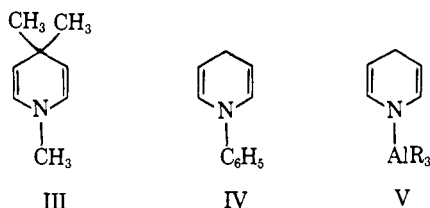


Table I.<sup>a</sup> Chemical Shifts (p.p.m.)

Compound	Protons at positions		
	2	3	4
I	5.87	4.50	3.05
II <sup>b</sup>	5.73	4.42	3.15
III <sup>c</sup>	5.51	4.11	...
IV <sup>d</sup>	6.27	4.53	2.98
V <sup>e</sup>	6.70	4.30	3.30

<sup>a</sup> Estimated precision  $\pm 0.03$  p.p.m. <sup>b</sup> The signal due to the N-H proton has not been identified. <sup>c</sup> No solvent (see ref. 3). <sup>d</sup> Solvent CCl<sub>4</sub>: M. Saunders and E. Gold, *J. Org. Chem.*, **27**, 1439 (1962). <sup>e</sup> Solvent pyridine: P. Lansbury and J. Peterson, *J. Am. Chem. Soc.*, **85**, 2236 (1963).

proton and protons 2 and 3. No evidence of coupling between the N-H proton and protons 4 is observed.



Compounds I and II have to be rigorously excluded from air since oxygen readily reacts with both materials. Methanolysis of I under neutral conditions is a slow reaction requiring several days to go to completion, but with base or acid the reaction is rapid and vigorous, often causing further reaction of the dihydropyridine.

*Acknowledgment.* We are indebted to Dr. J. B. Bush, Jr., for assistance in interpretation of the n.m.r. spectra, and to Dr. R. S. McDonald for assistance in interpretation of the infrared spectra.

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## The Second-Order Beckmann Reaction of an $\alpha$ -(Methylthio) Ketone Oxime

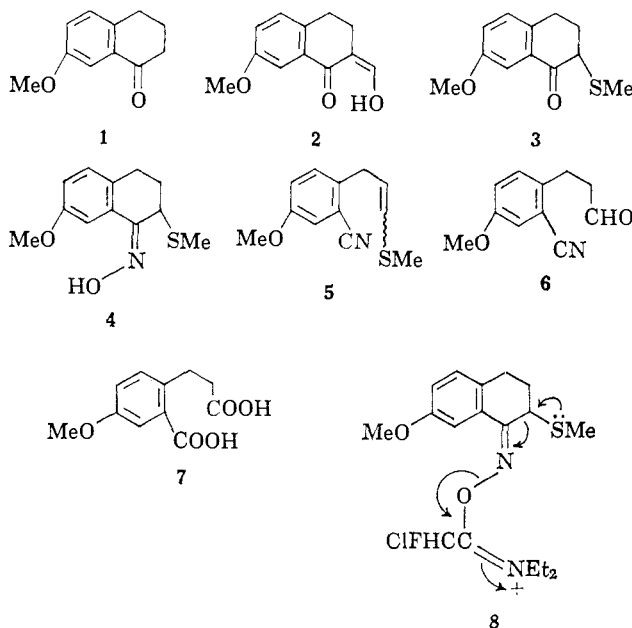
Sir:

We describe here a novel sequence of apparent general applicability to the purpose of oxidative cleavage of the bond between a ketone group and an adjacent methylene. This cleavage is useful in two ways, *viz.*, that direction of cleavage is governed by the steric control over product stability typical of Claisen-type condensations,<sup>1,2</sup> and that the termini of the cleaved bond are left in different oxidation states so that they may readily be separately modified.

7-Methoxytetralone (1) was formylated by the action of ethyl formate in tetrahydrofuran in the presence of sodium methoxide to yield the hydroxymethylene ketone 2,<sup>3,4</sup> m.p. 31.2–32.0°. The hydroxymethylene

(1) G. Stork and R. K. Hill, *J. Am. Chem. Soc.*, **79**, 495 (1957).  
(2) For a recent example of a formylation clearly not governed by the stability of the more stable enolate, see P. Grafen and R. B. Turner, *Tetrahedron Letters*, 3935 (1964), and S. W. Pelletier, R. L. Chappell, and P. C. Parthasarathy, *ibid.*, 41 (1965).  
(3) Acceptable analyses and concordant spectra have been obtained for all new compounds.  
(4) V. S. Gaid, R. P. Gandhi, I. C. Lakshumna, and S. M. Mukherji, *J. Indian Chem. Soc.*, **33**, 1 (1956), report 2 as a liquid; semicarbazone, m.p. 210°. We find for the semicarbazone m.p. 199.7–200.6°; isoxazole, m.p. 75–76.5°.

