ical stability, II (and its *p*-chloro derivative) being recovered unchanged after refluxing for many hours in reagents as diverse as concentrated NaOH, $LaAlH_4$–tetrahydrofuran, sodium in ethanol, concentrated HCl, and 20% H_2SO_4. There is no apparent steric interference with protonation on nitrogen, and the compounds are bases, readily dissolved in dilute acids and recovered by basification. This behavior is unexpected if one considers 1,3-diazetidines to be the nitrogen analogs of the acid-labile acetals, a comparison apparently not accurate, perhaps due to the unreactivity of the diprotonated species.[8]

Acknowledgment. We are grateful to Professor R. C. Fort for his assistance in the determination of the ^{13}C–H satellite spectra.

(8) As suggested by a referee.

(9) To whom correspondence and requests for reprints should be directed at the School of Medicine, Case Western Reserve University, Cleveland, Ohio.

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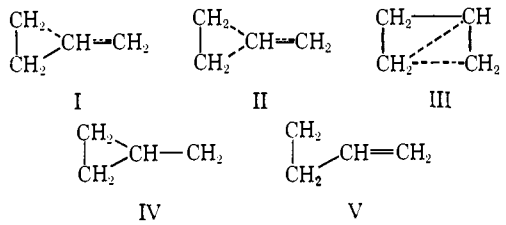
A Nonclassical Free Radical[1]

Sir:

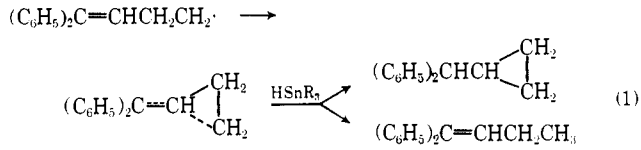
Molecular orbital calculations have helped to explain rate and product data for carbonium ion reactions of cyclobutyl, cyclopropylcarbinyl, and allylcarbinyl compounds by implicating a common, nonclassical intermediate.[2,3] Such calculations for radical systems suggest that nonclassical free radicals should also be intermediates in some reactions. Howden and Roberts[2] calculated that nonclassical radical I should be more stable than bicyclobutyl radical III, cyclopropylcarbinyl radical IV, or allylcarbinyl radical V, although the stabilization is small relative to that in the corresponding cation.[4]



I II III

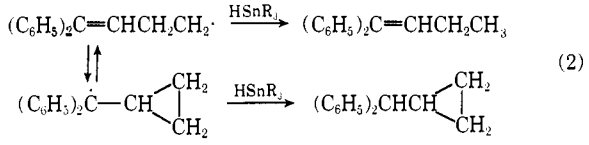
IV V

Compelling experimental evidence for nonclassical radicals appears to be lacking. Wilt and coworkers[6,7] have suggested that the 7-norbornenyl radical and the 2,3-dibenzo-7-norbornenyl radical may be nonclassical, but the suggestion is based on qualitative and incomplete rate comparisons. Howden[8] found that the ratio of products from the (γ,γ-diphenylallyl)carbinyl radical is nearly constant over the range 110–150°, a result consistent with a nonclassical radical intermediate (eq 1). Equilibrating classical radicals (eq 2) were thought less



(1)

likely because the equilibrium constant should be



(2)

strongly temperature dependent while the ratio of rate constants for hydrogen abstraction might well be insensitive to temperature. Direct formation of the nonclassical radical (eq 1) from the substrate (the peracetate) was thought unlikely in view of the small effect of structure on rate.[8]

Recent studies of homoallylic radical systems indicate, however, that there is no general need to postulate nonclassical structures for such species.[9,10] In fact, there is some indication that the 3-methylcyclopropylcarbinyl radical is a classical species.[10]

We wish to report evidence that 7-norbornenyl is a nonclassical radical. A convenient method for generating a free radical is reduction of an organic halide with an organotin hydride.[11–13] Reduction of either *syn*- or *anti*-7-bromonorbornene with tri-*n*-butyltin deuteride in hexane leads to the *same* 7-deuterionorbornene. The yield is about 80%, and there are no other volatile products. That the same product is obtained and that it is a norbornene is evident from the nmr spectra (Figure 1) and from identity of its glpc retention time with that of norbornene. That 7-deuterium in the product is *anti* is based on a recent reassignment[14] of the signal at τ 8.93 to the *anti*-7-hydrogen of norbornene (Figure 1).

