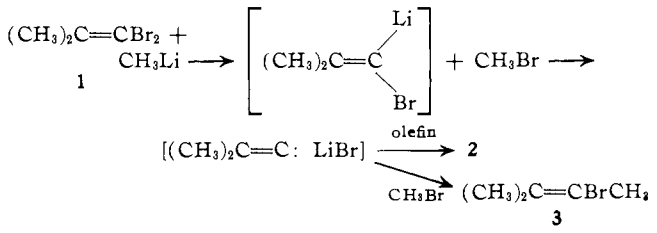
hydrogens. Thus, the spectrum of the product obtained from isobutylene (**2**, $R_1 = R_2 = CH_3$, $R_3 = H$) showed the resonances of the ring methyls (singlet) at τ 8.85, the methylene (seven peaks) centered at τ 9.21, and the olefinic methyls (four peaks) centered at τ 8.24.

2-Bromo-3-methyl-2-butene (**3**) was formed in all the reactions of **1**, methyllithium, and olefins. The yields of **3** were in inverse relation to those of the olefin adducts **2**. With weakly nucleophilic olefins, such as ethylene or vinyl chloride, only traces of methylenecyclopropanes were formed, and **3** was the major product. These results suggest that an intermediate is formed which can react with olefin or methyl bromide. The variation in yield of **2** with olefin structure is that expected of an electrophilic intermediate. It is suggested that lithium–bromine exchange occurs and is followed by, at least, partial loss of lithium bromide.[7]



Attempts to trap the α-halolithium intermediate by carbonation were unsuccessful. No products of insertion of the isopropylidene carbene into carbon–hydrogen bonds have yet been found.

(7) A more precise formulation of the intermediate cannot now be given. The extent to which a metal halide leaves an α-halo metal compound to produce a carbene is a problem with all α-eliminations: see G. L. Closs and L. E Closs, *J. Am. Chem. Soc.*, **85**, 99 (1963).

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The Quadricyclic Carbonium Ion. Solvolysis of 7-Quadricyclo[2.2.1.$0^{2,6}$.$0^{3,5}$]heptane Derivatives

Sir:

Because of their relation to the 7-norbornadienyl system[1] we have examined carbonium ion-forming reactions of 7-quadricyclo[2.2.1.$0^{2,6}$.$0^{3,5}$]heptane derivatives (I).[2] Confirming the recent report by Richey and Buckley[3] we find that these molecules are remarkably reactive compared to their 7-norbornyl analogs (II). This dramatic rate enhancement naturally raises the question of how best to represent charge delocalization in the intermediate carbonium ion. We have attempted to prepare the fluoroborate of I in sulfur dioxide as we did from the diene chloride (IIIb)[1] but the n.m.r. spectrum, which appeared to be that of a mixture, was too complex to be of value.

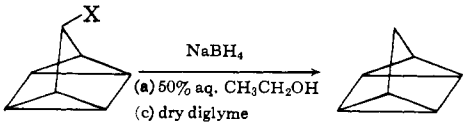
Subsequently, we solvolyzed the quadricyclic chloride (Ia) in 50% aqueous ethanol at 50° containing an excess of sodium borohydride to trap the intermediate carbonium ion according to Brown's procedure.[4]

(1) P. R. Story and M. Saunders, *J. Am. Chem. Soc.*, **84**, 4876 (1962): P. R. Story, L. C. Snyder, D. C. Douglass, E. W. Anderson, and R. L. Kornegay, *ibid.*, **85**, 3650 (1963).

(2) The quadricyclic compounds (I) were prepared by photolysis of the appropriate diene (III) (ref. 1) according to Hammond's procedure (ref. 6). Structures were established by n.m.r. analysis and by thermal conversion (170°) to the corresponding diene isomer (III). Satisfactory analyses were obtained for all new compounds.

(3) H. G. Richey, Jr., and N. C. Buckley, *J. Am. Chem. Soc.*, **85**, 3057 (1963).

Careful analysis of the hydrocarbon fraction of the product by v.p.c. revealed only quadricyclene (Ib)[5,6] and a trace (<1%) of an unknown material. Even



Ia, c Ib

Ia, X = Cl
b, X = H
c, X = OBs
d, X = OH
e, X = OCH_2CH_3

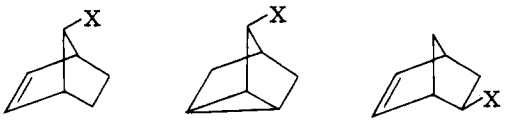
more remarkably, reaction of the *p*-bromobenzenesulfonate (Ic) with sodium borohydride in dry diglyme[7] at 40° produced only quadricyclene (Ib) along with a trace (<1%) of material with the same retention time as norbornadiene.

