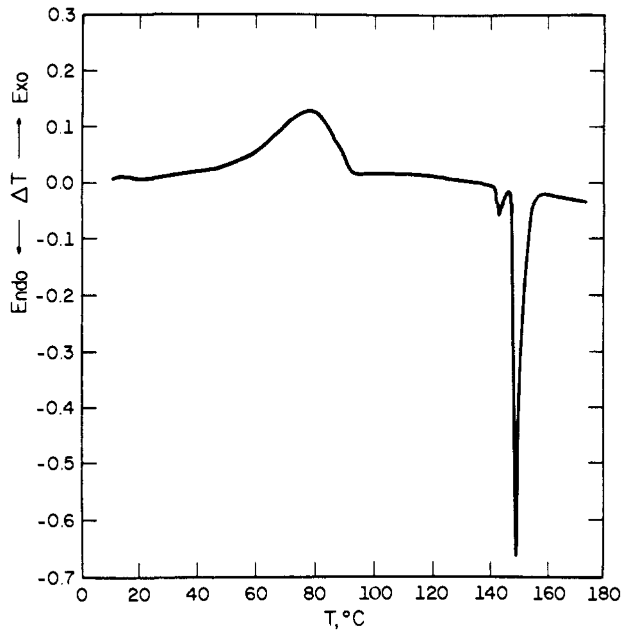

Figure 1. Thermogram of 0.98 mg of *trans*-**2** and 3.68 mg of *cis*-**2** in 10.42 mg of Dow-Corning 704 silicon oil. For calibration, 1.22 mg of 50:32:18 Sn-Pb-Cd eutectic has been included. The exotherm at *ca.* 77° arises from the isomerization; the endotherm at 148° arises from fusion of the eutectic.

librium, too little *trans*-**2** is present to allow direct determination of K_{eq} (and hence ΔG) by nmr.

Direct determinations of ΔH of isomerization have been made *via* differential scanning calorimetry using a DuPont 900 thermal analyzer. Although neat mixtures of *cis*- and *trans*-**2** can be obtained by irradiation in (and subsequent evaporation of) liquid butane, these mixtures were semicrystalline and the phase changes (*i.e.*, crystallization and melting) which attended the trans–cis isomerization during thermal analysis complicate data interpretation. These problems were circumvented by conducting the isomerization in a nonvolatile inert solvent. Irradiation and analysis were performed in Dow-Corning 704 silicon diffusion pump oil. To circumvent calibration difficulties which might attend the use of the silicon oil, a weighed sample of 50:32:18 tin–lead–cadmium eutectic,[11] mp 148°, was included in each run as an internal standard. The ΔH_{fus} of the alloy was predetermined. A sample thermogram is shown in Figure 1. By this technique, a ΔH value of -9.0 ± 1.0 kcal/mol has been obtained for the trans–cis isomerization. Assuming negligible differences between the ΔH values for solution and vaporization of the two isomers, this value is approximately $\Delta H_g°$.

Efforts to obtain similar thermal data for the analogous bicyclo[6.1.0]nonane isomers have been forestalled by extraneous reactions which occur at the higher temperature required for trans–cis isomerization. In this instance, ΔG can be obtained directly *via* equilibration and is -2.9 kcal/mol at 158° in cyclohexane, a value in close accord with that reported for bicyclo[6.1.0]nonan-2-one.[3,12]

Acknowledgment. This work was supported by an unrestricted DuPont Young Faculty Grant.

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[11] C. D. Hodgman, Ed., "Handbook of Chemistry and Physics," 44th ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1962–1963, p 1536.

[12] K. B. Wiberg and A. de Meijere, *Tetrahedron Lett.*, 59 (1969).

[13] Alfred P. Sloan Foundation Research Fellow, 1970–1972.

[14] National Science Foundation Trainee, 1969–1972.

