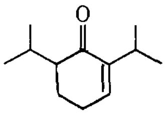

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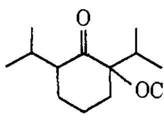

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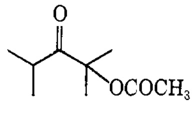

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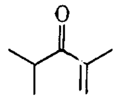

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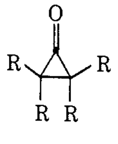

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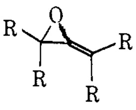

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actions.[1,2] Even if formed, both types of compounds would be expected to interact with the $FeBr_2$ produced to give the product-determining oxyallyl–Fe(II) complex **3**.

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The Orientation Dilemma in Alkaline Halogenation of 2-Butanone[1,2]

Sir:

Because orientations appear to be different in alkaline deuteration[3,4] and iodination[5] of 2-butanone (I), it has been suggested[6] that enolization is not the mechanism for NaOH-induced halogenations of aliphatic ketones in aqueous solution. A nonenolizing rate-determining step involving hypohalite anion and unenolized ketone was proposed.[6]

The orientation of deuteration of I, shown in Table I, indicates that each enolizable methyl hydrogen (on C-1, C_1–H) is no more electrophilic than each methylene hydrogen (on C-3, C_3–H). Evidently electronic destabilization of an adjacent enolate by an alkyl substituent is insignificant.

Table I. Relative Rates of H–D Exchange of Hydrogens of I in D_2O

Temp, °C	[I], *M*	[NaOD], *M*	k_{C_1-H}/k_{C_3-H}[a,b]	% at C_1H_3[c]
35	1.4–1.7	0.009–0.041	0.97 ± 0.04[d]	59 ± 2
0	1.1–2.2	0.039	0.95 ± 0.10[d]	59 ± 6
30	1.8	0.10	1.00[e]	60

[a] Relative rates on a per hydrogen basis. [b] Exchange followed to 1 half-life by comparing integrated nmr signals of C-1 and C-3 hydrogens with the C-4 hydrogens as internal standard. [c] Calculated per cent of rate at these three (of the five) enolizable hydrogens. [d] Reference 3. [e] Reference 4.

The orientation of base-induced halogenations of I is commonly thought to indicate that methyl hydrogens are much more reactive. Since neither 1-bromo-2-butanone(II) nor 3-bromo-2-butanone (III) is stable under the reaction conditions, the initial ratio of II to III has been inferred from products of further reaction. The most thorough previous study (NaOH-induced iodination) reported HCI_3 (97%), $CH_3CH_2CO_2H$ (IV, yield undetermined), and CH_3CHICO_2H (13%), which could result from initial enolization at either C-1 or C-3, indicating that only 0–13% of C-3 enolization occurs.[5] Cullis and Hashmi reasoned that any $CH_3COCHICH_3$ formed would yield $CH_3COCI_2CH_3$ rapidly because NaOH-induced iodination of bromoacetone is 800 times faster than that of acetone.[7] Since no diiodo acids were found, it was though "more plausible . . . that initial attack occurs exclusively at the methyl group."[5,8]

Our product study refutes this conclusion that methyl hydrogens are much more reactive than ethyl CH_2 hydrogens in base-induced halogenation, and thus obviates the need for different rate-determining steps for alkaline halogenation and deuterium exchange. Our reaction conditions were 0.50 *M* NaOH, 0.094 *M* NaOBr, and 0.021 *M* I in aqueous solution at 25°. The reaction is homogeneous for 2.5 half-lives. The following products were determined by glc after 120 sec (7.5 half-lives): $CH_3CH_2CO_2H$ (IV, 57 ± 1%), $CH_3CHOHCO_2H$ (V, 42 ± 3%), CH_3CO_2H (VI, 5.5 ± 1%), $CHBr_3$ (88 ± 2%), and CBr_4 (6.6 ± 1%). The material balance is 101 ± 5% based on I. These products account for consumption of 3.49 ± 0.08 mol of NaOBr per mol of I. By uv, 3.25 ± 0.12 mol of NaOBr per mol of I was consumed. Under the same conditions, II yields IV but *no* V; III yields V and VI but *no* IV. Therefore, the 57% of IV formed arises from initial bromination at C-1. Since 57% is within experimental error of the values for deuteration in Table I, this is just as expected if enolization is the rate-determining step for base-induced bromination also.

