tion cyclize. This renders difficult the defense of any mechanism for the oxygenation of primary Grignard reagents in which the initial step is the addition of the Grignard reagent to oxygen, and in which the carbon oxygen bond thus formed is never thereafter ruptured.[8] On the other hand, the results conform to the predictions of mechanisms involving free-radical intermediates, since the tendency of the 5-hexenyl radical to cyclize to the cyclopentylmethyl radical is well documented.[2,5,9] The most reasonable pathways are those involving one-electron transfer from the Grignard reagent, reactions 1 and 2 being possible steps in such

$$RMgX + O_2 \longrightarrow R\cdot + XMgO_2 \quad (1)$$

$$RMgX + ROO\cdot \longrightarrow R\cdot + ROOMgX \quad (2)$$

mechanisms. Reaction 1 might be an initiation step of a chain process or simply the first step of a nonchain process. Reaction 2 might be a propagation step of a chain process. In any event, the cyclization of the 5-hexenyl radical would then compete with other reactions destroying that species.[10] Ample precedent and analogy for these reactions exists in the work of others, the most extensive pertinent studies being those of Russell and co-workers, who have presented evidence that many carbanion oxidations proceed *via* similar one-electron transfer processes, and specifically suggested the inclusion of Grignard oxidations in this family.[11]

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(8) C. Walling and S. A. Buckler, *J. Am. Chem. Soc.*, 77, 6032 (1955); also, C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, pp 465–466. The radical scavenger experiments of Walling and Buckler bear directly on chain processes only. As they recognized, it is possible that no effect of inhibitors was observed because these were insufficiently reactive radical traps.

(9) (a) C. Walling and M. S. Pearson, *J. Am. Chem. Soc.*, 86, 2262 (1964); (b) R. G. Garwood, C. J. Scott, and B. C. L. Weedon, *Chem. Commun.*, 14 (1965).

(10) Since the cyclization of 5-hexenyl cannot compete with cage reactions,[2] reaction 1 followed by cage recombination would lead exclusively to noncyclic alkyl hydroperoxide salt, an over-all result which is indistinguishable here from direct nucleophilic addition of the Grignard reagent to oxygen. If the usually formulated alkoxide producing reaction, $RMgX + ROOMgX \rightarrow 2\ ROMgX$,[8] is presumed to proceed *without* the intervention of radicals, and if it accounts for all the alkoxide, then at least 50% of the alkyl hydroperoxide must be produced through radical pathways. We prefer to postulate that it is 100%, but that the extent of cyclization is limited by competition of other reactions, including cage recombination, with the radical cyclization. It is possible that all noncyclic hydroperoxide arises in radical cage reactions and that all radicals escaping cage recombination cyclize, although the data certainly do not require this.

(11) A summary appears in G. A. Russell, E. G. Janzen, A. G. Bemis, E. J. Geels, A. J. Moye, S. Mak, and E. T. Strom, "Selective Oxidation Processes," Advances in Chemistry Series, No. 51, American Chemical Society, Washington, D. C., 1965, Chapter 10.

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Electron-Transfer Reaction of Radical Anions with Cholesteryl and Cyclocholestanyl Chlorides

Sir:

Garst and his co-workers[1] have investigated the reaction of sodium naphthalene radical anion with 5-hexenyl and cyclopentylmethyl bromides and chlorides. The olefinic halides gave mixtures of 1-hexene and methylcyclopentane, in the C_6 hydrocarbon products, while only the latter C_6 hydrocarbon was observed in the reaction of the halomethylcyclopentanes. These authors concluded that electron transfer from the radical anion results in the formation of a free radical and halide ion, that the olefinic radical is partially cyclized to cyclopentylmethyl radical, and that the two organic radicals are converted by a second mole of radical anion to carbanions, which are then protonated by solvent.

We wish now to report our results on the reaction of sodium biphenyl radical anion with cholesteryl chloride (I) and β-cyclocholestanyl chloride (II), from which we have arrived at substantially identical conclusions. Our work in this system derived from our interest in homoallylic and cyclopropylcarbinyl free radicals.[2] Reduction of the isomeric chlorides led to monomeric hydrocarbon products in good yields (58–84%). Chloride I gave only 5-cholestene (III), while chloride II gave mixtures of III and $3\alpha,5\alpha$-cyclocholestane (IV). These diverse results show that the radical and/or carbanion intermediates derived from I and II are different and do not equilibrate completely before being trapped, are consistent with our previous conclusions[2] regarding the nonexistence of nonclassical homoallylic radicals, and extend those conclusions to carbanions.