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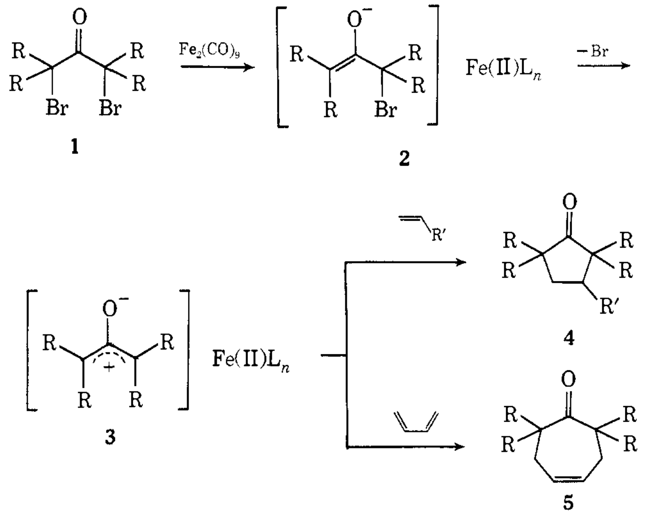
Mechanistic Aspects of the Reaction of α,α'-Dibromo Ketones and Iron Carbonyl. Reductive Rearrangements of Dibromo Ketones[1]

Sir:

We have recently reported the iron carbonyl assisted coupling of α,α'-dibromo ketones with unsaturated substrates which serves as a highly versatile method for the construction of a carbocyclic framework.[1,2] This paper presents evidence that the overall transformation proceeds by the route outlined in Scheme I:

Scheme I



initial reduction of the dibromide **1** with $Fe_2(CO)_9$ produces the iron enolate **2** (L = Br^-, CO, and solvent, etc.), which eliminates bromide ion to form the key oxyallyl–Fe(II) intermediate **3**; subsequent cyclocoupling with nucleophilic olefins or conjugated dienes yields the five- or seven-membered carbocycles **4** and **5**, respectively.

Formation of enolate species with α-bromo ketones was demonstrated by the reduction of 3-*endo*-bromocamphor with $Fe_2(CO)_9$[3] in dimethylformamide (DMF) containing 5% D_2O (60°, 17 hr) to give 3-*exo*-deuteriocamphor (87% d_1 and 13% d_0) in quantitative yield.[4] Dibromo ketones of type **1**, as usual, underwent successive debromination in moist solvent to produce the parent dialkyl ketones.

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[1] Carbon–Carbon Bond Formations Promoted by Transition Metal Carbonyls. III. Part II: R. Noyori, K. Yokoyama, S. Makino, and Y. Hayakawa, *J. Amer. Chem. Soc.*, **94**, 1772 (1972).

[2] R. Noyori, S. Makino, and H. Takaya, *ibid.*, **93**, 1272 (1971).

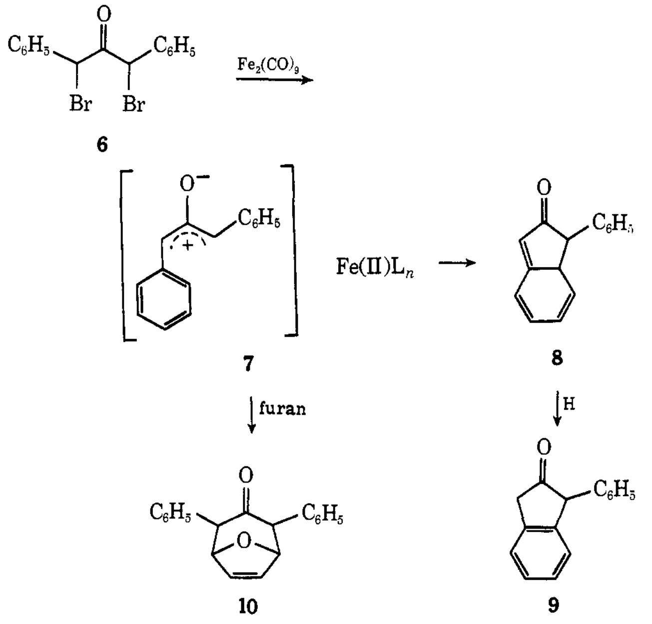
[3] Reaction was performed under a nitrogen atmosphere using the bromide (or dibromide) and $Fe_2(CO)_9$ in a mole ratio of 1:1.2. Iron pentacarbonyl was much less effective as a reducing agent. All new compounds gave correct elemental analyses and/or molecular peaks in exact mass spectra. Ir and nmr (with and without added $Eu(fod)_3$) were consistent with the structures assigned.

