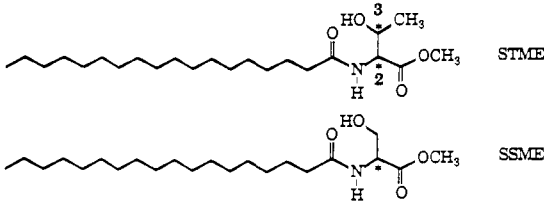Table IX. Correlation of Film Behavior at 25 °C with Chirality in Mixed Monolayer Films of Stearoylthreonine Methyl Ester (STME) and Stearoylserine Methyl Ester (SSME)

film mixture (1/1)	chirality (STME/SSME)	film behavior
L-STME/L-SSME	2S,3R/S	condensed
L-STME/D-SSME	2S,3R/R	expanded
L-*allo*-STME/L-SSME	2S,3S/S	condensed
L-*allo*-STME/D-SSME	2S,3S/R	expanded

chirality at the number 3 center plays a more passive role.

Table IX reveals that for 1/1 mixed films of SSME with STME, behavior similar to the condensed films of Table VIII occurs for mixtures where the chirality at STME center 2 is the same as that in SSME. For cases where the configuration at STME center 2 is opposite to that of SSME, behavior resembling the expanded monolayers of Table VIII occurs.

While the correlations discussed above are suggestive of particular interactions leading to chiral recognition, they do not allow one to get a true picture of what the specific interactions are at a molecular level. Unfortunately, crystal structures of the surfactants of this project could not be obtained, despite several attempts at growing suitable crystalline specimens. The CPK models of each surfactant were constructed, but modeling interactions with these failed to demonstrate any readily interpretable structure/property relationships which could explain the chiral discrimination observed in the surface films uniquely.

Conclusions

The chiral molecular recognition manifested in the monolayer films of the surfactants studied here is strongly phase-dependent, but no simple pattern related to headgroup geometry is apparent. Isotherms of enantiomeric and racemic SCME, in which the molecules of the film are tightly packed at all $\Pi > 0$, are distinct from one another at virtually all surface pressures. In contrast, the monolayers of DLCDME, which exist in a more expanded phase (liquid-expanded) below their collapse pressure, are independent of stereochemistry in this region.

The STMEs indicate the monolayer transition from the liquid-expanded (LE) to the liquid-condensed (LC) phase as the point at which chiral discrimination is readily detectable in this class of surfactant by the monolayer methods used (Π/A measurements and viscosities). Moreover, this LE–LC phase behavior is highly temperature-dependent in the range of study. Although the intermolecular interactions in the LC phase are obviously tighter than those in the LE phase, the viscosities of the threonine surfactants distinguish the LC phase from a two-dimensional solid, which would show no viscous flow at all.

For none of the surfactants studied was chiral recognition observed in the monolayers at film pressures below the equilibrium spreading pressure. Only in metastable or unstable monolayer states (or collapse states) did differences based on stereochemistry occur.

Comparisons of enantiomeric discrimination between monolayer films of a particular surfactant and its crystals (where chiral discrimination was always manifested) show that the sense of discrimination is the same in each case, since heterochiral interactions are favored (preference for pairwise interactions between chiral molecules of opposite configuration, rather than for interactions between molecules of the same configuration).

The two-component monolayer mixtures indicate that the degree of diastereomeric recognition is of the same order as the enantiomeric recognition for each surfactant studied. Examination of mixtures of the isomers of STME, and its mixtures with SSME, reveals a trend in film packing that implies that the chiral center α to the ester group (carbon 2) in STME plays a more dominant role than that of carbon 3 in determining the phase behavior, and thus the chiral recognition, observed in its monolayers.

The Anion Radical of Bicyclononatriene

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Abstract: The low-temperature potassium metal reduction of bicyclo[6.1.0]nona-2,4,6-triene (BCN) in DME leads to the formation of the previously observed open form of the homocyclooctatetraene anion radical (HCOT$^{\cdot-}$). Careful inspection of the EPR spectra recorded from these solutions, and some of those previously published, shows the presence of another species. This second species is best interpreted using a set of methylene proton coupling constants very similar to those of HCOT$^{\cdot-}$ (all within 10%) but much smaller endo and exo bridgehead coupling constants. Perdeuteration of the sp^2 carbons supports this interpretation. The only reasonable interpretation of the hyperfine pattern observed for the second anion radical is in terms of the closed (bicyclic) form. The closed anion radical (BCN$^{\cdot-}$) is favored under conditions involving more ion association and more complete reduction.

