olefins.[10] The production of both *cis*- and *trans*-$C_2H_2D_2$ in our experiments indicates that isomerically pure olefins are not obtained with the isomerically pure vicinal diboron compound. The reductive cleavage, or alkaline hydrolysis,[3] thus appears to be better suited to elucidation of stereochemistry in this type of organoboron derivative.

It is of interest to note the rather surprising similarity in the proton–proton spin-coupling constants for the *cis* and *trans* isomers of 1,2-bis(dichloroboryl)ethylene (17.5 and 19.6 Hz, respectively). The magnitudes of vicinal H–H couplings have been widely used to assess the stereochemistry of olefinic derivatives, on the premise that *cis* and *trans* proton–proton couplings have distinct and characteristic values (6 to 14 Hz and 11 to 18 Hz, respectively).[11] Exceptions to this generalization are known, particularly in vinyl derivatives of relatively electropositive elements.[12] The present results emphasize the need for caution in basing structural assignments on this criterion.

Acknowledgments. We thank Dr. R. B. Johannesen for obtaining the double resonance spectra and Dr. F. E. Brinckman for helpful discussions during the course of this work.

(10) M. F. Lappert and B. Prokai, *J. Organometal. Chem.* (Amsterdam), 1, 384 (1964)

(11) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," International Series of Monographs on Organic Chemistry, Vol. 5, Pergamon Press, New York, N. Y., 1959, p 85.

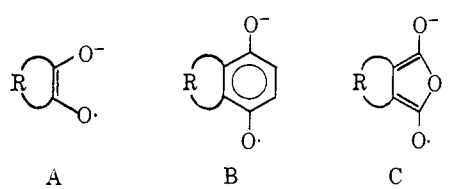
(12) T. Schaefer, *Can. J. Chem.*, 40, 1 (1962).

T. D. Coyle, J. J. Ritter
Inorganic Chemistry Section, National Bureau of Standards
Washington, D. C. 20234
Received August 18, 1967

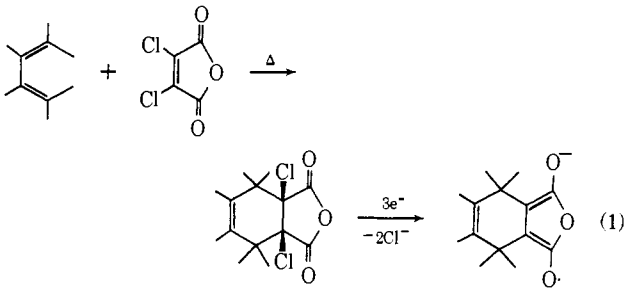
The Maleic Anhydride Radical Anion Grouping. A Useful Spin Label

Sir:

Studies of the effect of stereochemistry upon long-range splittings in esr spectra have been carried out using the semidione[1] (A) and semiquinone[2] (B) groups to introduce spin to the hydrocarbon group.[3] We wish to report studies using a third spin label group, maleic anhydride anion (C, which we shall call the "semifuraquinone" group). This group is particularly convenient to introduce into the rigid bicyclic systems which yield the most information. Reduction of vicintual dihalogenated compounds is well known to lead to elimination to form olefins. We have used this fact to generate semifuraquinones for esr studies[4] by *intra muros* reduction of Diels–Alder adducts of dichloromaleic anhydride[5] (eq 1). An alternate path is to carry out a one-electron reduction of the substituted maleic anhydride, prepared by using dimethyl acetyldicarboxylate as the dienophile, hydrolyzing the ester groups, and dehydrating with acetic anhydride.[6] The nonconjugated double bond of either adduct is catalytically reduced without dehalogenating or saturating the conjugated double bond.[7]



A B C



(1)

