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Bond Fixation in Annulenes. 15. A Titanium(0)-Mediated Synthesis of a Cyclooctatetraene. Probe of the Relative Size of the Interstitial Phenyl Substituent in 1,3-Dimethyl-2-phenylcyclooctatetraene by means of Racemization Kinetics[1]

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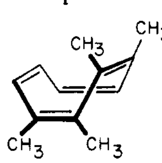
Abstract: A fully regiospecific synthesis of racemic 1,3-dimethyl-2-phenylcyclooctatetraene (**23a**) has been achieved on the basis of the expectation that *trans*-4-methyl-5-acetyl-4-cyclohexenyl phenyl ketone (**21a**) would undergo efficient titanium-(0)-promoted cyclization. The overall scheme allows for convenient replacement of one methyl substituent by a CD_3 group. Conditions were also found for arriving at bond shift isomer **23b** free of **23'b**. Cycloaddition of **23a** and *endo*-bornyltriazolinedione provided a diastereomeric pair of urazoles that were separated by fractional crystallization. Hydrolysis–oxidation led to (+)-**23a**, the rates of racemization of which were subsequently determined. When the data for 1,2,3-trimethylcyclooctatetraene for reference were used, k_{rac} was dissected into BS and RI rate constants. The dimethylphenyl derivative was thereby shown to be more dynamically mobile than its trimethyl congener. The probable sources of the greater conformational flexibility of **23a** are discussed.

Appreciable interest has arisen in the dynamic behavior of peripherally crowded cyclooctatetraenes.[1,3-5] Such compounds usually can be isolated as shelf-stable pairs of bond shift isomers, e.g., **1** and **2**, owing to heightened levels of steric strain which impede both ring inversion (RI) and bond shifting (BS) via planar localized (**3**) and weakly antiaromatic[3c] delocalized [8]annulene (**4**) transition states, respectively.[6] When methyl substituents are involved, the incremental increases in the barriers to both processes which are realized upon further substitution, i.e., di → tri → tetra, are seen to follow regular trends. The $\Delta\Delta G^\ddagger$ values are larger for RI than for BS because of the presumably greater steric demands present in **3** relative to **4**.[3c] Comparable influences



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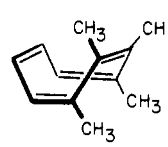

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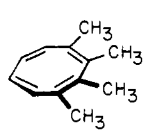

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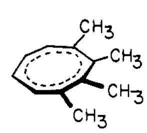

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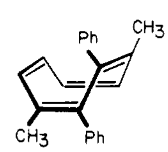
operate when pairs of *tert*-butyl groups are involved. Thus, 1,3-di-*tert*-butylcyclooctatetraene is conveniently resolved ($\Delta H^\ddagger_{RI}$ = 19.3 kcal/mol; $\Delta H^\ddagger_{BS}$ = 22.7 kcal/mol),[3d] whereas the 1,4-disubstituted congener is not ($\Delta H^\ddagger_{BS}$ = 14.8 kcal/mol).[1,4a] Here the decrease in spatial proximity is unmistakingly accompanied by increased conformational flexibility.

In a recent investigation designed to probe the relative steric consequences of phenyl vs. methyl substitution, the kinetic behavior cyclooctatetraenes **5** and **6** was extensively examined.[3f] It was uncovered that the $\Delta H^\ddagger_{BS}$ values for **5** (32.4 kcal/mol) and **6** (33.3 kcal/mol) are appreciably higher than that for **1** (28.1 kcal/mol). However, the magnitude of $\Delta H^\ddagger_{RI}$ found for **5** (27.1 kcal/mol) unexpectedly fell below that determined for **1** (28.5 kcal/mol). The dichotomy was rationalized in terms of out-of-plane spraying of the phenyl rings as in **7**, a description equivalent to assuming that the aryl groups probably do not pass through the [8]annulene plane simultaneously. Allowance was also made for angle



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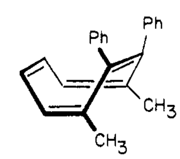

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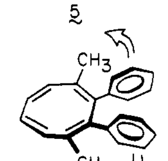

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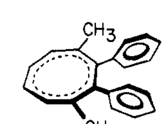

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bending, bond stretching, and in- and out-of-plane nuclear displacements by the medium-ring carbon atoms as a mechanism for spreading the total strain energy throughout the hydrocarbon framework. In contrast, arrival at **8**, a planar structure with equal bonds, should serve to restrict the conformational degrees of freedom just cited and cause **8** to be energetically less accessible than the tetramethyl counterparts.

The attainment of an enhanced understanding of the dynamic behavior of this class of compounds is considered to be both timely and important. In particular, the topological distinction made above between **7** and **8** demands further refinement. Since **5** and **6** each carry two phenyl substituents, matters may have been unnecessarily complicated. For this reason, attention has now been directed to three possible contiguously substituted dimethylphenylcyclooctatetraenes. The 1,3-dimethyl-2-phenyl example,

(1) Part 14: Paquette, L. A.; Hefferon, G. J.; Samodral, R.; Hanzawa, Y. *J. Org. Chem.* **1983**, *48*, 1262.

(2) (a) The Ohio State University Dissertation Fellow, 1977–1978. (b) NATO Postdoctoral Fellow of the Science Research Council, 1978–1980. (c) Graduate School Postdoctoral Fellow, 1979–1980.

