Bond Fixation in Annulenes. 16. Synthesis of the 1,2-Dimethyl-3-phenylcyclooctatetraene ⇌ 1,8-Dimethyl-2-phenylcyclooctatetraene Bond Shift Isomer Pair. Probe of the Relative Size of a Flanking Phenyl Substituent by means of Racemization Kinetics[1]

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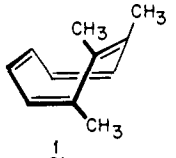
Abstract: Two synthetic approaches to the cyclooctatetraene bond shift isomers **3** ⇌ **4** were developed. The first began with a phenyl-substituted starting material (phenylsuccinic acid) and proceeded to introduce the two methyl groups by desulfonylative ring contraction of a bicyclic α,α'-disubstituted sulfone. The second had its origins in citraconic anhydride. The two carbonyl groups were differentiated by regiospecific conversion to bromo lactone **20**. Following stepwise introduction of the phenyl and second methyl substituents, a titanium(0)-promoted coupling was utilized to prepare **26**. Both pathways were dependent upon regioselective bromination–dehydrobromination of a bicyclo[4.2.0]octadiene to generate the cyclooctatetraene nucleus. Although **3** dominates over **4** in the equilibrium, it is possible to separate these bond shift isomers by cycloaddition with a triazolinedione. When recourse was made to the *endo*-bornyl-substituted dienophile, it was ultimately possible to obtain (−)-**3** and to determine its rate of racemization. The data indicate that the flanking phenyl group in **3** causes significant rate retardation relative to the trimethyl derivative. This finding contrasts with the behavior of **2** which racemizes more rapidly despite an interstitial phenyl substituent. The source of these dissimilar effects has been clarified by MM2 calculations, the details of which are presented.

Peripheral substitution of the cyclooctatetraene nucleus has emerged as a very powerful tool for evaluating the bond shifting (BS) and ring inversion (RI) energetics of [8]annulene systems.[3] The proximal positioning of alkyl and aryl groups impedes flattening of the thermodynamically more stable tub-shaped conformations associated with these medium-ring polyolefins. Independent isolation of bond shift isomers is thereby made possible. Furthermore, in chiral examples, resolution and the assignment of absolute configuration can readily be achieved.[4]

The dynamic behavior of 1,2,3-trimethylcyclooctatetraene (**1**) has been thoroughly studied.[4a,c] For this sytem, the barrier to bond shifting ($\Delta G^{\ddagger}_{25}$ = 26.5 kcal/mol) exceeds that associated with ring inversion ($\Delta G^{\ddagger}_{25}$ = 24.4 kcal/mol), as is usually the case.[3]



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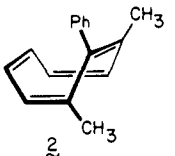

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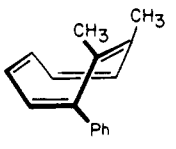

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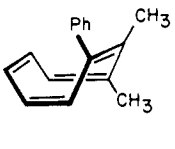

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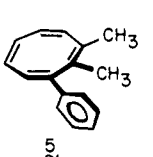
The preceding paper reports the overall racemization rate of optically active **2**.[1] Despite the fact that k_{rac} is a composite of k_{BS} and k_{RI}, the data provided information on the relative steric demands of a phenyl substituent when "sandwiched" between a pair of CH_3 groups on the exterior of an essentially planar eight-membered ring. Higher levels of steric perturbation generally come into play here because of reduced extracyclic angle size relative to that found in cyclohexane[5] and polycyclic aromatic systems.[6] Because accentuated in-plane congestion such as is present in **5**–**7** is less easily and consistently accessed in other ways,



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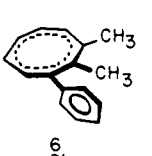

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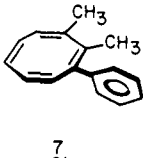

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we have presently undetaken preparation of the cyclooctatetraene isomer pair **3**/**4** in order to compare the impedance contributions of a flanking phenyl ring toward flattening under otherwise isomeric circumstances. Our goal was to provide added insight into the effect of intramolecular strain on the internal mobility of cyclooctatetraenes as gauged by the ease with which transition-state structures **5**–**7** are attained.

Results

Synthetic Protocols. Retrosynthetic analysis of the 1,2-dimethyl-3-phenyl- (**3**) and 1,8-dimethyl-2-phenylcyclooctatetraene (**4**) molecules suggested that the requisite substitution plans might

(1) Part 15: Paquette, L. A.; Gardlik, J. M.; McCullough, K. J.; Hanzawa, Y. *J. Am. Chem. Soc.*, preceding paper in this issue.

(2) (a) The Ohio State University Dissertation Fellow, 1977–1978. (b) NATO Postdoctoral Fellow of the Science Research Council, 1978–1980.

(3) Paquette, L. A. *Pure Apl. Chem.* **1982**, *54*, 987.

(4) (a) Paquette, L. A.; Gardlik, J. M. *J. Am. Chem. Soc.* **1980**, *102*, 5016. (b) Paquette, L. A.; Gardlik, J. M.; Johnson, L. K.; McCullough, K. J. *Ibid.* **1980**, *102*, 5026. (c) Paquette, L. A.; Gardlik, J. M. *Ibid.* **1980**, *102*, 5033. (d) Paquette, L. A.; Hanzawa, Y.; McCullough, K. J.; Tagle, B.; Swenson, W.; Clardy, J. *Ibid.* **1981**, *103*, 2262. (e) Hanzawa, Y.; Paquette, L. A. *Ibid.* **1981**, *103*, 2269. (f) Paquette, L. A.; Hanzawa, Y.; Hefferon, G. J.; Blount, J. F. *J. Org. Chem.* **1982**, *47*, 265. (g) Paquette, L. A.; Hefferon, G. J.; Samodral, R.; Hanzawa, Y. *Ibid.* **1983**, *48*, 1262.

(5) (a) Shapiro, B. L.; Gattuso, M. J.; Hepfinger, N. F.; Shone, R. L.; White, W. L. *Tetrahedron Lett.* **1971**, 219. (b) Allinger, N. L.; Tribble, M. T. *Ibid.* **1971**, 3259. (c) DeBeule, H.; Tavernier, D.; Anteunis, M. *Tetrahedron* **1974**, *30*, 3573. (d) Eliel, E. L.; Manoharan, M. *J. Org. Chem.* **1981**, *46*, 1959.

(6) (a) House, H. O.; Koepsell, D. G.; Campbell, W. J. *J. Org. Chem.* **1972**, *37*, 1003 and earlier references cited therein. (b) House, H. O.; Koepsell, D.; Jaeger, W. *Ibid.* **1973**, *38*, 1167. (c) Clough, R. L.; Kung, W. J.; Marsh, R. E.; Roberts, J. D. *Ibid.* **1976**, *41*, 3603. (d) Gust, D. *J. Am. Chem. Soc.* **1977**, *99*, 6980. (e) Clough, R. L.; Roberts, J. D. *J. Org. Chem.* **1978**, *43*, 1328. (f) Gust, D.; Patton, A. *J. Am. Chem. Soc.* **1978**, *100*, 8175. (g) Patton, A.; Dirks, J. W.; Gust, D. *J. Org. Chem.* **1979**, *44*, 4749. (h) Gust, D.; Fagan, M. W. *Ibid.* **1980**, *45*, 2511.