Splittings for semifuraquinones from adducts of butadiene[8] (**1C**), cyclohexadiene[9] (**2C**), the saturated cyclohexadiene adduct[10] (**3C**), cyclopentadiene[11] (**4C**), and the saturated cyclopentadiene adduct[12] (**5C**) are compared with values for the other spin labels in Table I. From the 7.0-gauss methyl splitting of *cis*-dimethylsemidione,[13] ρ_α (the π spin density at the carbons to which the alkyl groups are attached) is about 0.30 (using a reasonable $|Q_{CH_3}{}^H|$ of 23 gauss). For 2,3-dimethylbenzosemiquinone, the methyl splitting of 1.714 gauss[14] yields a ρ_α of 0.075. The β splittings of **1C** give ρ_α of about 0.19 (taking the average dihedral angle as 30°, then $|Q_\beta{}^H| \approx 1.5|Q_{CH_3}{}^H|$[15]). Assuming the H_a splitting in **2** and **3** to be directly proportional to ρ_α, and using the ρ_α values derived above for the semidiones and semiquinones, ρ_α values for **2C** and **3C** are interpolated to be 0.187 and 0.203 from the H_a splittings. This shows that the H_a splittings in **2** and **3** are essentially proportional to ρ_α.

The 0.2-gauss H_γ splitting of **1C** shows that detectable spin density reaches a γ-vinyl group even without β

(1) (a) G. A. Russell and K-Y. Chang, *J. Am. Chem. Soc.*, 87, 4381 (1965); (b) G. A. Russell, G. Holland, and K-Y. Chang, *Tetrahedron Letters*, 1955 (1967); (c) G. A. Russell, G. Holland, and K-Y. Chang, *J. Am. Chem. Soc.*, in press.

(2) (a) D. Kosman and L. M. Stock, *ibid.*, 88, 843 (1966); (b) D. Kosman and L. M. Stock, *Tetrahedron Letters*, 1511 (1967).

(3) The high degree of σ character of the spin-carrying nitrogen orbital of iminoxy radicals makes spin delocalization in these radicals a considerably different problem. See R. O. C. Norman and B. C. Gilbert, *J. Phys. Chem.*, 71, 14 (1967), for long-range splittings in these systems.

(4) Reductions were carried out at room temperature in the Varian flat quartz cell; splittings were determined using a Varian V-4502 spectrometer and benzoquinone anion as calibration standard (a_H = 2.42 in DMSO: J. Gendell, J. H. Freed, and G. K. Fraenkel, *J. Chem. Phys.*, 37, 2832 (1962)).

(5) Dichloromaleic anhydride adducts of cyclopentadiene and some methylated butadienes are reported by A. M. Clifford and C. E. Glaim, U. S. Patent 2,391,276 (1945) (*Chem. Abstr.*, 40, 3136 (1946)).

(6) O. Diels and K. Alder, *Ann.*, 479, 236 (1931).

(7) For dibromomaleic anhydride adduct reductions see O. Diels and K. Alder, *ibid.*, 478, 137 (1930).

(8) Generated by reduction of 3,6-dihydrophthalic anhydride prepared by the method of N. P. Sopov and V. S. Miklashevskaya, *J. Gen. Chem. USSR*, 26, 2133 (1956).

(9) Generated by reduction of the dichloromaleic anhydride adduct (mp 241–243°) prepared by refluxing the components in toluene.

(10) Generated by reduction of the saturated dichloromaleic anhydride derivative (mp 210–220° dec).

(11) Generated both from the dichloromaleic anhydride adduct of cyclopentadiene (mp 193–194°, lit.[5] 188–189°) and from the maleic anhydride derivative, prepared by treatment of the acid[6] with acetic anhydride (mp 145–147°). The esr spectra were identical.

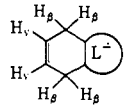
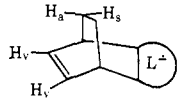
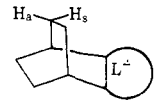
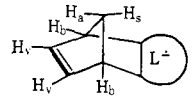
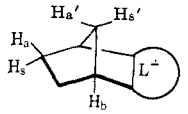
(12) From the maleic anhydride derivative, prepared by treatment of the acid[6] with acetic anhydride (mp 95–97°; lit.[6] 98–99°).

(13) G. A. Russell, E. T. Strom, E. R. Talaty, and S. A. Weiner, *J. Am. Chem. Soc.*, 88, 1998 (1966).

(14) S. B. Venkatranen, B. G. Segal, and G. K. Fraenkel, *J. Chem. Phys.*, 30, 1006 (1959).