(3) (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.

(4) (a) Lyttle, M. H.; Streitwieser, A., Jr.; Kluttz, R. Q. *J. Am. Chem. Soc.* **1981**, *103*, 3232. (b) Allinger, N. L.; Frierson, M.; Van-Catledge, F. A. *Ibid.* **1982**, *104*, 4592.

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(6) Paquette, L. A. *Pure Appl. Chem.* **1982**, *54*, 987.

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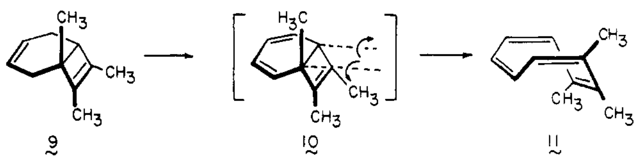
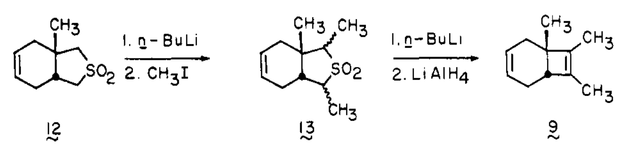
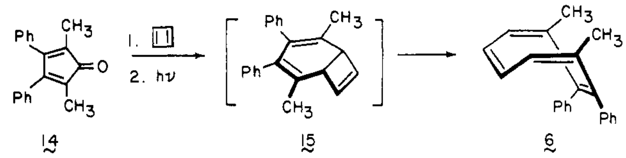
wherein the aryl substituent is situated interestitially between the two alkyl groups, is dealt with here. The companion paper describes our investigation relating to the other two isomers.[7]

Results

In the past, we have avoided the problems associated with the direct introduction of groups onto a preexisting cyclooctatetraene ring[8] by first elaborating a bicyclo[4.2.0]octadiene such as **9**. Since the cyclohexene double bond in dienes of this type is more reactive than the cyclobutene π linkage toward pyridinium hydrobromide perbromide, it becomes an easy matter to arrive at **10** via a bromination–dehydrobromination sequence. Due to the thermodynamic instability of bicyclo[4.2.0]octatrienes, valence isomerization ensues to deliver the cyclooctatetraene. Importantly, the requisite disrotatory central bond cleavage proceeds under strict orbital symmetry control[9] via exclusive electronic reorganization within the cyclohexadiene ring to deliver a single [8]annulene bond shift isomer, viz., **10** → **11**. Previously, 1,7,8-trimethylbicyclo-



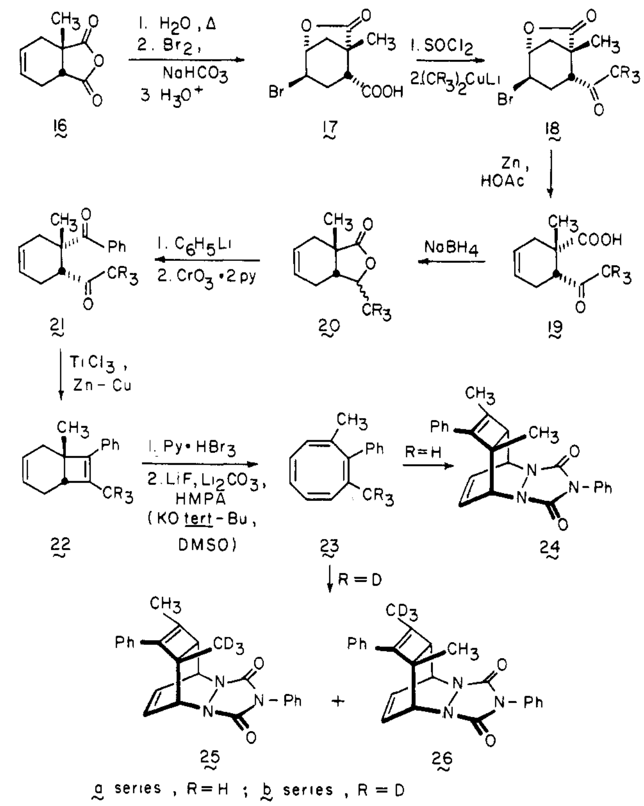




octatriene (**9**) was made available by α,α'-dimethylation of sulfone **12** and desulfonylative ring contraction of **13** by the Photis procedure.[3a,10] Obviously, the present need to place a phenyl substituent at the 8-position as in **22** could not be approached readily in an analogous manner. Nor was the route deployed to gain access to **6**[3f] (i.e., **14** → **15** → **6**) extrapolatable to the present circumstances because the appropriately substituted cyclopentadienone is unavailable. Cyclobutadiene addition to an *o*-benzoquinone comprises an alternative first step toward substituted cyclooctatetraenes,[1,3d,11] but the dimethylphenyl derivative required in the present instance is also unknown.

