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Evidence for the Reactive Spin State of 1,4-Dehydrobenzenes

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Abstract: Two approaches have been used to investigate the spin state(s) of 1,4-dehydrobenzenes produced in the solution thermolysis of diethynyl olefins. One method relies on the "spin correlation effect" which postulates a relationship between the spin state of a caged radical pair and the ratio of cage and escape reactions (C/E) which may occur in the pair. When the 2,3-di-*n*-propyl-1,4-dehydrobenzene biradical (**4**) abstracts hydrogen from 1,4-cyclohexadiene, a radical pair is generated. If a mixture of 1,4-cyclohexadiene-d_0 and -d_4 is employed, it is possible, by performing a VPC–MS analysis, to determined the C/E ratio leading from the radical pair to the reduced product, *o*-dipropylbenzene (**10**). When this method was applied to the reaction of (*Z*)-4,5-diethynyl-4-octene (**3**), C/E was found to be 0.6, independent of the concentration of 1,4-cyclohexadiene (between 0.1 and 10 M) in the chlorobenzene reaction solution. This result indicates the presence of the singlet state of **4** in the reaction of **3**. Additional support for this analysis came from the reaction of 3,4-dimethyl-1,5-hexadiyn-3-ene (**11**) in hexachloroacetone solvent in a ^{1}H NMR probe. The single polarized signal (emission) observed is attributed to the major product of the reaction, 1,4-dichloro-2,3-dimethylbenzene (**12**), obtained by chlorine abstraction from the solvent. The interpretation of this result indicates solvent trapping of the singlet state of the intermediate 2,3-dimethyl-1,4-dehydrobenzene, consistent with the chemical trapping study. These experimental approaches indicate that at least a substantial portion of the products formed from 1,4-dehydrobenzenes at elevated temperatures arise from the singlet state of the biradical. This suggests that either the singlet is the ground state or, if the triplet is lower in energy, the rate of intersystem crossing from the singlet must be $\leq 10^9$ s^{-1} at 200 °C.

In spite of the efforts of numerous investigators to generate and study the chemistry of 1,4-dehydrobenzene (**1**),[1,2] the spin states populated under the reaction conditions have yet to be characterized. This is a particularly intriguing problem because the singlet and triplet states are presumed to be close in energy and because of the failure of theoretical treatments to reach a consensus in predicting the ground electronic state (Table I).[3-8]

Wilhite and Whitten[4] reported a detailed ab initio study in which three calculations were performed: a full SCF-MO treatment of both the singlet and triplet electronic states, a limited configuration interaction (CI) calculation, and a many-determinant CI treatment. The simplest calculation predicted that the energy of the triplet biradical lies well below that of the singlet. Inclusion of CI in the calculations, however, led to a much smaller predicted difference in the singlet and triplet biradical energies. The smallest energy difference was predicted in the full CI calculation which placed the triplet state 3.5 kcal/mol below the singlet. In these calculations, the geometry of 1,4-dehydrobenzene was somewhat arbitrarily taken to be that of benzene. Wilhite and Whitten were careful to point out that, given the small singlet–triplet energy difference found, a calculation performed at the equilibrium geometry might lead to an inverted ordering of the electronic states. Because the geometry was fixed in their treatment, no prediction was made concerning the relative positions on the energy surface of the biradical structure **1a** and its bicyclic isomer butalene **1b** (which would be expected to have a much shorter 1,4 distance than benzene).

1a **1b**

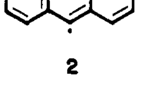

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Table I. Calculated Energies of 1,4-Dehydrobenzene Structures

	relative energy of structures, kcal/mol		
	1		**2**
	triplet	singlet	singlet
Wilhite and Whitten (1971)[4] SCF–MO–CI	0	+3.45	
Dewar et al. (1974)[5] MINDO/3 (lim/CI)	+5	0 ($\Delta H_f = +117$ kcal/mol)	+36
Washburn et al. (1979)[8] ab initio 4-31G (no CI)	0	(+82)	+94
Mueller (1973)[7] modified MINDO/2 (no CI)	0	(+24)	+18
Noell and Newton (1979)[6] ab initio GVB (4-31G)	+1.4	0	(~77)

Dewar and Li[5] reported a MINDO/3 study in which geometry optimization was carried out for the singlet and triplet electronic states. The singlet biradical was predicted to be 6.2 kcal/mol more stable than the triplet. An investigation of the singlet surface led to the prediction that butalene lies in a relative energy minimum, 35.9 kcal/mol above the singlet biradical. The transannular bond in butalene was predicted to be 1.667 Å long.

A generalized valence bond (GVB) calculation of the 1,4-dehydrobenzene energy surface was recently reported by Noell and Newton.[6] These authors performed limited geometry optimization for the singlet and triplet states. They concluded that the lowest energy structure of 1,4-dehydrobenzene is the singlet biradical and that the bicyclic butalene structure lies in a local energy minimum very roughly estimated to be 77 kcal/mol higher. The triplet biradical was calculated to have an energy slightly above that of the singlet (1.4 kcal/mol), though the difference

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[1] For a review, see: (a) Levin, R. H. "Reactive Intermediates"; Jones, M.; Moss, R. A., Eds.; J Wiley: New York, **1978**, Vol. I. See also: (b) Bergman, R. G. *Acc. Chem. Res.* **1973**, *6*, 25. (c) Breslow, R.; Napierski, J.; Clarke, T. C. *J. Am. Chem. Soc.*, **1976**, *98*, 570.

[2] (a) Lockhart, T. P.; Mallon, C. B.; Bergman, R. G. *J. Am. Chem. Soc.*, **1980**, *102*, 5976. (b) Lockhart, T. P.; Comita, P. B.; Bergman, R. G., preceding paper in this issue.

[3] For early theoretical treatments see: (a) Gheorghiu, M. D.; Hoffman, R.; *Rev. Roum. Chim.* **1969**, *14*, 947. (b) Roberts, J. D.; Streitweiser, A.; Regan, C. M. *J. Am. Chem. Soc.* **1952**, *74*, 4579.

