taken on a Cary 14 and the infrared spectra on a Perkin-Elmer 237-B spectrometer.

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The Structure of Boron Halide Complexes of α-Halo Ketones

Sir:

Molecular addition complexes between ketones and boron trihalides (BX_3) have been known since 1877;[1] however, the structures of the complexes have received limited attention. Infrared[2,3] and dipole moment[4] data on several adducts give evidence for oxygen–boron bonds. We wish to report detailed information regarding the geometry of the carbonyl carbon of boron halide complexes of α-chloropinacolone (Ia) and α-bromopinacolone (Ib) obtained by variable-temperature nuclear magnetic resonance (nmr) studies.

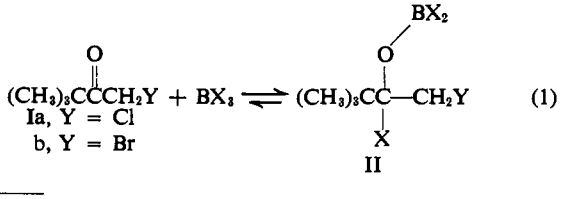
The nmr spectra[5] of Ia and Ib show sharp singlets for the methylene and *t*-butyl protons, which do not change as the temperature is lowered to −20°. On the other hand, the resonance of the methylene protons of complexes of Ia and Ib formed in the presence of excess BCl_3 and BBr_3 are temperature variant and generally appear as an AB pattern below 10°. Parameters describing nmr spectra at −10° are given in Table I.

Table I. Nmr Data of α-Halo Ketones and Complexes at −10°

System	δ_{H_a}, τ	δ_{H_b} τ	J_{ab}, cps	δ_{CH_3}, τ
$(CH_3)_3CCOCH_2Cl$	5.58[a]	....	..	8.80
$(CH)_3CCOCH_2Br$	5.77[a]	....	..	8.78
$(CH_3)_3CCOCH_2Cl + BF_3$ (excess)	5.53[a]	....	..	8.72
$(CH_3)_3CCOCH_2Cl + BCl_3$ (excess)	5.60	5.83	13	8.78
$(CH_3)_3CCOCH_2Cl + BBr_3$ (excess)	5.17	5.80	13	8.78
$(CH_3)_3CCOCH_2Br + BF_3$ (excess)	5.67[a]	....	..	8.63
$(CH_3)_3CCOCH_2Br + BCl_3$ (excess)	5.70	5.87	12	8.75
$(CH_3)_3CCOCH_2Br + BBr_3$ (excess)	5.23	5.85	12	8.72

[a] A singlet was observed for H_a and N_b.

The observed AB pattern can be rationalized by addition of BCl_3 or BBr_3 across the carbon–oxygen double bond (eq 1) to yield II in which the methylene protons are adjacent to a magnetically asymmetric center[6] and



(1)

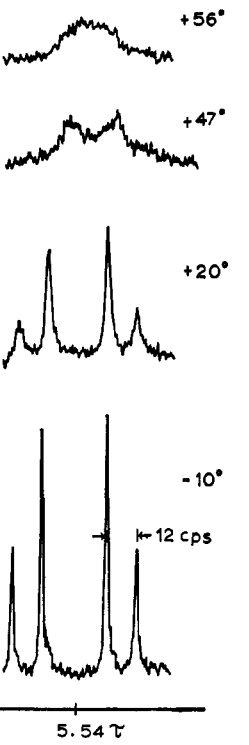
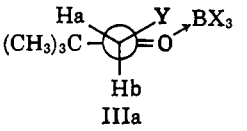
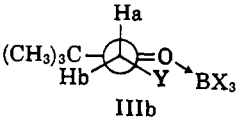


Figure 1. Temperature dependence of the nmr spectrum of the methylene protons of the α-bromopinacolone–boron tribromide complex.

are nonequivalent. An intermediate involving an sp^2-hybridized carbonyl carbon is highly unlikely since the energy required for the methylene protons to become



IIIa



IIIb

magnetically equivalent, such as IIIa ⇄ IIIb,[7] would be small. *Therefore the carbon to which the oxygen is bonded must be tetrahedral.*

Variable temperature spectra of the methylene region of α-bromopinacolone plus BBr_3 are shown in Figure 1. An AB pattern is observed at −10° and is unchanged with further decreases in temperature. As the temperature is raised the lines of the quartet start to coalesce, and at 56° a broad peak is observed in the methylene region. This change in absorption pattern is characteristic of two species in equilibrium (eq 1). When the rate of interconversion is rapid on the nmr time scale, the methylene protons can become equivalent. Reversible reactions involving starting material must account for this change in absorption since α-bromopinacolone can be recovered (91% by vpc analysis) by decomposition of the complex with sodium bicarbonate solution and extraction into methylene chloride.