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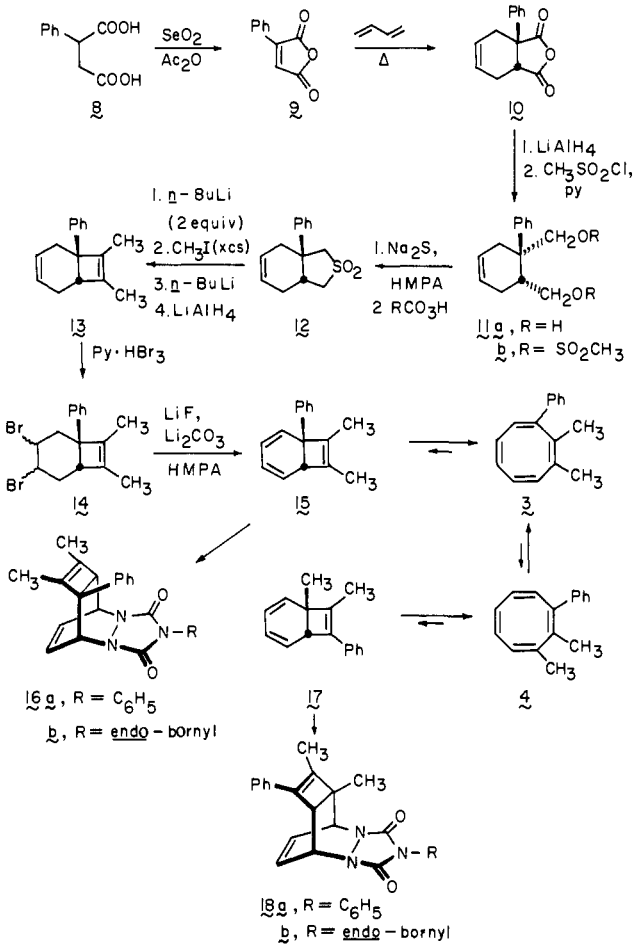
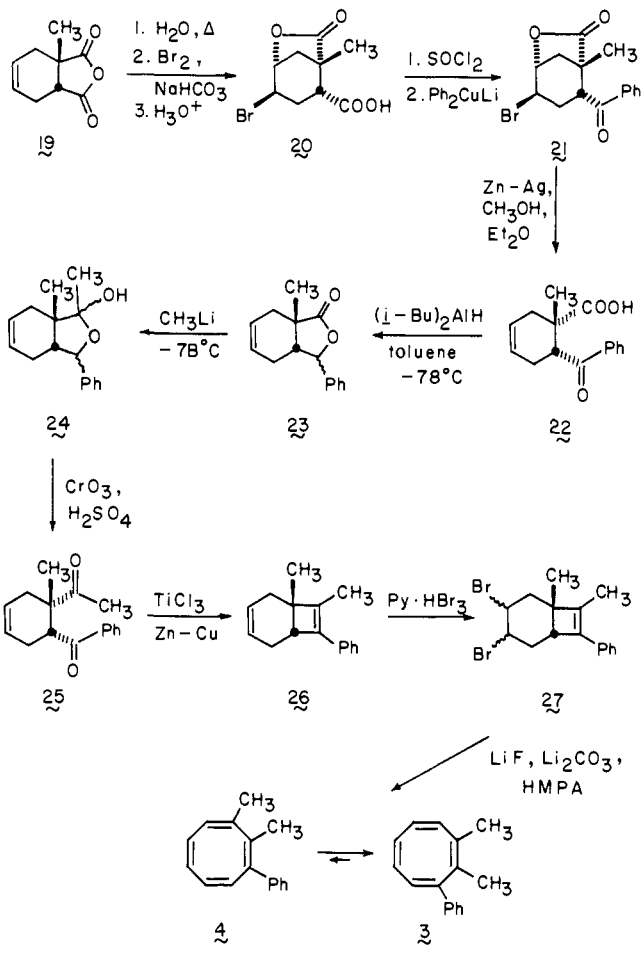
Scheme I



Scheme II



prove particularly well suited to a comparative analysis of tandem approaches. Thus, phenylmaleic anhydride (**9**) emerges as a logical precursor to sulfone **12** and bicyclo[4.2.0]octadiene **13** (Scheme I) when viewed in the context of the Photis ring contraction procedure.[7] Alternatively, a titanium(0)-mediated synthesis of bicyclooctadiene **26** was considered feasible in light of earlier work from this laboratory,[1] as long as diketone **25** could be made available (Scheme II). Proper assessment of both options would make known practical considerations which could well bias future synthetic undertakings in this area.

With commercially available phenylsuccinic acid (**8**) in hand, its direct conversion to **9** by concurrent oxidation–dehydration was achieved with high efficiency (94%) upon heating with selenium dioxide in acetic anhydride.[8] This dienophile entered readily into Diels–Alder reaction with butadiene under autoclave conditions (160 °C) to deliver the bicyclic intermediate **10** (92%). The classical four-step transformation of **10** into **12** proved once again to be highly serviceable. Submission of **12** to sequential α,α'-dimethylation and desulfonylative ring contraction led to the isolation of **13** in 42% overall yield. Generation of dibromide **14** from **13** was achieved by selective bromination of the cyclohexene double bond with pyridinium hydrobromide perbromide. The lack of any complications due to electrophilic attack on the four-membered ring once again attested to the widely divergent nucleophilicities of these two π bonds.

With the stage now set for entry via **15** to target cyclooctatetraene **3**, we proceeded to subject **14** to dehydrobromination with lithium fluoride and lithium carbonate in hexamethylphosphoramide at 60 °C. Under these conditions, essentially quantitative conversion to a mixture of **3** and **4** was realized. As will be seen below, the percentage of **3** in this mixture (80–85%) reflects the fact that complete equilibration had occurred between the pair of [8]annulenes. A variety of other conditions was examined for transforming **14** exclusively into **3**. However, the **3** → **4** interconversion could not be arrested and significantly lower yields were realized.

At this point, it was discovered that treatment of this mixture of cyclooctatetraenes with *N*-phenyltriazolinedione afforded a separable mixture of **16a** (66%) and **18a** (12%). This Diels–Alder procedure served to fractionate cleanly the bond shift isomers and to implicate bicyclo[4.2.0]octadiene **17** as a viable valence tautomer of **4**. Unfortunately, the small quantities of **18a** attainable in this manner caused it to be a rather elusive substance.

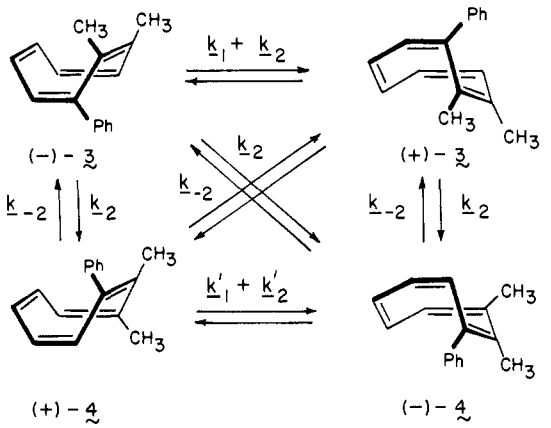
Nonetheless, independent hydrolysis–oxidation of the two urazoles afforded isomerically pure samples of **3** and **4** as colorless oils following chromatography on Florisil. While the methyl groups of **3** appear at δ 1.78 and 1.63 in $CDCl_3$, those of **4** are seen at 1.93 and 1.73. The electronic spectra are also distinctive, the $\lambda_{max}^{isooctane}$ for **3** (244 nm, log ϵ 4.16) appearing hypsochromically shifted from that of **4** (246 nm, log ϵ 3.79).