Solvolysis of quadricyclic chloride (Ia) in 50% aqueous ethanol at 46.3° gave a first-order rate constant of 1.03×10^{-5} sec.$^{-1}$. Comparison with *anti*-7-norbornenyl chloride (IVa)[8] reveals that Ia is less reactive by a factor of only 100. While it is not possible to make a direct comparison with the corresponding saturated chloride (IIa),[8] the tosylate (IVb) is reported to be *ca.* 10^{11} times more reactive than IIb.[9] Consequently, Ia is probably about 10^8–10^9 more reactive than 7-norbornyl chloride (IIa). These relative rate factors are in good agreement with those reported by Richey and Buckley.[3] Interestingly, Ia is only *ca.* one-tenth as reactive as cyclopropylcarbinyl chloride under the same conditions.[10]

If Ia is solvolyzed in 50% aqueous ethanol containing a slight excess of sodium bicarbonate at 50°, the principal products are quadricyclic (Id,e) and account for 75% of the total yield (80–90%). However, under these conditions 18% of the product consists

II
IIa, X = Cl
b, X = OTs

III
IIIa, X = H
b, X = Cl
c, X = OAc
d, X = OH
e, X = OCH_2CH_3



IV
IVa, X = Cl
b, X = OTs

V
Va, X = Cl
b, X = OBs

VI
VIa, X = Cl
b, X = OTs

of dienes (IIId,e).[11] Two unidentified materials accounted for 7% of the product. One of these (*ca.* 3%) was highly unstable and visibly diminished with time. The diene isomer (III) is clearly of lower energy than

(4) H. C. Brown and H. M. Bell, *J. Org. Chem.*, **27**, 1928 (1962): *J. Am. Chem. Soc.*, **85**, 2324 (1963).

(5) W. G. Dauben and R. L. Cargill, *Tetrahedron*, **15**, 197 (1961).

(6) G. S. Hammond, N. J. Turro and A. Fischer, *J. Am. Chem. Soc.*, **83**, 4674 (1961).

(7) S. Winstein, A. H. Lewin, and K. C. Pande, *ibid.*, **85**, 2324 (1963).

(8) W. G. Woods, R. A. Carboni, and J. D. Roberts, *ibid.*, **78**, 5653 (1956).

(9) S. Winstein, M. Shatavsky, C. Norton, and R. B. Woodward, *ibid.*, **77**, 4183 (1955).

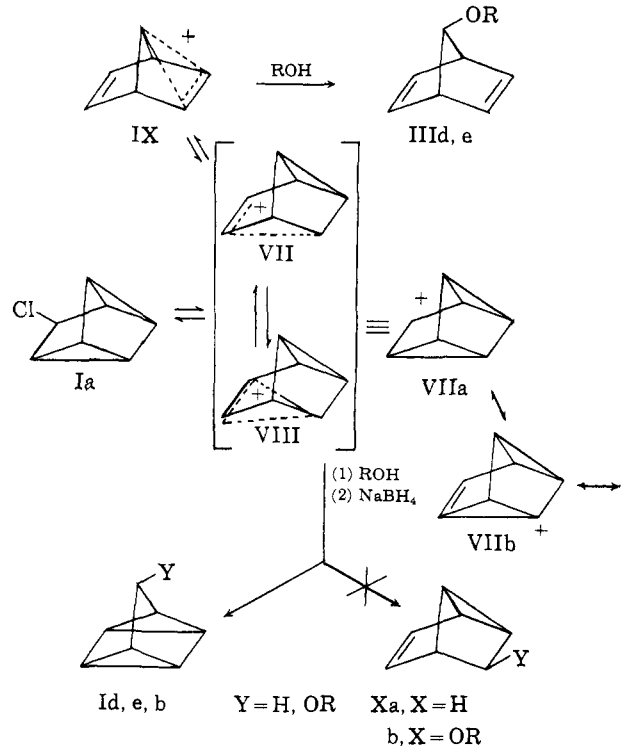
(10) E. F. Cox, M. C. Caserio, M. S. Silver, and J. D. Roberts, *ibid.*, **83**, 2719 (1961)

(11) The mal reversion of Ia to IIIb is only 50% complete at 170° after 5 hr. in carbon tetrachloride solution. Thermal reversion is negligible below 100°.

the quadricyclic (I) since Ib is converted essentially completely to norbornadiene (IIIa) at 200°.[5,6] Furthermore, we find that quadricyclic derivatives (Ia,d,e) are converted rapidly and completely to their corresponding diene isomers (III) in dilute acid. Solvolysis of Ia in 50% aqueous ethanol without sodium bicarbonate yields only dienes (IIId and IIIe, 41%) and what appear to be acid-catalyzed solvent addition products (55%).