[4] Wilhite, D. L.; Whitten, J. L. *J. Am. Chem. Soc.* **1971**, *93*, 2858.

[5] Dewar, M. J. S.; Li, W.-K. *J. Am. Chem. Soc.* **1974**, *96*, 5569.

[6] Noell, J. O.; Newton, M. D. *J. Am. Chem. Soc.* **1979**, *101*, 51.

[7] Mueller, K., private communication.

[8] Washburn, W. N.; Zahler, R. *J. Am. Chem. Soc.* **1978**, *100*, 5873.

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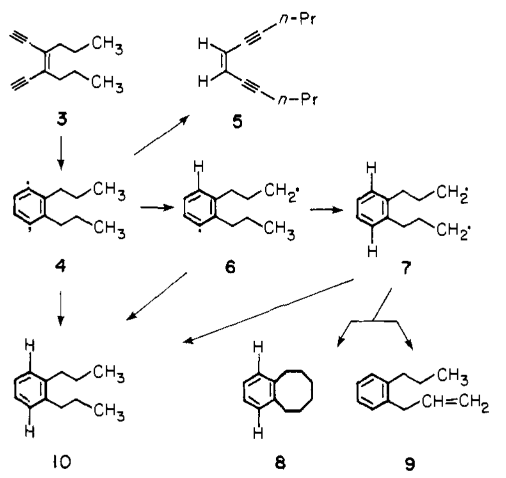
Scheme I



calculated for the two biradicals appears to be less than the uncertainty of the calculations.

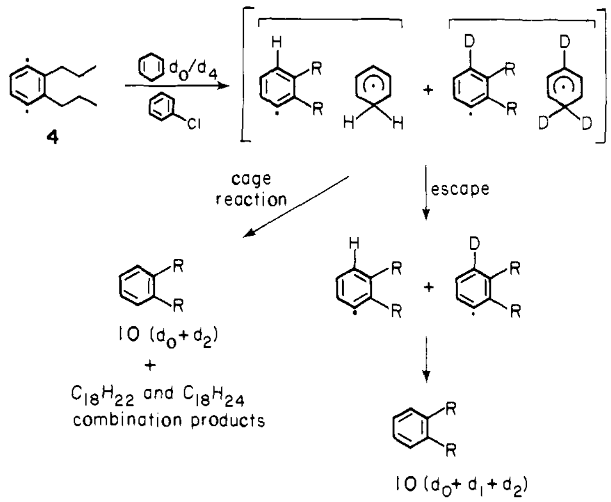
To date, the only reported experimental attempt to determine the spin state of a 1,4-dehydroaromatic is that of Chapman and co-workers,[9] who generated 9,10-dehydroanthracene (**2**) in a matrix at 8 K and searched, without success, for an ESR signal which would have indicated population of the triplet state. In this paper we detail our efforts to determine the number and description of the reactive spin states of the 1,4-dehydrobenzenes generated by the thermal reaction of diethynyl olefins at higher temperatures in solution. Our approach relies upon chemical trapping experiments, supported by chemically induced dynamic nuclear polarization (CIDNP) studies.

Results and Discussion

Chemical Trapping Studies. One approach to determining the spin states present in solution involved an attempt to distinguish between the chemical reactivity of the triplet and singlet states of 1,4-dehydrobenzene. We chose to work with diethynyl olefin **3** which generates 2,3-dipropyl-1,4-dehydrobenzene (**4**) in a well-characterized thermal reaction (Scheme I).[2] Because radical pairs are generated by abstraction reactions of **4**, the task reduces to finding a way to differentiate the reactivity of singlet and triplet radical pairs.[10] The spin correlation effect (SCE)[11] postulates that radical pair reactivity is related to the spin state of the crossing).[13] singlet radical pairs may undergo both cage[12] and escape reactions but a spin prohibition against cage reactions limits triplet pairs to cage escape (in the absence of intersystem crossing).[13] In order to detect the presence of singlet and triplet radical pairs generated by trapping of singlet and triplet **4**, we must distinguish between the cage and escape pathways leading to product formation; the magnitude of the ratio of cage/escape reactions should reflect the spin state of the radical pair generated from **4**.

Scheme II illustrates the cage and escape reactions that can occur in the radical pair generated by hydrogen transfer from 1,4-cyclohexadiene to biradical **4**. While the combination products (see ref 2b for possible structures of these materials) are unique to cage reaction,[15] **10** is produced both by cage disproportionation and cage escape; it is necessary, therefore, to determine the extent to which the cage and escape reaction pathways contribute to the yield of **10**. It is possible to perform this analysis if a mixture of 1,4-cyclohexadiene-d_0 and -d_4 is used in the reaction solution. Consider first the reaction of **4** with cyclohexadiene-d_0. The cage reactions which the radical pair (formed by hydrogen transfer to **4**) may undergo include transfer of a second hydrogen atom to give **10**-d_0 and combination to produce C_{18} products. Escape of the aryl radical from the solvent cage, followed by abstraction of hydrogen or deuterium from trapping agent, will give **10**-d_0 and -d_1 in the ratio 1:1 in the absence of a deuterium isotope effect. By a similar analysis, if **4** initially interacts with deuterated trapping agent, **10** formed by cage reactions will contain two deuteria while cage escape will lead to **10**-d_1 and -d_2 in the ratio 1:1. In summary, cage reaction will lead to only **10**-d_0 and -d_2 (1:1 ratio) and escape reactions of the radical pair should give **10**-d_0, -d_1, and -d_2 in the ratio 1:2:1. Because **10**-d_1 is unique to the cage escape reaction channel, it is possible to dissect the experimentally observed ratio of **10**-d_0, -d_1, and -d_2 (obtained by