The product ratio, IV/III, from reduction of chloride II was observed to be independent of the hydrogen atom donating ability of the reaction medium (as classified on the Bridger–Russell scale[3]), using benzene, toluene, tetralin, and a 1 *M* solution of triphenyltin hydride in benzene as solvents, but depended quite markedly on the concentration of the sodium biphenyl radical anion and on the temperature of the reaction. For example, reaction of II with 0.01 *M* sodium biphenyl in 1,2-dimethoxyethane at 25° gave 11% IV and 89% III while reaction of II with 1.0 *M* sodium biphenyl at 25° gave 20% IV and 80% III. Reaction of II in 1.0 *M* sodium biphenyl at −20° yielded 41% IV and 59% III, while reaction at −70° yielded 60% IV and 40% III.

In each experiment the reaction was quenched after several minutes by addition of water to destroy excess radical anion, steam distillation to remove biphenyl, and column chromatography on 10% silver nitrate on neutral alumina; IV was obtained by elution with olefin-free *n*-pentane and III by elution with 5% benzene in Skellysolve B. Compounds IV and III were identified by comparison with authentic samples.[4]

Our results indicate that the course of the reduction of II involves the initial transfer of an electron from the radical anion to the chlorine atom resulting in the loss of chloride ion and formation of the cyclocholestanyl free radical V.[5]

(1) J. F. Garst, P. W. Ayers, and R. C. Lamb, *J. Am. Chem. Soc.*, 88, 4260 (1966).

(2) See, *inter alia:* S. J. Cristol and D. I. Davies, *J. Org. Chem.*, 29, 1282 (1964), and S. J. Cristol, G. D. Brindell, and J A. Reeder, *J. Am. Chem. Soc.*, 80, 635 (1958).

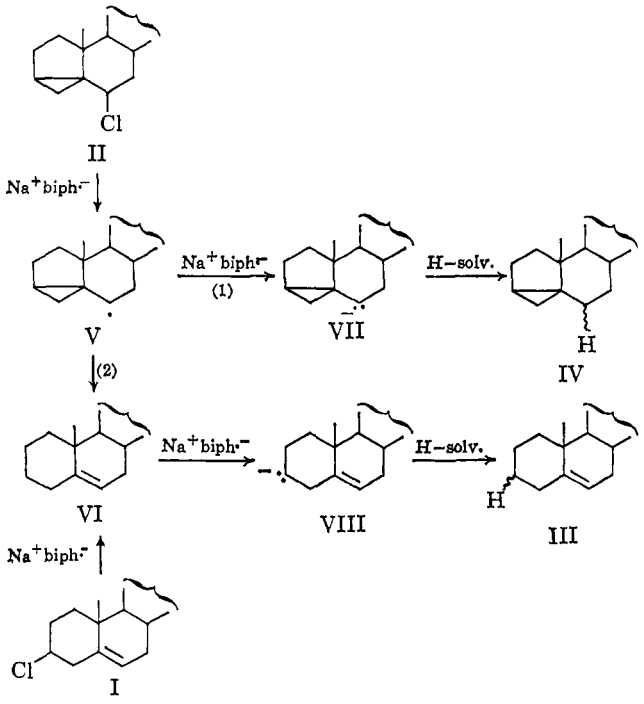
(3) R. F. Bridger and G. A. Russell, *ibid.*, 85, 3754 (1963).

(4) IV reported by F. S. Prout and B. Riegel, *ibid.*, 74, 3190 (1952); III reported by W. G. Dauben and R. H. Takemura, *ibid.*, 75, 6302 (1953).

(5) Dissociative electron capture by alkyl halides with resulting formation of halide ion and alkyl radical has been reported: R. F. Claridge and J. E. Willard, *ibid.*, 87, 4992 (1965).

The radical V would appear to have three important choices: (a) it may abstract a hydrogen atom from the surrounding medium to give the cyclocholestane IV, (b) it may be reduced by another molecule of radical anion to form the corresponding carbanion VII, or (c) it may rearrange to the allylcarbinyl radical VI, which may have similar choices. That choice a is unimportant is shown by the lack of dependency of the product ratio on the hydrogen atom donor ability of the medium. Competition between the other choices is required to rationalize our results. The reaction sequence proposed is outlined in scheme I.