In order to account for the high stability of molecules in which conjugation is interrupted in one or more places by aliphatic groups, some 43 years ago Winstein and Adam[1] extended the concept of aromaticity to include homoaromatic compounds. The
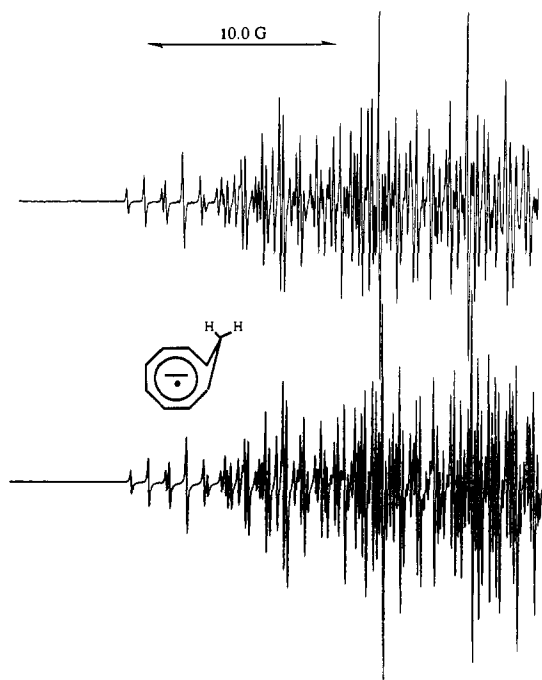
Figure 1. Upper: EPR spectrum at −63 °C of the anion radical of HCOT, generated via the sodium reduction of BCN in DME. Lower: Computer simulation generated with the coupling constants 12.28 (1 H), 4.77 (1 H), 0.93 (2 H), 2.04 (2 H), 5.11 (2 H), and 5.30 G (2 H) and a peak-to-peak line width of 0.07 G.

essential feature of homoaromatic character is the union of an unsaturated segment with a cyclopropane moiety, structure I. The

I
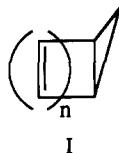
first suggestion of homoaromaticity was advanced by Thiele to explain the decreased acidity of the methylene protons in cyclo-heptatriene relative to those of cyclopentadiene.[2] This explanation is, of course, incorrect, but homoaromaticity has turned out to be very important in controlling the chemistry of a number of cationic organic systems, including[3] the homotropylium cation,[4] the bicyclo[3.1.0]hexenyl cation,[5] and the homocyclopropenyl cation.[6]

The first report of an anionic homoannulene system came from the same laboratory (S. Winstein's) that developed the original concept.[7] This report describes the reduction of bicyclo-[6.1.0]nona-2,4,6-triene (BCN), reaction 1, generating the

BCN   HCOT·⁻   HCOT²⁻
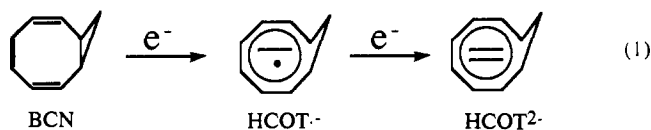
homo[8]annulene anion radical (HCOT·⁻) in dimethoxyethane

(DME), and its analysis via EPR spectroscopy. Unfortunately, there is a very poor correlation between their empirical EPR spectrum and their computer-drawn simulation. Their EPR analysis was, in fact, later shown to be flawed by Smentowski et al.,[8] but in the same issue that contained the original report, Katz and Talcott[9] reported a set of EPR coupling constants in liquid ammonia that are much closer to those accepted to be true. The key coupling constants are those of the C_9 protons, which would be three bonds removed from the nearest sp^2 carbon in the closed form of the anion radical. Under these conditions they would necessarily have relatively small coupling constants.[9] Thus, the large splittings observed by Katz and Talcott,[9] 12.0 and 4.8 G for the internal and external protons, respectively, clearly support the assignment of the open structure to the anion radical.

