4,4-Diphenylcyclohexa-2,5-dienylidene: Rearrangement via an Isobenzene Pathway

Peter K. Freeman* and James K. Pugh

Department of Chemistry, Oregon State University, Corvallis, Oregon 97331

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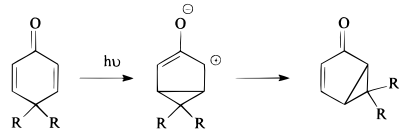
Pyrolytic decompostition of the Li salt of the tosylhydrazone of 4,4-diphenyl-2,5-cyclohexadienone produces a mixture of products which includes biphenyl, *p*-terphenyl, the azine of 4,4-diphenyl-2,5-cyclohexadienone, and *o*-terphenyl. ^{13}C labeling studies and computational results (semiempirical AM1 and density functional B3LYP/6-31G* molecular orbital calculations) elucidate the mechanistic pathway for the formation of *o*-terphenyl. A single mechanism is involved which proceeds through formation of an isobenzene species followed by subsequent phenyl and hydrogen migrations.

The photochemistry of the cyclohexadienone chromophore has been known for some time.[1] Early work focused on the photochemical rearrangement of the sesquiterpene α-santonin and its route to product formation.[2] This led to a decade of intensive studies on the 2,5-cyclohexadienone system during the 1960s that elucidated the mechanistic pathway for rearrangement.[3] Evidence has been developed for a sequence of steps that is formally represented by a $[{}_{\pi}2_a + {}_{o}2_a]$ reaction.[4] The mechanism includes a zwitterionic intermediate as outlined in Scheme 1.

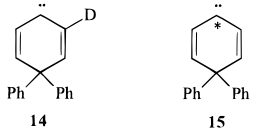
With this background, it was logical to investigate the carbene analogue. If a singlet carbene were generated that contained the electron pair in the σ orbital, then a similar rearrangement might well occur. Carbene **4** could undergo an allylcarbinyl−cyclopropylcarbinyl rearrangement to generate zwitterion **5**. A 1,4 sigmatropic shift would then produce bicyclic bivalent **6** as in Scheme 2.

Previously we have investigated carbene rearrangements of 4,4-diphenylcyclohexa-2,5-dienylidene (**4**).[5] Thermal degradation of the lithium salt of the tosylhydrazone of ketone **7** gave seven products. Five of the products could be identified and are shown in Scheme 3. The azine (**11**) was formed in 51% yield, with the volatile monomeric components (6.4%) present in a percent composition ratio of 24.8 (**9**):9.2 (**10**):46.7 (**12**):5.8 (**13**); a fifth component (13.4%) remains unidentified. This work focuses on the mechanistic formation of *o*-terphenyl (**12**), the major monomeric product. This product is unique to the diaryl-substituted cyclohexadienylidene intermediates for no ortho products were isolated from analogous 4,4-dialkylcyclohexadienylidenes.[6] It is known that the photochemistry of 4,4-diphenylcyclohexadienones can lead to similar products via a carbocation intermediate followed by a phenyl migration.[7] If there were a proton source available during the tosylhydrazone degradation, a carbocation could form to provide a route to *o*-terphenyl formation. To test the sensitivity of the decomposition to protic impurities, tosylhydrazone **8** was converted to its sodium salt with sodium hydride and photolyzed in THF in the presence of 1 equiv of deuterium oxide.[5] No deuterium was found to be incorporated into the *o*-terphenyl. This provides evidence that the *o*-terphenyl is formed via a carbene rearrangement and not through a carbocation intermediate.

Scheme 1



A first thought was to consider the formation of *o*-terphenyl using monodeuterated diphenylcyclohexadienylidene (**14**).[5] Using this experimental approach, three alternative mechanistic schemes were evaluated. Our current investigation utilizes diphenylcyclohexadienylidene with a ^{13}C enhancement at C-1 (**15**). The following mechanistic schemes follow the path of both the deuterium and the proposed ^{13}C label. Scheme 4 starts with the rearrangement of diphenylcyclohexadienylidene (**4a**) to bicyclic carbene **6a** (**6b**). A cyclopropylcarbinyl to allylcarbinyl ring cleavage produces **16a** (**16b**). A 1,2-phenyl shift generates carbene **17a** (**17b**). Hydrogen (deuterium) migration leads to *o*-terphenyl with equal proportions of



(1) Schuster, D. I. *Acc. Chem. Res.* **1978**, *11*, 65 and references therein.

(2) Barton, D. H. R. *J. Chem. Soc.* **1958**, 3314.

(3) (a) Zimmerman, H. E. *Adv. Photochem.* **1963**, *1*, 183. (b) Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1961**, *83*, 4486. (c) Zimmerman, H. E.; Crumrine, D. S.; Dopp, D.; Huyfter, P. S. *J. Am. Chem. Soc.* **1969**, *91*, 434. (d) Zimmerman, H. E.; Epling, G. A. *J. Am. Chem. Soc.* **1972**, *94*, 7806. (e) Schuster, D. I.; Liu, K. C. *J. Am. Chem. Soc.* **1971**, *93*, 6711.