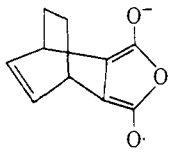
(15) For a recent discussion see T. M. McKinney and D. H. Geske, *J. Am. Chem. Soc.*, 89, 2806 (1967).

Table I. Splitting Constants (gauss) for Some Radicals Showing Long-Range Splittings[a]

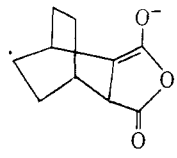
Compd	Radical	Assignment	Semifuraquinone (C)	Semidione (A)	Semiquinone (B)
1		H_β H_v	6.56 (4 H) 0.20 (2 H)		
2		H_a H_v H_s	1.55 (2 H) 1.18 (2 H) 0·33 (2 H)	2.60 (2 H)[1b] {0.41 (4 H)	{0.49 (4 H)[1c]; 0.54 (4 H)[2b] 0.18 (2 H); 0.125 (2 H)
3		H_a H_s	1.36 (4 H) 0.27 (2 H)	2.09 (4 H)[1a] Unresolved	0.40 (4 H);[1c] 0.45 (4 H)[2b] 0.09 (4 H); unresolved
4		H_a H_v, H_s H_b	1.41 (1 H) 0.79 (3 H) 0.40 [2 H)		0.80 (1 H)[b, 2a] 0.40 (3 H) Unresolved
5		H_a H_a H_b H_s H_s'	1.03 (1 H) 2.04 (2 H) {0.37 (2 H) {0.27 (2 H) 0.47 (1 H)	6.54 (1 H)[1a] {2.43 (4 H) Unresolved 0.41 (1 H)	{0.66 (3 H)[b] Unresolved Unresolved Unresolved

[a] Semifuraquinones in DMSO–0.05 *M* Bu_4NClO_4, electrolytic;[4] semiquinones and semidiones in DMSO containing KO-*t*-Bu except examples from ref 2b which are in acetonitrile. [b] S. F. Nelsen and B. M. Trost, *Tetrahedron Letters*, **46**, 5737 (1966).

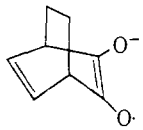
bridging to force it toward the α-carbons. A two-carbon bridge allows more effective spin delocalization than a one-carbon bridge, although the α- and γ-carbons should be slightly closer in the latter case. Table I demonstrates that the H_v splitting is *not* directly proportional to ρ_α, since the H_v splitting of the semidione **2A** is relatively much smaller than the ρ_α value would predict. This is not consistent with spin reaching the vinyl π system by simple physical overlap of the label and vinyl π systems. It is consistent with a rapid equilibrium between open and closed forms[2] as **2C** and **2C′** (or resonance between these forms). The corresponding closed form of the semidione (**2A′**) should be relatively less favorable because of greater electron localization in it.



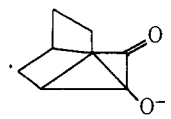
2C



2C′



2A



2A′

The size of the H_s splittings is also not proportional to ρ_α; here again the semidiones have "too small" splittings (**3A**, **5A**). The labeled bicycloheptane systems **5A** and **5C** (Figure 1) show remarkably different splittings[16] (resolution is so poor for **5B** that these data are almost useless); the huge H_a' splittings and remarkably large bridgehead splittings of **5A** are simply