A second motive for developing Scheme II had now surfaced. The sulfone route is seen to necessarily proceed via **15**, the disrotatory opening of which provides **3** as the first-formed cyclooctatetraene. In contrast, bromination–dehydrobromination of **26** leads to **17** whose electrocyclic central bond cleavage should deliver **4** initially. Consequently, the development of suitably controlled conditions for effecting the **26** → **17** transformation might well allow this isomer to be prepared in usable quantities.

Distinction between the two carbonyl groups in **19** was simply achieved by conversion to **20**,[9] formation of the acid chloride, and condensation with lithium diphenylcuprate. Phenyl ketone **21**, which gave every indication of being stereochemically homoge-

(7) (a) Photis, J. M.; Paquette, L. A. *J. Am. Chem. Soc.* **1974**, *96*, 4715. (b) Paquette, L. A.; Photis, J. M. *Org. Synth.* **1977**, *57*, 53.
(8) Hill, R. K. *J. Org. Chem.* **1961**, *26*, 4745.
(9) Corey, E. J.; Sachdev, H. S. *J. Org. Chem.* **1975**, *40*, 579.

Scheme III

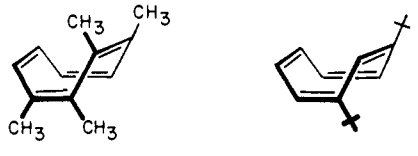


neous, underwent reduction in the presence of zinc–silver couple in high yield (94.5%) to **22**. The goal of arriving at **25** was realized without event. Diisobutylaluminum hydride reduction of **22** gave lactone **23** which in turn provided lactol **24** when treated with methyllithium. Upon exposure of **24** to the Jones reagent, oxidation occurred in part with loss of the methyl group and return to **23**. The major product proved, however, to be the desired **25** (52%). The ensuing reductive cyclization of this diketone with titanium trichloride and freshly prepared zinc–copper couple furnished **26** in 82% purified yield.

There now remained the demanding task of transforming **26** into **4**. While the requisite bromination step proceeded well, subsequent dehydrobromination could not be effected under conditions adequately mild to ensure the integrity of this cyclooctatetraene. The cleanest and most efficient route again involved the use of lithium fluoride and lithium carbonate in hexamethylphosphoramide. As before, bond shift isomer **3** predominated heavily (80–85%) over **4** in the mixture.

Our desire to acquire reasonable quantities of **4** was frustrated in yet another direction when it was uncovered that (−)-*endo*-bornyltriazolinedione entered very selectively into Diels–Alder reaction with these [8]annulene bond shift isomers. Within our limits of detection, **16b** was found to constitute <97% of the urazole mixture. Threefold recrystallization of the product from diisopropyl ether afforded colorless crystals, mp 82–86 °C, having $[\alpha]^{20}_D$ +34.9° in ethanol. The diastereomeric purity of this sample was ascertained by taking advantage of an observation made in another study[10] that the chemical shift of the bridgehead methyl group of the *endo*-bornyl moiety often reflects its distinctive chemical environment at 300 MHz or greater. In the present instance, all three bornyl methyl singlets were cleanly twinned, and the degree of diastereomeric enrichment was ascertained to be 84%.

Carefully controlled hydrolysis–oxidation of **16b** gave **3** as a colorless oil, $[\alpha]^{30}_D$ −76.7° in diglyme. The levorotatory nature of this hydrocarbon suggests that it possesses the absolute configuration given by formula **3**. This designation, which is based upon the established stereochemistries of (−)-**1**,[4a] (−)-**28**,[4b] and (−)-**29**,[4d] is of some interest, but understandably not crucial to the kinetic studies which follow.



Freshly prepared samples of (−)-**3** were dissolved in purified diglyme and immediately placed in a 1-dm polarimeter cell maintained at 42.2 and 52.5 °C by means of a circulating constant temperature bath. The rotations at 546 nm were recorded as a function of time, and plots of -ln α vs. time afforded straight lines whose slopes are equal to $2(k_1 + 2k_2)$[4a] where k_1 and k_2 refer to ring inversion and bond shifting, respectively (see Scheme III). For rates measured at 62.6 °C, recourse was made to a sealed ampule technique. The data compiled for duplicate runs at each temperature, together with the activation parameters, are summarized in Table I.

Table I. Summary of Racemization Rate Data for (−)-3

temp, °C	k, s^{-1}	corr coeff
42.2 ± 0.2	1.97×10^{-5}	0.9999
	2.11×10^{-5}	0.9998
51.2 ± 0.3	5.98×10^{-5}	0.9999
	6.13×10^{-5}	0.9999
62.6 ± 0.3	2.09×10^{-4}	0.9984
	2.08×10^{-4}	0.9999
19.5[a]	1.05×10^{-6}	
25[a]	2.25×10^{-6}	
30[a]	4.39×10^{-6}	
40[a]	1.57×10^{-5}	

$\Delta H^{\ddagger}_{(25\,°C)} = 23.4$ kcal/mol
$\Delta S^{\ddagger}_{(25\,°C)} = -5.7$ eu
$\Delta G^{\ddagger}_{(25\,°C)} = 25.2$ kcal/mol
$E_{act} = 24.0$ kcal/mol

[a] Extrapolated values.

Discussion

Simple inspection of the racemization rate constants and associated activation parameters provides at least an approximate answer to the problem stated in the introduction. Thus, k_{rac} for (−)-**3** is seen to be 21 times slower than that for (+)-**2** at 40.0 °C, but to compare more closely to that determined for the trimethyl derivative **1** (k_{rac}(**1**)/k_{rac}(**3**) = 4.3 at 42.2 °C). Therefore, the combined sum of ring inversion (RI) and bond shifting (BS) pathways leading from (−)-**3** to (+)-**4** (Scheme III) is more energetically competitive with the sum of those leading from (+)-**1** to (±)-**1**. Interestingly, concurrent RI and BS in (+)-**2** are considerably more facile. The overall trend is evident from the ordering of the $\Delta G^{\ddagger}_{(25\,°C)}$ values for the three systems: **3**, 25.2 kcal/mol; **2**, 24.3 kcal/mol; **1**, 23.1 kcal/mol. Additionally, the Me–Ph–Me substitution plan generates the more negative entropy of activation (-14.9 eu for **2**; -6.1 eu for **1**; -5.7 for **3**).

A completely rigorous evaluation of the dynamic behavior of the specific cyclooctatetraene involved here must take into account the fact that the reacting system can racemize by two distinctively different processes (RI and BS, alone and in tandem). Detailed kinetic analysis of such a system is rather complex since there are 16 concurrent unimolecular processes which interconnect (−)-**3** with three other molecules (Scheme III). Our present inability to obtain **4** in optically active form precludes the possibility of evaluating k_1', k_2', and k_{-2} directly. On the other hand, the combined experimental results for **1**–**3** indicate that k_1 and k_2 may be usefully approximated by the assumption that $k_1 \approx 20k_2$ in 1,2,3-trisubstituted cyclooctatetraenes at +30 °C.[1,3] In these terms, it can be calculated that k_1 and k_2 for **3** are roughly 25 and 20 times smaller than the values for **2** and **1**, respectively.

Consequently, the flanking phenyl group in **3** acts in a manner that causes it to impede flattening of the [8]annulene ring to an extent which is significantly larger than the effect of the third methyl group in **1**. In contrast, the interstitial phenyl group in **2** exerts a steric influence that is somewhat less than of a methyl group!

In an effort to delineate the source of the dissimilar effects, recourse has been made to molecular mechanics calculations using Allinger's MM2 program.[11] With only two exceptions to be noted subsequently, the necessary parameters proved to be inherent to the program or were otherwise available.[12,13] The definition of

(10) Klobucar, W. D.; Paquette, L. A.; Blount, J. F. *J. Org. Chem.* **1981**, *46*, 4021.