(4) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie/Academic: Weinheim, 1970.

(5) Freeman, P. K.; Swenson, K. E. *Tetrahedron* **1982**, *38*, 3737.

(6) (a) Fry, A. J. *J. Am. Chem. Soc.* **1965**, *87*, 1816. (b) Jones, M., Jr.; Harrison, M.; Rettig, K. R. *J. Am. Chem. Soc.* **1969**, *91*, 7462. (c) Berdick, R. H.; Levin, R. H.; Wolf, A. D.; Jones, M., Jr. *J. Am. Chem. Soc.* **1973**, *95*, 5087. (d) Wolf, A. D.; Kane, V. V.; Levin, R. H.; Jones, M. *J. Am. Chem. Soc.* **1973**, *95*, 1680. (e) Kane, V. V.; Wolf, A. D.; Jones Jr., M., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 2643. (f) Jones, M., Jr. *Acc. Chem. Res.* **1974**, *7*, 415.

(7) Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1961**, *83*, 4486.

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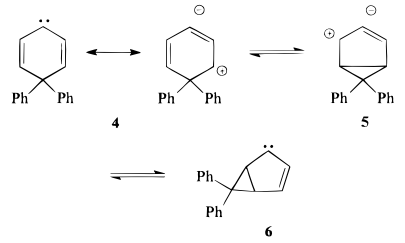
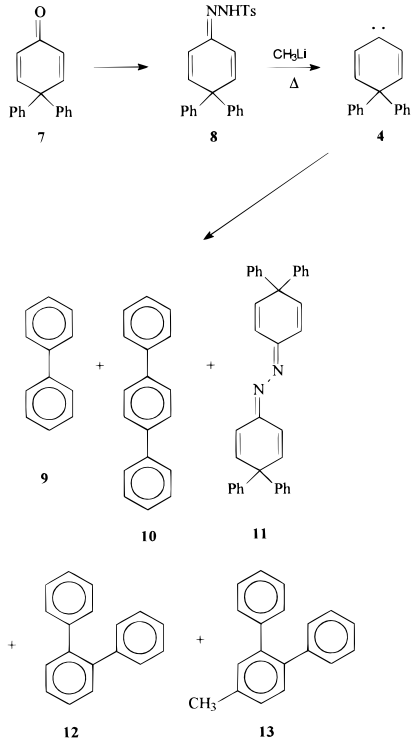
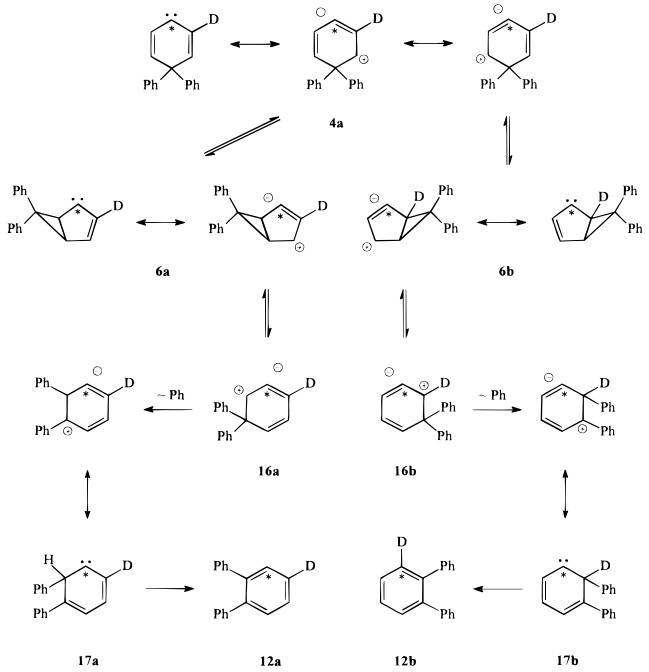
Scheme 2



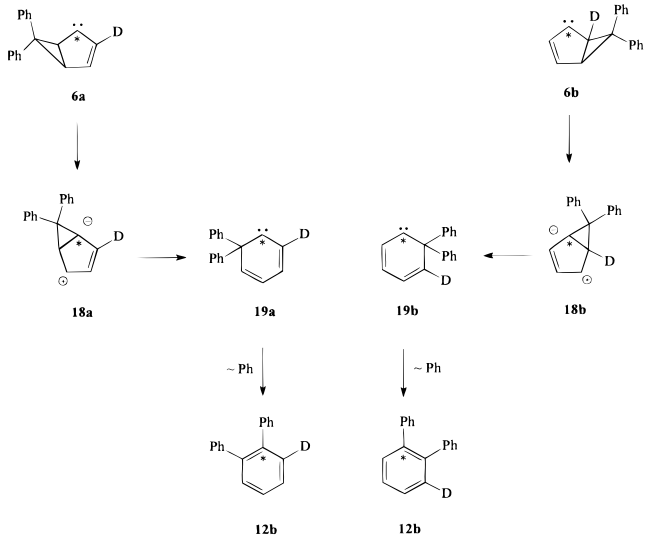
Scheme 3



Scheme 4



Scheme 5



12a and **12b**. In this mechanistic scheme a ^{13}C label would be at position 3 of the central benzene ring.

