

(7) R. Breslow and R. Peterson, *J. Am. Chem. Soc.*, **82**, 4426 (1960).

(8) E. Bourcart, *Chem. Ber.*, **22**, 1368 (1889). In this paper it is reported that treatment of the ketone with ethanolic magnesia yields a compound with empirical formula $C_{13}H_{10}O$, but the product is not described further!

(9) G. Hesse and F. Urbanek, *Chem. Ber.*, **91**, 2733 (1958).