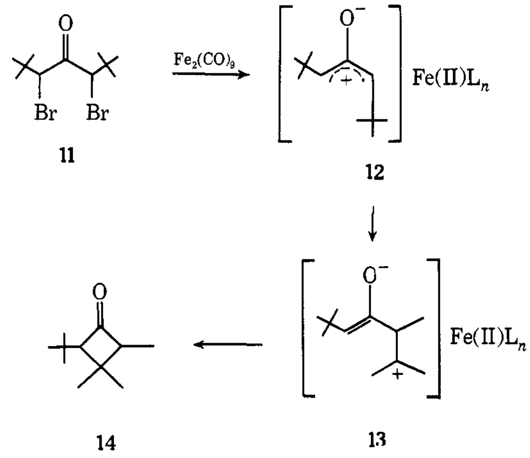
[4] *Cf.* R. R. Sauers and C. K. Hu, *J. Org. Chem.*, **36**, 1153 (1971).

We have observed four types of reductive rearrangements of dibromo ketones which demonstrate the intermediacy of **3** in the product-determining step. The dipolar ion **3** can act as an allylic cation, since the negative charge is masked by interacting with the Fe(II) ion.

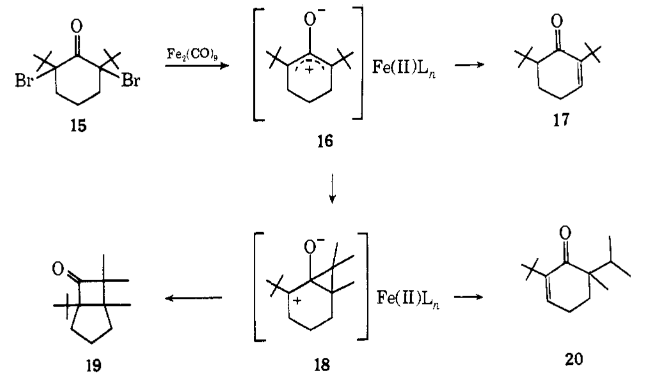
Reaction of the dibromide **6** with $Fe_2(CO)_9$ in dry benzene (25°, 12 hr) gave the indanone derivative **9** as the sole isolable product (70% yield). The transformation could be interpreted in terms of the electrocyclization **7**[5] → **8** followed by aromatization.[6] As expected, the reduction of **6** in a mixture of benzene and furan (1:1.5, v/v) gave the bicyclic adduct **10** (cis: trans = 50:50) in 90% yield.[7]

Treatment of the dibromo ketone **11** with $Fe_2(CO)_9$ in benzene (80°, 2 hr) gave rise to the cyclobutanone **14**, $\nu_{C=O}^{CCl_4}$ 1764 cm^{-1}, in 70% yield (cis:trans = 86:14). The formation of **14** can be accounted for by assuming the neopentyl-type rearrangement **12** → **13**.[5,8]