Alternatively, bicyclic carbene **6a** (**6b**) could undergo a 1,4 suprafacial alkyl shift to produce **18a** (**18b**). Cyclopropylcarbinyl to allylcarbinyl cleavage would generate carbene **19a** (**19b**) (Scheme 5). Phenyl migration from either would result in *o*-terphenyl with the deuterium label solely in the ortho position (**12b**). The ^{13}C label in this example would be located at position 1 of the center ring. Both the alkyl shift (**6** → **18**) and the 1,2 phenyl migration have literature precedence.[8]

The third mechanistic pathway is analogous to that suggested by Dannenberg and Gross to explain the carbenoid decomposition of a steroidal cyclohexadienone tosylhydrazone.[9] Consecutive phenyl and hydrogen migrations generate carbene **20a** (**20b**) (Scheme 6). In the final step, carbene **20a** would be expected to exhibit more facile migration of the hydrogen over deuterium based upon the deuterium isotope effect (k_H/k_D should be in the range of 1.0−1.5).[10] Allowing for the isotope effect, this mechanism would lead to a ratio of **12a** to **12b** of 70−75:25−30. The ^{13}C label would end up at position 4 of the central ring. The experimental results from the deuterated study gave a product ratio of 31 ± 8.8:69 ± 8.8 of **12a** to **12b**. On the basis of these results none of the proposed mechanistic schemes could alone account for the observed product ratio. At best it could be a combination of different pathways.[5] There are, however, some points of concern in the deuterium tracer experiment. The low incorporation of deuterium in the experimental sample (42%) clouds the issue. This left a large amount of nondeuterated *o*-terphenyl that complicated the deuterium analysis which was based on natural abundance ^{13}C NMR analysis and geminal (^{13}CCD) isotope effects.

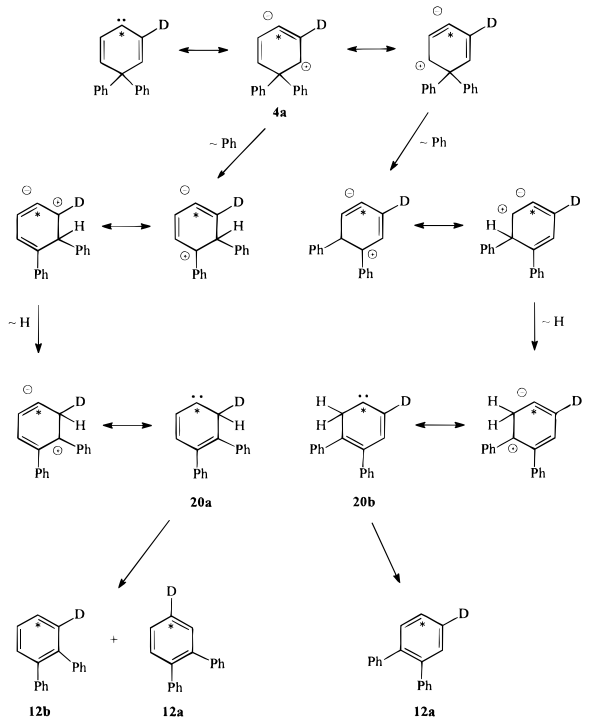
A reassessment of the deuterium labeling experiment reveals that only Scheme 5 can be ruled out completely.

(8) (a) Kirmse, W. *Carbene Chemistry*, 2nd ed.; Academic Press: New York, 1971; pp 457−462. (b) Baron, W. J.; DeCamp, M. R.; Hendrick, M. E.; Jones, M., Jr.; Levin, R. H.; Sohn, M. B. *Carbenes*; Wiley: New York, 1973; pp 32−40.

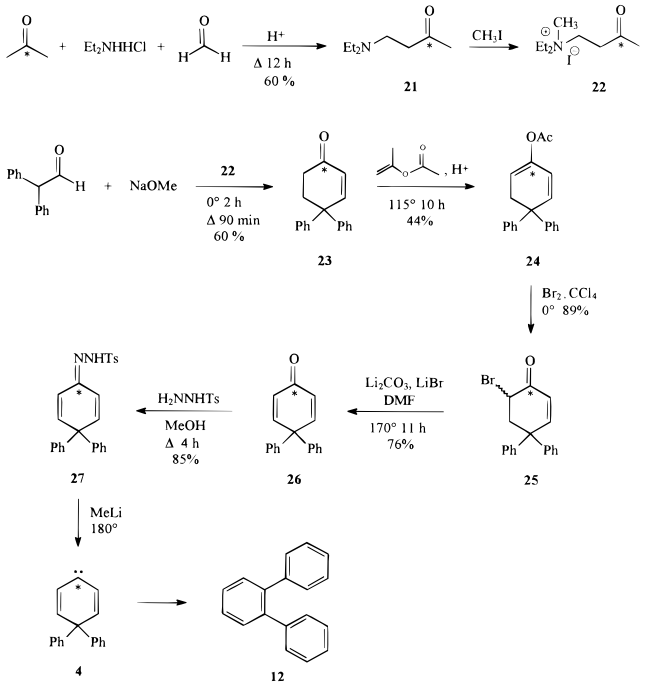
(9) Dannenberg, H.; Gross, H. J. *Tetrahedron* **1965**, *21*, 1611.

