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CYCLIZATION OF ACETYLENIC ALKYL RADICALS[1a]

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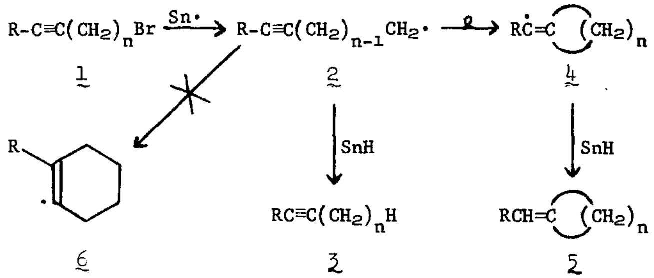
In connection with studies on the cyclization of organometallic derivatives obtained from acetylenic halides of general formula 1,[2] it became evident that free-radical processes involving intermediate radical 2 might be important in competitive reactions. Although some work has been reported by Julia[3] on intramolecular cyclizations of related acetylenic radicals, the general characteristics of such species are still relatively undefined. Accordingly, we have examined the radicals derived from a series of bromides in which the carbon chain separating the reactive center and the acetylenic unit is varied in length.



An unambiguous method for the production of 2 from 1 involves reduction with tri-*n*-butyltin hydride, a reaction whose mechanism is well established as a radical chain process.[4] Once formed, 2 can abstract hydrogen from tin hydride to give the simple reduction product 3, or it may rearrange to cyclic radical 4 prior to hydrogen abstraction thereby yielding cyclic product 5. The results given in Table I are for reductions performed by adding 1.1 equiv of a 10% solution of tri-*n*-butyltin hydride in benzene to an 0.07 *M* solution of halide in benzene (1.8 mole-percent of AIBN as an initiator) and heating to reflux for 36 hr. The yields of distilled hydrocarbon products ranged from 85% to quantitative.

The following conclusions can be drawn from the tabulated data: Cyclization of 1 with n = 4 gives ylidenecyclopentanes in an exceptionally efficient process which should be of synthetic utility. Cyclization is not observed under these reaction conditions with $n \neq 4$ or 5. This is true for $n = 3$ even at high dilution. When $n = 5$, partial cyclization occurs with a phenyl substituent on the acetylenic group but not with an alkyl substituent, confirming the expected stabilization of cyclic radical 4 when R = C_6H_5. The proportion of cyclic product for $n = 5$, R = C_6H_5 was increased by lowering the concentration of the reactants, indicating that the amount of cyclization is determined by the rate of hydrogen abstraction by 2 from the tin hydride relative to rearrangement of 2 to 4, and not by preliminary equilibration of 2 and 4. Cyclization is remarkably specific in that bond formation uniformly occurs at the acetylenic carbon nearest the radical center.[5] (Careful glpc analysis utilizing authentic samples of the expected products from alternate cyclic radical 6 assured that less than 1% of the reaction proceeded *via* this intermediate.)

TABLE I

1		3	5
n	*R*		
2	C_6H_5	99%	-
3	C_6H_5	99%	-
3	C_6H_5	99%	- (0.007 *M* halide)
4	C_6H_5	-	99%
4	*n*-C_5H_{11}	-	99%
5	C_6H_5	50%	50%
5	C_6H_5	25%	75% (0.018 *M* halide)
5	*n*-C_5H_{11}	98%	-

The second method employed for the generation of radical 2 from halide 1 was reaction with lithium biphenyl. This reagent reduces alkyl halides by electron transfer to halogen and fragmentation to an alkyl radical and halide ion.[6] This system is more complex than the tin hydride reductions, since competitive electron transfer to other acceptor sites in the molecule can occur, and in addition, radical species can be further reduced to carbanionic (*i.e.*, organolithium) centers. The data presented in Table II were obtained from reactions in which the halide, 0.15 equiv of biphenyl and 2.2 equiv of metallic lithium, were stirred in tetrahydrofuran until the dark green color of the biphenyl radical-anion persisted. Not unexpectedly, these reductions are less selective than those described above, but good yields of hydrocarbon products were generally obtained. Notable among the new materials are the dehydrohalogenation products 7 and 8. These are undoubtedly derived from normal elimination processes with the biphenyl radical-anion functioning as the base.[7] Cyclization to 5 is again efficient with the

$n = 4$ substrates, some cyclic product is found for $n = 5$, $R = C_6H_5$ (but not with R = alkyl), and no cyclization is observed for $n = 2$. These observations therefore parallel the tin hydride reactions reasonably well and confirm the latter results.