Scheme II



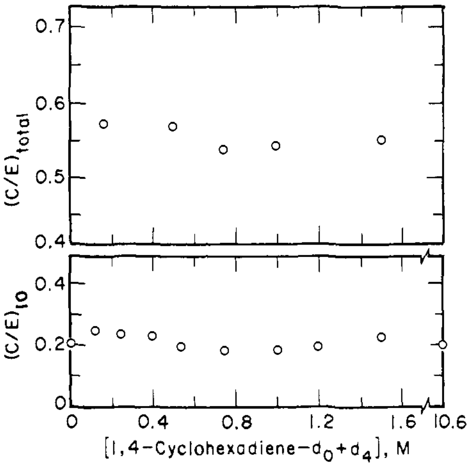


Figure 1. Ratio of cage to escape products (C/E) observed in the reaction of **3** (0.01 M, 195 °C) as a function of 1,4-cyclohexadiene concentration. Upper plot shows C/E for both **10** and C_{18} combination products. Lower plot shows C/E for product **10** alone.

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(9) Chapman, O. L.; Chang, C. C.; Kolc, J. *J. Am. Chem. Soc.* **1976**, *98*, 5703.

(10) The spin state of the radical pair should accurately reflect the spin state of the biradical. A similar approach has been employed in the study of the singlet and triplet carbenes; see: Roth, H. D. *Acc. Chem. Res.* **1977**, *10*, 85.

(11) (a) For a recent study see: Engel, P. S.; Bishop, D. J.; Page, M. A. *J. Am. Chem. Soc.* **1978**, *100*, 7009. (b) Perhaps the most convincing demonstration of a SCE is that of: Closs, G. L.; Trifunac, A. D. *J. Am. Chem. Soc.* **1969**, *91*, 4554. (c) For a less supportive discussion see: Koenig, T. In "Free Radicals"; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. I, Chapter 3.

(12) The term "cage reaction" as applied in this discussion is meant to denote bimolecular reactions which take place within the geminate radical pair, i.e., combination and disproportionation.

(13) Since the lifetime of solvent-caged radical pairs is ca. 10^{-10} and the rate of intersystem crossing is ca. 10^8 s^{-1},[14] triplet-singlet interconversion should have an insignificant effect on the product distribution.

(14) Kaptein, R. *Adv. Free-Radical Chem.* **1975**, *5*, 338.

(15) That $C_{18}H_{22}$ and $C_{18}H_{29}$ hydrocarbons are formed solely by cage combination is demonstrated by the observation that, when **3** was allowed to react in the presence of cyclohexadiene-d_0 and -d_4, these products contained only zero, two, and four deuteria/molecule. Random combination of aryl and cyclohexadienyl radicals would have led to appreciable formation of the d_1 and d_3 isomers.

mass spectroscopic analysis) into the relative contributions of the cage and escape pathways; when the yield of combination products is added to the yield of **10** produced by cage reaction, the ratio of cage to escape products (C/E) is obtained.

It is impossible to predict, a priori, the relative amounts of cage and escape reaction for a given singlet radical pair (the SCE postulates that C/E for a triplet pair is zero). For this reason an experimentally observed ratio of C/E by itself will provide limited quantitative information about the relative amounts of singlet and triplet **4** present in solution. The analysis is broadened, however, by consideration of the kinetic relationships in Scheme I. Conservation of spin (in the cyclization reaction) requires that biradical **4** is initially generated in the singlet state. *If* the triplet is the ground state or is thermally accessible, the ratio of trapping of the singlet biradical to intersystem crossing to triplet **4** will depend on the concentration of trapping agent in solution.[16] With low concentrations of cyclohexadiene intersystem crossing should be at its maximum value whereas a high concentration of the trapping agent will scavenge **4** more efficiently and the amount of intersystem crossing observed should be at a minimum.

Compound **3** (0.01 M) was allowed to react at 195 °C in a chlorobenzene solution which contained added cyclohexadiene (d_0:d_4 = 1:4) ranging in concentration from 0.01 to 10.6 M. The data obtained by combined VPC and VPC–MS analysis are plotted in Figure 1. The ratio C/E (0.55) did not vary, within experimental error, over the range 0.2–1.6 M cyclohexadiene. The ratio of C/E was experimentally difficult to determine for the entire product spectrum at low concentrations of cyclohexadiene;[17] the ratio of cage and escape reactions leading to product **10**, however, may be readily determined by VPC–MS analysis alone. As the lower plot in Figure 1 shows, the ratio C/E for product **10** (0.20) was independent of cyclohexadiene concentration from 0.01 to 10.6 M.

Unfortunately, there is some confusion in the literature about the quantitative values for C/E to be expected for singlet and triplet radical pairs; a good discussion of this problem (with specific application to azo compound decompositions) is given in a recent review by Engel.[18a] It now seems well accepted that radical pairs generated initially as triplets will have significantly lower C/E values than those generated as singlets (one exception to this appears to occur in photochemical α cleavage of ketones[18b]). However, the quantitative values vary somewhat. In azo compound decompositions low values ($\leq$ca. 0.1) seem to be generally found for triplet-sensitized decompositions and higher values (0.4–0.6) for singlets. One of the best models for our system is the reaction of singlet and triplet diphenylmethylene with toluene, since there, as in our case, the radical pairs are generated by hydrogen transfer. In that system C/E for the singlet is 0.3, and for the triplet it is zero.[11b] With the assumption that our system behaves similarly, the C/E value of 0.55 obtained in the 1,4-dehydrobenzene case suggests strongly that a significant portion (and possibly 100%) of the products formed from 1,4-dehydrobenzenes under our conditions arise from the singlet state of the biradical. It would be most useful to test this conclusion by generating triplet **4**. Unfortunately, attempts to induce several diethynylethylenes to cyclize upon photochemical activation have met with failure; cis–trans isomerization and polymerization are the only processes observed.