The anion radical of HCOT disproportionates to the dianion and neutral BCN in a manner similar to that of cyclooctatetraene (COT). In contrast to COT^{2-}, which can be stored in tetra-hydrofuran (THF) for years at room temperature, $HCOT^{2-}$ de-protonates this solvent, except at low temperatures, due to its inability to delocalize charge as efficiently as does the planar π analogue.[9,10] The much stronger basicity and the ability of $HCOT^{2-}$ to deprotonate some solvents are accounted for by its very negative reduction potential. The first half-wave potential for the reduction of BCN appears in the region characteristic of a conjugated triene.[11] The $E_{1/2}$'s of COT and BCN in THF with 0.2 M tetra-n-butylammonium perchlorate are −1.96 and −2.55 V, respectively, while the difference between the first and second half-wave potentials of BCN (to anion radical and dianion) is similar to that of COT.[11] All of this might suggest the formation of the closed triene anion radical, structure II, as a first step in the reduction, followed by ring opening.

II

In liquid ammonia, the anion radical of HCOT in the presence of solvated electrons can be produced under the condition of low current densities. However, at higher current densities a different anion radical is produced, which has been identified as that of methylcyclooctatetraene.[9] $HCOT^{2-}$ has also been shown to rapidly deprotonate ammonia, leaving a planar cyclononatrienyl anion.

The only solvent system that seems capable of sustaining the HCOT anion radical is DME, in which much of the EPR work has been carried out.[7,8,12] However, even in this solvent, poor correspondence between even the best computer simulations and the actual EPR spectra,[8] which has been attributed to line-width effects by Smentowski et al.,[8] indicates the possible presence of another radical or a misinterpretation of the coupling constants. Due to the importance of this anionic homoaromatic system and the vast amount of literature devoted to it,[7–12,13] we were motivated to unravel this remaining mystery involving HCOT·⁻ and in doing so have found the closed form of the anion radical.

Results and Discussion

The reduction of BCN with small amounts of potassium metal in DME results in orange solutions that yield EPR spectra at −30 °C that appear exactly like those reported earlier.[8] The previously reported simulations are not in very good agreement with the real

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(2) Garratt, P. J. *Aromaticity*; McGraw-Hill: London, 1971.

(3) (a) Grutzner, J. B.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1981**, *103*, 1372. (b) Paquette, L. A.; Kekula, M. J.; Ley, S. V.; Traynor, S. G. *J. Am. Chem. Soc.* **1977**, *99*, 4756. (c) Haddon, R. C. *J. Org. Chem.* **1979**, *44*, 3608.

(4) (a) Warner, P.; Harris, D. L.; Bradley, C. H.; Winstein, S. *Tetrahedron Lett.* **1970**, *4013*. (b) Keller, C. E.; Petit, R. *J. Am. Chem. Soc.* **1966**, *88*, 604, 606.

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(8) Smentowski, F. J.; Owens, R. M.; Faubion, B. D. *J. Am. Chem. Soc.* **1968**, *90*, 1537.

(9) Katz, T. J.; Talcott, C. *J. Am. Chem. Soc.* **1966**, *88*, 4732.

(10) Ley, S. V.; Paquette, L. A. *J. Am. Chem. Soc.* **1974**, *96*, 6670.

(11) Anderson, L. B.; Broadhurst, M. J.; Paquette, L. A. *J. Am. Chem. Soc.* **1973**, *95*, 2198.

(12) Moshuk, G.; Petrowski, G.; Winstein, S. *J. Am. Chem. Soc.* **1968**, *90*, 2179.