(11) QCPE Program 395, 1980 version, Indiana University, Bloomington, IN.

Table II. Calculated and Observed Enthalpies of Activation for Cyclooctatetraene Ring Inversion (kcal/mol)

substituent	E ground state	E transition state	$\Delta G^{\ddagger}_{exptl}$	$\Delta H^{\ddagger}_{exptl}$	$\Delta H^{\ddagger}_{calcd}$
1,2,3,4-tetramethyl[4a]	16.1	45.2	31.8	28.5	29.1
1,2,3-trimethyl (**1**)[4b]	13.7	37.0	24.3	22.5	23.3
1,3-dimethyl-2-phenyl (**2**)	10.8	30.1	23.1	18.7	19.3
1,2-dimethyl-3-phenyl (**3**)	9.1	32.9	25.2	23.4	23.8
1,8-dimethyl	10.8	30.7			19.9
phenyl	5.6	19.8			14.2
methyl	9.6	22.2			12.6
	8.5	20.3			11.8

three types of trigonal carbon atoms was initially required. The first two must serve to distinguish between the individual sets of stretching, bending, and torsional constants unique to the single and double bonds of the cyclooctatetraene nucleus, while the third must relate to those carbon atoms that constitute the phenyl substituent.

Whereas all compounds were calculated to exist in ground-state tub conformations, their transition states were constrained to a planar geometry by suitable torsional restriction. In contrast, exocyclic atoms could achieve non-zero dihedral angles as the result of out-of-plane bending modes. We recognize that thermally activated cyclooctatetraenes need not in reality be fully planar at the height of their RI transition states, since pseudorotational motions are entirely conceivable. However, calculations to model such alternate pathways are not easily achieved. Moreover, initial calculations revealed that planar transition states adequately conform to the experimental data.

Preliminary studies led to computed $\Delta H^{\ddagger}$ values which are 2–3 kcal/mol greater than those determined by experiment, and these differences were seen to increase systematically with enhanced peripheral steric congestion of the cyclooctatetraene. Since a substantial portion of the steric energy of these transition states is associated with bending terms and a major part of the energy of bending is a result of the 135° endocyclic bond angle, the C—C=C bending constant was decreased by 8%. While this modification caused no change in the calculated ground-state energies, it did decrease the energies of the planar transition states such that the calculated $\Delta H^{\ddagger}$ terms now averaged only 0.6 kcal/mol in excess of the experimental values (Table II).

For those compounds that carry a phenyl substituent, the normal bond length and stretching force constant selected are those used by Mislow.[14] It was necessary to define a torsional constant about the single bond between the phenyl and cyclooctatetraene rings. The V_2 term was selected to produce added stabilization to the conformation in which the phenyl ring is in conjugation with a double bond. The $V_2 = 2.000$ should be compared to the values of 1.704 and 8.479 for the single and double bonds, respectively, in the cyclooctatetraene ring.[13]

The calculated $\Delta H^{\ddagger}$'s for the compounds listed in Table II, which range from 11.8 to 29.1 kcal/mol, provide a broad spectrum of values upon which to base an interpretation of the special features of the isomeric 1,2-dimethyl-3-phenyl- and 1,8-dimethyl-2-phenylcyclooctatetraenes. For the unsubstituted, monosubstituted, and disubstituted derivatives, there exists limited experimental data. The experimental $\Delta H^{\ddagger}$ for cyclooctatetraene is estimated at less than 13.7 kcal/mol[15] on the basis of coalescence data and an assumed $\Delta S^{\ddagger} = 0$. For fluorocyclooctatetraene, the $\Delta G^{\ddagger}$ is 12 kcal/mol.[16] Thus, the calculated value for the parent hydrocarbon obtained in this study falls well within the proper range.

A methyl or phenyl group increases $\Delta H^{\ddagger}$, phenyl the more so. The reported $\Delta G^{\ddagger}$ of 14.8 kcal/mol for isopropylcyclooctatetraene[17] is similar to that of the calculated $\Delta H^{\ddagger}$ for the phenyl derivative. The free energy of ring inversion of 8-methylcyclooctatetraenylmethyl *O*-methylmandelate[18] is estimated as 18.4 kcal/mol. This substantially increased value, which is a direct result of vicinal substitution, is similarly reflected in our calculated $\Delta H^{\ddagger}$ for 1,8-dimethylcyclooctatetraene.

Of more relevance to the present undertaking is the close agreement between calculated and experimental enthalpies of activation for 1,2,3-trimethyl- and 1,2,3,4-tetramethylcyclooctatetraene.[4c] Clearly, the force field adequately represents those intramolecular interactions operative in these highly substituted compounds. This close agreement is pivotal to our analysis of the dimethyl phenyl derivatives.

The calculated $\Delta H^{\ddagger}$ for 1,2-dimethyl-3-phenylcyclooctatetraene (**3**) is slightly larger than that for 1,2,3-trimethylcyclooctatetraene (**1**), whereas that for 1,3-dimethyl-2-phenylcyclooctatetraene (**2**) is distinctly smaller. This ordering is in agreement with the experimental values. The source of this interesting difference resides in the phenyl group, more specifically its conformation in the ground and transition states. For the flanking phenyl group in **3**, the calculated dihedral angles are 25° and 87° for the ground and transition states, respectively. As concerns isomer **2**, the interstitial phenyl group is already twisted at a 60° dihedral angle in the ground state and rotates only an additional 25° (to 85°) while proceeding to the transition state.

The seemingly dissimilar effects of the phenyl group may consequently be readily explained on the basis of those differences unique to the particular set of ground and transition states. The ground-state energy of **3** is higher than that of **2** because of the eclipsing of a phenyl and a methyl in the former compound. Additionally, the torsional angle of the phenyl ring in **2** is more well suited for progress toward the transiton state. The transition-state energies of the isomeric compounds indicate that once a perpendicular conformation is achieved by the phenyl ring, the interstitial placement of the aryl substituent leads to lower nonbonded interactions between phenyl and methyl groups than between methyl and methyl in the compound with a flanking phenyl group.

Conclusion

In summary, we note that three major conclusions can be drawn from the present study. First, heavy contiguous peripheral substitution of a cyclooctatetraene frame apparently does not deter the molecule from adopting a ground-state tub conformation. However, important energy differences can appear depending upon how comfortably various substituent groups can tolerate each other sterically.

Second, our calculations have uncovered that a pendant phenyl ring will rotate out of conjugation with a neighboring cyclooctatetraene double bond when it is otherwise eclipsed by a methyl group. This phenomenon raises the ground-state energy while simultaneously preorienting the aryl unit for more facile access

(12) Allinger, N. L.; Frierson, M.; Van-Catledge, F. A. *J. Am. Chem. Soc.* **1982**, *104*, 4592.
(13) The authors thank Professor Allinger for providing us with his computational results for the parent cyclooctatetraene hydrocarbon arrived at by application of the MMP2 force-field procedure.
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to planar or quasiplanar transition states. The observable effect is a more rapid rate of racemization relative to isomers where an initial dihedral angle relationship is of much smaller magnitude.

