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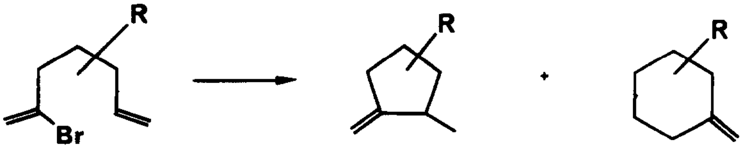
FIVE VS SIX MEMBERED RING FORMATION IN THE VINYL RADICAL CYCLIZATION

Gilbert Stork* and Robert Mook, Jr.

Department of Chemistry, Columbia University
New York, New York 10027

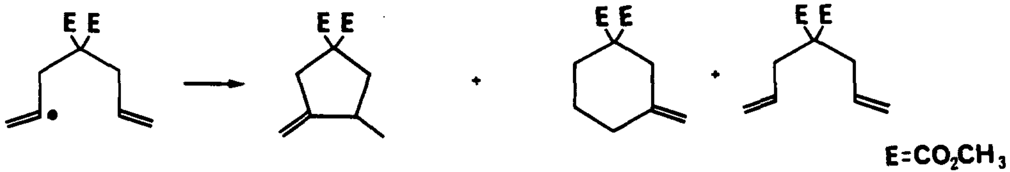
Summary: The ratio of methylenecyclopentane to methylenecyclohexane derivatives observed in the vinyl radical cyclization increases with the concentration of substrate and tin hydride. This is interpreted to mean that these cyclizations are under thermodynamic control at low concentrations.

In the original paper which demonstrated the feasibility of vinyl radical cyclization[1], we reported a number of cases which might, a priori, have led either to a methylenecyclohexane or to a methylenecyclopentane derivative. The formation of methylenecyclohexanes varied from significant to exclusive and was not easily reconciled with well-established observations involving the cyclization of alkyl radicals [2]. We were, therefore, led to consider, some time ago [3], that the ratios we had originally observed might reflect thermodynamic rather than kinetic control: In the vinyl radical cyclization, the initially formed cyclic radical is homoallylic and has available an easy rearrangement path [4] to a thermodynamic equilibrium which, in a given case, might well be in favor of a methylenecyclohexane.



We now report the results we obtained on this problem. They show unambiguously that the kinetic product, in a vinyl radical cyclization involving the possible formation of either a five or a six membered ring, is normally a methylenecyclopentyl radical. This may then be trapped by a hydrogen atom donor; or it may rearrange and end up as a methylenecyclohexane. If this picture is correct, the exact ratio of five and six rings should be dependent, inter alia, on the hydrogen donor concentration.

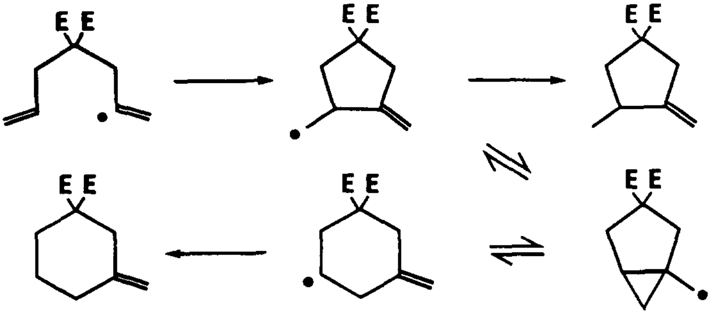
We were, indeed, able to show that the ratio of methylenecyclopentane formed in a given case increases dramatically as the concentration of the hydrogen donor, specifically tributyl tin hydride, was increased. A typical example involves the cyclization of 1 to 2 and 3. We had originally observed that this cyclization leads to a 3:1 ratio of 2 over 3 with 0.02 M Bu_3SnH. Our more recent work [3] has shown that in 1.7 M solution the ratio