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(1) Supported in part by research grants from the National Institutes of Health and the National Science Foundation.

(2) For further details, see R. P. Dunlap, Ph.D. Thesis, Massachusetts Institute of Technology, July 1972.

(3) J. Warkentin and O. S. Tee, *J. Amer. Chem. Soc.*, **88**, 5540 (1966).

(4) C. Rappe, *Acta Chem. Scand.*, **20**, 2236 (1966); C. Rappe and W. H. Sachs, *J. Org. Chem.*, **32**, 4127 (1967).

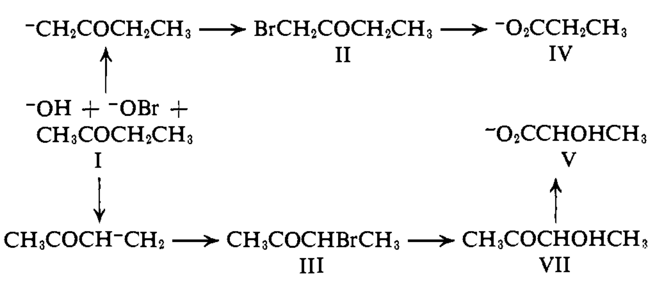
(5) C. F. Cullis and M. H. Hashmi, *J. Chem. Soc.*, 2512 (1956); 1548, 3080 (1957).

(6) C. Rappe, *Acta Chem. Scand.*, **20**, 1721 (1966); **21**, 857, 1823 (1967); **22**, 219 (1968).

(7) R. P. Bell and O. M. Lidwell, *Proc. Roy Soc., Ser. A*, **176**, 88 (1940).

(8) This conclusion that "Hofmann" orientation to an unalkylated position should be preferred in kinetically controlled alkaline enolizations was predicted earlier (E. D. Hughes, *Nature* (*London*), **147**, 813 (1941); H. M. E. Cardwell, *J. Chem. Soc.*, 2442 (1951)) and is consistent with the positive (+1.0) Hammett reaction constant for enolization of substituted acetophenones by aqueous NaOH at 25° (J. R. Jones, R. E. Marks, and S. C. S. Rao, *Trans. Faraday Soc.*, **63**, 111 (1967)) and the fact that alkyl substituents often retard the overall rate of attack by anionic bases (D. P. Evans and J. J. Gordon, *J. Chem. Soc.*, 1434 (1938); J. Warkentin and C. Barnett, *J. Amer. Chem. Soc.*, **90**, 4629 (1968); and ref 4 and 5). However, when one allows for ground-state free-energy differences between different ketones in solution, electronic effects of alkyls are insignificant, and steric effects become significant only when there are two alkyls or one large alkyl (*e.g.*, *tert*-butyl) on the enolizing carbon.

CBr_4 is formed slowly from $CHBr_3$. V could be formed from III by either (1) hydrolysis of III to acetoin (VII) followed by successive halogenations at C-1 and hydrolytic cleavage to V or (2) successive enolizations and brominations at C-1, hydrolytic cleavage to $CH_3CHBrCO_2^-$, and hydrolysis to V. The second possibility requires that enolization of III at C-1 be faster than hydrolysis of III. However, after 57% of III was hydrolyzed to VII in the absence of NaOBr, none (<5%) of the remaining III had enolized, as shown by lack of deuterium incorporation by nmr. Hence V is formed *via* VII.



Thus, in the NaOH-induced bromination of I in aqueous solution at 25°, each hydrogen on C-1 and C-3 of I is attacked *equally* fast (±5%) to form a sodium enolate, and the resulting II and III rapidly give bromoform, plus sodium propionate and sodium lactate (*via* acetoin), respectively.

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Stereochemistry of Metal Anion Substitutions on Carbon[1]

Sir:

The reaction of alkali metal salts of various metal anions with alkyl halides and tosylates has become a standard method of preparing carbon–metal bonds as illustrated by reaction 1.[2,3]

The extremely rapid reaction rate of anions of Sn, Ge, Pb, Co (cobalamine), and others with alkyl halides has prompted the name "supernucleophile."[4-6] In almost all cases studied this reaction has been found to proceed with inversion of configuration.[4,7,8]