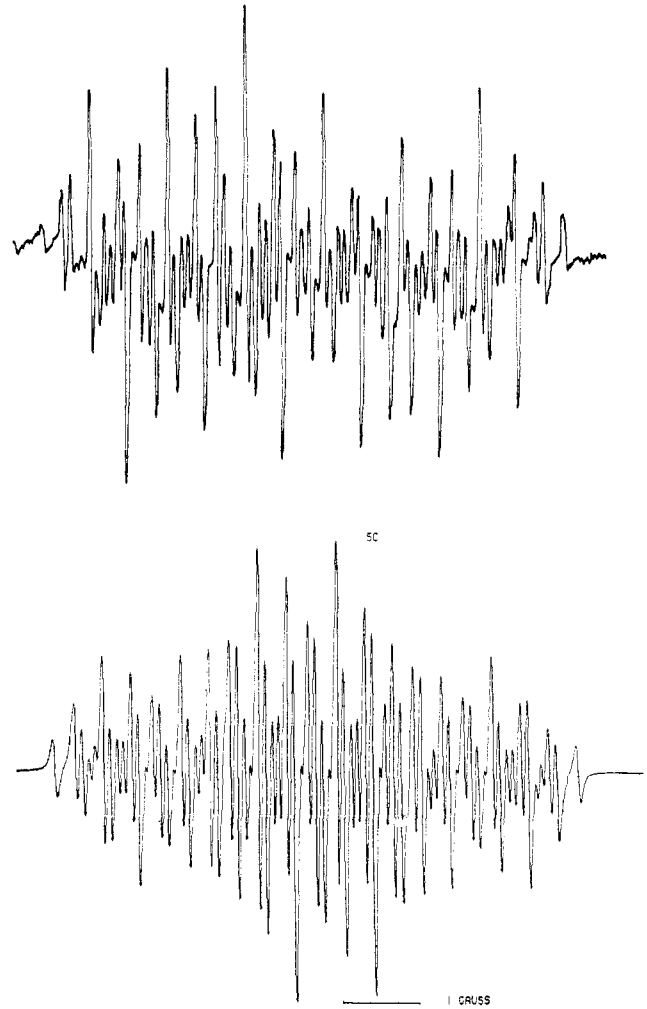


Figure 1. The esr spectrum of **5C** and a simulation (below) using the splittings of Table I and a 0.05-gauss line width with Lorenzian line shape.

(16) Obviously we have not *proven* that **5C** (or any radical anion mentioned in this article) has the structure proposed. Until a sufficient number of such systems have been investigated, it is not possible to say what results for long-range splittings are "anomalous." 2,3-Norbornadione does give the spectrum reported by Russell[1a] under electrolytic conditions.

not found for **5C**. Obviously other factors than ρ_α influence these splittings. Even the presumably small geometrical changes caused by lengthening of the C_α–C_α' distance in going from A to C spin labels may be of great importance in determining the size of splittings.

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Stephen F. Nelsen, Errol D. Seppanen
Department of Chemistry, University of Wisconsin
Madison, Wisconsin 53706
Received August 1, 1967

Book Reviews

The Amino Sugars. The Chemistry and Biology of Compounds Containing Amino Sugars. Volume IIB. Metabolism and Interactions. Edited by ENDRE A. BALAZS, Institute of Biological and Medical Sciences, Retina Foundation and Harvard Medical School, Boston, Mass., and ROGER W. JEANLOZ, Harvard Medical School and Massachusetts General Hospital, Boston, Mass. Academic Press Inc., 111 Fifth Ave., New York, N. Y. 1966. xviii + 516 pp. 16.5 × 23 cm. $22.00.

Volume IIB of this four-volume treatise deals with the metabolism of some amino-sugar-containing molecules. It follows directly on the preceding volume which was concerned with the distribution of these compounds in a wide variety of biological forms. Volume IIB also deals with interactions of amino-sugar-containing molecules with cells and viruses.

As stated in the editors' preface to this treatise it was felt that "a summary of the present knowledge, with a comprehensive review of the literature, prepared by scientists currently working in this field, would provide a starting point for the newcomer to the field and would also serve the expert in the broadening of his interest." The editors set out to fulfill two purposes in the preparation of this major treatise on the amino sugars. These were (1) to survey the chemistry, physical chemistry, and biochemistry of all naturally occurring and synthetically prepared amino-sugar-containing molecules, and (2) to present a critical and interpretative account of the biological and medical importance of these molecules.

Volume IIB of the treatise was designed to consider a review of the metabolism of the amino sugars and the amino-sugar moieties of macromolecules, and to review the interaction of amino sugars, glycosaminoglycans, glycoproteins, and glycolipids with different macromolecules, and finally with viruses, cells, and whole organisms. The fact that these goals were established by the editors at once presented the difficult job of selecting the areas to be covered in this volume.