Third, a phenyl ring positioned in a "knife-edge" orientation between a pair of flanking methyl groups introduces less nonbonded steric interactions than a methyl group in a comparable environment.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 467 spectrophotometer. The ^{1}H NMR spectra were determined with Varian T-60 and Bruker HX-90 instruments, and apparent splittings are given in all cases. Mass spectra were measured with an AEI-MS9 spectrometer at an ionization energy of 70 eV. Polarimetric measurements were made with a Perkin-Elmer Model 241 polarimeter. Microanalytical determinations were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

Phenylmaleic Anhydride (9). To a mechanically stirred slurry of selenium dioxide (127.8 g, 1.61 mmol) in freshly distilled acetic anhydride (600 mL) was added phenylsuccinic acid (195.0 g, 1.01 mol), and this mixture was heated at reflux for 12 h, during which time it turned from yellow to black. While still hot, the mixture was filtered through a Celite pad to remove precipitated selenium salts. The filtrate was cooled, and 106.5 g of the anhydride was collected. Subsequent solvent evaporation afforded an additional 62.4 g of product (94.3% total yield). Recrystallization from benzene–hexane afforded **9** as pale yellow crystals: mp 119–120 °C (lit.[8] mp 119–119.5 °C); IR (KBr, cm^{-1}) 3120, 1850, 1750, 1630, 1250; ^{1}H NMR ($CDCl_3$) δ 8.0 (m, 2 H), 7.55 (br m, 3 H), 7.00 (s, 1 H).

***cis*-4-Phenylcyclohexene-4,5-dicarboxylic Acid Anhydride (10).** A 2-L rocking autoclave was charged with **9** (110.2 g, 0.63 mol), freshly distilled butadiene (300 mL), hydroquinone (5 g), and dioxane (300 mL). This mixture was shaken at 160 °C for 24 h, cooled, and concentrated in vacuo. The residual oil was distilled through an L-shaped tube (sand bath temperature 220 °C and 0.01 torr) to give 133.3 g (92%) of **10** as a yellowish oil, essentially pure by ^{1}H NMR, which was utilized directly without additional purification: IR (neat, cm^{-1}) 3050, 2960, 1855, 1790, 1220; ^{1}H NMR ($CDCl_3$) δ 7.32 (m, 5 H), 6.0 (m, 2 H), 3.5 (m, 1 H), 2.70 (br m, 4 H); *m/e* calcd (M^+) 228.0786, obsd 228.0790.

***cis*-1-Phenyl-8-thiabicyclo[4.3.0]non-3-ene 8,8-Dioxide (12).** To a mechanically stirred refluxing slurry of lithium aluminum hydride (33.78 g, 0.89 mol) in anhydrous tetrahydrofuran (350 mL) was added dropwise under nitrogen a solution of **10** (48.79 g, 0.214 mol) in the same solvent (175 mL). The reaction mixture was heated at reflux for 48 h, cooled, quenched by the careful addition of sodium sulfate decahydrate (100 g), and stirred until the solid turned white. The insolubles were separated by filtration, placed in a Soxhlet extractor, and extracted with ether. The combined organic phases were dried and concentrated, and the resulting solid was recrystallized from ethyl acetate–hexane to furnish 41.05 g (88.0%) of diol **11a**, as a tan solid: mp 89–92 °C; IR ($CHCl_3$, cm^{-1}) 3350, 2890, 1490, 1440, 1030; ^{1}H NMR ($CDCl_3$) δ 7.25 (m, 5 H), 5.55 (m, 2 H), 4.15 (br s, 2 H), 3.8–3.4 (m, 4 H), 2.35 (m, 3 H), 1.85 (m, 2 H).

To a cooled (−5 °C) solution of **11a** (9.70 g, 44.5 mmol) and freshly distilled triethylamine (23 mL, 0.166 mol) in dry dichloromethane (130 mL) was added dropwise with stirring 10 mL (0.129 mol) of methanesulfonyl chloride. The mixture was stirred at room temperature for 4 h, poured into water, and extracted with dichloromethane (3 × 50 mL). The organic phase was washed with 10% hydrochloric acid (3 × 30 mL) and saturated brine (2 × 40 mL) prior to drying and solvent evaporation. There was isolated 19.31 g (100%) of dimesylate **11b** as a brown oil which was used without further purification: ^{1}H NMR ($CDCl_3$) δ 7.4 (m, 5 H), 5.7 (m, 2 H), 4.5–3.8 (series of m, 4 H), 2.84 (s, 3 H), 2.78 (s, 3 H), 2.6–1.95 (series of m, 5 H).

An anhydrous slurry of sodium sulfide in hexamethylphosphoramide (HMPA; possible carcinogen—careful handling is advocated) was prepared by distillation of the water–HMPA fraction (bp 36–120 °C at 30 torr) from a mixture of 99.0 g (0.413 mol) of sodium sulfide nonahydrate and 500 mL of HMPA. To the cooled slurry was added mesylate **11b** (50.0 g, 0.101 mmol), and the reaction mixture was stirred with heating at 110 °C for 20 h under a nitrogen atmosphere, cooled, poured into water (1000 mL), and extracted with petroleum ether (4 × 500 mL). The combined extracts were washed with water (5 × 1000 mL) and saturated brine (1000 mL), dried, and evaporated. The residue was chromatographed on alumina (elution with 5% ether in pentane) to yield a colorless liquid that was further distilled. There was obtained 16.5 g (71%) of bicyclic sulfide as a colorless liquid, bp 100–110 °C (0.5 torr), which solidified on standing: ^{1}H NMR ($CDCl_3$) δ 7.3 (m, 5 H), 5.6 (m, 2 H), 3.4–2.6 (m, 5 H), 2.55 (m, 2 H), 1.98 (m, 2 H).

To a mechanically stirred solution of the sulfide (2.65 g, 12.3 mmol) in ether (40 mL) cooled to 0 °C was added 33.20 mL of a 0.7813 N solution of monoperphthalic acid in ether (24.6 mmol). Upon completion of the addition, the reaction mixture was stirred at room temperature for 18 h and concentrated on a rotary evaporator. The residue was poured into 10% sodium hydroxide solution, and the product was extracted into dichloromethane (2 × 50 mL). The combined organic layers were washed with saturated brine (50 mL), dried, and evaporated to furnish sulfone **12** (2.97 g, 97.6%) as a colorless, crystalline solid: mp 156–157 °C (from acetone–hexane); IR ($CHCl_3$, cm^{-1}) 2970, 2880, 1490, 1300, 1230, 1110; ^{1}H NMR ($CDCl_3$) δ 7.30 (m, 5 H), 5.7 (m, 2 H), 3.6–3.0 (m, 5 H), 2.75 (m, 2 H), 1.95 (m, 2 H); *m/e* calcd (M^+) 248.0871, obsd 248.0879.

Anal. Calcd for $C_{14}H_{16}O_2S$: C, 67.71; H, 6.50; S, 12.91. Found: C, 67.74; H, 6.60; S, 12.63.

***cis*-1-Phenyl-7,8-dimethylbicyclo[4.2.0]octa-3,7-diene (13).** A cold (−78 °C), magnetically stirred solution of **12** (14.0 g, 0.056 mol) in dry tetrahydrofuran (350 mL) was treated under nitrogen with *n*-butyllithium in hexane (70 mL of 1.6 M, 0.112 mol). After 0.75 h, methyl iodide (40 g, 0.280 mol) dissolved in 50 mL of the same solvent was added dropwise during 30 min. The reaction mixture was stirred at −78 °C for 4 h, allowed to come to room temperature, and stirred for an additional 6 h. Water (50 mL) was next added, and most of the tetrahydrofuran was removed in vacuo. The residue was taken up in water (500 mL) and extracted with dichloromethane (3 × 150 mL). The combined organic layers were washed with water (500 mL), dried, and evaporated to give 16.2 g of dimethylated sulfone as a nearly colorless oil that crystallized on standing.