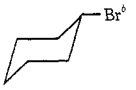
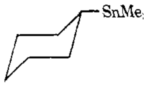
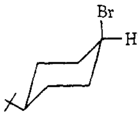
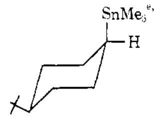
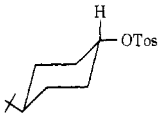
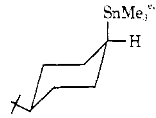
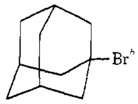
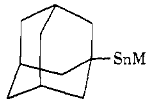
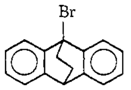
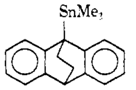
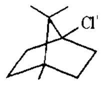
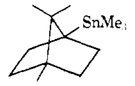
However, the observation that 1-bromo-1-methyl-2,2-diphenylcyclopropane reacted with trimethyltin lithium with retention of configuration[9] and the ready reaction of certain metal anions with bromobenzene[2] suggests that a mechanism other than the assumed S_N2 reaction could be occurring in some cases.[10]

We have studied the reaction of trimethyltin lithium with some alkyl halides and tosylates to test for other stereochemistry and possibly other mechanisms. The

$$\mathrm{Me_3SnLi + RX \longrightarrow RSnMe_3 + LiX} \qquad (2)$$

results are shown in Table I.

Table I. Products[a] and Stereochemistry of Reaction 2 in Tetrahydrofuran at 25°

Structure of RX	Reaction time, hr	Yield, %	Product	Stereochemistry
 Br[b]	1–2	51	 $SnMe_3$[c]	
 Br, H[d]	3.5	30	 $SnMe_3$[e,f], H	Retention
 H, OTos[g]	12	63	 $SnMe_3$[e,f], H	Inversion
 Br[h]	3.5	57	 $SnMe_3$	Retention
 Br	2.5	85	 $SnMe_3$	Retention
 Cl[i]	5	66	 $SnMe_3$	Retention

[a] All new compounds had analyses and nmr consistent with the indicated structures. [b] From Aldrich Chemical Co. [c] See R. C. Putnam and H. Pu, *Can. J. Chem.*, **44**, 1343 (1966). [d] Prepared from 66% trans, 34% cis alcohol. The nmr indicated that the bromide was 78–80% axial (cis). See ref 7. [e] See text for structure proof. [f] Greater than 95% was of the indicated configuration. [g] Pure *trans*-tosylate was prepared by the method of S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, **77**, 5574 (1955). A mixture of *cis*- and *trans*-tosylates afforded mostly cis tin compound and much olefin. [h] Identical with structure prepared by H. J. Berwin, Thesis, University of California, San Diego, 1970. See also W. Hanstein, H. J. Berwin, and T. G. Traylor, *J. Amer. Chem. Soc.*, **92**, 7476 (1970). [i] Prepared in a previous investigation: S. Winstein and T. G. Traylor, *ibid.*, **78**, 2597 (1956).

The products of reaction of *trans*-4-*tert*-butylcyclohexyl tosylate and *cis*-4-*tert*-butylcyclohexyl bromide with Me_3SnLi have almost identical nmr spectra having an Me_3Sn singlet at τ 9.87. However, the reaction of the 4-*tert*-butylcyclohexyl Grignard with Me_3SnCl produced a compound whose nmr spectrum was

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(1) Supported by the Air Force Office of Scientific Research (Grant No. AFOSR-69-1639C).

(2) C. E. Coates, M. L. H. Green, and K. Wade, "Organometallic Compounds," Vol. I, Methuen, London, 1967, p 457.

(3) F. R. Jensen and D. D. Davis, *J. Amer. Chem. Soc.*, **93**, 4047 (1971).

(4) R. E. Dessy, R. L. Pohl, and R. B. King, *ibid.*, **88**, 5121 (1966).

(5) R. B. King and M. B. Bisnette, *J. Organometal. Chem.*, **7**, 311 (1967).

(6) G. N. Schrauzer and E. Deutsch, *J. Amer. Chem. Soc.*, **91**, 3341 (1969).

(7) F. R. Jensen, V. Madan, and D. H. Buchanan, *ibid.*, **92**, 1414 (1970).

(8) G. M. Whitesides and D. J. Boschetto, *ibid.*, **91**, 4313 (1969).

(9) K. Sisido, S. Kozima, and K. Takizaiva, *Tetrahedron Lett.*, 33 (1967).

(10) See also R. E. Dessy and P. M. Weissman, *J. Amer. Chem. Soc.*, **88**, 5124 (1966).