(10) (a) Freeman, P. K.; Hardy, T. A.; Balyeat, J. R.; Wescott, L. D., Jr. *J. Org. Chem.* **1977**, *42*, 3356. (b) Nickon, A.; Huang, F.; Weglein, R.; Matsuo, K.; Yogi, H. *J. Am. Chem. Soc.* **1979**, *96*, 5264. (c) Kirmse, W.; von Schultz, H. D.; Arold, H. *Justus Liebigs Ann. Chem.* **1968**, *711*, 22.

Scheme 6



Scheme 7

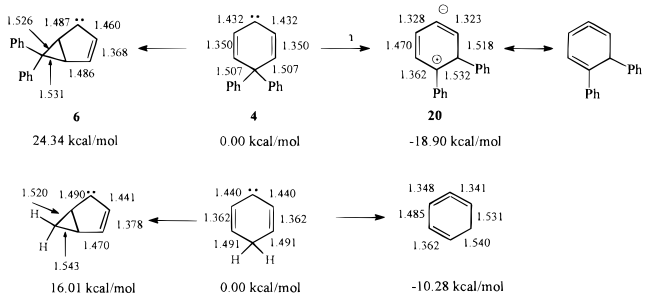


Both Schemes 4 and 6 could theoretically give natural abundance ^{13}C NMR spectra that are very similar. With this in mind, a labeling study employing ^{13}C enhancement at C-1 was carried out to clear up the mechanistic picture.

Results and Discussion

Synthesis of ^{13}C-Enhanced Diphenylcyclohexadienylidene. Our first route to incorporate the ^{13}C label was to utilize acetic-*1*-^{13}C acid as the synthetic precursor, convert this to an acid chloride and then use Stille coupling[11] with tetravinyltin to synthesize methyl vinyl ketone. All attempts at this reaction sequence led to extremely low or no yields of desired product. Other methods also based on the acid chloride (cuprate addition, MnI_2 coupling, and Grignard reagent chemistry) were unsuccessful. We next focused our attention on the use of a Mannich base product from the reaction of diethylamine hydrochloride, acetone, and paraformaldehyde. By using acetone-*2*-^{13}C diluted with reagent grade acetone, diethylamino-2-butanone (**21**) was synthesized in 60% yield with a calculated 6.63% ^{13}C enhancement (vide infra) at the carbonyl carbon (Scheme 7). Adding 1 equiv of iodomethane yielded the methiodide of diethylamino-2-butanone (**22**). Diphenylacetaldehyde, the methiodide, and base were combined to form the Robinson annulation product 4,4-diphenylcyclohex-2-enone (**23**) in 60% yield. To introduce the second double bond, an α-phenylseleno ketone was synthesized followed by hydrogen peroxide elimination, but again low yields prevented us from using this method. Instead, heating **23** at reflux in the presence of isopropenyl acetate formed the enol acetate (**24**) in 44% yield. Typical yields from this reaction are 60−80%, but unfortunately a slight excess of heat upon workup caused reversion to starting material and subsequent repetition of the synthetic step. Bromine was added to the enol acetate to give 6-bromo-4,4-diphenycyclohex-2-enone (**25**) in 89% yield. Dehydrohalogenation followed to yield 4,4-diphenyl-2,5-cyclohexadienone (**26**) which was converted to the tosylhydrazone (**27**) by adding tosylhydrazine. FAB mass spectral analysis shows ^{13}C enhancement to 6.55 ± 0.98%. The imine carbon exhibits a 3.98-fold ^{13}C enhancement. The yield was 65% for the two steps. 4,4-Diphenylcyclohexadienylidene (**4**) was generated by first converting to the lithium salt with methyllithium and then heating to 180 °C. After the thermal degradation of the tosylhydrazone, *o*-terphenyl was isolated by a combination of silica gel chromatography and preparative gas chromatography.

Scheme 8



Analysis of the Labeling Study. Semiempirical AM1 calculations were carried out on the key entities in the competing rearrangement pathways, and density functional B3LYP/6-31G(d) calculations were employed for nonphenylated analogues for the purpose of comparison (Scheme 8). Given in this scheme are the relative $\Delta H°_f$ values (AM1) and electronic energies plus zero point energies (B3LYP/6-31G(d)), respectively, in kcal/mol. The competition would be between a skeletal rearrangement to a bicyclocarbenoid species (Schemes 4 and 5) and a 1,2 phenyl migration (Scheme 6). If one looks at the thermodynamic picture, a clear pathway leading to **20** is supported. This intermediate lies 43.24 kcal/mol below **6** and 18.90 kcal/mol below initial carbene **4** and is, in

(11) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.