For these reasons, a phenomenologically new cyclooctatetraene synthesis was sought which offered tangible signs of being both broad in scope and fully compatible with the controlled installation of aryl substituents. In this regard, McMurry's titanium-induced intramolecular reductive coupling of carbonyl groups to olefins was viewed as particularly attractive.[12] The procedure had previously been shown to be tolerant of phenyl substituents and to produce cyclobutenes efficiently. Therefore, we set bicyclooctatriene **22** as one initial synthetic target and initiated a program aimed at the preparation of diketone **21a**. As shown in Scheme I, this intermediate can be readily obtained from the well-known citraconic anhydride–butadiene adduct **16**[13] by means of initial

Scheme I



hydrolysis and chemospecific conversion to bromo lactone **17**.[14] With the tertiary carboxylic acid functionality temporarily transformed into a lactone unit, it becomes possible to operate on the free secondary carboxyl residue without complication. Conversion of **17** to its acid chloride was accomplished uneventfully, as was the subsequent condensation with lithium dimethylcuprate,[15] provided that recourse was made to inverse addition in the latter step. Following reduction of **18a** with zinc dust in acetic acid to regenerate the γ,δ-unsaturated carboxylic acid moiety, selective reduction of the acetyl group was carried out with sodium borohydride. Cyclization occurred spontaneously during the workup procedure to deliver lactone **20a** as a mixture of epimers. Introduction of the phenyl substituent was next realized through reaction of **20a** with phenyllithium. Oxidation of the resulting lactone with Collins reagent[16] accomplished the desired conversion to **21a** without loss of configuration at the enolizable center.

When this diketone was subjected to reduction with titanium trichloride and zinc–copper couple, bicyclic diene **22a** was isolated in 97% yield after flash chromatography and molecular distillation. Regioselective bromination of **22a**, followed by treatment with a stirred slurry of lithium fluoride and lithium carbonate in HMPA at 65 °C,[17] afforded the desired cyclooctatetraene as a distillable, colorless liquid. Its room temperature 90-MHz ^{1}H NMR spectrum (in C_6D_6) consists of two distinguishable methyl signals. The CH_3 group which has no styrene character appears slightly downfield of the one which does (δ 1.83 vs. 1.79) and is slightly coupled (J = 1.2 Hz) to its neighboring vinylic proton. Variable-temperature studies gave no evidence of coalescence for these absorptions. Nor was the existence of an equilibrium with a bicyclo[4.2.0]octatriene tautomer apparent. Nevertheless, both

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(8) (a) Schröder, G. "Cyclooctatetraen"; Verlag Chemie: Weinheim/Bergstr., West Germany, 1965. (b) Paquette, L. A. *Tetrahedron* **1975**, *31*, 2855. (c) Fray, G. I.; Saxton, R. G. "The Chemistry of Cyclooctatetraene and Its Derivatives"; Cambridge University Press: New York, 1978.
(9) Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Verlag Chemie: Weinheim/Bergstr., West Germany, 1971.
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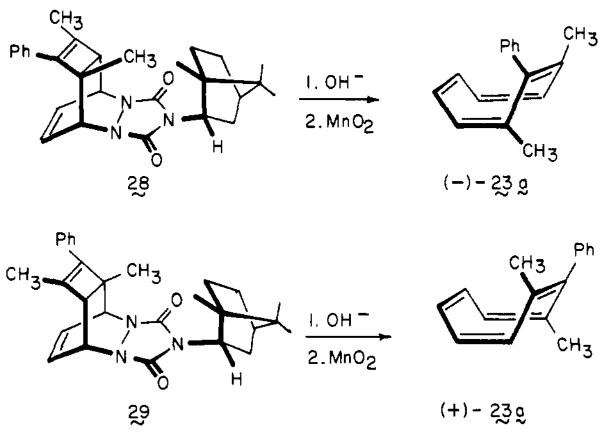
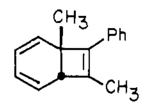
(15) (a) Posner, G. H.; Whitten, C. E. *Tetrahedron Lett.* **1970**, 4647. (b) Posner, G. H.; Whitten, C. E.; McFarland, P. E. *J. Am. Chem. Soc.* **1972**, *94*, 5106. (c) Fox, T.; Froborg, J.; Magnusson, G.; Thoren, S. *J. Org. Chem.* **1976**, *41*, 3518. (d) Paquette, L. A.; Snow, R. A.; Muthard, J. L.; Cynkowski, T. *J. Am. Chem. Soc.* **1978**, *100*, 1600; **1979**, *101*, 6991.
(16) Ratcliffe, R.; Rodehorst, R. *J. Org. Chem.* **1970**, *35*, 4000.
(17) King, P. F.; Paquette, L. A. *Synthesis* **1977**, 279.

Scheme II



valence tautomerism and bond shifting operate under these conditions.

For example, treatment of **23a** with *N*-phenyltriazolidinedione in refluxing benzene leads to adduct **24** in fair yield. This observation confirms the presence of low-level equilibrium concentrations of **27** but does not rule out the possible generation of its isomers. The heightened reactivity of **27** in Diels–Alder cycloaddition results from the unsubstituted nature of its 1,3-diene unit.



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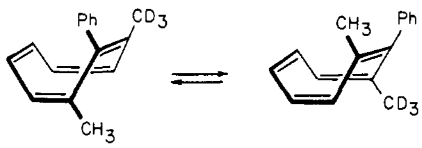
In order to assess the bond shifting question, the acid chloride of **17** was coupled with $(CD_3)_2CuLi$ to provide **18b**. Like its unlabeled counterpart, **18b** was carried through Scheme I in order to gain access to **22b**. With this diene in hand, bromination and dehydrobromination were performed, the latter with proper control of conditions (KO-*t*-Bu, Me_2SO) and temperature (20 °C), and the carefully purified cyclooctatetraene was seen to exhibit only a narrow upfield doublet at δ 1.83 in C_6D_6. Thus, it was possible to generate **23b** free of **23′b**. When this sample was warmed to



23b **23′b**

50 °C for 2 h, a singlet due to **23′b** at δ 1.7. arose in proportion to a decrease in the 1.83 signal. In line with this finding, treatment of pure **23b** with *N*-phenyltriazolinedione in benzene at the reflux temperature gave rise to an equimolar mixture of **25** and **26**.