If the ground state of **4** is a triplet but intersystem crossing from the singlet is slow relative to unimolecular and bimolecular reaction, exclusive trapping of the singlet state will be observed at all concentrations of cyclohexadiene. One way to increase k_{isc} might be to perform the reaction in a brominated solvent; the presence of bromine either in a reacting substrate or in the solvent is known from excited-state chemistry to increase intersystem crossing rates (the heavy-atom effect).[19] When **3** was allowed to react in bromobenzene solution, the ratio of C/E was found again to be independent of cyclohexadiene concentration (Figure 2). As before, the large value of C/E (ca. 0.64) suggests the exclusive formation of the singlet radical pair. The ratio C/E for product **10** (0.20) was also independent, within experimental error, of the concentration of cyclohexadiene.

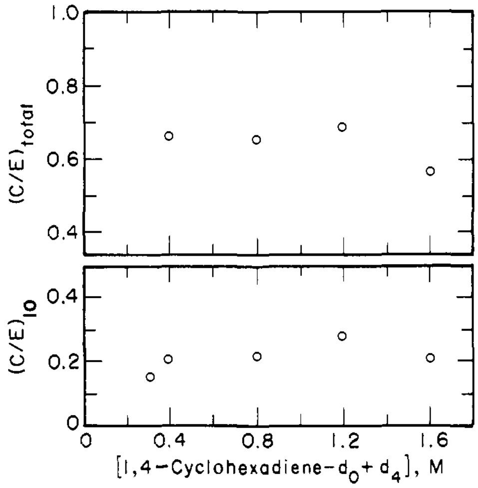

Figure 2. Ratio of cage to escape products (C/E) observed in the reaction of **3** (0.01 M, 195 °C) in bromobenzene solution as a function of added 1,4-cyclohexadiene. Upper plot shows C/E for **10** and C_{18} combination products. Lower plot shows C/E for product **10** alone.

In the accompanying study[2] it was shown that both **4** and **6** are trapped by 1,4-cyclohexadiene. Thus, in the spin state study described above two radical pairs were generated (from **4** to **6**) at low concentrations of cyclohexadiene and a single pair (from **4**) at high concentrations. However, **6** is presumed to be produced from **4** without a change in spin multiplicity, therefore the spin state analysis above may still be appropriate: this is strongly supported by the observation that the ratio C/E was independent of cyclohexadiene concentration even though the relative amounts of trapping of biradical **4** and **6** varied considerably.

There are several alternatives to the conclusions drawn from the chemical trapping data. First, although the ratio C/E was found to have a value (ca. 0.6) which strongly suggests the presence of singlet **4**, the same value would have been obtained if extremely rapid intersystem crossing produced an equilibrium ratio of singlet and triplet **4** at all concentrations of cyclohexadiene. If this were the case, the ratio C/E would reflect a component of both the singlet (C/E > 0.6) and triplet (C/E = ca. 0) radical pairs. Another way to explain the results is that k_{isc} and k_S[SH] are competitive, but k_T[SH] is very slow and fails to generate an appreciable amount of the triplet radical pair. It is difficult to imagine a factor that would lead to such an appreciable difference in the reactivity of singlet and triplet **4** toward cyclohexadiene. A final possibility, which cannot be ruled out, is that k_{isc} is too slow to produce an observable amount of triplet **4** under the reaction conditions, even it the triplet state is equal to or lower in energy than the singlet. Unfortunately, the lifetimes of 1,4-dehydrobenzene biradicals are limited by ring opening and other unimolecular reactions, even in the absence of bimolecular reaction channels. Generation of 1,4-dehydrobenzenes at lower temperature might favor intersystem crossing over other reaction pathways;[20] the rapid aromatization of cyclic diethynyl olefins at ambient temperature, observed by Masamune[21] and Sondheimer[22] and their co-workers, suggests one approach.

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(16) The ratio of cyclohexadiene-d_0 and -d_4 was held constant, but the total concentration of trapping agent was varied.

(17) At low concentrations of trapping agent, the yield of **10** plus combination products was very small. Because **10** overlaps slightly with unimolecular product **9** in the VPC trace, small amounts of **10** were difficult to accurately measure. Likewise, because they refer to several isomeric, long retention time products, VPC integration of $C_{18}H_{22}$ and $C_{18}H_{24}$ was not accurate when low yields were produced in the reaction.

(18) (a) Engel, P. S. *Chem. Rev.* **1980**, *80*, 99. (b) Lewis, F. D.; Magyar, J. G. *J. Am. Chem. Soc.* **1973**, *95*, 5973.

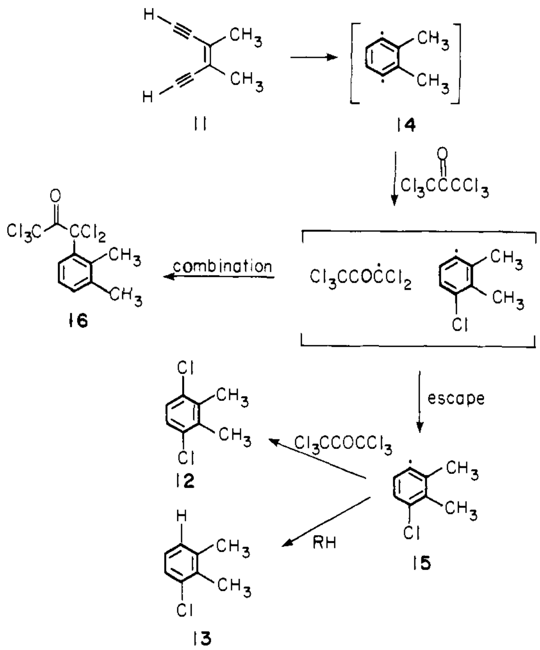
(19) Turro, N. J. In "Modern Molecular Photochemistry"; Benjamin/Cummings, Co.: Menlo Park, 1978; pp 191–193.

(20) Reference 19, pp 187–190.

(21) Darby, N.; Kim, C. U.; Salaun, J. A.; Shelton, K. W.; Takada, S.; Masamune, S.; *Chem. Commun.*, **1971**, 1516.