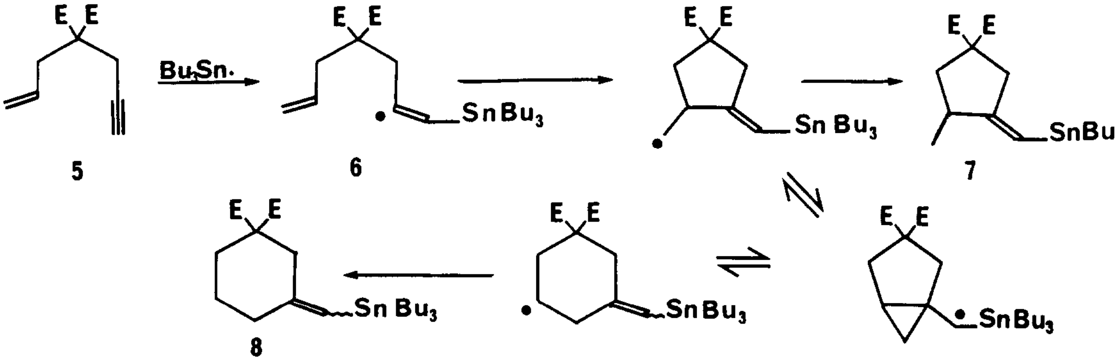
1 2 3 4

becomes ≥ 97:1 in favor of the methylenecyclopentane 2 [5]. It is a striking illustration of the great effectiveness of vinyl radical cyclizations, that, even in neat tributyl tin hydride, the reaction still largely gives the cyclized product 2 rather than the simple dehalogenation product 4 (ratio of 2 to 4= 4.4:1).

It is clear that the process illustrated in the following scheme is operative.



We have made related observations with the tin radical-mediated ethynyl cyclization. In this recently discovered reaction [6], the cyclizing intermediate (cf 6) is a vinyl radical β-substituted by a trialkylstannyl group. Here again, the gradual increase in the ratio of methylenecyclopentane 7 to methylenecyclohexane 8 (see Table) is in complete accord with the mechanistic picture of scheme I.



Table

Molar concentration of Bu_3SnH	; enyne 5	Product ratio 7 : 8
.02	; .02	1 : 4
.3	; .25	4 : 1
.7	; .6	18 : 1
2.2	; 1.9	≥ 100 : 1

Acknowledgment: We thank the National Institutes of Health and the National Science Foundation for their support of this work.

References and Notes

1). G. Stork and N.H. Baine, J. Am. Chem. Soc., 104, 2321 (1982).

2) See, for instance, M. Julia, Acc. Chem. Res., 4, 386 (1971); M. Julia, Pure and Appl. Chem., 15, 167 (1967).

3) This material is taken from the Ph.D. dissertation of Robert Mook, Jr. Columbia University, N.Y. 1984. cf. Dissertation Abstracts, 46B, 2669 (1985).

4) A.L.J. Beckwith and G. Phillipon, J. Chem. Soc., Chem. Communications, 658 (1971).

5) The ratios of products were determined by capillary vpc at 180 --> 270°C and by ^{1}H NMR(200 MHz), after removal of starting material and/or uncyclized dehalogenated product by chromatography or silica with 10% ethyl acetate-petroleum ether. The retention times were 4 < 2 < 3. ^{1}H NMR 2 : δ 4.92 (br s, ^{1}H ; C=C$\underline{H_2}$), 1.09 (d, J = 6Hz ; CH_3). 3: 4.75 (br s, 2 H; C=C$\underline{H_2}$). The vinylstannane products 7 and 8 could be converted into 2 and 3 by destannylation upon stirring overnight with silica gel.

6) G. Stork and R. Mook, in preparation.

7) We thank Dr. A.L.J. Beckwith for his courtesy in arranging that the publication reporting his own results be delayed until ours could be sent. See A.L.J. Beckwith and D.M. O'Shea, Tetrahedron Letters, accompanying communication.

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