Although kinetic analysis of the **23b** ⇄ **23′b** interconversion was clearly possible, this phase of our study was not pursued when it became known that comparable success could not be realized with the isomer pair having the phenyl substituent on the flank.[7]

However, heating of **23a** with enantiomerically pure (−)-*endo*-bornyltriazolinedione[18] resulted in conversion to the diastereomeric adducts **28** and **29** (Scheme II). Three recrystallizations of this material from a 1:1 ethyl acetate–petroleum ether solvent system afforded sharp-melting, colorless platelets of improved optical rotation, $[\alpha]_D^{20}$ +25.4° in ethanol. Upon alkaline hydrolysis and oxidation of this purified diastereomer with manganese dioxide at low temperature, the desired cyclooctatetraene was obtained as a colorless dextrorotatory oil. Should the absolute configuration of (+)-**23a** correspond to that of (+)-1,2,3-trimethylcyclooctatetraene,[3a] its stereoformula would be as indicated and **29** would then be the progenitor urazole (Scheme II). However, this point is only tangentially relevant.

Samples of (+)-**23a** produced in this way were immediately dissolved in purified diglyme, placed in a 1-dm polarimeter cell, and allowed to racemize in the 19.5–40.0 °C temperature range. The first-order kinetic data derived from these experiments are compiled in Table I. To facilitate comparison, analogous data for the trimethyl congener are summarized in Table II.

Table I. Summary of Racemization Rate Data for (+)-**23a** (Diglyme Solution)

temp, °C	k, s^{-1}	corr coeff
19.5 ± 0.2	3.642×10^{-5}	0.9996
	3.734×10^{-5}	0.9993
30.0 ± 0.2	1.205×10^{-4}	0.9997
	1.121×10^{-4}	0.9996
40.0 ± 0.2	3.415×10^{-4}	0.9995
	3.071×10^{-4}	0.9993

$\Delta H^{\ddagger}_{(25\,°C)} = 18.7$ kcal/mol
$\Delta S^{\ddagger}_{(25\,°C)} = -14.9$ eu
$\Delta G^{\ddagger}_{(25\,°C)} = 23.1$ kcal/mol
$E_{act} = 19.3$ kcal/mol

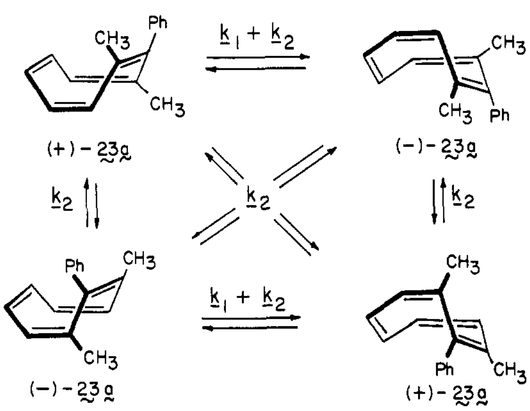
Table II. Summary of Racemization Rate Data for (−)-**11** (Diglyme Solution)[a]

temp, °C	k, s^{-1}	corr coeff
34.0 ± 0.1	$3.09\ (\pm 0.01) \times 10^{-5}$	0.9999
	$3.21\ (\pm 0.01) \times 10^{-5}$	0.9999
42.3 ± 0.1	$9.36\ (\pm 0.09) \times 10^{-5}$	0.9995
	$8.23\ (\pm 0.04) \times 10^{-5}$	0.9991
50.5 ± 0.3	$2.22\ (\pm 0.01) \times 10^{-4}$	0.9990
	$2.10\ (\pm 0.01) \times 10^{-4}$	0.9999

$\Delta H^{\ddagger}_{(25\,°C)} = 22.5$ kcal/mol
$\Delta S^{\ddagger}_{(25\,°C)} = -6.1$ eu
$\Delta G^{\ddagger}_{(25\,°C)} = 24.3$ kcal/mol
$E_{act} = 23.1$ kcal/mol

[a] Data taken from ref 3a and Gardlik, J. M. Ph.D. Thesis, The Ohio State University, 1978.

Scheme III



Discussion

To conform with earlier precedent,[3] we shall hereafter refer to the rates of ring inversion and bond shifting as k_1 and k_2, respectively. In the case of (+)-**23a**, both processes proceed with loss of optical activity. Scheme III also makes allowance for the incursion of ring inversion *with* bond shifting (diagonal arrows). When due consideration is given to the entire kinetic profile, the overall racemization rate (k_{rac}) can be shown to equal $2(k_1 + 2k_2)$.[3a]

With the availability of extensive data pertaining to the 1,2,3-trimethylcyclooctatetraene example (**11**),[3a] it becomes possible to approximate the values of k_1 and k_2 for **23a**. Thus, the k_1/k_2 ratio for **11** in the 34.0–50.6 °C region is seen to be remarkably constant at 19. On the assumption that this kinetic