(22) Wong, H. N. C.; Sondheimer, F. *Tetrahedron Lett.* **1980**, 217.

Scheme III



CIDNP Experiments. We were interested in obtaining other, independent evidence for the spin state(s) produced upon thermal reaction of 1,2-diethynyl olefins. CIDNP appeared to be an especially promising technique, although we expected that attempts to observe CIDNP at the temperature required for the reactions reported here would present some technical difficulties. As previously reported,[2] when **3** was heated in the probe of a ^{1}H NMR spectrometer at 160 °C, emission was observed in signals due to the vinyl and terminal methyl and methylene protons of the alkyl side chains of **9**. The location of the protons in **9** which showed emission indicates that biradical **7** is the molecule in which the CIDNP effects arose. The following observations are inconsistent with S–T mixing and indicate instead an $S-T_-$ mixing mechanism.[23] (1) The protons α and β to the radical centers showed the same polarization; this indicates that the sign of the hyperfine interaction has no effect on the spectrum. (2) All of the polarized signals were emissive; normally, for polarizing radicals with a g value difference of zero, a mixture of enhanced absorption and emission (multiplet effect) is observed. The $S-T_-$ mechanism has been observed at high magnetic fields only in small biradicals (unpaired electrons separated by fewer than ca. 10 carbon atoms).[23,24] The interpretation of these effects is problematical and led us to search for other systems in which the CIDNP results would be more easily deciphered.

A more straightforward CIDNP analysis may be obtained by looking for polarization effects in the products of bimolecular reaction of the 1,4-dehydrobenzene biradical. This approach has been applied to the thermal reaction of 2,3-dimethylhexa-1,5-diyn-3-ene (**11**, Scheme III). When a solution of **11** in hexachloroacetone (0.1 M) was heated to 160 °C in the probe of a 90-MHz ^{1}H NMR spectrometer, the spectrum obtained showed an emission in the aromatic region (Figure 3). VPC analysis of the solution after reaction showed the formation of 1,4-dichloro-2,3-dimethylbenzene (**12**) and 1-chloro-2,3-dimethylbenzene (**13**) (relative yields, ca. 3:1). Only minor amounts of other products were detected by VPC. The emission observed during the thermal reaction of **11** is assigned tentatively to the aromatic protons of **12**. The broad proton absorption in the alkyl region of the solution after complete reaction (Figure 3, spectrum c) is attributed to polymerization products formed as a result of the relatively high concenctrations of **11** in the NMR experiment.

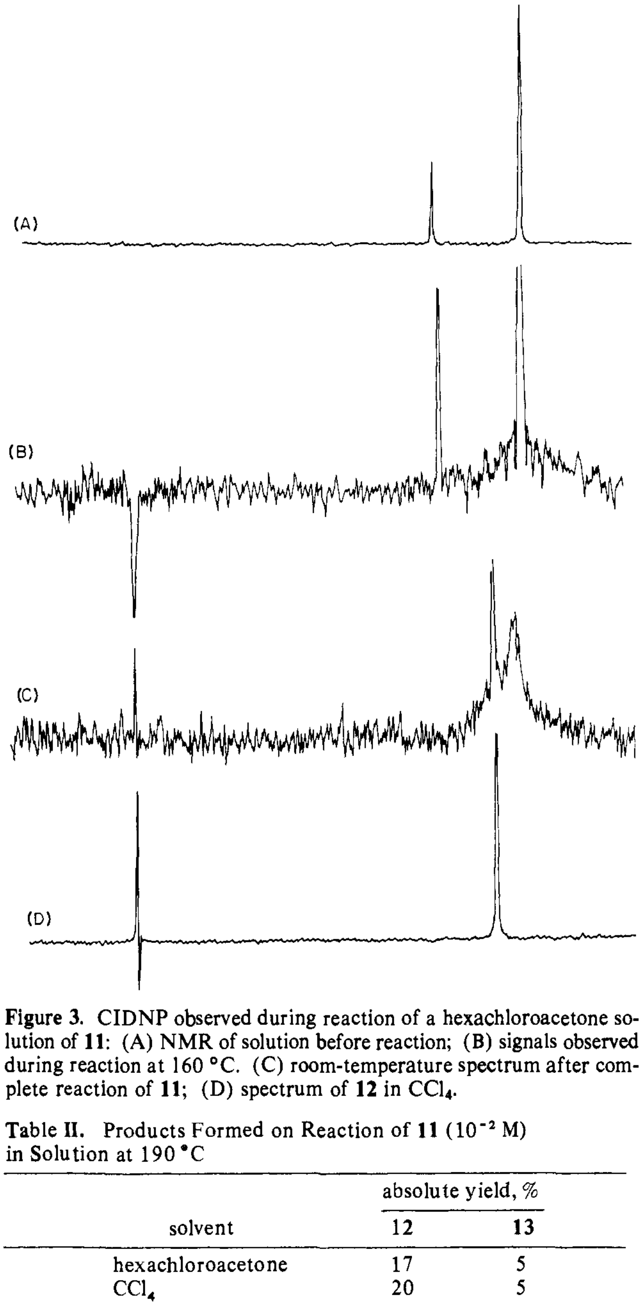


Figure 3. CIDNP observed during reaction of a hexachloroacetone solution of **11**: (A) NMR of solution before reaction; (B) signals observed during reaction at 160 °C. (C) room-temperature spectrum after complete reaction of **11**; (D) spectrum of **12** in CCl_4.

Table II. Products Formed on Reaction of **11** (10^{-2} M) in Solution at 190 °C

	absolute yield, %	
solvent	12	13
hexachloroacetone	17	5
CCl_4	20	5

Thermal reaction of dilute solutions of **11** (0.01 M) in hexachloroacetone and CCl_4 gave results (Table II) similar to the NMR experiment. Product **12** was isolated from a CCl_4 solution reaction by preparative VPC and characterized by IR, ^{1}H NMR, and HRMS.