Quite obviously, solvolysis of quadricyclic chloride (Ia) and diene chloride[1,12] does not lead to a common carbonium ion intermediate. In like manner V and VI do not solvolyze to a common carbonium ion intermediate.[13a] We suggest that by analogy to the tricyclic system (V)[13] charge delocalization in the 7-quadricyclic carbonium ion could well be represented by the symmetrical homoallylic ion (VII) and/or by the unsymmetrical bicyclobutonium ion (VIII). These intermediate ions could easily leak over to the diene ion (IX) to give the observed diene products (IIId,e). Under no circumstances, however, have we been able to observe the expected tricyclic olefin (X). Even sodium borohydride reduction of Ia failed to produce any of the known Xa[14] which could have been detected in the hydrocarbon product in concentrations as low as 0.5%. It becomes necessary to argue, then, that resonance structure VIIb does not assume sufficient importance to cause accumulation of X as does the corresponding structure in the solvolysis of V.[13] The absence of X does not appear to be simply a matter of ground state energies since Xa is formed from IIIb and appears to be unstable relative to both Ib and IIIa.

This interpretation of charge delocalization in I would explain the comparable reactivity of I and V and why the effect of the cyclopropyl groups is not linearly additive as noted by Richey and Buckley.[3] This situation is highly reminiscent of the epimeric diene carbonium ions investigated by DePuy,[15] which



were not interconvertible, nor was the effect of the double bonds additive. Consequently, by analogy to the 7-norbornadienyl carbonium ion[1,12] and to DePuy's system[15] it is perhaps not too surprising that the effect of the cyclopropyl groups is not additive. The quadricyclic system seems to offer another example of what we call "charge delocalization priority."

(12) S. Winstein and C. Ordronneau, *J. Am. Chem. Soc.*, **82**, 2084 (1960).
(13) (a) S. Winstein and E. M. Kosower, *ibid.*, **81**, 4399 (1959); (b) S. Winstein, H. M. Walborsky, and K. Schreiber, *ibid.*, **72**, 5795 (1950).
(14) P. R. Story, *ibid.*, **83**, 3347 (1961).
(15) C. H. DePuy, I. A. Ogawa, and J. C. McDaniels, *ibid.*, **82**, 2398 (1960).

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BOOK REVIEWS

Biochemical Frontiers in Medicine. HARRIS BUSCH, Ed., M.D., Ph.D., Professor of Pharmacology, Chairman, Dept. of Pharmacology, Baylor College of Medicine, Houston, Texas. Medical Book Department, Little, Brown and Co., Boston 6, Mass. 1963. 16 × 24 cm. 364 pp. Price, $12.50.

At a time when knowledge in biochemistry is accumulating at so rapid a rate, the need for books that integrate the relationship of advances in biochemistry with medicine is great indeed. To accomplish this end, a book is needed which assists in the understanding of biochemical fundamentals and their pertinence to medicine rather than the collection of biochemical facts. In spite of its promising name, "Biochemical Frontiers in Medicine," edited by Harris Busch, fails to achieve this objective. It fails to communicate both the significant nature and the excitement of these frontiers to its medical audience. Thus it falls back to become just another catalog of biochemical phenomena in medicine, of which there is now quite a number.

In eight chapters by five authors, this book deals with selected topics in the biochemistry of genetics, metabolic diseases, cancer, chemotherapy, diagnostic methods, and pathology. As might be expected from a book by multiple authors, homogeneity is lacking and there is variation in style and quality. The chapter by O. Bodansky is superior and provides good reading. The biochemical bases of laboratory tests which aid the diagnosis and management of pheochromocytoma, carcinoid, jaundice, and porphyria are summarized lucidly and succinctly.

In the chapter entitled "Biochemical Pathology," E. Farber demonstrates the impact of recent advances in biochemistry and electron microscopy upon current thinking and trends in research in pathology. Two of the most basic cellular pathologic alterations, necrosis and the accumulation of lipids by cells, are discussed in terms of the biochemical and metabolic responses to injury and alterations in the ultrastructure of the cell.

The action of selected purine analogs as therapeutic agents for cancer is discussed by R. Parks in terms of their chemistry and mechanisms of action. A report on these antimetabolites which have met with clinical success seems both pertinent and timely at a period when the state of knowledge in organic and biochemistry has made the design of more effective antitumor agents both feasible and practical. The synthesis of penicillin, its mechanism of action, and the problem of drug resistance are also reviewed.

In two chapters, genetically determined disorders of carbohydrate, amino acid, and protein metabolism are described in routine fashion. Clinical manifestations of the diseases, laboratory findings, metabolic defect, genetics of transmission, treatment, and prognosis are outlined.

The chapter on the biochemical basis of genetic aberrations discusses chromosomal structure, the chemistry of DNA and