(18) (a) Gardlik, J. M.; Paquette, L. A. *Tetrahedron Lett.* **1979**, 3597. (b) Paquette, L. A.; Doehner, R. F., Jr. *J. Org. Chem.* **1980**, *45*, 5105.

inequality will be reasonably characteristic[19] of the 1,2,3-trisubstitution pattern somewhat above room temperature, we have solved the preceding equation for $k_1 = 15k_2$ and also for $k_1 = 20k_2$ at 30 °C where k_{rac} for (+)-**23a** equals 1.16 × 10^{-4} s^{-1}. These computations provide a k_1 value of 5.15–5.25 × 10^{-5} s^{-1} and show k_2 to fall in the range of 2.64–3.40 × 10^{-6} s^{-1}. Comparison of these rate constants with the (extrapolated) value for **11** at 30 °C reveals that **23a** quite probably enters into ring inversion with approximately 6-fold greater facility than **11**. Bond shifting also occurs more readily (5.7–7.4) in the dimethylphenyl derivative.

That the replacement of the central methyl group in **11** by a phenyl substituent allows for more ready flattening of the [8]-annulene ring can also be gauged by the activation parameters associated with racemization of these two cyclooctatetraenes (Table I and II). The differences in $\Delta H^{\ddagger}$ and E_{act} (3.8 kcal/mol) are seen to be approximately 3 times larger than the $\Delta G^{\ddagger}$ gap. The dimethylphenyl substitution plan also lends itself to a lower entropy of activation.

These findings agree in direction with the experimentally determined $\Delta H^{\ddagger}_{RI}$ values for **5** and **1**[6] as noted earlier. Must we conclude that a phenyl group is effectively small than methyl in those planar alternate transition states which presumably are central to the ring inversion process? The ordering is opposite to that observed for bond shifting in **1** and **5**,[6] and also reversed when compared to the conformational energies of a lone phenyl or methyl group on a cyclohexane ring (2.87 and 1.74 kcal/mol, respectively).[20]

Proper comparison with the racemization behavior of **3** and/or **4** where the phenyl group no longer is directly involved in major buttressing strain would obviously be useful. This facet of the problem forms the subject of the accompanying paper.[7] Suffice it to say that we have found no existing quantified data concerning phenyl buttressing effects. Can it be that the benzene π cloud is capable of greater steric compression than methyl when circumstances dictate? Or does the cyclooctatetraene ring begin to buckle in response to increased levels of peripheral steric perturbation?

The decreased barrier to racemization in **23a** (relative to **11**) can without any doubt be ascribed to the onset of lesser strain interactions while proceeding to its transition state from its ground state. Consequently, adequate consideration must also be given to the possibility that tub-shaped **23a** suffers from meaningful steric congestion not present in **11**. Were this situation to pertain and the two activated complexes to prove otherwise isoenergetic, **23a** would obviously be the more prone to racemization. Further refinement of these questions follows in the sequel.

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.

Bromo Keto Lactone 17. The citraconic anhydride–butadiene adduct (**16**)[13] was subjected to bromolactonization as described elsewhere.[14] Lithium dimethylcuprate was prepared by dropwise addition of a freshly prepared, ethereal methyllithium solution to a cold (−10 °C), stirred slurry of cuprous iodide (4.0 g) in dry ether (100 mL). The addition was discontinued (ca. 40 mL) when the yellow precipitate of methylcopper was no longer in evidence. The clear solution was cooled to −50 °C, stirred for an additional 20 min, and subsequently added dropwise to a cold (−78 °C), stirred solution of the acid chloride of **17**[7] (5.6 g) in anhydrous tetrahydrofuran–ether (1:3, 100 mL) under argon. The reaction mixture was stirred for 30 min and treated dropwise with saturated ammonium chloride solution (100 mL). During a further 30 min of stirring, the solution was allowed to warm to room temperature, after which it was filtered through Celite. The layers of the filtrate were separated, the aqueous phase was extracted with ether (50 mL), and the combined organic solutions were washed with saturated brine (100 mL), dried, and evaporated. There was obtained 4.2, g (82%) of **18a** as long, colorless needles: mp 121–122 °C (from ether–pentane); IR (KBr, cm^{-1}) 3000, 2990, 1790, 1720, 1640, 1355, 1160, 1085, 1075, 970, 940; ^{1}H NMR ($CDCl_3$) δ 4.7 (m, 1 H), 4.47 (m, 1 H), 3.2–2.2 (series of m, 5 H), 2.15 (s, 3 H), 1.27 (s, 3 H); *m/e* calcd (M^+) 260.0049, obsd 260.0053.

Anal. Calcd for $C_{10}H_{13}BrO_3$: C, 46.00; H, 5.02. Found: C, 46.05; H, 4.96.

Analogous reaction of lithium di(methyl-d_3)cuprate with the same acid chloride (5.6 g, 17.8 mmol) afforded 4.1 g (78%) of **18b** as a colorless solid, mp 108–110 °,c, which was not further purified: IR (Nujol, cm^{-1}) 1780 and 1705 (weak C–D stretch at 2000); ^{1}H NMR, same as for the protio derivative except for the absence of the δ 2.15 singlet; *m/e* calcd (M^+) 263.0237, obsd 263.0245.