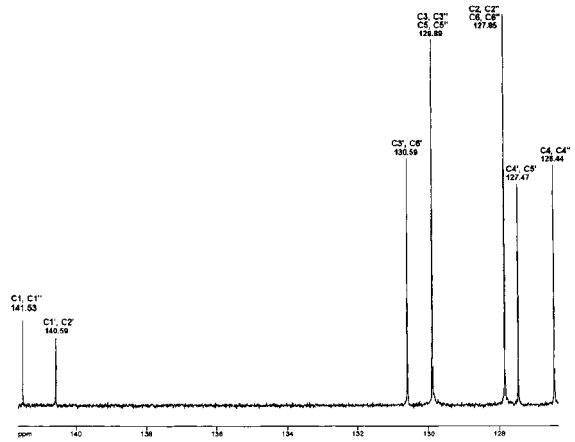
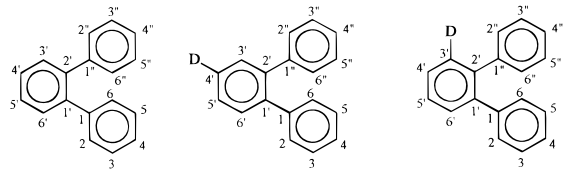


Figure 1. ^{13}C NMR spectra of *o*-terphenyl standard.

Scheme 9



12 **12a** **12b**

fact, an isobenzene species.[12,13] The pathway from **4** to **6** is endothermic by 24.34 kcal/mol. The stabilities of the intermediates in the analogous nonphenylated rearrangements, relative to 3-carbena-1,4-cyclohexadiene, provide a similar picture (Scheme 8).

These results strongly suggest that the favored product would be that formed from an initial phenyl migration as outlined in Scheme 6. These computational results are also in agreement with the experimental analysis. The ^{13}C NMR chemical shift assignments of product *o*-terphenyl were made by using tabulated data for substituent effects on benzene[14] and by the effect of deuterium at known positions.[5] Experimentally the incorporation of the deuterium at C3′ and C4′ led to a splitting of the ^{13}C signals at 130.5 (C3′, C6′) and 127.4 (C4′, C5′) ppm, leaving four signals at 130.5, 130.4, 127.4, and 127.3 ppm (Scheme 9). Figures 1 and 2 show the ^{13}C NMR of standard *o*-terphenyl and our ^{13}C-enriched *o*-terphenyl formed in the pyrolysis of the lithium salt of **27**. To gain an idea of the normal relative peak size, the ^{13}C spectra of seven standard solutions of *o*-terphenyl (1 M soln in $CDCl_3$) were obtained. Table 1 shows the relative peak size as measured against the peak at 127.85 ppm for both normal and ^{13}C-enriched *o*-terphenyl.

As can be seen from the ^{13}C spectra on partially labeled *o*-terphenyl, only the peak at 127.47 ppm shows clear enhancement of the signal. This corresponds to enriched

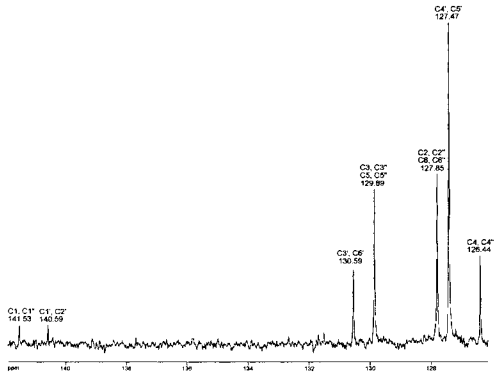


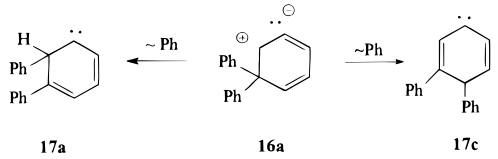
Figure 2. ^{13}C NMR spectra of ^{13}C-enriched *o*-terphenyl.

Table 1. Relative Intensities of ^{13}C NMR Peaks

chemical shift[a]	relative peak size for standard *o*-terphenyl[b]	relative peak size for ^{13}C enhanced *o*-terphenyl[b]
126.44	0.534 ± 0.032	0.562
127.47	0.496 ± 0.049	2.081
127.85	1.000	1.000
129.89	1.221 ± 0.149	0.963
130.59	0.551 ± 0.045	0.507
140.59	0.198 ± 0.050	0.117
141.53	0.211 ± 0.010	0.129

[a] Measured in ppm relative to TMS. [b] Relative to the peak at 127.85 ppm.