This stereochemical result cannot be accounted for readily in terms of either a single classical radical or equilibrating classical radicals. For VI to accommodate this result requires either a highly stereospecific reaction of the unhindered, classical C_7 radical or re-

(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work (Grant 1396-A4).

(2) M. E. H. Howden and J. D. Roberts, *Tetrahedron Suppl.*, 2, 403 (1963).

(3) R. J. Piccolini and S. Winstein, *ibid.*, 2, 423 (1963).

(4) The best description of the cation appears to be bishomoallyl structure II.[5]

(5) See, *e.g.*, (a) H. G. Richey, Jr., and J. M. Richey, *J. Am. Chem. Soc.*, 88, 4971 (1966); (b) P. von R. Schleyer and G. W. Van Dine, *ibid.*, 88, 2321 (1966); (c) references cited in ref 5a,b.

(6) J. W. Wilt and A. A. Levin, *J. Org. Chem.*, 27, 2319 (1962).

(7) J. W. Wilt, G. Gutman, W. J. Ranus, Jr., and A. R. Zigman, *ibid.*, 32, 893 (1967).

(8) M. E. H. Howden, Ph.D. Thesis, California Institute of Technology, 1962.

(9) L. K. Montgomery, J. W. Matt, and J. R. Webster, *J. Am. Chem. Soc.*, 89, 923 (1967).

(10) L. K. Montgomery and J. W. Matt, *ibid.*, 89, 934 (1967).

(11) (a) H. G. Kuivila, L. W. Menapace, and C. R. Warner, *ibid.*, 84, 3584 (1962); (b) H. G. Kuivila and L. W. Menapace, *J. Org. Chem.*, 28, 2165 (1963); (c) H. G. Kuivila in "Progress in Organometallic Chemistry," F. G. A. Stone and R. West, Ed., Academic Press Inc., New York, N. Y., 1964, p 64.

(12) F. D. Greene and N. N. Lowry, *J. Org. Chem.*, 32, 875 (1967).

(13) L. Kaplan, *J. Am. Chem. Soc.*, 88, 4531 (1966).

(14) K. Tori, K. Aono, Y. Hata, R. Muneyuki, T. Tsuji, and H. Tanida, *Tetrahedron Letters*, 9 (1966).

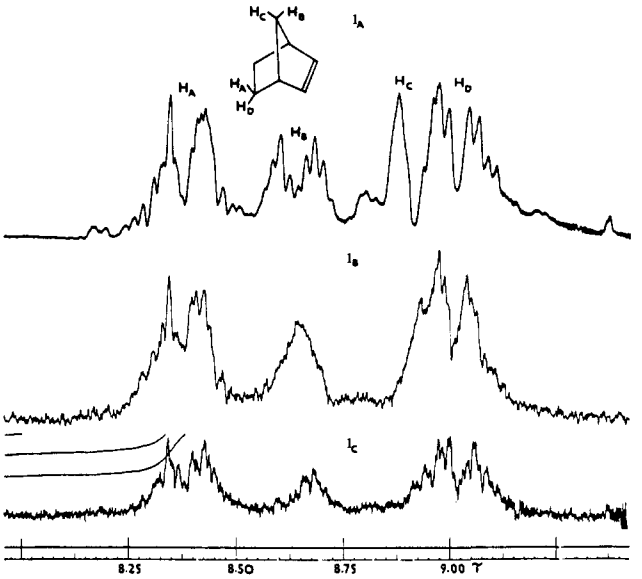
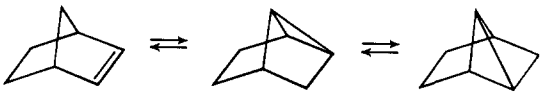


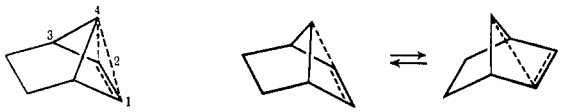
Figure 1. Nmr spectra at 100 Mc: (I_A) norbornene; (I_B) *anti*-7-deuterionorbornene from *anti*-bromide; (I_C) *anti*-7-deuterionorbornene from *syn*-bromide.

action of a cyclopropylcarbinyl radical at a carbon which does not have radical character. The steric factor is too small, and there is no precedent for reaction of the latter type. Either VII or equilibrating nonclassical radicals VIII can accommodate the result.