***trans*-4-Methyl-5-acetylcyclohexene-4-carboxylic Acid (19a).** A mixture of **18a** (3.7 g, 14.2 mmol), zinc dust (9.3 g, 142 mg-atom), and glacial acetic acid (100 mL) was stirred and heated at 50 °C for 24 h. Most of the solvent was removed in vacuo, and the resulting oil was taken up in ether (100 mL). This ethereal solution was washed with water (200 mL) and 10% sodium bicarbonate solution, acidified with concentrated hydrochloric acid, and extracted with ether (2 × 100 mL). The combined ethereal layers were washed with saturated brine (100 mL), dried, and evapoprated to give **19** as a colorless, crystalline solid (1.85 g, 72%): mp 110–114 °C; ^{1}H NMR ($CDCl_3$) δ 5.55 (m, 2 H), 3.0–1.6 (series of m, 5 H), 2.08 (br s, 3 H), 1.20 (s, 3 H); *m/e* calcd (M^+) 182.0943, obsd 182.0947.

Treatment of **18b** (4.5 g) with freshly prepared zinc–silver couple (8.0 g) in ether–methanol (2:1, 150 mL) at room temperature for 24 h was followed by filtration and evaporation of the filtrate. The oily residue was taken up in ether and washed with 1% sodium bicarbonate solution (200 mL; the sodium salt of the keto acid tended to precipitate from solution). The organic phase was removed and the aqueous layer and precipitate were acidified to pH 1 with concentrated hydrochloric acid. This solution was extracted with dichloromethane (2 × 10 mL) and the combined organic layers were washed and saturated brine (100 mL), dried, and concentrated. There was isolated 3.0 g of **19b**, the ^{1}H NMR spectrum of which lacked the methyl absorption at δ 2.08.

Reductive Cyclization of 19a to Lactone 20a. A magnetically stirred solution of **19a** (1.85 g, 10.2 mmol), sodium bicarbonate (1.43 g, 17 mmol), and sodium borohydride (1.0 g, 26.3 mmol) in water (60 mL) was stirred at room temperature for 1 h, made acidic (pH 1-2) by the careful addition of concentrated hydrochloric acid, and extracted with ether (3 × 50 mL). The combined organic layers were washed with water (100 mL) and brine (100 mL) prior to drying. Solvent evaporation afforded 1.14 g (67%) of **20a** as a yellowish oil: IR (neat, cm^{-1}) 1780; ^{1}H NMR ($CDCl_3$) δ 5.60 (m, 2 H), 4.3–3.8 (m, 1 H), 2.4–1.7 (series of m, 5 H), 1.35 (d, *J* = 8 Hz, 3 H), 1.25 (s, 3 H).

Comparable reduction of **19b** (3.0 g) at 0 °C gave 2.6 g of **20b** as an oil which slowly crystallized; *m/e* calcd (M^+) 169.1182, obsd 169.1188; the ^{1}H NMR spectrum was devoid of the doublet at δ 1.35.

Lactol Formation. A cold (−78 °C) solution of **20a** (1.14 g, 6.852 mmol) in dry ether (40 mL) was treated under a nitrogen atmosphere with 20 mL of a 1.8 M solution of phenyllithium in benzene–ether (7:3, 3.6 mL). The reaction mixture was stirred at −78 °C for 30 min, allowed to come to room temperature, and carefully treated with 50 mL of water. The aqueous phase was extracted with ether (2 × 50 mL), and the combined organic layers were washed with water (100 mL) and brine (100 mL) prior to drying. Solvent evaporation left a white solid which was chromatographed on silica gel. Pentane elution removed biphenyl. Continued elution with 20% ether in pentane afforded 1.4 g (83%) of lactol as colorless crystals: mp 145–152 °C (from ether–hexane); IR (KBr, cm^{-1}) 3420; ^{1}H NMR ($CDCl_3$) δ 5.4 (m, 2 H), 4.1–3.5 (m, 1 H), 2.70 (s, 1 H), 2.4–1.4 (series of m, 5 H), 1.15 (d, *J* = 8 Hz, 3 H), 1.10 (s, 3 H); *m/e* calcd (M^+) 244.1463, obsd 244.1466.

Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.68; H, 8.19.

Analogous treatment of **20b** (2.6 g, 15.4 mmol) and ultimate chromatography on Florisil (elution with 20% ether in hexane) gave 3.2 g (84%) of lactol-d_3 as a colorless solid. The doublet at δ 1.15 was lacking in its ^{1}H NMR spectrum; *m/e* (M^+) at 247 was observed, but was too transient for high resolution meaurement.

***trans*-4-Methyl-5-acetyl-4-cyclohexenyl Phenyl Ketone (21a).** A nitrogen-blanketed flame-dried flask was charged with dry dichloromethane (30 mL, freshly distilled from BaO) and pyridine (2.37 mL, 29.6 mmol). The reaction vessel was cooled in an ice bath and chromium trioxide (1.48 g, 14.8 mmol) was added in one portion. The stirred

(19) While the 1,4-dimethyl-2,3-diphenyl systems exhibit a comparable k_1/k_2 ratio of 16–26 at 100–120 °C, that for the 1,2,3,4-tetramethyl congener is seen to be much lower (1.2–2.1) for comparably elevated temperatures (120–160 °C).