(13) For some examples, see: (a) Ogliaruso, M.; Winstein, S. *J. Am. Chem. Soc.* **1967**, *89*, 5290. (b) Ogliaruso, M. *J. Am. Chem. Soc.* **1970**, *92*, 7490. (c) Warner, P.; Winstein, S. *J. Am. Chem. Soc.* **1971**, *93*, 1284. (d) Fray, G. I.; Saxton, R. G. *The Chemistry of Cyclooctatetraene and Its Derivatives*; Cambridge University Press: New York, 1978; pp 262–291 and references therein.
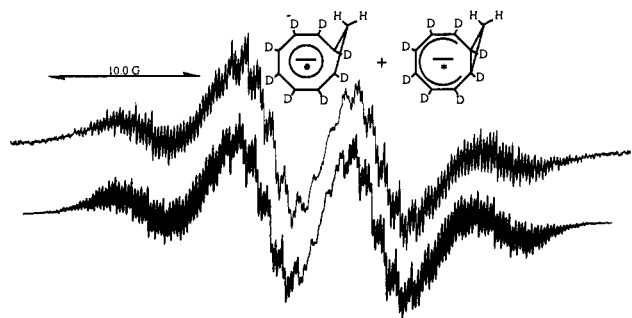
Figure 2. Upper: EPR spectrum at −30 °C of the anion radical of 1,2,3,4,5,6,7,8-octadeuteriobicyclo[6.1.0]nonatriene (BCN-d_8·−), generated via the potassium reduction of 1,2,3,4,5,6,7,8-octadeuteriobicyclo-[6.1.0]nonatriene (BCN-d_8) in DME, superimposed upon that at −30 °C for HCOT-d_8. Lower: Computer simulation generated with the coupling constants shown in structures IV and VI, peak-to-peak line widths of 0.20 G for BCN-d_8·− and 0.13 G for HCOT-d_8·−, and [BCN-d_8·−]/[HCOT-d_8·−] = 1.7. This simulation also includes a 20 mol % contribution from the representative d_7 closed and open species.

spectra (as per the author's admission[8]). Refinement of the coupling constants brings the simulation into excellent agreement with the real spectrum. The resolution is improved when sodium metal is used in the reduction (Figure 1), but the spectrum could be fit with coupling constants that are very similar to those used to fit the spectrum resulting from the potassium reduction. However, the central portion of the spectrum reported by Smentowski et al.[8] at −96 °C could not be fit with the refined coupling constants. Neither could that of Winstein, which was recorded at nearly the same temperature. There is obvious deviation in the intensities and the number of EPR lines toward the central portions of these spectra and the computer-drawn simulations using the accepted a_H's. It seemed to us that this must be due to the presence of another anion radical with a smaller total spectral width. Since the large total spectral width obtained from HCOT·− is due to the very large coupling from the endo C_9 proton, we felt some light could be shed upon the problem through the examination of the anion radical of 1,2,3,4,5,6,7,8-octa-deuteriohomo[8]annulene (BCN-d_8).

The potassium reduction of BCN-d_8 in DME led to an anion radical solution whose EPR pattern must consist of two superimposed spectra at −30 °C (Figure 2). The two broad features (doublet) separated by 5.2 G about the spectral center cannot be from the same radical which yields the multitude of hyperfine lines that appear throughout the spectrum. The two nonequivalent protons of HCOT-d_8·− must result in four peaks (two pairs) of equal intensities with superimposed hyperfine deuterium splittings, assuming a sufficiently narrow line width. The four observable main packets of peaks are in approximately a 1:4:4:1 intensity ratio. The spacing and relative intensities are inconsistent with those predicted for any logical combination of nuclei in a single radical. Were the intensity ratio due to a line-broadening process, the deuterium hyperfine lines would be accordingly broadened out of observability.

Presumably, one of the two radicals is HCOT-d_8·−. To account for the obvious doublet of multiplets underlying the inner pair from HCOT-d_8·−, the second radical must have a single-proton coupling constant that is large (5.2 G) relative to all other hyperfine splittings. It is clear that the spectrum for HCOT-d_8·− has one large proton splitting (12.9 G) and resolved deuterium splittings, while the second radical, with its relatively small proton splittings (5.2 G for the largest), has consequent crowding of the remaining hyperfine pattern, resulting in unresolved deuterium couplings.