The mechanism shown in Scheme III is proposed to explain the reaction of **11** in hexachloroacetone. By analogy to the thermal chemistry of **3**, cyclization of **11** gives the 2,3-dimethyl-1,4-dehydrobenzene biradical (**14**) which may abstract chlorine from solvent to produce a solvent-caged radical pair. Cage escape of the aryl radical (**15**) and abstraction of a second chlorine atom from the solvent give **12**. Hydrogen abstraction reactions of **14** and **15** lead to **13**. The pentachloroacetonyl radicals generated by loss of chlorine may attack **11**; this is presumed to be responsible for the modest yield of aromatic products. Cage reaction between **15** and the pentachloroacetonyl radical to give **12** (by transfer of a second chlorine atom) is considered unlikely for energetic reasons. Cage combinations of the paired radicals is a more likely reaction mode and may be presumed to occur to some extent; however, no evidence for formation of the high molecular weight

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[23] Closs, G. L. In "Chemically Induced Magnetic Polarization"; Muus, L. T., et al., Eds.; D. Reidel Publishing Co.: Boston, 1977; pp 225–257. See also Ref 14, pp 370–373.

[24] Kaptein, R.; van Leeuwen, P. W. N. M.; Huis, R.; *Chem. Phys. Lett.* **1976**, *41*, 264. Kaptein, R.; Frater-Schroeder, M.; Oosterhoff, L. J. *Ibid.* **1971**, *12*, 16.

combination product (**16**) was found by VPC–MS analysis.

The observed polarizations may be interpreted by application of Kaptein's rules[14] (eq 1). Because the aromatic signal appeared

$$\Gamma = \mu\epsilon\Delta g A_i \qquad (1)$$

in emission, the product of the four parameters must be negative. Assuming the escape product compound **12** to be the product responsible for the emission signal, we assign ϵ a negative value. The g value of **15** should be less than that of the pentachloroacetonyl radical (cf. g values of phenyl (2.0025) and dichloromethyl (2.0080))[25] so $\Delta g = (-)$. The hyperfine coupling constant in phenyl radicals is positive for the ortho, meta, and para hydrogens, so $A_i = (+)$.[26] The remaining parameter, μ, must be assigned a value which makes the product of the right-hand side negative since the polarization attributed to **12** was emissive; the sign of μ, therefore, is minus. This supports the conclusion that the spin state of the polarizing radical pair is singlet. It should be noted, however, that this conclusion depends upon the critical assumption that the polarization arises from escape, rather than cage, product. If the CIDNP arises from the aromatic resonances of a recombination product, which then rapidly decomposes to intractable material, or if a second chlorine can be transferred from Cl_3COCCl_2 to the chlorophenyl radical in the cage, the sign of μ would be reversed. Both these possibilities seem less likely than the mechanism outlined in Scheme III, however, and we feel the CIDNP study provides at least circumstantial support for the isotope labeling results.

Conclusions

The CIDNP result obtained in the reaction of **11** supports the chemical trapping study which indicates the presence of singlet state intermediates in the reaction of **3**. The failure to detect evidence for the population of triplet **4** or **14** in these studies may be due to the short lifetime of the 1,4-dehydrobenzene intermediates under the reaction conditions. A slow intersystem crossing rate will preclude observation of the triplet biradical even if it is the lowest energy state. The lifetime of 2,3-dialkyl-substituted 1,4-dehydrobenzenes may be estimated from the parameters previously obtained for **4**;[2] at 200 °C, unimolecular ring opening occurs with a half-life of ca. 10^{-8}–10^{-9} s^{-1}. Therefore, if the ground electronic state of 1,4-dehydrobenzenes **4** and **14** is the triplet, population from the singlet must occur with a rate constant $\leq 10^9$ s.

Experimental Section

General Data. Descriptions of the NMR, IR, and mass spectrometers used and the method of preparation of solution and CIDNP reaction samples are described in the accompanying paper.[2b]

Preparative VPC was performed on a Varian 90P instrument. Analytical VPC was conducted on either a Perkin-Elmer 3920 or a Perkin-Elmer Sigma 3 chromatograph. Both were equipped with flame ionization detectors (FID) and were interfaced with a Spectra Physics Autolab System 1 computing integrator. The VPC columns used in the work reported here were the following: for preparative VPC, 10 ft × $^1/_4$ in. glass 10% SF-96 on 60/80 Chrom W; for analytical VPC, 9 ft × $^1/_8$ in. stainless steel 10% SF-96 on 100/120 Chrom W-AW/DMCS; for VPC–MS analyses, 30-m glass capillary SP2100 wall-coated open tubular (WCOT) column.

Synthesis. 2-Bromo-3-butyne. A procedure for a similar reaction has been outlined by Ashworth, Whitman, and Whiting.[27] A dry ether solution (18 mL) of 1-butyn-3-ol (22.2 g, 0.317 mol) and pyridine (0.22 mL) was placed in a three-neck flask fitted with an addition funnel, an argon inlet, and a reflux condenser. To the argon-flushed flask cooled to 5 °C was added an ether solution (12 mL) of freshy distilled PBr_3 (42.5 g, 0.317 mol) over 4 h. Reaction was complete at the end of the addition (VPC analysis on preparative instrument, 45 °C). Water was carefully added to the clear orange-brown reaction solution until fuming ceased. The organic phase was separated and washed with 50 mL of an aqueous $NaHCO_3$ solution followed by a wash with 50 mL of brine. The ether solution was dried over $MgSO_4$; distillation through a Ta wire column at 1 atm gave 13.6 g (32% yield) of 2-bromo-3-butyne (>98% pure, as determined by VPC): bp 83–90 °C; ^1H NMR (CCl_4) δ 1.90 (d, 3 H, J = 7 Hz), 2.53 (d, 1 H, J = 2.5 Hz), 4.51 (d of q, 1 H, J = 7, 2.5 Hz); IR (thin film) 3300, 2950, 2120, 1430, 1370, 1300, 1180, 1090, 1060, 990, 970, 855 cm^{-1}. Anal. Calcd for C_4H_5Br: C, 36.13; H, 3.75. Found: C, 35.95, H, 3.76.