Since many amino-sugar-containing macromolecules are intimately involved in a score of biological processes the choice of material to be reviewed in this volume naturally has led to the exclusion of several topics which understandably would make the volume unwieldy in size. It is regrettable, however, that such limitations have led as one example to a cursory review of the interactions of glycoproteins and the role of heparin in the prevention of blood coagulation. The editors chose this solution to their problem rather than enlarge the treatise, hoping that the specialized areas dealing with the biological and pharmacological aspects of this type of interaction could be followed more intensively by a interested reader in other sources.

The volume includes 14 chapters, each one of which is reviewed by a specialist in the area under discussion. The first of these is a survey of the metabolism of amino sugars. The observation made by Ledderhose in 1878 of a nitrogenous reducing substance in chitin was the starting point for studies on this widely diversified group of biological compounds. Among the wide range of aspects covered in this chapter are the many studies concerned with the origin of the C skeleton, by utilizing in recent years ^{14}C-labeled glucose. The origin of the amino group has been followed with ^{15}N-labeled compounds, and it is shown from many of these studies that glutamine plays a contributing role in the synthesis of hexosamine, and presumably many amino-sugar-containing compounds. Much of this introductory chapter deals with detailed pathways which have been uncovered in recent years. Much emphasis is placed on the role of UTP-activated systems leading to the synthesis of the cell wall structure of bacteria. The concluding half of the chapter concerns degradative pathways leading to the further utilization of the constituent sugars and N.

The second chapter of this volume (No. 39 of the treatise) is a detailed discussion of the metabolism of glycosaminoglycans. The authors show that most studies of this field have depended within recent years on the utilization of isotopes of carbon, sulfur, and hydrogen. This chapter follows very logically after the previous chapter in which the work of Leloir on uridine coenzymes was enlarged on in the synthesis of saccharides. The UDP-N-acetylglucosamine, and UDP-D-glucuronic acid were shown in that chapter to be precursors for the glycosaminoglycans.

Further evidence for this comes from the observation that the uridine nucleotide sugars are included in the biosynthesis of chitin, cellulose, and other polysaccharides. In this chapter more details are included for the varied metabolic paths leading to formation of the glycosaminoglycans, and to their catabolism.

The next chapter is a review of glycoproteins, glycopeptides, and glycolipids. Among the topics covered are effects of steroids on the glycosaminoglycans of connective tissue. One of the interesting aspects of this survey is a review of the so-called "sexual skin" of several primates, notably that of the baboon and mandrill. The presence of glucosamine and glucuronic acid has been shown in the exudates of this special connective tissue. Some detailed studies are included of the tissue glycosaminoglycans, which are shown to be connected to proteins. It is shown, for example, that during swelling of this sexual skin, as also in the rooster comb, there is a correlation between water content and glycosaminoglycans, mainly of hyaluronic acid. Three short chapters on hexosaminidases, neuraminidases, and enzymes degrading glycosaminoglycans include pertinent studies on these enzymes. The sulfatases of glycosaminoglycans are covered in a brief chapter. The activation and inhibition of enzymes by polyanions which contain amino sugars are discussed in a short chapter followed by one very good chapter on chemical and physical changes brought about in glycoproteins by radiation and oxidation–reduction systems.

After a very brief treatment of the blood-group substances, the subject of immunochemistry is covered. This chapter in the opinion of the reviewer is the most valuable one in this volume as it gives a very comprehensive coverage of many aspects of this topic which are difficult to find individually in the literature. There is a very good but short review of the blood-group substances.

The concluding chapters are concerned with the interaction of glycoproteins and viruses, cells, and tissues, this being perhaps the most interesting aspect of the metabolism of the amino-sugar compounds. The growth-promoting and regulating nature of these compounds is documented in detail.

The volume concludes with a very well-annotated bibliography and comprehensive index. The size of the volume (516 pp) is remarkable considering the tremendous survey encountered between its covers. As a reference work it is unexcelled for those working in the field of amino sugars. It will remain as such for a long time to come, with appropriate revisions being made to update the volume. It is unlikely that this volume will serve a useful purpose for a newcomer to the field as it covers such a wide diffuse area. Certain chapters are excellent, however, notably the one on immunochemistry.

The book is well produced and the editors are to be congratulated in providing a useful contribution to the biochemical literature.

E. R. M. Kay
Department of Biochemistry, University of Toronto
Toronto 5, Ontario