A number of such experiments show that the intensity of the EPR signal for HCOT-d_8·− increases relative to that of the second radical with increasing temperature, and this phenomenon is reversible. However, the second radical increases in concentration relative to HCOT-d_8·− with further reduction (longer exposure of the solution to the potassium mirror). The second radical cannot be observed if sodium metal is used to reduce the BCN. The EPR
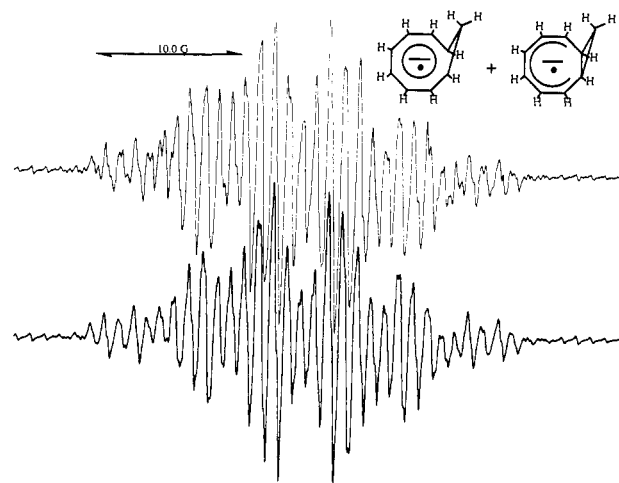

Figure 3. Upper: EPR spectrum at −30 °C of the anion radical of bicyclo[6.1.0]nonatriene (BCN·−), generated via the potassium reduction of BCN in DME, superimposed upon that at −30 °C for HCOT·−. Lower: Computer simulation generated with the coupling constants shown in structures III and V, peak-to-peak line widths of 0.20 G for HCOT·− and 0.27 G for BCN·−, and [BCN·−]/[HCOT·−] = 10.0.
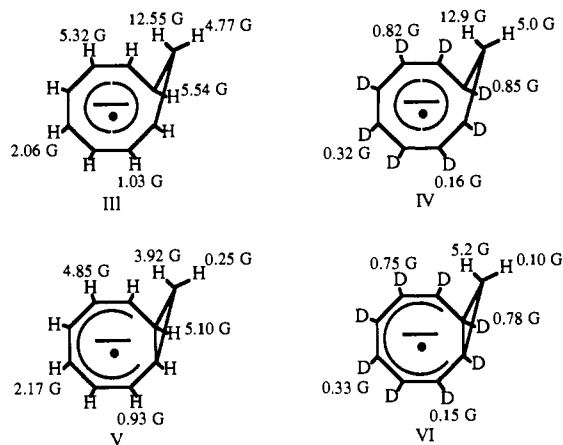
signal for the anion radical of HCOT-d_8·− can be simulated using nearly the same spectral parameters, after adjusting for gyromagnetic ratio differences (a_D/a_H = 1/6.5), that we used to fit the spectrum for HCOT·−.

The perprotiated form of the second radical was generated by simply exposing the BCN–DME solution to the potassium mirror at −30 °C for longer time periods and then recording the EPR spectra at low temperature (−30 °C). The resulting EPR spectrum is best simulated using single-proton couplings of 3.92 and 0.25 G and four pairs of protons (Figure 3). The remainder of the spectrum of the second radical is due to four pairs of protons that have coupling constants that are very similar in magnitude to those of HCOT·−. *The spectral parameters are consistent with those expected for the closed form of the anion radical* (BCN·−, structure II). The averages of the ring proton coupling constants in the open and closed forms of the anion radical are 3.49 and 3.26 G, respectively, as compared to the 3.21-G splitting for the vinyl protons in the cyclooctatetraene anion radical.[14] It should be noted that again the sodium reduction does not result in production of the second radical. However, when potassium iodide is added to a DME solution of the sodium anion radical salt, the second radical appears.

The spectral parameters used to analyze the EPR spectrum of BCN·−, after adjusting for the gyromagnetic ratio differences between H and D and for increases in the bridgehead a_H's, were then used to generate a simulation of the second radical observed after the BCN-d_8 reduction (Figure 2). The fit proved to be excellent. Computer simulations of the spectra expected for mixtures of the anion radicals (BCN-d_8·− and HCOT-d_8·−) are also in excellent agreement with the empirical results. The coupling constants for the four potassium anion radicals are summarized in structures III–VI.