(20) Eliel, E. L.; Manoharan, M. *J. Org. Chem.* **1981**, *46*, 1959 and relevant references cited therein.

reaction mixture was allowed to warm to room temperature and a solution of lactol (600 mg, 2.46 mmol) in dry dichloromethane (10 mL) was added during 5 min. After an additional hour, the supernatant was decanted from the tarry precipitate which was triturated with boiling ether (2 × 20 mL). The combined organic layers were eluted through a short column of Florisil. The eluate was concentrated in vacuo, and the residue was dissolved in ether. Hexane was added unitl the solution become cloudy, causing 182 mg of starting lactol, mp 147–150 °C, to crystallize. The mother liquor was concentrated in vacuo, and the resulting oil was molecularly distilled (120 °C and 0.1 torr) to give 350 mg (58%) of **21a** as a colorless oil: IR (neat, cm^{-1}) 1705, 1670; ^1H NMR ($CDCl_3$) δ 7.7–7.1 (m, 5 H), 5.52 (m, 2 H), 3.4–2.15 (series of m, 5 H), 2.09 (s, 3 H), 1.33 (s, 3 H); *m/e* calcd (M^+) 242.1307, obsd 242.1313.

Analogous treatment of the trideuteriomethyl derivative (240 mg) afforded 190 mg of **21b** lacking the δ 2.09 singlet in its ^1H NMR spectrum; *m/e* calcd (M^+) 245.1495, obsd 245.1500.

1,7-Dimethyl-8-phenylbicyclo[4.2.0]octa-3,7-diene (22a). Zinc–copper couple was prepared by adding to zinc dust (9.87 g, 150 mg-atom) in deoxygenated water (40 mL) solid cupric sulfate (750 mg, 4.7 mmol). The black suspension was agitated by purging with nitrogen for 10 min, filtered under nitrogen, washed sequentially with deoxygenated water, acetone, and ether, dried under high vacuum, and stored under argon.

In an argon-blanketed flame-dried flask was placed titanium trichloride (940 mg, 6.7 mmol) and 1,2-dimethoxyethane (20 mL, doubly distilled first from CaH_2, then from sodium benzophenone ketyl). Magnetic stirring was initiated, zinc–copper couple (1.54 g) was added, and the reaction mixture was heated at reflux for 1 h under argon. A solution of **21a** (75 mg, 0.31 mmol) in dry dimethoxyethane (20 mL) was added during 9 h by means of a syringe pump, and heating was continued for an additional 12 h. An addition 75-mg sample of **21a** was introduced, and the cycle was repeated as before. At this point, the reaction mixture was cooled to room temperature, vacuum filtered through a pad of Florisil under argon, and evaporated. The residue was taken up in pentane (20 mL), washed with water (2 × 20 mL) and brine (20 mL), and dried. Solvent removal afforded **22a** (126 mg, 97%) as a colorless oil. The analytical sample was obtained from chromatography on Florisil (pentane elution) and molecular distillation: IR (neat, cm^{-1}) 3080–2820, 1492, 1450, 1370, 760, 685, 668; ^1H NMR ($CDCl_3$) δ 7.15 (s, 5 H), 5.75–5.50 (m, 2 H), 2.6–1.9 (series of m, 5 H), 1.80 (s, 3 H), 1.34 (s, 3 H); *m/e* calcd (M^+) 210.1408, obsd 210.1412.

Anal. Calcd for $C_{16}H_{18}$: C, 91.37; H, 8.63. Found: C, 91.44; H, 8.55.

Comparable treatment of **21b** (190 mg) furnished **22b** (135 mg), the ^1H NMR of which lacked the singlet at δ 1.80; *m/e* calcd (M^+) 213.1597, obsd 213.1601.

1,3-Dimethyl-2-phenylcyclooctatetraene (23a). To a solution of **22a** (133 mg, 0.63 mmol) in a mixture of carbon tetrachloride (6 mL) and glacial acetic acid (6 mL) was added pyridinium hydrobromide perbromide (200 mg, 0.62 mmol) in one portion. Following 12 h of stirring at room temperature, the reaction mixture was poured into water (75 mL) 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 brine (100 mL) prior to drying and solvent evaporation. The resulting oily dibromide was dissolved in dry hexamethylphosphoramide (10 mL, distilled from CaH_2), treated with lithium fluoride (165 mg, 6.34 mmol) and lithium carbonate (470 mg, 6.34 mmol), and stirred with heating at 60–65 °C for 20 h under nitrogen. The reaction mixture was 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 to give a yellow oil (96.6 mg) which was chromatographed on Florisil (2 g, pentane elution). Solvent removal and molecular distillation (100 °C, 0.1 torr) afforded **23a** (56 mg, 42% overall) as a colorless oil: ^1H NMR (C_6D_6) δ 7.2 (s, 5 H), 6.0–5.3 (m, 5 H), 1.83 (d, *J* = 1.2 Hz, 3 H), 1.79 (s, 3 H); *m/e* calcd (M^+) 208.1252, obsd 208.1248.

Bromination of **22b** (235 mg, 1.1 mmol) in the predescribed manner afforded 510 mg of dibromide as a brown oil. This material was dissolved in dry dimethyl sulfoxide (5 mL) and added dropwise during 5 min to a stirred solution of potassium *tert*-butoxide in the same solvent (10 mL) at room temperature. The black solution was stirred for 45 min, poured into ice water (25 mL), and extracted with pentane (3 × 25 mL). The combined extracts were washed with water (2 × 50 mL) and brine (50 mL), dried, and evaporated (no heat!). The resulting oil (90 mg) was subjected to rapid preparative TLC on silica gel (elution with hexane) in a cold room. The hydrocarbon purified in this manner exhibits in C_6D_6 a narrow doublet (*J* = 1.2 Hz) at δ 1.83 indicating the presence of **23b** and not **23'b**. When this sample was heated at 60 °C for 2 h, a singlet at δ 1.70 due to **23'b** arose in proportion to a decrease in the 1.83 signal (C_6H_6 as internal standard).