In the spectrum of α-chloropinacolone plus BCl_3, the central lines of the quartet are distinguishable at tem-

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(2) B. Susz and P. Chalandon, *Helv. Chim. Acta*, **41**, 1332 (1958).
(3) M. Lappert, *J. Chem. Soc.*, 817 (1961).
(4) P. Chalandon and B. Susz, *Helv. Chim. Acta*, **41**, 697 (1958).
(5) Spectra were obtained on a Varian Associates A-60 spectrometer equipped with a variable temperature probe using 30% w/w solutions in carbon tetrachloride.
(6) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York N. Y., 1959 p 379.
(7) Mizushima, *et al.*,[8] have shown that chloroacetone exists in two molecular forms in solution. The dihedral angle between the C_1–Cl and the C_2–O planes in the less polar form is *ca.* 150° and that of the more polar form between 0 and 30°. Since rotation about the C_1–C_2 bond is likely to be rapid on the nmr scale, the methylene protons in either conformation will become magnetically equivalent.
(8) S. Mizashima, T. Shimanouchi, T. Miyazawa, I. Ichishima, K. Kuratuni, I. Nakagawa, and N. Shido, *J. Chem. Phys.*, 21, 815 (1953).

peratures as high as 54°. An increase in the vapor pressure of the sample prevented nmr measurements above this temperature. A characteristic AB pattern is also observed for α-chloropinacolone and BBr_3. Analysis of recovered ketone showed it to be a mixture of α-chloropinacolone (56%) and α-bromopinacolone (13%), which results from slow exchange of the α-chloro substituent. Only α-bromopinacolone (89%) is recovered from the α-bromopinacolone–boron trichloride complex. This is probably due to the fact that chloride is a better leaving group than bromide and BBr_3 is a stronger acceptor than BCl_3. The chemical shifts of the nonequivalent protons of the α-chloropinacolone–boron tribromide complex parallel those of the α-bromopinacolone–boron tribromide complex, signifying a dominating influence of the boron halide moiety. Chemical shifts of the α-bromopinacolone– and α-chloropinacolone–boron trichloride complexes are consistent with this postulate.

The spectra of α-bromopinacolone plus BCl_3 are unique in that they contain an additional peak in the vicinity of the *t*-butyl (τ 8.45) and methylene (τ 5.13) regions at temperatures below 10°. The additional peaks merge with the methylene quartet and *t*-butyl resonance as the temperature is raised. This occurs as the quartet is coalescing. This is characteristic of three species in equilibrium. A 2:1 complex has been postulated[9] to account for additional peaks found in the nmr spectrum of BCl_3 complexes of N,N-dimethylformamide.

Nonequivalence of methylene protons was not observed at temperatures as low as −30° when BF_3 was used as the complexing agent. The absence of a magnetically asymmetric center in the BF_3 complexes or rapid interconversion of equilibrating species at −30° can account for the results (eq 2). This is consistent

$$(CH_3)_3CC(=O)CH_2Y + BF_3 \rightleftharpoons (CH_3)_3CC(=O{\rightarrow}BF_3)-CH_2Y \qquad (2)$$

with the relative acceptor ability of boron halides,[10,11] $BBr_3 > BCl_3 > BF_3$, and results obtained by Coyle and Stone[12] on BH_3 and BF_3 complexes of diethyl sulfide. One would expect the tendency for BF_3 to ionize to be smaller than BCl_3 or BBr_3 because of the stronger boron–fluorine bond and smaller steric requirements of BF_3.

Addition of Lewis acids to α-halo ketones is expected to be more facile than to simple ketones. The lower basicity of the former makes coordination with boron halides less favorable. Unfortunately, attempts to extend this study to complexes of 3-pentanone with BBr_3 were unsuccessful because of rapid polymerization of the solution. A detailed discussion of the energies of activation of several processes described herein will be the subject of a separate publication.

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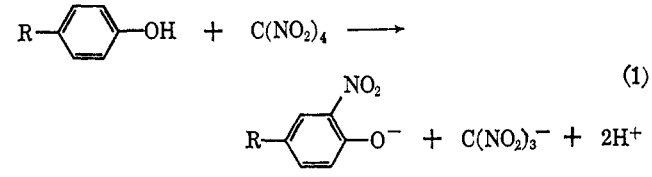
Tetranitromethane. A Reagent for the Nitration of Tyrosine and Tyrosyl Residues of Proteins[1]

Sir:

The suitability of reagents for chemical modification of enzymes depends not only on their specificity toward a particular functional group but also on the reaction conditions. Available procedures for nitration,[2] while effective with stable aromatic compounds, employ conditions too severe to be applicable to biological macromolecules.

Attention was directed to the potential usefulness of tetranitromethane (TNM).[3] While this reagent had been employed to modify the biological function of proteins,[4] its chemical specificity was not examined. Since earlier studies had indicated that TNM could serve to nitrate phenols,[5] our initial efforts were aimed at the reaction with tyrosine and its derivatives as here reported.

Typical conditions involve the addition of 5 μl of TNM (42 μmoles) to 3 ml of a 10^{-4} *M* solution of tyrosine, buffered at pH 8.0 with 0.05 *M* tris(hydroxymethyl)aminomethane hydrochloride (Tris-Cl) at 20°. The products of the reaction are trinitromethane (nitroform), protons, and a nitrated derivative of tyrosine having an absorption maximum of 428 mμ. For kinetic studies, the high molar absorptivity of the nitroformate anion (ϵ_{350} 14,400)[6] provides a most sensitive and convenient parameter of this reaction (Figure 1). At pH 8, nitration displaces two protons and produces 1 mole of nitroformate/mole of tyrosine, suggesting the formation of 3-nitrotyrosine as in eq 1.



(1)

In support of this interpretation, chromatographic analysis of the nitration reaction mixture, using the Spinco Model 120B amino acid analyzer according to the procedure of Spackman, *et al.*,[7] revealed the presence of a substance eluting in the position corresponding to authentic 3-nitrotyrosine, *i.e.*, 228 ml relative to the elution of phenylalanine at 213 ml. Material eluting

(1) This work was supported by Grants-in-Aid HE-07297 from the National Institutes of Health of the Department of Health, Education and Welfare.

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