C4′ and C5′. If Scheme 4 were in effect, the ^{13}C label would be located at C3′ and C6′. To keep mechanistic choices simple, we have not considered above in Scheme 4 a phenyl migration in the opposite direction (**16a** → **17c**). At this point, however, it is clear that since **16a** → **17a** does not occur, it is unlikely that **16a** → **17c** would be operative (eq 1). Likewise, Scheme 5 would have given enhancement at C1′ and C2′. On the basis of these results, the only pathway in operation is Scheme 6. This also reflects the thermodynamic picture revealed in the AM1 and B3LYP/6-31G(d) calculations. With these new findings in hand, we have clear evidence to support the mechanism of Scheme 6, free of the ambiguity of the deuterium study.



17a **16a** **17c** (1)

Computational Details

Geometry optimizations for the phenylated substrates were obtained using AM1 semiempirical calculations[15] in the Spartan 4.1.1 suite of programs.[16] The density functional theory module included in the Gaussian 94 suite of programs[17] was used, employing Becke's three-parameter hybrid functional[18]

(12) (a) Bettinger, H. F.; Schreiner, P. R.; Schaefer, H. F., III; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1998**, *120*, 5741. (b) Hopf, H.; Berger, H.; Zimmermann, G.; Nüchter, U.; Jones, P. G.; Dix, I. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1187. (c) Roth, W.; Hopf, H.; Horn, C. *Chem. Ber.* **1994**, *127*, 1765. (d) Christl, M.; Braun, M.; Müller, G. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 473. (d) Janoschek, R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 476.

(13) The geometry reported in ref 12a for isobenzene at the B3LYP/DZP level is in close agreement with that at the B3LYP/6-31G* level.

(14) Levy, G. C.; Lichter, R. L.; Nelson, G. L. *Carbon-13 Nuclear Magnetic Resonance Spectroscopy*, 2nd ed.; Wiley-Interscience: New York, 1980; pp 111−112. (b) Pretsch; Clerc; Seibl; Simon. *Spectral Data for Structure Determination of Organic Compounds*, 2nd ed.; Springer-Verlag: Berlin, 1989; pp C120−C125.

(15) Dewar, M. J.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4499.

(16) Spartan IBM version 4.1.1. Wavefunction, Inc., Irvine, CA, 1991−1997.

(17) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. GAUSSIAN 94, Revision B.2, Gaussian, Inc., Pittsburgh, PA, 1995.

(18) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

with the gradient-corrected correlation functional of Lee, Yang, and Parr[19] for the nonphenylated analogues using the 6-31G* basis set.[20] Once structures had converged, frequency calculations at the same level of theory were carried out to ensure each molecule was an energy minimum.

Experimental Section

General Methods. Solvents were purchased from Mallinckrodt Chemical and Fischer Scientific and used without further purification. Reagent grade chemicals were purchased from Aldrich Chemical.

***2*-^{13}*C*-4-Diethylamino-2-butanone (21).** The procedure of Wilds, Nowak, and McCaleb was followed.[21] Diethylamine hydrochloride (22.00 g, 200 mmol), paraformaldehyde (8.400 g, 280 mmol), acetone (70 mL), methyl alcohol (10 mL), 35% HCl (0.25 mL), and acetone-*2*-^{13}*C* (99% ^{13}C at C-2) (4.00 g, 67.72 mmol) were added to an oven-dried 250 mL round-bottom flask fitted with a reflux condenser and magnetic stir bar. The mixture was heated for 12 h in a 70 °C oil bath at which time a light-yellow solution remained. The mixture was allowed to cool to room temperature. Fresh sodium hydroxide solution (8.2 g, 5.4 M in H_2O, 205 mmol) was prepared and cooled in a refrigerator. The yellow reaction solution was transferred to a separatory funnel, and the cold base was added. Et_2O (25 mL) was added, and the two layers were separated. The aqueous layer was extracted with Et_2O (2 × 25 mL). The combined ether extracts were washed with a saturated sodium chloride solution (2 × 20 mL). The combined aqueous layers were washed with Et_2O (2 × 20 mL); then the combined ether layers were dried for 1 h over sodium sulfate. The final solution was filtered and concentrated using a rotary evaporator. Final purification was done by reduced pressure spinning band distillation (12.5 Torr, 18 in. × ~3/8 in. column with jacket heated to 50−60 °C). The product was collected as a light yellow to colorless liquid that is calculated to be 6.6% labeled at position 2 (which is in agreement with the analysis of tosylhydrazone **27**, vide infra) (17.06 g, 60%): bp 72−75 °C at 12.5 Torr; $n^{24}_D = 1.4300$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.69 (t, 2H, J = 7.45 Hz.), 2.52 (t, 2H, J = 7.23 Hz.), 2.45 (q, 4H, J = 7.15 Hz.), 2.11 (s, 3H), 0.96 (t, 6H, J = 7.15 Hz.).