3,4-Dimethylhexa-1,5-diyn-3-ol. An oven-dried three-neck flask was fitted with an addition funnel, condenser, thermometer, and an argon inlet. Magnesium turnings (2.45 g, 0.10 mol), dry ethyl ether (10 mL), and a small amount of $HgCl_2$ were added. After the solution became cloudy, the reaction flask was cooled to 10 °C and an ethyl ether (65 mL) solution of 2-bromo-3-butyne (13.6 g, 0.10 mol) was added over 1.5 h. A clear, faint yellow solution resulted. The solution was cooled to −15 °C and methyl ethynyl ketone (6.9 g, 0.10 mol) dissolved in ethyl ether (70 mL) was added over 1 h. A white precipitate formed after the addition was half complete. After the addition, the solution was warmed to room temperature over 0.5 h and poured into a cold, saturated aqueous NH_4Cl solution. The organics were isolated, and the aqueous phase was washed three times with ethyl ether. The combined ethyl ether solutions were washed with 150 mL of brine and then dried over Na_2SO_4. Concentration on a rotary evaporator gave a somewhat volatile reddish oil. The crude product was purified by passing through a pad of silica gel with a mixture of petroleum ether and ethyl ether as eluant (7:3 v/v). Static vacuum distillation (0.03 torr) of the oil gave 8.4 g (>98% pure as determined with preparative VPC) of 3,4-dimethylhexa-2,5-diyn-3-ol (70%) as a colorless oil. The alcohol was formed as a mixture of diastereomers (5:1 ratio) which could be separated by preparative VPC (column temperature, 100 °C): NMR of major diastereomer ($CDCl_3$) δ 1.33 (d, 3 H, J = 7.5 Hz), 1.54 (s, 3 H), 2.19 (d, 1 H, J = 2.5 Hz), 2.46 (s, 2 H, OH, acetylenic H), 2.65 (m, 1 H, J = 7.5, 2.5 Hz); IR thin film) 3250, 3220, 2980, 2110, 1710, 1440, 1370, 1250, 1090, 1030, 1000, 970, 720 cm^{-1}. Anal. Calcd for $C_5H_{10}O$: C, 78.65; H, 82.5. Found: C, 78.36; H, 8.23.

2,3-Dimethylhexa-1,5-diyn-3-ene (11). A 25-mL three-neck flask was fitted with an argon inlet, addition funnel, and a stopcock through which aliquots could be removed. After the flask was flushed with argon, 3,4-dimethylhexa-1,5-diynol (1.65 g, 0.011 mol) and pyridine (3.5 mL) were added. The mixture was cooled to 5 °C, and a solution of $POCl_3$ (1.98 g, 1.2 mL, 0.013 mol) in pyridine (1.7 mL) was added with stirring over 30 min. The reaction was monitored by preparative VPC (column temperature 98 °C). After the addition of $POCl_3$, little reaction had occurred, so the mixture was warmed slowly to room temperature. After 1 h at room temperature the reaction was complete. The dark reaction mixture was poured over ice with petroleum ether and H_2O rinses. The organic layer was separated, and the aqueous phase was washed three times with petroleum ether. The combined organics were washed with 10% aqueous HCl until acidic by litmus and then washed with H_2O to pH 4. The petroleum ether solution was dried over Na_2SO and concentrated to give 0.63 g (50% yield) of an orange oil (>95% pure by VPC). Crystallization of *cis*- and *trans*-2,3-dimethylhexa-1,5-diyn-3-ene (ratio 1:3) at −70 °C gave further purified product. The geometric isomers were isolated by column chromatography on silica gel (petroleum ether eluant). Cis isomer: NMR ($CDCl_3$) δ 1.88 (s, 6 H), 3.17 (s, 2 H); IR (thin film) 3310, 3020, 2935, 2874, 2108, 1445, 1386, 1250, 1156, 1103 cm^{-1}. Trans isomer: NMR ($CDCl_3$) δ 2.02 (s, 6 H), 3.36 (s, 2 H); IR (thin film) 3318, 2970, 2940, 2872, 2002, 1735, 1445, 1378, 1265, 1235, 1166, 1098, 800 cm^{-1}; HRMS precise mass calcd for C_8H_8 104.0625, found for *cis*-**11** 104.0623 and found for *trans*-**11** 104.0622.

Thermal Reactions. Reaction of 2,3-Dimethylhexa-1,5-diyn-3-ene (11) in Chlorinated solvents. CCl_4 (MCB spectral quality) was used without additional purification. Hexachloroacetone was purified by repeated distillation at 50 torr through a vacuum-jacketed glass helices packed column. **11** was purified by preparative VPC (column temperature 85 °C). Octane was used as an internal standard in the thermal reactions. Yields of products were determined by reference to the internal standard with the assumption that the response factor of the starting material and products was the same.[28] Pyrolyzed solutions were dark, Guinness-brown, suggesting the occurrence of substantial polymerization. Reaction product **12** was isolated from the CCl_4 reaction mixture by preparative VPC (column temperature 135 °C) and identified by NMR, IR, and HRMS (see below). Compound **13** was identified by its mass spectrum (*m/e* 140). No evidence for **16** was detected by VPC–MS analysis of the hexachloroacetone solution reaction. In the CCl_4 reaction a product with *m/e* 256, 258, 260, and 262 was detected; this may have been formed by cage combination of aryl radical **15** and the trichloromethyl radical. 1,4-dichloro-2,3-dimethylbenzene (**12**); NMR (CCl_4) δ 2.33 (s, 6 H), 6.98 (s, 2 H); IR (CCl_4) 3020, 2940, 1875, 1458, 1413, 1389, 1264,

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(25) See ref 14, p 332.