To an ice-cooled solution of this material (16.2 g, 0.056 mol) in dry dioxane (80 mL) was added *n*-butyllithium in hexane (35 mL of 1.6 M, 0.056 mol) while under a nitrogen atmosphere. The reaction mixture was allowed to warm to room temperature and transferred via canula to a refluxing slurry of lithium aluminum hydride (10.64 g, 0.280 mol) in dry dioxane (800 mL), also under a nitrogen atmosphere. Following 20 h at a reflux temperature, the mixture was cooled and excess hydride was decomposed by careful addition of Glauber's salt and a little water. The white solid was separated by filtration and washed with pentane. The combined filtrates were washed with water (5 × 1.5 L) and saturated brine (1.5 L) before drying. The solvent was evaporated to give 10.9 g of a yellow oil that was chromatographed on alumina (elution with pentane). There was isolated 4.94 g (42%) of **13** as a clear, colorless liquid. Double molecular distillation furnished the analytical sample (bp 70 °C at 0.1 torr): IR (neat, cm^{-1}) 3020, 2920, 1490, 1450, 720, 690; ^{1}H NMR ($CDCl_3$) δ 7.16 (m, 5 H), 5.70 (m, 2 H), 2.85–2.0 (m, 5 H), 1.55 (s, 6 H); *m/e* calcd (M^+) 210.1408, obsd 210.1413.

Anal. Calcd for $C_{16}H_{18}$: C, 91.37; H, 8.63. Found: C, 91.37; H, 8.68.

1,2-Dimethyl-3-phenyl- ⇄ 1,8-Dimethyl-2-phenylcyclooctatetraene (3 ⇄ 4). To a nitrogen-blanketed, magnetically stirred solution of **13** (187 mg, 0.89 mmol) in acetic acid (8 mL) and carbon tetrachloride (8 mL) was added pyridinium hydrobromide perbromide (358 mg, 1.12 mmol). The reaction mixture was stirred at room temperature until all the solid had dissolved (ca 8 h) and poured into water (100 mL). The layers were separated, and the aqueous phase was extracted with carbon tetrachloride (2 × 40 mL). The combined organic layers were washed with 5% sodium bisulfite solution (100 mL) and saturated brine (100 mL) prior to drying and solvent evaporation. There was isolated 314 mg (95.3%) of dibromide as a yellow oil.

The dibromide was added in one portion to a mechanically stirred slurry of lithium fluoride (257 mg, 9.89 mmol) and lithium carbonate (714 mg, 9.72 mmol) in dry hexamethylphosphoramide (10 mL). The reaction mixture was stirred and heated at 60 °C under nitrogen for 22 h, cooled, poured into water (40 mL), and extracted with petroleum ether (6 × 50 mL). The combined organic layers were washed with water (4 × 20 mL) and brine (20 mL), dried, and evaporated. There was obtained 185 mg (100%) of a mixture of **3** and **4**: ^{1}H NMR ($CDCl_3$) δ 7.10 (m, 5 H), 6.10–5.5 (m, 5 H), and broadened singlets at 1.80, 1.65, 1.50, and 1.20.

Formation of *N*-Phenyltriazolinedione Adducts. To a magnetically stirred solution of cyclooctatetraenes **3** ⇄ **4** (211 mg, 1.01 mmol) in ethyl acetate (20 mL) was added 186 mg (1.06 mmol) of freshly sublimed *N*-phenyltriazolinedione. The reaction mixture was heated at reflux under nitrogen for 24 h, cooled, and evaporated. The resulting brown oil was chromatographed on silica gel (elution with 15% ethyl acetate in petroleum ether) to give 44.9 mg (11.6%) of **18a** and 254 mg (65.6%) of **16a**, both as white crystalline solids.

For **18a**: mp 170–172 °C (from ethyl acetate–hexane); IR (KBr, cm^{-1}) 2940, 1770, 1710, 1500, 1405, 1075; ^{1}H NMR ($CDCl_3$) δ 7.41 (m, 5 H), 7.23 (s, 5 H), 6.45–5.85 (sextet of d, J = 5 and 2 Hz, 2 H), 5.35–5.10 (t of d, J = 5 and 2 Hz, 1 H), 4.8–4.6 (d of d, J = 6 and 2

Hz, 1 H), 3.2–2.9 (br m, 1 H), 1.85 (d, J = 1.5 Hz, 3 H), 1.50 (s, 3 H); m/e (M^+) calcd 383.1634, obsd 383.1641.

Anal. Calcd for $C_{24}H_{21}N_3O_2$: C, 75.17; H, 5.52; N, 10.96. Found: C, 74.92; H, 5.52; N, 10.93.

For **16a**: mp 201–202 °C (from ethyl acetate–pentane); IR (KBr, cm^{-1}) 3060, 2940, 1770, 1710, 1500, 1405; ^1H NMR ($CDCl_3$) δ 7.35 (m, 10 H), 6.60–5.95 (m, 2 H), 5.35–4.90 (m, 2 H), 3.45–3.15 (br m, 1 H), 1.50 (br s, 6 H); m/e calcd (M^+) 383.1634, obsd 383.1638.

Anal. Calcd for $C_{24}H_{21}N_3O_2$: C, 75.17; H, 5.52; N, 10.96. Found: C, 75.28; H, 5.60; N, 10.96.

Hydrolysis–Oxidation of 16a. A solution of **16a** (100 mg, 0.26 mmol) and sodium hydroxide (104 mg) in isopropyl alcohol (6 mL) was heated at reflux under nitrogen for 1 h. The reaction mixture was cooled in an ice bath, acidified to pH 1–2 with 3 N hydrochloric acid, and made basic (pH 9) by addition of 3 N ammonium hydroxide. Pentane (10 mL) and manganese dioxide (230 mg, 2.64 mmol) were added, and stirring was resumed for an additional 3 h. The contents were transferred to a separatory funnel with the aid of some water and pentane, and the layers were separated. The aqueous phase was extracted with pentane (2 × 10 mL), and the combined organic layers were washed with ice-cold 10% hydrochloric acid (20 mL), water (3 × 20 mL), and brine (20 mL) prior to drying and evaporation (no heat!). The residual oil was chromatographed on Florisil (pentane elution) to afford 30 mg (55%) of **3** as a colorless oil: UV (isooctane) λ_{max} 244 nm (log ϵ 4.16); ^1H NMR ($CDCl_3$) δ 7.20 (s, 5 H), 6.2–5.5 (m, 5 H), 1.78 (d, J = 1 Hz, 3 H), 1.63 (d, J = 1 Hz, 3 H); m/e calcd (M^+) 208.1252, obsd 208.1256.

Hydrolysis–Oxidation of 18a. The preceding procedure was utilized to convert 78 mg (0.2 mmol) of **18a** to **4** (20 mg, 50%) as a colorless oil after Florisil chromatography: UV (isooctane) 246 nm (log ϵ 3.79); ^1H NMR ($CDCl_3$) δ 7.25 (m, 5 H), 6.2–5.5 (m, 5 H), 1.93 (t, J = 2 Hz, 3 H), 1.73 (d, J = 1 Hz, 3 H); m/e calcd (M^+) 208.1252, obsd 208.1256.

Reaction with *endo*-Bornyltriazolinedione. To a magnetically stirred solution of cyclooctatetraenes **3** and **4** (600 mg, 2.87 mmol) in ethyl acetate (20 mL) under nitrogen was added freshly sublimed (–)-*endo*-bornyltriazolinedione (1.00 g, 4.26 mmol), and heating at the reflux temperature was maintained for 24 h. The reaction mixture was cooled and evaporated, and the resulting brown oil was chromatographed on silica gel (elution with 10% ethyl acetate in petroleum ether) to furnish 750 mg (59%) of a mixture of **16b** and **18b** as a crystalline white solid: mp 185–190 °C; IR ($CHCl_3$, cm^{-1}) 2940, 1750, 1700, 1415, 1390; ^1H NMR ($CDCl_3$) δ 7.25 (s, 5 H), 6.15 (m, 2 H), 5.0 (br m, 2 H), 4.26–4.09 (m, 1 H), 3.15 (br s, 1 H), 2.04–1.56 (m, 7 H), 1.55 (s, 6 H), 0.95 (s, 3 H), 0.87 (s, 3 H), 0.79 (s, 3 H).