ketone was treated<sup>5</sup> with methyl thioisylate<sup>6</sup> and potassium acetate in ethanol to afford the 2-methoxy-7-methoxytetralone<sup>3</sup> (3), m.p. 70–70.6°. The crude yield in the two steps is quantitative; the yield of first crop after two recrystallizations is 59%. With hydroxylamine hydrochloride and sodium hydroxide in boiling ethanol, 3 afforded a single oxime<sup>3</sup> 4, m.p. 107.9–108.8°, in 64% yield. Its infrared spectrum displayed the usual pair of bands for free and intramolecularly hydrogen-bonded hydroxyl at 2.79 (sharp) and 3.06  $\mu$  (broad, strong). Its n.m.r. spectrum showed the following absorptions (in p.p.m. on the  $\delta$ -scale): =NOH, broadened singlet at 9.13<sup>7</sup> (its position being concentration dependent); -SMe, sharp singlet at 2.15; CHSMe, triplet centered at 4.82,  $J = 3.7$  c.p.s.



The oxime 4 was subjected to the Beckmann rearrangement of second order<sup>8</sup> under various conditions, to give methyl 3-(2-cyano-4-methoxyphenyl)prop-1-enyl thioether<sup>3</sup> (5) as a semisolid mixture of *cis* and *trans* isomers. The assignment of structure to 5 rests on elemental analysis and i.r. and n.m.r. spectra. The infrared spectrum displays a sharp band at 4.48  $\mu$  (-CN) and new bands<sup>9</sup> at 10.31 and 10.73  $\mu$ , one of which should be assigned to the *trans*-disubstituted double bond. The n.m.r. spectrum displays complex absorption in the vinyl region: at least 15 bands between 5.14 and 6.25, and two sharp singlets for the sulfur-bound methyl groups, at 2.19 and 2.28, area ratios (by integration) 1.7:1.

The vinyl thioether 5 was subjected to hydrolysis by the action of a 1:1 solution of 15% aqueous perchloric acid in ethanol for 30 min. on the steam bath. Conditions vigorous enough to hydrolyze the thioether are

(5) L. G. S. Brooker and S. Smiles, *J. Chem. Soc.*, 1723 (1926).  
(6) D. T. Gibson, *ibid.*, 2637 (1931).  
(7) *Cf. inter alia*, N. S. Bhacca, *et al.* "NMR Spectra Catalogue," Vol. 2, Varian Associates, Inc., Palo Alto, Calif., 1963, spectra numbers 501 and 614.  
(8) (a) *Cf. inter alia*, R. K. Hill, *J. Org. Chem.*, **27**, 29 (1962); (b) A. Hassner and W. A. Wentworth, *Chem. Commun.*, 44 (1965). The footnotes of these two references constitute a useful bibliography.  
(9) *Cf.* L. J. Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen and Co., Ltd., London, 1958, p. 46.

such as to cause some loss of the product aldehyde<sup>3</sup> **6**, probably by aldol condensation. The aldehyde was obtained as an oil in 50% yield. Its dinitrophenylhydrazone<sup>3</sup> melted at 199–200°. The aldehyde was further characterized by oxidation with Jones' reagent, then hydrolysis of the nitrile, to give the diacid<sup>3</sup> **7**, m.p. 196–197°. It was identical with a sample prepared from ketone **1** by permanganate oxidation.

The reaction conditions and course for the Beckmann cleavage are of interest. The rearrangement of oximes of 5- and 6-membered ketones is distinctly sluggish.<sup>10</sup> The tosylate of oxime **4** required boiling for 12 hr. in pyridine for its rearrangement to proceed about seven-eighths to completion. From such conditions, we recovered **5** in yields up to 35% (after purification by chromatography), and 10% of pure oxime. It is possible that this sluggishness of reaction in our example is owing to slow formation of tosylate from hindered oxime, as conduct of the reaction on the mesylate proceeds to give 38% of product and no recoverable oxime in appreciably shorter time.

A third alternative method is to conduct the reaction in a novel manner suggested by a recent publication of Cross, *et al.*<sup>11</sup> Treatment of the oxime **4** in dioxane solution with dry, freshly prepared 2-chloro-1,1,2-trifluoroethyl-diethylamine for 30 min. at 70° affords the product **5** in quite variable yields up to 48%, and oxime recovery exceeds 20%. We suggest that this quite mild reaction proceeds as indicated in **8**.

Although such a formulation of the reaction course places it within the general framework characteristic of the second-order Beckmann rearrangement as suggested in Hill's valuable article,<sup>3a</sup> this may be the first report<sup>12</sup> of such a rearrangement wherein the electron source which causes fragmentation is an unshared pair on sulfur. Hill refers to an article by Barltrop and Morgan<sup>13</sup> as having reported such an example. They describe the rearrangement of some oximes having on the  $\beta$ -carbon a 2-nitrophenylthio group or a 2,4-dinitrophenylthio group. Even though some of the product amides were too unstable to characterize, they appear to have been formed in all cases, as acid hydrolysis was required for the liberation of product fragments which would correspond to those expected from the alternative course we describe. We suggest that the difference in reaction course between our results and those of Barltrop may be ascribed to the presence of a thioether so substituted with electron-withdrawing groups that the lone pair on sulfur required for our reaction is practically unavailable in his cases.