In all of the EPR experiments, raising the temperature results in the replacement of the closed form with the open form of the anion radical, and this phenomenon is thermally reversible. This is made evident by comparing the spectrum shown in Figure 2 with that in Figure 4. Figure 4 shows the EPR spectrum recorded at +28 °C of the same anion radical as that whose spectrum is shown in Figure 2. Note that the spectrum dominated by the 5.2-G doublet is not present at this higher temperature. At temperatures above −30 °C, there is a noticeable decrease in the EPR signal intensity of both anion radicals over the period of time that is required to acquire the spectra. This is presumably due to the previously reported deprotonation of solvent.[10] As long as

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III: 12.55 G, 5.32 G, 4.77 G, H 5.54 G, 2.06 G, 1.03 G

IV: 0.82 G, 12.9 G, 5.0 G, D 0.85 G, 0.32 G, 0.16 G

V: 3.92 G, 4.85 G, 0.25 G, H 5.10 G, 2.17 G, 0.93 G

VI: 0.75 G, 5.2 G, H 0.10 G, D 0.78 G, 0.33 G, 0.15 G

Figure 4. Upper: EPR spectrum at 28 °C of the anion radical of HCOT-d_8[·−], generated via the potassium reduction of 1,2,3,4,5,6,7,8-octadeuteriobicyclo[6.1.0]nonatriene (BCN-d_8) in DME (same solution as for the spectrum in Figure 2). However, now note the absence of a signal for BCN-d_8[·−]. Lower: Computer simulation generated with the coupling constants shown in structure IV. This simulation also includes a 20 mol % contribution from the representative d_7 open species.

Scheme I

the ring opening of the bicyclic anion radical is slow relative to the disproportionation, the reactions shown in Scheme I seem to account for all of the observations reported here and elsewhere.

The neutral bicyclic compound accepts the electron from the metal, and the resulting anion radical is involved in an equilibrium with its valence tautomer, the open form. This is slow as compared to the subsequent disproportionation of HCOT[·−]. The apparent significant energy barrier to ring opening is in agreement with the prediction, based upon molecular orbital symmetries, that both disrotatory and conrotatory ring openings are disallowed processes for this system.[15] The closed form is stabilized relative to the open form by ion association with K^{+}, as evidenced by the fact that the addition of potassium iodide to solutions of the open anion radical results in formation of the closed anion radical. Ion association is known to stabilize less delocalized substituted cyclooctatetraene anions more than it does the more delocalized systems.[16] It is unlikely that the closed form of the anion radical would undergo further reduction to a closed dianion; thus the addition of more metal leads to the reduction of HCOT[·−] to the HCOT dianion, which can undergo electron transfer with BCN or alternatively can deprotonate the solvent, accounting for the facts that the addition of more potassium metal results in the replacement of the open form with the closed form and that the EPR signal intensity slowly decreases with time.

INDO calculations carried out on this system do support the fact that the endo and exo proton splittings are more than twice as large in the open form of the anion radical as they are in the closed form.[15] The fact that the endo proton coupling constant of the closed anion radical is larger in the deuteriated material than in the perprotiated material was not totally unexpected. Perdeuteriation of one moiety of an anion radical has been previously observed to cause an increase in the spin density of the other moiety. Specifically, deuteriation of the cyclooctatetraenyl moiety in the phenylcyclooctatetraene anion radical results in increases in the ortho and meta proton coupling constants in the benzene ring.[17]