Anal. Calcd for $C_{28}H_{33}N_3O_2$: C, 75.81; H, 7.50; N, 9.47. Found: C, 75.45; H, 7.52; N, 9.30.

This material was recrystallized three times from diisopropyl ether to provide fine white crystals [mp 82–86 °C, $[\alpha]^{20}_D$ + 34.9° (c 8.9, C_2H_5OH)], shown to be enriched to the extent of 84% of **16b** by 300-MHz ^1H NMR analysis of the methyl region.

Preparation of Bromo Keto Lactone 21. Anhydride **19** was hydrolyzed and subjected to bromolactonization in accordance with earlier precedent.[9] A suspension of **20** (20.0 g, 0.076 mol) in dry benzene (200 mL) was treated with 65 mL of thionyl chloride, and heating was continued for 3 h to effect dissolution. The reaction mixture was cooled and evaporated to provide the acid chloride as a yellow solid that was used immediately.

Lithium diphenylcuprate was generated by dropwise addition of freshly prepared phenyllithium (1.9 M, 240 mL) to a slurry of cuprous iodide (43.4 g) in dry ether (100 mL) with cooling (0 °C) under nitrogen. The cuprate was then cooled to –78 °C and added dropwise during 1.5 h to a cold (–78 °C), stirred solution of the acid chloride in anhydrous tetrahydrofuran (200 mL). Stirring was continued for an additional hour at –78 °C before warming to room temperature, quenching by gradual addition of saturated ammonium chloride solution (200 mL), and filtration through Celite. The phases were separated, and the aqueous layer was extracted with ether (2 × 200 mL). The combined organic phases were washed with saturated ammonium chloride (500 mL) and brine solutions (500 mL) prior to drying. Removal of solvent afforded a brown solid that was triturated with hexane to remove biphenyl and recrystallized from ether–hexane. There was obtained 11.5 g (47%) of **21** as a colorless crystalline solid: mp 174–175 °C; IR (Nujol, cm^{-1}) 1770 and 1660; ^1H NMR ($CDCl_3$) δ 7.95–7.70 (m, 2 H), 7.6–7.25 (m, 3 H), 4.8–4.4 (m, 1 H), 4.2–3.8 (m, 1 H), 3.0–2.0 (m, 5 H), 1.17 (s, 3 H); m/e calcd (M^+) 322.0205, obsd 322.0212.

Anal. Calcd for $C_{15}H_{25}BrO_3$: C, 55.75; H, 4.65. Found: C, 55.65; H, 4.65.

***trans*-4-Methyl-5-benzoylcyclohexene-4-carboxylic Acid (22).** Zinc dust (8.22 g) was stirred with 10% hydrochloric acid (50 mL) for 4 min, the supernatant was decanted off, and the residual metal was washed with acetone (2 × 50 mL) and ether (50 mL). A suspension of silver acetate (350 mg) in boiling glacial acetic acid (50 mL) was added, and the mixture was stirred for 1 min. The darkening Zn–Ag couple was then decanted from the acetic acid, washed with ether (2 × 50 mL) and methanol (50 mL), and used immediately.

Bromo lactone **21** (5.00 g, 15.5 mmol) was added as a slurry in ether (50 mL) to the freshly prepared couple in ether–methanol (1:1, 100 mL), and stirring was continued for 18 h. The metal was filtered off, and solvent was removed in vacuo to provide a light yellow oil that was treated with dilute sodium bicarbonate solution (2.64 g in 50 mL of water) and acidified to pH <1 with concentrated hydrochloric acid. The resulting solution was extracted with dichloromethane (2 × 100 mL), and the combined organic phases were washed with brine (100 mL), dried, and evaporated. There was isolated 3.57 g (94.5%) of **22** as a crystalline white solid: mp 180–183 °C; m/e calcd (M^+) 244.1099, obsd 244.1105.

Reductive Cyclization of 22 to Lactone 23. Diisobutylaluminum hydride (120 mL of 1 M in hexane) was added via syringe to a cold (–78 °C), magnetically stirred solution of **22** (5.0 g, 20.5 mmol) in anhydrous toluene (200 mL) under an atmosphere of argon. After 4 h at –78 °C, water (50 mL) was cautiously added, the reaction mixture was allowed to warm to room temperature, and the resulting gel was poured into ether (200 mL) and 10% hydrochloric acid solution (200 mL). After thorough shaking, the layers were separated, and the ethereal phase was further extracted with 10% hydrochloric acid (100 mL). The combined aqueous layers were extracted with ether (200 mL), and the ethereal layers were washed with brine (100 mL) prior to drying and solvent evaporation. There was obtained 4.7 g (94%) of **23** as a colorless crystalline solid: mp 106–107 °C (from ether–pentane); IR (Nujol, cm^{-1}) 1780; ^1H NMR ($CDCl_3$) δ 7.33 (s, 5 H), 5.73 (m, 2 H), 4.93 (d, J = 10 Hz, 1 H), 2.6–1.7 (series of m, 5 H), 1.25 (s, 3 H); m/e calcd (M^+) 228.1150, obsd 228.1156.

Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.90; H, 7.05. Found: C, 78.59; H, 7.00.

***trans*-4-Methyl-5-benzoyl-4-cyclohexenyl Methyl Ketone (25).** A solution of ethereal methyllithium (25 mL of 1.8 M) was added dropwise to a cold (–78 °C), magnetically stirred solution of **23** (5.0 g, 20.5 mmol) in anhydrous ether (175 mL). Stirring was continued for a further 2 h at –78 °C prior to dropwise addition of saturated ammonium chloride solution (50 mL). The layers were separated, the aqueous phase was extracted with ether, and the combined organic solutions were washed with saturated brine (100 mL) and dried. Removal of solvent under reduced pressure afforded **24** (5.2 g, 97%) as a colorless solid: mp 115–116 °C (from ether–hexane); IR (KBr, cm^{-1}) 3390; ^1H NMR ($CDCl_3$) δ 7.2 (m, 5 H), 4.53 (m, 2 H), 2.7–1.7 (series of m, 6 H), 1.43 (s, 3 H), 1.07 (s, 3 H); m/e calcd (M^+) 244.1463, obsd 244.1468.

The lactol (3.07 g, 12.6 mmol) was dissolved in acetone (50 mL), and Jones reagent (from 5.06 g of chromium trioxide, 12.6 mL of water, and 4.40 mL of concentrated sulfuric acid) was added rapidly over 2 min. The reaction mixture was stirred for 15 min before water and isopropyl alcohol (150 mL each) were added. Solids were removed by filtration through a Celite pad, and the filter cake was rinsed with ether until the filtrate was colorless. The isopropyl alcohol was removed on a rotary evaporator, and the aqueous residue was extracted with ether (4 × 100 mL). The combined organic layers were dried and concentrated to leave a residue that was chromatographed on silica gel (elution with 5% ethyl acetate in petroleum ether). The diketone was obtained as a pale yellow oil (1.58 g, 51.9%) that was used without further purification: ^1H NMR ($CDCl_3$) δ 7.4 (m, 5 H), 5.5 (m, 2 H), 3.4–2.2 (series of m, 5 H), 2.10 (s, 3 H), 1.35 (s, 3 H); m/e calcd (M^+) 242.1307, obsd 242.1315.