(10) For elegant work on the mechanistic details of the Beckmann rearrangement, consult the papers of R. Huisgen, *et al.*, *e.g.*, *Ann.*, **602**, 127 (1957); **604**, 191 (1957); *Ber.*, **90**, 1844, 1850 (1957)

(11) L. H. Knox, E. Velarde, S. Berger, D. Cuadriello, and A. D. Cross, *J. Org. Chem.*, **29**, 2187 (1964). We are indebted to Dr. Cross for a discussion of his results prior to publication.

(12) The first report may be that of E. Vinkler and K. Autheried, *Acta Univ. Szeged. Acta Phys. Chem.*, **2**, 105 (1948); *Chem. Abstr.*, **44**, 6399 (1950). We are unable to ascertain relevant details from the abstract.

(13) J. A. Barltrop and K. J. Morgan, *J. Chem. Soc.*, 4486 (1960).

(14) DuPont Fellow, summer 1963.

Robert Luis Autrey, Peter W. Scullard<sup>14</sup>

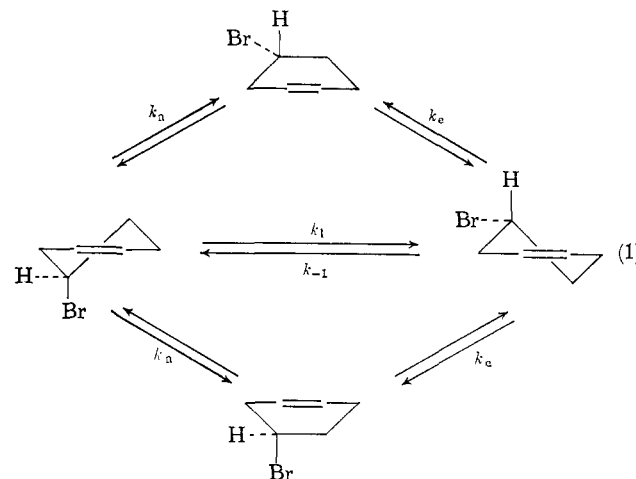
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## The Interconversion Barrier and Conformational Preference of Bromine in 4-Bromocyclohexene

Sir:

The interconversion barriers of many cyclic compounds, *e.g.*, cyclohexane<sup>1</sup> and derivatives,<sup>2,3</sup> have been determined using variable temperature n.m.r. spectroscopic methods. Related studies at low temperatures have been very fruitful in providing conformational preferences of groups substituted in cyclohexyl rings.<sup>4</sup> One of the major remaining problems in conformational analysis is the cyclohexenyl ring; this report concerns the energy of the half-chair-half-chair interconversion of 4-bromocyclohexene and the conformational preference of the 4-bromo group in this ring system.



The various rate constants (eq. 1) were determined for a 30% by volume solution of 4-bromocyclohexene in perdeuteriovinyl chloride as solvent with tetramethylsilane (TMS) as internal standard using a Varian HR-60 spectrometer with a special low temperature probe.

At temperatures above  $-140^\circ$ , the rate of the interconversion (eq. 1) is sufficiently rapid that a single, complex time average HCB $\pi$  resonance is observed. As the temperature is lowered below  $-145^\circ$ , the HCB $\pi$  proton resonance broadens and separates into two peaks in a manner similar to that reported for cyclohexane<sup>1</sup> and the halocyclohexanes. In the case of 4-bromocyclohexene, the peaks are effectively completely separated at  $-159^\circ$  with a broad signal occurring at  $254.5 \pm 0.9$  c.p.s. downfield from TMS and a relatively sharp peak  $281.8 \pm 0.8$  c.p.s. downfield from TMS. The upfield, broad peak was assigned to the axial hydrogen (equatorial bromine) and the downfield, sharper peak to the equatorial hydrogen on the basis of known chemical shifts of cyclohexyl axial and equatorial hydrogens<sup>5</sup> and respective coupling constants as functions of dihedral angles between protons.<sup>6</sup>

The chemical shifts at various temperatures are reported in Table I.

From the observed separation of the peaks with temperature, the sum of the two residence times,  $\tau$  (=

(1) F. R. Jensen, D. S. Noyce, C. H. Sederholm, and A. J. Berlin, *J. Am. Chem. Soc.*, **84**, 386 (1962).

(2) L. W. Reeves and K. O. Stromme, *Can. J. Chem.*, **38**, 1241 (1960).

(3) A. J. Berlin, Ph.D. Dissertation, University of California, Berkeley, 1961.

(4) A. J. Berlin and F. R. Jensen, *Chem. Ind.* (London), 998 (1960).

(5) R. U. Lemieux, R. K. Kullnig, H. G. Bernstein, and W. G. Schneider, *J. Am. Chem. Soc.*, **80**, 6098 (1958).

(6) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).