TABLE II

	1	Yield	3	5	7	8	Other
n	R						
2	n-C_4H_9	70%	99%	-	-	-	
2	C_6H_5	~ 30%	55%	-	-	39%	polymer
3	C_6H_5	95%	7%	26%	52%	-	
3*	C_6H_5	-	11%	37%	40%	-	
3*	n-C_3H_7	80%	88%	-	12%	-	
4	n-C_5H_{11}	85%	-	99%	-	-	
4	C_6H_5	98%	4%	93%	3%	-	
4**	C_6H_5	-	6%	85%	1%	-	8% 1-phenyl-1-hexene
5	n-C_5H_{11}	100%	94%	-	-	3%	3% 5,6-dodecadiene
5	C_6H_5	93%	15%	15%	56%	-	

* The alkyl chloride was used.
** The bromide was added dropwise to an excess of lithium biphenyl solution.

In order to check on the possibility of anion involvement in these reductions, several reactions were quenched with deuterium oxide. The cyclic product 5 was unlabeled, indicating either that organometallic intermediates are not involved or that they do not survive the reaction conditions. Evidence against the latter possibility was secured by slowly adding a solution of halide ($n = 4$, $R = C_6H_5$) to a large excess of radical-anion solution. Under these conditions, favorable for anion formation, 5 incorporated 24% of one deuterium. Furthermore, the amount of noncyclic product (3 plus its reduction product 1-phenyl-1-hexene) increased from 4% to 14%. This information suggests that carbanion 9 can be formed under the appropriate conditions and that at least some of this species survives the reaction conditions, but that 9 is most likely not extensively involved in the standard free-radical reactions. In addition, it appears that carbanionic cyclizations may be less facile than those of 2 in view of the greater amount of acyclic products under conditions favoring carbanion production.

$RC{\equiv}C(CH_2)_{n-2}CH{=}CH_2$

7

8

9

$R\dot{C}{=}\bar{C}(CH_2)_nX$

10

Finally, attention should be drawn to the one striking difference between the two reduction methods, namely the presence of substantial amounts of benzylidenecyclobutane from the n = 3, R = C_6H_5 substrate (but not with R = alkyl) in the radical-anion system. Note also that changing the halogen from bromide to chloride increased the amount of cyclization. Several explanations can be advanced to account for these observations. Both reductions may involve radical **2** exclusively, but since cyclization is dependent upon the relative rates of hydrogen abstraction by **2** and its rearrangement to **4**, the cyclization may be effectively prevented in the presence of the very good hydrogen donor, tin hydride, but compete with abstraction from poorer donors (presumably tetrahydrofuran) in the radical-anion system. The radical-anion reduction may be mechanistically different; for example, benzylidenecyclobutane may arise by a carbanionic pathway. (However, deuterium incorporation in the cyclic product was not observed.) Alternatively, cyclization could be initiated by *electron transfer to the phenylacetylenic moiety*, and the radical-anion **10** could then yield radical **4** by an intramolecular carbanionic displacement on the halogen center. Available polarographic data[8] on similar acetylenic compounds indicate that one-electron reduction of the triple bond should be favored over electron transfer to the alkyl chloride center and reasonably competitive with donation to the bromide site. Thus, the enhanced cyclization with the chloride might be attributed to increased formation of **10** from this material over the bromide. We are currently in the process of evaluating the importance of non-radical cyclization pathways as a source of benzylidenecyclobutane and the other cyclic products obtained in the lithium biphenyl reductions.

References

1. a. Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work. b. Alfred P. Sloan Research Fellow 1968-1970. c. Public Health Service Predoctoral Fellow 1966-1968.
2. D. J. Keyton, Ph.D. Thesis, Indiana University, 1968. See also: S. A. Kandil and R. E. Dessy, *J. Amer. Chem. Soc.*, **88**, 3027 (1966); H. R. Ward, *ibid.*, **89**, 5517 (1967); H. G. Richey, Jr., and A. M. Rothman, *Tetrahedron Lett.*, 1457 (1968).
3. M. Julia, *Rec. Chem. Progr.*, **25**, 3 (1964).
4. H. G. Kuivila, *Accounts of Chem. Research*, **1**, 299 (1968).
5. Similar specificity is observed with the olefinic counterpart of **2**: C. Walling, J. H. Cooley, A. A. Ponoras, and E. J. Racah, *J. Amer. Chem. Soc.*, **88**, 5361 (1966).
6. B. J. McClelland, *Chem. Rev.*, **64**, 301 (1964); J. F. Garst, P. W. Ayers, and R. C. Lamb, *J. Amer. Chem. Soc.*, **88**, 4260 (1966); S. D. Sargent, J. N. Cron, and S. Bank, *ibid.*, **88**, 5363 (1966).
7. J. K. Crandall and D. J. Keyton, *Chem. Commun.*, 1069 (1968).
8. L. Meites, "Polarographic Techniques," Interscience Publishers, New York, N. Y., 1965, pp 671-711.