VI

In systems without a rigid framework, structures like VII are expected to be favored,[2] but rigid systems are



VII VIII

also stabilized by including 1,4 overlap along with 2,4 overlap.[15]

Results of application of the kinetic criterion for delocalization, in this and in other systems, will be reported soon.

(15) The numbering system used for VII emphasizes the homoallylic portion of the molecule.

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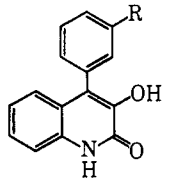
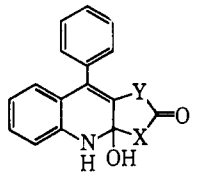
The Synthesis of Cyclopenin[1]

Sir:

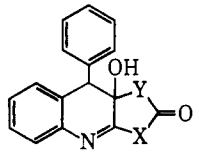
Cyclopenin, $C_{17}H_{14}N_2O_3$, a metabolite first isolated[2] from *Penicillium cyclopium* and later[3] from *Penicillium viridicatin*, in dilute acid solution loses its optical activity with concomitant appearance in high yield of 3-hydroxy-4-phenyl-2-quinolone (viridicatin, I, R = H),[2-4] carbon dioxide, and methylamine. To accommodate these observations, a quinolinooxazolidinone structure (IIa or IIIb) was assigned[2] to cyclopenin; fusion at the 3,4 positions of the quinoline also was postulated.[5] In each case, the isomer with the oxygen and N–CH_3 interchanged was also a contender.



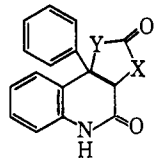
I



IIa, X = NCH_3; Y = O
b, X = O; Y = NCH_3

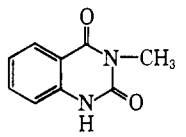


IIIa, X = NCH_3; Y = O
b, X = O; Y = NCH_3

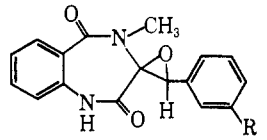


IVa, X = NCH_3; Y = O
b, X = O; Y = NCH_3

Reinvestigation[3,4,6] showed that a phenolic metabolite, cyclopenol, accompanied cyclopenin and that cyclopenol is also labile to mild acid, yielding 3′-hydroxyviridicatin (I, R = OH). Oxidation of cyclopenin[4] with hydrogen peroxide–acetic acid gave anthranilic acid, benzoic acid, benzaldehyde, and in particular 3-methyl-2,4-quinazolinedione (V). Biosynthetic studies[4,7] showed that anthranilic acid and phenylalanine were incorporated into cyclopenin, that the carbon dioxide evolved in the viridicatin transformation derived from the anthranilic acid carboxyl, and that this carbon remained in the quinazoline V. None of the previous proposals (II, III, and IV) is compatible with these data, and a new structural proposal,[4] the benzodiazepine VI, was made for cyclopenin. Further support was provided by the strong amide absorption in the ir and the one proton singlet at δ 4.04 in the nmr, assigned to the benzylic hydrogen.



V



VI

Although a strong case can be made for VI, some anomalies remained. Particularly striking was the

(1) Supported in part by the U. S. Army Research Office, Durham, N. C.

(2) A. Bracken, A. Pocker, and H. Raistrick, *Biochem. J.*, 57, 587 (1954).

(3) J. H. Birkinshaw, M. Luckner, Y. S. Mohammed, K. Mothes, and C. E. Stickings, *ibid.*, **89**, 196 (1963).

(4) Y. S. Mohammed and M. Luckner, *Tetrahedron Letters*, 1953 (1963).

(5) J. T. Edward, *Ann. Rept. Progr. Chem.* (Chem. Soc. London), **51**, 247 (1954).

(6) M. Luckner and Y. S. Mohammed, *Tetrahedron Letters*, 1987 (1964).

(7) M. Luckner and K. Mothes, *ibid.*, 1035 (1962); *Arch. Pharm.*, **296**, 18 (1963).