Experimental Section

Perdeuteriated Cyclooctatetraene. A 50-mL round-bottom bulb was charged with about 0.85 grams of Ni(Acac)$_2$, and the bulb was connected to the vacuum line and evacuated. Dry THF (30 mL) was then distilled into the round-bottom bulb using a dry ice–acetone solution (−70 °C). The bulb was then kept in the dry ice–acetone solution so that deuteriated acetylene could be condensed into the THF solution. The production of deuteriated acetylene was performed on the same vacuum line by dripping approximately 50 mL of D$_2$O onto 100 g of CaC$_2$, resulting in the production of 1.25 mol of acetylene-d_2, which was condensed into the 50-mL bulb. The chemical reaction between water and calcium carbide is very exothermic. Therefore, some unreacted water will vaporize and possibly condense in the reaction bulb. To eliminate this possibility two U-tubes were placed between the reaction bulb and the three-neck flask
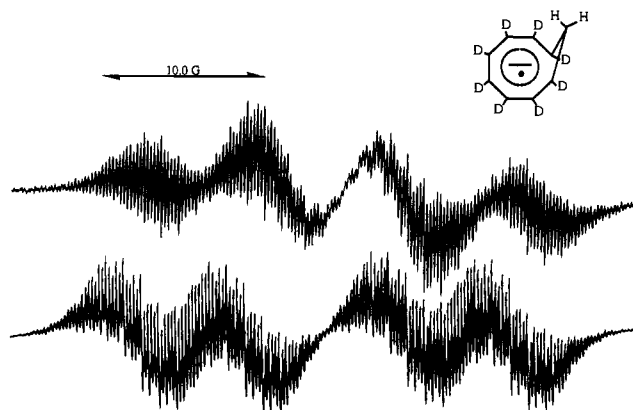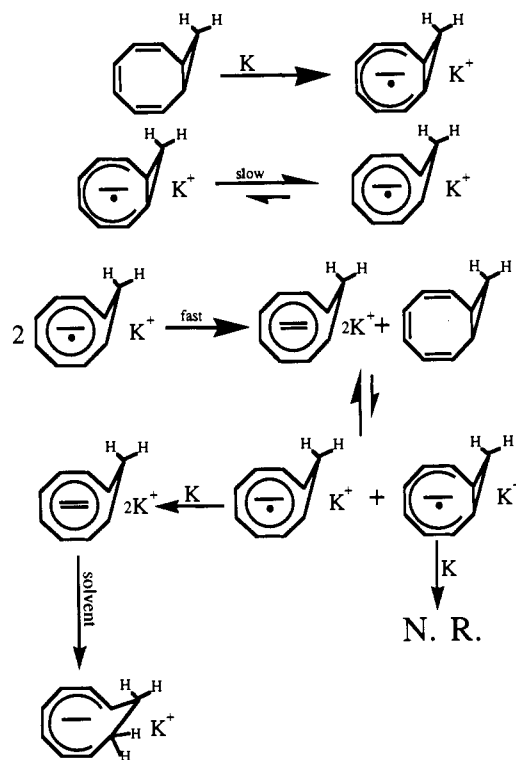
(15) Brewer, D. A.; Schug, J. C.; Ogliaruso, M. A. *Tetrahedron* **1975**, *31*, 69.

(16) Stevenson, G. R.; Ocasio, I. *J. Am. Chem. Soc.* **1976**, *98*, 890.

(17) Stevenson, G. R.; Burton, R. D.; Reiter, R. C. *J. Am. Chem. Soc.* **1992**, *114*, 399.

where the CaC$_2$/D$_2$O reaction was taking place. One U-tube was submerged in an ice bath and was charged with CaC$_2$ to convert any vaporized D$_2$O to acetylene-d_2. To condense any residual D$_2$O, a second U-tube was submerged in an acetone bath which had been cooled to approximately −50 °C. When the THF solution becamse saturated with acetylene-d_2, the bulb was submerged in liquid N$_2$ to condense any residual acetylene-d_2. Once all the acetylene-d_2 was condensed and the solution was frozen solid, the bulb was sealed from the line and enclosed in a 500-mL steel bomb. The bomb was submerged in a 90 °C oil bath for 15 h and shaken periodically. The bomb was then cooled in an ice bath and opened. The materials in the bomb were removed and dissolved in about 300 mL of diethyl ether. The solution was dried with magnesium sulfate and gravity-filtered. The ether was evaporated under a stream of dry nitrogen. The remaining dark liquid was then vacuum distilled at 30 Torr. A yellow liquid was collected over the temperature range 40–50 °C. Mass spectral analysis is consistent with perdeuteriated [8]annulene (93% isotopic purity) mixed with heptadeuteriated [8]-annulene (7% isotopic purity).

Bicyclo[6.1.0]nona-2,4,6-triene. BCN was prepared by the addition of the cyclooctatetraene dianion to methylene chloride as previously

described.[18] It was purified via three vacuum distillations at 30 Torr. The octadeuteriobicyclo[6.1.0]nona-2,4,6-triene was prepared in an identical manner with the use of perdeuteriated cyclooctatetraene as described above.