Formation of the *N*-Phenyltriazolinedione Adduct. A solution of **23a** (56 mg, 0.26 mmol) in benzene (2 mL) was heated to 50 °C and treated with an excess of *N*-phenyltriazolinedione dissolved in ethyl acetate (2 mL). The reaction mixture was heated at reflux under a nitrogen atmosphere for 48 h, cooled to room temperature, and deposited on 1 g of Florisil. This solid was placed atop a 4-g column of Florisil and eluted first with hexane and finally with 10% ethyl acetate in hexane. The latter solvent system eluted 20 mg of **24** as a colorless crystalline solid: mp 157–159 °C (from ethyl acetate–hexane); ^1H NMR ($CDCl_3$) δ 7.45 (m, 5 H), 7.31–7.19 (7, 5 H), 6.4–6.05 (m, 2 H), 5.15–4.95 (m, 2 H), 2.78 (m, 1 H), 1.89 (d, *J* = 1.2 Hz, 3 H), 1.63 (s, 3 H); *m/e* calcd (M^+) 383.1634, obsd 383.1641.

Formation of the *endo*-Bornyltriazolinedione Adduct. A sample of unpurified **23a** (1.5 g) was immediately dissolved in ethyl acetate (50 mL), heated to the reflux temperature under argon, and treated with a solution of (−)-*endo*-bornyltriazolinedione[18] (2.0 g) in ethyl acetate (10 mL). Heating was continued for an additional 48 h, and the solution was cooled and evaporated. The residue was chromatographed on silica gel (30 g) (elution with 5 → 10% ethyl acetate in petroleum ether) to give 950 mg of **28**/**29**. Three recrystallizations of this material from ethyl acetate–petroleum ether (1:1) afforded colorless crystalline platelets: mp 268–269 °C; $[\alpha]^{20}_{578}$ +26.4°, $[\alpha]^{20}_{546}$ +30.1°, $[\alpha]^{20}_{436}$ +52.4°, $[\alpha]^{20}_{365}$ +80.2°, $[\alpha]^{20}_D$ +25.4° (*c* 8.1, C_2H_5OH); ^1H NMR ($CDCl_3$) δ 7.25 (m, 5 H), 6.20 (m, 1 H), 6.02 (m, 1 H), 4.92 (t, *J* = 5.5 Hz, 1 H), 4.81 (d, *J* = 5.5 Hz, 1 H), 4.22 (m, 1 H), 2.68 (d, *J* = 3.9 Hz, 1 H), 2.4 (dd, *J* = 12.8 and 5.5 Hz, 1 H), 2.0–1.1 (series of m, 8 H), 1.85 (s, 3 H), 1.60 (s, 3 H), 0.96 (s, 3 H), 0.87 (s, 3 H), 0.80 (s, 3 H).

Anal. Calcd for $C_{28}H_{33}N_3O_2$: C, 75.81; H, 7.50; N, 9.47. Found: C, 75.67; H, 7.57; N, 9.28.

Hydrolysis–Oxidation of (−)-*endo*-Bornyltriazolinedione Adduct 29. A solution of **29** (396 mg, 0.89 mmol) and sodium hydroxide (1 g) in isopropyl alcohol (100 mL) was heated at reflux under nitrogen for 20 h. The cooled mixture was made acidic by addition of 3 N hydrochloric acid and subsequently made basic with 3 N ammonium hydroxide solution. Ether (100 mL) was added, the two-phase mixture was cooled in ice, and activated manganese dioxide (1 g, 11.5 mmol) was introduced. After 20 min of stirring at 0 °C, the solid was separated by filtration, and the filtrate was evaporated at 0 °C. The residual brown oil was purified by Florisil chromatography at −45 °C (elution with ether–petroleum ether, 1:10) to give 120 mg of (+)-**23a**, with spectra identical with those reported above: $[\alpha]^{20}_D$ +19.5° (*c* 32, ether). In a second run, 150 mg of **29** led to 80 mg of (+)-**23a** with the same optical rotation.

Determination of Racemization Rates. The samples of optically active (+)-**23a** produced as indicated above were immediately dissolved in purified diglyme (distilled from Na–K alloy) (120 mg/4 mL; 80 mg/2.5 mL). The first solution was used for the kinetic runs at 40 and 30 °C and the second for the 1.5 °C determinations. All rotations were measured at the α_{546} mercury line. An aliquot of the solution (ca. 1 mL) was transferred to a thermostated polarimeter tube (1 dm) and allowed to equilibrate for a few minutes, at which point an accurate timer was started. Readings of α were taken at appropriate time intervals. The slopes of the mean plots of −ln α vs. time were determined by a linear least-squares analysis of the experimental data points in each case. Rate constant values are given in Table I. In each experiment, the infinity point read 0° after some heating to complete the racemization. The ^1H NMR spectra of select recovered samples showed only **23a** to be present.

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