***cis*-1,8-Dimethyl-7-phenylbicyclo[4.2.0]octa-3,7-diene (26).** Zinc–copper couple was prepared by treating zinc dust (9.81 g, 150 g-atom) in deoxygenated water (40 mL) with copper sulfate (750 mg, 4.7 mmol). The black suspension was agitated by purging with a stream of nitrogen for 10 min. Following filtration, the couple was washed in turn with deoxygenated water, acetone, and ether, dried under high vacuum, and stored under argon.

Titanium trichloride (2.59 g, 16.8 mmol) and the couple (4.24 g) were added to dry, freshly distilled (from CaH_2 and then benzophenone ketyl) dimethoxyethane (100 mL) while the system was being swept by nitrogen. The resulting slurry was heated at reflux under nitrogen for 1 h with efficient stirring. Diketone **25** (206 mg, 0.85 mmol) dissolved in dry dimethoxyethane (50 mL) was introduced over 10 h via a syringe pump, and the reaction mixture was heated a second time, cooled, and filtered through Florisil under nitrogen (hexane elution). The eluate was evaporated to give **26** (293 mg, 82%) as an air-sensitive colorless liquid that was not further purified. The hydrocarbon appeared to be entirely stable if kept in ether solution in a refrigerator: ^1H NMR ($CDCl_3$) δ 7.4 (m, 5 H), 5.6 (br m, 2 H), 2.4–1.7 (series of m, 5 H), 1.78 (s, 3 H), 1.20 (s, 3 H); m/e calcd (M^+) 210.1408, obsd 210.1413.

Bromination–Dehydrobromination of 26. Treatment of **26** (185 mg, 0.89 mmol) with pyridinium hydrobromide perbromide in the predes-

cribed manner afforded a dibromide mixture (300 mg) that was directly subjected to elimination with LiF and Li_2CO_3 in HMPA as before. There was isolated 150 mg (82%) of a mixture of **3** and **4** identical with that encountered earlier (^1H NMR analysis).

Hydrolysis–Oxidation of (−)-*endo*-Bornyltriazolinedione Adduct 16b. A solution of **16b** ($[\alpha]^{24}_D$ + 39.6°, 100 mg, 0.226 mmol) and sodium hydroxide (350 mg, 8.75 mmol) in isopropyl alcohol was heated at reflux under nitrogen for 24 h. The reaction mixture was cooled in an ice bath, acidified to pH 1 with 3 N hydrochloric acid, and finally made basic to pH 9 with 3 N ammonium hydroxide. Pentane (10 mL) and activated manganese dioxide (300 mg, 3.45 mmol) were added, and the resulting mixture was stirred at room temperature for 40 min before being filtered. The solid was washed once with cold pentane (10 mL). The aqueous phase of the filtrate was extracted with pentane (10 mL), and the combined organic layers were washed with cold water (3 × 10 mL) and brine (2 × 10 mL) prior to drying and solvent removal at room temperature on a rotary evaporator. The brown oily residue was chromatographed on Florisil (6 g) at −78 °C (pentane elution) to give 30 mg of a colorless oil. This was dissolved in $CDCl_3$, and the ^1H NMR spectrum showed ca. 30% of **4** to be present along with **3**. The $CDCl_3$ was carefully removed and to the remaining 29 mg was added 1.07 g of diglyme and the specific rotation was determined: $[\alpha]^{30}_D$ −76.7°, $[\alpha]^{30}_{578}$ −81.9°, $[\alpha]^{30}_{546}$ −100.0°, $[\alpha]^{30}_{436}$ −279.1°.

Determination of Racemization Rates for (−)-3. The procedure described in the accompanying paper[1] was followed. A summary of the resulting data is given in Table I.

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Chemiluminescence Mechanism of Cyclic Hydrazides Such as Luminol in Aqueous Solutions

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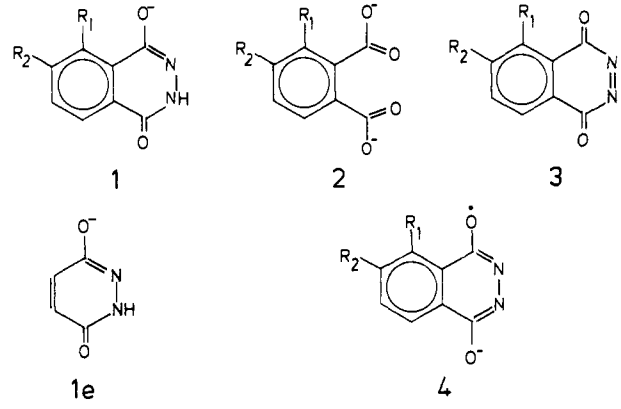
Abstract: Independently of the mode of oxidation, the first critical intermediate on the chemiluminescent pathway of luminol is a hydroperoxide. Below its pK_a it decomposes into oxygen and the parent hydrazide. At higher pH, the monoanion of the hydroperoxide expels nitrogen and yields a monoprotonated dicarboxylate. The latter is chemiexcited to some extent.

Being among the longest known synthetic chemiluminescing compounds, cyclic hydrazides **1** have been the subject of countless investigations starting with the famous paper by Albrecht[1] in 1928 (Chart I). Though the literature is replete with many suggestions, not much has emerged in the way of hard facts concerning the reaction mechanism. Elegant work in the laboratory of White et al.[2,3] has nevertheless revealed the main cornerstones of hydrazide chemistry. In aprotic solvents such as Me_2SO the overall stoichiometry was shown to involve the consumption of 1 mol each of the hydrazide dianion and O_2 to yield 1 mol of the dicarboxylate **2** and N_2. In each case the corresponding dicarboxylates have been proved to be the emitting species. Furthermore, the reaction of the two-electron oxidized hydrazide (the diazaquinone **3**) with H_2O_2 was shown to yield chemiluminescence as well.[4,5] In protic solvents, particularly water, chemiluminescence presupposes not only the presence of the hydrazide and a dioxygen species but also that of an oxidant.[6] Due to the sluggishness of the initial reaction step, kinetic investigations beyond it were not possible in the above studies.

In aqueous solutions the rate of the primary oxidation can be dramatically enhanced by means of radiolysis.[7] In a recent publication the quantum yield of radiolytically initiated luminol chemiluminescence was shown to be around 1%.[8] Characteristic features of radiolysis will now be briefly described insofar as they are relevant to hydrazide oxidation. Subject to ionizing radiation water decomposes to yield the radicals e_{aq}^-, H·, and OH·. By addition of N_2O e_{aq}^- is converted into OH· radicals. In oxygenated solutions e_{aq}^- and H· reduce O_2 to superoxide (O_2^{-}·). In the presence of the anions N_3^-, CO_3^{2-}, SCN^-, Br^-, and ClO_2^- the OH· radical produces the one-electron oxidants N_3·, CO_3^{-}·, $(SCN)_2^{-}$·, Br_2^{-}·, and ClO_2·, respectively. When the solution contains several solutes they compete for the radicals present and the competition is governed by the rate constants and the concentration of the solutes.

Chart I[a]



[a] a, R_1 = H, R_2 = H; b, R_1 = NH_2, R_2 = H; c, R_1 = H, R_2 = NH_2; d, R_1 = H, R_2 = $N(CH_3)_2$.

The above-mentioned one-electron oxidants produce one single radical species **4** upon reaction with a particular hydrazide.[9,10] This species, identified as the diazasemiquinone radical, quantitatively dismutes upon self-recombination (reaction 1) into the

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