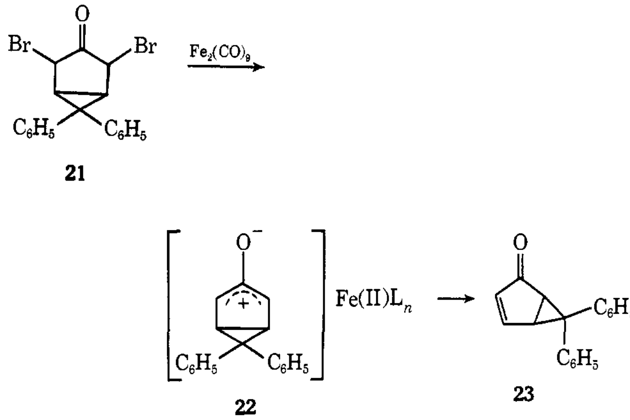




Debromination of **15** in benzene (20°, 3 hr) gave a mixture of the cyclobutanone **19** (80% yield), $\nu_{C=O}^{CCl_4}$ 1757 cm^{-1}, and the cyclohexenones **17** (15%) and **20** (3%). No trace of 1-*tert*-butyl-5,7,7-trimethylbicyclo[3.1.0]heptan-6-one was detected. Reaction in DMF at 20° gave solely **17** (95%). The intermediary carbocations **16** and **18** could explain the observation.[9]



The reactive species **22** derived from the dibromo ketone **21** in benzene at 60° (or in DMF at 25°) underwent the known cationic [1,4] sigmatropic rearrangement[10] to give the enone **23** in 95% yield.



Further evidence for the intermediacy of **3** during the reduction of dibromo ketones was obtained by trapping with nucleophiles. The reduction of 2,6-dibromo-2,6-diisopropylcyclohexanone in DMF at 25° gave the unsaturated ketone **24** in 82% yield, while in CH_3OH a mixture of **24** (24%) and the methoxy ketone **25** (69%, 61:39 mixture of stereoisomers) was produced. No skeletal changes were observed. The reduction of **1** (R = CH_3) with $Fe_2(CO)_9$ in DMF in the presence of 2.4 equiv of CH_3COONa (25°, 12 hr) gave the acetoxy ketone **26** (60%) along with the unsaturated ketone **27** (20%).[11]

Cyclopropanones **28**[12] or allene oxides **29**,[13] species structurally related to **3**, could satisfactorily explain the above findings only in part. Moreover, these species appear too labile under the reaction conditions used to be reasonable intermediates for intermolecular re-

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(5) Detailed configuration is unknown.

(6) F. G. Bordwell and R. G. Scamehorn, *J. Amer. Chem. Soc.*, **93**, 3410 (1971).

(7) For the cycloaddition of allyl cations to furan, see H. M. R. Hoffmann and D. R. Joy, *J. Chem. Soc. B*, 1182 (1968).

(8) W. Kirmse and H. Urbach, *Chem. Ber.*, **105**, 840 (1972).

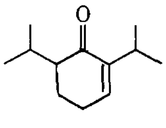
(9) *Cf.* C. D. Poulter and S. Winstein, *J. Amer. Chem. Soc.*, **94**, 2297 (1972); J. R. Salaün and J. M. Conia, *Chem. Commun.*, 1579 (1971).

(10) H. E. Zimmerman, D. S. Crumrine, D. Döpp, and P. S. Huyffer, *J. Amer. Chem. Soc.*, **91**, 434 (1969).

(11) Electrolytic, two-electron reduction of **1** (R = CH_3) was recently reported: J. P. Dirlam, L. Eberson, and J. Casanova, *ibid.*, **94**, 240 (1972). For the reduction of dibromo ketones with Zn–Cu couple, see H. M. R. Hoffmann, K. E. Clemens, E. A. Schmidt, and R. H. Smithers, *ibid.*, **94**, 3201 (1972).

(12) N. J. Turro, *Accounts Chem. Res.*, **2**, 25 (1969).

(13) R. L. Camp and F. D. Greene, *J. Amer. Chem. Soc.*, **90**, 7349 (1968).



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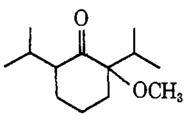

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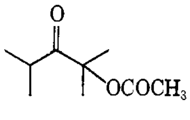

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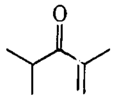

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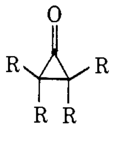

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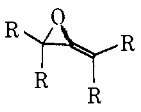

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actions.[1,2] Even if formed, both types of compounds would be expected to interact with the $FeBr_2$ produced to give the product-determining oxyallyl–Fe(II) complex **3**.

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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.