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1161, 1136, 1030, 833, 590 cm^{-1}; HMRS precise mass calcd for $C_8H_8Cl_2$ 174.0003, found 173.9999.

Reaction of 4,5-Diethynyloct-4-ene (3) in Cyclohexadiene-d_0 and -d_4. Compound **3** was isolated >99% pure by preparative VPC and promptly dissolved in chlorobenzene to give a solution 0.01 M in **3**. Undecane was added as an internal standard, and the initial concentration of **3** was determined by comparison of the integrated analytical VPC peak areas. Cyclohexadiene-d_0 and -d_4 were added to the chlorobenzene solution of **3** in a pyrolysis tube which was promptly sealed. After reaction for 15 min at 195 °C, the solutions were very light yellow. The reacted solutions were analyzed by analytical VPC (initial temperature 150 °C for 15 min; increase at 5 °C/min; hold at 220 °C for 20 min) and the product yields determined by reference to the internal standard. The relative yields of **10**-d_0, -d_1, and -d_2 were determined by VPC-MS analysis (WCOT capillary column; initial temperature 110 °C; increase at 4 °C/min; hold at 220 °C). The ratio of cyclohexadiene-d_0 and -d_4 used was 1:4. With this ratio, **10**-d_0 and -d_2 were formed in nearly equal yield (k_H/k_D is 4). The ratio of C/E was determined as follows: cage escape (E) is the only source of **10**-d_1; escape gives **10**-d_0, -d_1, and -d_2 in the ratio 1:2:1. Therefore, the escape component of **10**-d_0 and -d_2 is half the yield of **10**-d_1. The remainder of **10**-d_0 and -d_2 was formed by cage reactions (C) and was added to the yield of the high molecular weight combination products to give the yield of cage products.

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Binding and Transport of Alkali and Alkaline Earth Metal Ions by Synthetic Macrolides Containing Tetrahydropyran Rings

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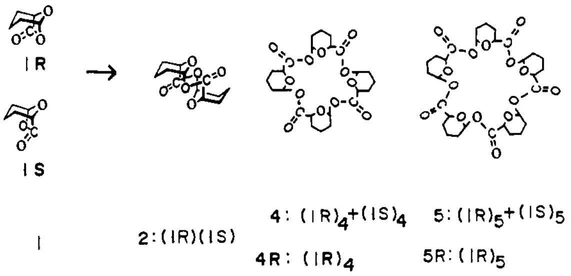
Abstract: Ion binding and transport abilities of 10-, 20-, and 25-membered macrolides (**2**, **4**, and **5**, respectively) consisting of alternating tetrahydropyran and ester moieties were evaluated mainly by extraction equilibrium and transport experiments of various metal picrates. The macrodilide **2** was totally ineffective in ion binding and transport. The ion extraction constants of the macrotetrolide **4** and the macropentalide **5** were found to be in the order of ~10–10^2, and their ion selectivity sequences were $Cs^+ > Rb^+ > K^+ > Na^+ > Li^+$ and $Ba^{2+} > Ca^{2+}$. The transport rate of metal picrates mediated by **4** and **5** through organic liquid membranes decreased in the order, $Cs^+ > Rb^+ > K^+ > Ba^{2+} > Ca^{2+} \simeq Na^+ > Li^+$, the selectivity of K^+ over Na^+ being ~2–3. Separated measurements of ion uptake and ion release, along with the selectivity sequences above, suggested that the ion uptake step was rate determining in the transport of metal picrates by **4** and **5**. These ion binding properties and transport behaviors are discussed in comparison with those of some natural and synthetic ionophores.

Introduction

There have been found in nature a variety of macrocyclic antibiotics which show a high degree of cation selectivity and act as ionophores to permeate specific ions through biological membranes.[1] Such elaborate functions displayed by these antibiotics have been elucidated to a considerable extent, particularly with recent advances in crystallographical and spectroscopical techniques. On the other hand, since the epoch-making discovery of crown ethers by Pedersen,[2] numerous multidentate macrocyclic ligands aiming at specific ion and substrate selectivities have been designed and their characteristic binding behaviors have been quantitatively investigated.[3] Some of these synthetic macrocyclic ligands have been studied as model carriers for transport of cations across cell membranes by naturally occurring ionophores.[4]



Recently, the authors succeeded in the highly selective synthesis of 10-, 20-, and 25-membered macrocyclic oligoesters (macrodilide **2**, macrotetrolide **4**, macropentalide **5**, respectively) by cationic ring-opening polymerization of (±)-6,8-dioxabicyclo[3.2.1]octan-7-one (**1**) at −40 °C.[5-7] In addition, optically active macrotetrolide (**4R**) and macropentalide (**5R**) were prepared in a similar manner from (+)-(1*R*,5*R*)-6,8-dioxabicyclo[3.2.1]octan-7-one (**1R**).[8-10] These macrolides are composed of alternating tetrahydropyran ring and ester moieties, and they bear structural resemblance to nonactin which is a 32-membered naturally occurring macrotetrolide. Nonactin has been shown to be influential in the regulation of metabolic behavior and is thought to act by selectively enhancing the transport of potassium ion through cell

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(10) All the macrolides used in this work are sufficiently pure; elemental analysis $(C_6H_8O_3)_n$ (n = 2, 4, and 5), C, H; no impurity was detected by GPC, IR, or ^1H and ^{13}C NMR techniques. Their structures were established by X-ray analysis. Previously, it was reported erroneously that a 30-membered cyclic hexamer was produced from both racemic and optically active 6,8-dioxabicyclo[3.2.1]octan-7-one, on the basis of the molecular weight determination by vapor pressure osmometry. Recent X-ray analysis has disclosed that it is actually a 25-membered cyclic pentamer. The error was due to the formation of a molecular complex of the cyclic pentamer with chloroform, whose molecular weight was close to that of the cyclic hexamer.

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