***2*-^{13}*C*-4-Diethylamino-2-butanone Methiodide (22).** Freshly distilled *2*-^{13}*C*-4-diethylamino-2-butanone (17.06 g, 119.1 mmol) was placed in a 50 mL round-bottom flask. The flask was fitted with a pressure equalizing dropping funnel and nitrogen inlet and then cooled to 0 °C in an ice bath. Methyl iodide (17.06 g, 120.2 mmol) was added to the dropping funnel and dripped into the amine slowly over the course of 30 min. CAUTION: this is an extremely exothermic reaction. The methyl iodide should be added slowly. After complete addition, the mixture was allowed to sit for 2 h in the ice bath and then an additional 2 h in a 0 °C refrigerator. Upon removal, the semicrystalline methiodide was washed with cold Et_2O (10 mL) and the Et_2O decanted. The Et_2O wash was repeated (2 × 10 mL). The methiodide was dissolved in MeOH (50 mL) and stored under nitrogen. No further purification was attempted.

***1*-^{13}*C*-4,4-Diphenylcyclohex-2-enone (23).** The general procedure of Johnson, Szmuszkovicz, Rogier, Hadler, and Wynberg was followed.[22] A magnetic stir bar and MeOH (100 mL) were added to a 500 mL round-bottom flask. Sodium metal (4.11 g, 178.7 mmol) was slowly added to the flask, after which time the flask was fitted with a pressure-equalizing dropping funnel and nitrogen bubbler and cooled in an ice bath. CAUTION: addition of the sodium too fast can lead to a very vigorous reaction. After the sodium was dissolved, diphenylacetaldehyde (23.55 g, 120.0 mmol) in benzene (100 mL) was placed in the dropping funnel and added quickly to the sodium methoxide solution. The dropping funnel was then charged with the cold methiodide (**22**) prepared from diethylamino-2-butanone (17.06 g, 119.1 mmol) as described above. The methiodide was added over a period of 120 min. Stirring was continued for 2 h at ice bath temperatures. The ice bath was replaced by an oil bath and the mixture heated at reflux for 90 min. The resultant orange mixture was cooled to room temperature and transferred to a separatory funnel. A 10% HCl solution was added until the aqueous layer was no longer basic to litmus paper. Cold H_2O (50 mL) was added, and the two layers were separated. The aqueous layer was extracted with cold Et_2O (3 × 90 mL). The combined organic layers were extracted once with a saturated sodium chloride solution. Finally, the combined aqueous layers were washed once with ether (90 mL). The organic layers were combined and dried over sodium sulfate. The solvent was removed by rotary evaporation, and an orange oil was collected. Upon cooling to room temperature, crystals started to form in the oil. Cold EtOH was added and immediately light-yellow crystals started to form. The solution was gently warmed and then cooled in a 0 °C refrigerator for 3 h. Crystals were collected by vacuum filtration and dried in the open air for 24 h. Cyclohex-2-enone **23** (17.75 g, 60%) was obtained: mp 90−91 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (m, 11H), 6.21 (d, 1H, J = 10.26 Hz), 2.71 (t, 2H, J = 6.48 Hz.), 2.42 (t, 2H, J = 6.36 Hz).

***2*-^{13}*C*-5,5-Diphenyl-2-acetoxy-1,3-cyclohexadiene (24).** The procedure of Moffett and Weisblat was followed.[23] *1*-^{13}*C*-4,4-Diphenylcyclohex-2-enone (**23**) (17.5 g, 70 mmol), *p*-toluenesulfonic acid monohydrate (0.9 g, 4.73 mmol), and isopropenyl acetate (70 mL) were placed in a 500 mL round-bottom flask. The flask was fitted with a single-piece distillation apparatus and placed in an oil bath. The solution was slowly distilled (oil bath temperature of 115 °C) for 10 h, with periodic replacement of the isopropenyl acetate. The dark amber solution left in the pot was allowed to cool to room temperature and left overnight. Solid $NaHCO_3$ (5.50 g, 66 mmol) was added to the mixture with stirring; then the solution was transferred to a separatory funnel. The flask was washed with Et_2O and ice water, both of which were added to the separatory funnel. The two-phase mixture was separated, and the aqueous layer was washed with Et_2O. The combined Et_2O extracts were then washed with a saturated NaCl solution. The combined aqueous layers were washed with Et_2O. The combined organic layers were then dried briefly over sodium sulfate, filtered by vacuum filtration, and then concentrated by rotary evaporation (50 °C, ~10 Torr). The solution was transferred to a beaker, the flask was washed with EtOH, and the wash was added to the beaker. The resultant amber mixture was allowed to cool to room temperature, and more EtOH (~ 50 mL) was added. The material was placed in a refrigerator for 2 h. Crystallization was induced by scratching with a glass stirring rod. The light tan crystals were collected by vacuum filtration and dried in a vacuum oven for 2 h (~10 Torr, 50 °C). ^{1}H NMR analysis showed about a 50/50 mixture of starting material (**23**) to product (**24**). At this time the crystals were collected and placed in a round-bottom flask. The isopropenyl acetate reaction was run a second time as above. The amber reaction mixture was allowed to cool to room temperature and then concentrated in vacuo (~3 Torr) to a volume of about 50 mL. Excess isopropenyl acetate was then removed carefully in vacuo at temperatures not exceeding 30 °C until crystals started to form. The mixture was then transferred to a beaker, and cold Et_2O was added. The final solution was placed in a refrigerator for 3 h at which time the crystals were collected by vacuum filtration and dried. ^{1}H NMR showed complete conversion to product. The enol acetate **24** was collected as off-white crystals (8.93 g, 44%): mp 102−105 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (m, 11H), 6.34 (d, 1H, J = 10.07 Hz.), 5.90 (dd, 1H, J = 2.11, 10.18 Hz.), 5.50 (dt, 1H, J = 1.99, 4.63 Hz.), 3.01 (d, 2H, J = 4.65 Hz.), 2.11 (s, 3H).