Scheme I



It would be predicted from this sequence that increased radical anion concentration should favor conversion of the radical V to the carbanion VII over its isomerization to the radical VI, as is observed, and the dependence upon concentration also requires that the rearrangement occurs at the radical stage rather than at the carbanion stage. Thus, if all radical V were reduced to carbanion VII, a decrease in radical anion concentration should not lead to increased amounts of III.

The strong temperature dependence of the product ratio IV/III is a reflection of the difference in activation energies between the electron-transfer reaction and the rearrangement reaction. That reaction 2 has an activation energy is an interesting confirmation of our conclusions regarding the nonexistence of nonclassical homoallylic free radicals.

The fact that no rearrangement occurred in the reduction of I (III being the sole product) suggests that radical VI is more stable than V, so that the reverse of reaction 2 is not observed. Attempts to trap carbanions VII and VIII by rapid carbonation of the reaction mixtures yielded none of the possible carboxylic acids. Carbanions VII and VIII must abstract protons from solvent very rapidly.

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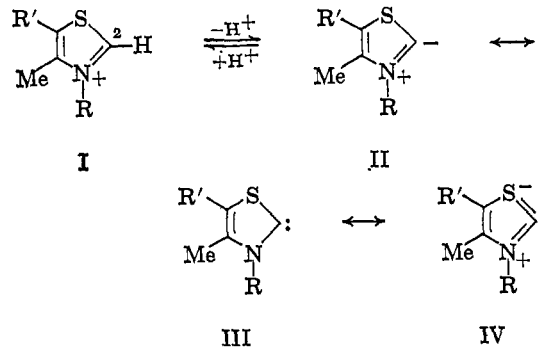
Hydrogen–Deuterium Exchange in Some Heterocyclic Cations Containing Nitrogen and Sulfur

Sir:

The importance in the mechanism of thiamine action of ionization at C_2 of the thiazolium ring (I) has been rigorously established by Breslow and others.[1] The



factors causing the lability of H_2 and their quantitative significance are, however, not well understood. Recently we showed by a study of the rates of deprotonation of a series of azoles and azolium salts (in which the number of nitrogens and the positioning of the positive charge were varied) that coulombic and inductive effects are major rate-enhancing factors:[2] that the positive charge in I should be worth *ca.* 10^{10} in rate and the α nitrogen *ca.* 10^5. We now wish to amplify our initial conclusions to include sulfur–nitrogen systems as necessary background for a later consideration of the importance of the carbene structure (III) and d–σ overlap (IV)[3] in the stabilization of II.

Two other groups have rationalized the acidity of I. Hafferl[4] discovered that 3,4-dimethylthiazolium iodide (V) and N,N′-diphenylimidazolinium chloride (VI) exchange at almost the same rate and concluded that III is an important rate-enhancing factor whereas IV is not. These authors, however, chose a poor model (the N,N′-dimethylimidazolium cation deprotonates 10^3 times more slowly than VI) and relied on some misinterpreted data of Wanzlich.[5] Haake[6] compared the exchange rates, nmr chemical shifts, and $J_{C^{13}-H}$ for the 3,4-dimethyloxazolium cation (VII) and V (rates 40:1; $J_{C^{13}-H}$ = 247:218 cps), and concluded that high s character in the C–H bond was a dominant factor. The use of $J_{C^{13}-H}$ as a measure of s character

(1) R. Breslow, *J. Am. Chem. Soc.*, **80**, 3719 (1958), and other papers; F. H. Westheimer, *Advan. Enzymol.*, **24**, 467 (1962).
(2) R. A. Olofson, W. R. Thompson, and J. S. Michelman, *J. Am. Chem. Soc.*, **86**, 1865 (1964), and unpublished results.
(3) R. A. Olofson, J. M. Landesberg, K. N. Houk, and J. S. Michelman, *ibid.*, **88**, 4265 (1966).
(4) W. Hafferl, R. Lundin, and L. L. Ingraham, *Biochemistry*, **2**, 1298, (1963).
(5) D. M. Lemal, R. A. Lovald, and K. I. Kawano, *J. Am. Chem. Soc.*, **86**, 2518 (1964).
(6) P. Haake and W. B. Miller, *ibid.*, **85**, 4044 (1963).