General Procedures. The reductions were carried out by allowing solutions of the bicyclo[6.1.0]nona-2,4,6-triene to come into contact with

the freshly distilled metal mirrors at −78 °C in vacuo. The EPR spectra were recorded with an IBM (Bruker) ER-200D spectrometer equipped with an IBM variable-temperature unit.

(18) Katz, T. J.; Garratt, P. J. *J. Am. Chem. Soc.* **1964**, *86*, 5194.

A Route to Artificial Glycoconjugates and Oligosaccharides via Enzymatically Resolved Glycals: Dramatic Effects of the Handedness of the Sugar Domain Upon the Properties of an Anthracycline Drug

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Abstract: Racemic, fully synthetic glycals of considerable structural variety may be kinetically resolved via enzymatically mediated transesterification using Lipase PS-30 from *Pseudomonas cepacia* as catalyst and vinyl acetate as acyl donor. This methodology provides convenient access to a pool of optically enriched D- and L-glycals. These glycals may be employed as building blocks, both as glycosyl donors and glycosyl acceptors, to generate artificial oligosaccharides. Thus the D-glucal analogue **7**, bearing a phenyl group at C-5, was converted to the corresponding 1,2-anhydrosugar(s) **8/9**, which could be coupled directly to a second glycal. Alternatively, the 1,2-anhydrosugar could be converted to the corresponding β-glycosyl fluoride **14** or β-glycosyl sulfoxides **18a,b**. Both **14** and **18a,b** were glycosylated, with a glycal or a terminating sugar, in good yield. Conversely, the L-glucal analogue **3** was employed as a glycosyl acceptor, with L-fucosyl fluoride(s) (α:β = 1:1) as the glycosyl donor, to furnish the artificial "L,L"-disaccharide **17**. Enzymatically resolved L- and D-glycals were also used to construct novel glycoconjugates of daunomycinone with di-*sym*-collidinyliodonium perchlorate as the coupling reagent. By employing each antipode of the 5-phenyl analogue of galactal, (+)- and (−)-**25**, as glycosyl donor, a pair of diastereomeric 5′-phenyl analogues of daunomycin **22** and **23**, was obtained. These two compounds differ only in the handedness (L or D) of their carbohydrate sectors, yet exhibit markedly different biological properties. Interestingly, X-ray crystal structure determinations for **22** and **23** reveal fundamentally different overall molecular shapes for the two compounds.

Background

Whereas remarkable progress has been made in oligosaccharide assembly,[1] a fully satisfying, straightforward solution to oligosaccharide synthesis still remains to be achieved. With an eye toward this ultimate goal, it is well to pursue possibilities which might conveniently lend themselves to iteration and minimize the number of steps in the construction of the array. In this context, the use of glycals in the assembly of oligosaccharides and other glycoconjugates was seen to have considerable advantages.

It had long been known, primarily through the pioneering efforts of Lemieux and Thiem, that glycals function well as glycosyl donors, being activated by a variety of E+ reagents.[2] The ability to transform glycals into 1,2-anhydrosugars,[3] 1,2-sulfonylaziridinosugar equivalents,[4] glycosyl fluorides,[5] phenylthio glycosides,[5] and n-pentenyl glycosides[5] has broadened their applicability as glycosyl donors. These earlier developments are summarized in Scheme I.[3–6]

A major advantage of glycals in complex constructions would lie in the simplification which they offer in protecting-group and activating-group strategies. These manipulations, as well as the coupling (glycosylation) reactions themselves, lie at the heart of oligosaccharide and glycoconjugate construction. Thus, in a glycal-based paradigm, only three hydroxyl groups need be dif-

ferentiated. Furthermore, given the range of possibilities described above, the glycal linkage can be seen as a poised, readily actuatable glycosyl donor.

For the proposed new approach to gain full impact, it was necessary for glycals to be incorporated in syntheses, not only as glycosyl donors, as in the past, but as glycosyl acceptors. The overall logic of the approach is presented in Scheme II. In the first cycle, glycal A_1 functions as a glycosyl acceptor while glycal D_1, suitably activated, is the glycosyl donor. A coupling reaction would lead to disaccharide D_2, wherein the stereochemistry of the glycosidic bond and the nature of X are permutable from a menu of glycal assembly processes (see Scheme I above). Disaccharide

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