***1*-^{13}*C*-6-Bromo-4,4-diphenylcyclohex-2-enone (25).** A modified procedure of Zimmerman, Hackett, Juers, McCall,

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and Schröder was followed.[24] 5,5-Diphenyl-2-acetoxy-1,3-cyclohexadiene (**24**) (8.24 g, 29 mmol) was placed in a 250 mL round-bottom flask. To this was added CCl_4 (50 mL), and the flask was fitted with a magnetic stirrer and pressure equalizing dropping funnel. The flask was then cooled in an ice bath. Cold bromine (1.5 mL, 31 mmol) was added dropwise to the mixture over the course of 60 min. The solution was stirred at 0 °C for 3 h. Upon removal, the dark yellow mixture was washed with a saturated sodium bicarbonate solution (60 mL). The two layers were separated, and the aqueous layer was washed with Et_2O (2 × 50 mL). The combined organic layers were dried over sodium sulfate for 30 min. The solution was filtered by vacuum filtration and then concentrated by rotary evaporation to a dark yellow oil. The oil was stirred with ether and then placed in a 0 °C refrigerator. Crystallization was induced by scratching the surface of the beaker with a glass stir rod. The material was left in the refrigerator overnight. Upon removal, the off-white crystals were collected via vacuum filtration and dried. α-Bromo ketone **25** was obtained (8.33 g, 89%): mp 102−105 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (m, 10H); 6.32 (d, 1H, J = 10.18 Hz), 4.71 (dd, 1H, J = 13.52, 4.69 Hz), 3.26 (ddd, 1H, J = 13.20, 4.70, 2.34 Hz), 3.17 (t, 1H, J = 13.46 Hz).

***1*-^{13}*C*-4,4-Diphenyl-2,5-cyclohexadienone (26).** The procedure of Zimmerman, Hackett, Juers, McCall, and Schröder was followed.[20] 6-Bromo-4,4-diphenylcyclohex-2-enone (**25**) (5.60 g, 17.1 mmol), lithium carbonate (4.36 g, 59 mmol), lithium bromide (4.95 g, 57 mmol), and dimethylformamide (50 mL) were placed in a 200 mL round-bottom flask. A magnetic stir bar was added, and the flask fitted with a reflux condensor and nitrogen bubbler. The solution was heated to 170 °C with an oil bath and stirred at reflux for 11 h under nitrogen in a darkened hood. After the mixture cooled, a white solid was observed in the bottom of the flask. The dark amber solution was filtered by vacuum filtration to remove the inorganic salts. It was heated with a warm water bath and concentrated in vacuo. The thick amber residue was mixed with Et_2O. Immediately crystals formed. These were dissolved by the addition of MeOH. The solution was transferred to a separatory funnel, more Et_2O was added, and the solution was washed with H_2O. The layers were separated, and the organic layer was washed with saturated sodium chloride. The combined aqueous layers were washed with Et_2O and then with benzene. The combined organic layers were dried over sodium sulfate, concentrated by rotary evaporation, and crystallized from EtOH. Dienone **26** was collected as light brown crystals (3.20 g, 76%): mp 122−124 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (m, 12H), 6.34 (d, 2H, J = 10.20 Hz.).

***1*-^{13}*C*-4,4-Diphenyl-2,5-cyclohexadienone Tosylhydrazone (27)**. *p*-Toluenesulfonhydrazide (2.23 g, 12 mmol), *1*-^{13}*C*-4,4-diphenyl-2,5-cyclohexadienone (**26**) (2.95 g, 12 mmol), and a magnetic stir bar were placed in a 100 mL round-bottom flask. MeOH (50 mL) was added, and the solution was heated at reflux (70 °C oil bath) for 4 h. The mixture was allowed to cool to room temperature and then placed in a 0 °C refrigerator overnight. Upon removal, light-yellow crystals had formed. Tosylhydrazone **27** was obtained (4.24 g, 85%): mp 139−140 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, 2H, J = 8.18 Hz.), 7.23 (m, 12H), 6.74 (dd, 1H, J = 10.29, 2.26 Hz.), 6.54 (dd, 1H, J = 10.29, 1.59 Hz.), 6.47 (dd, 1H, J = 10.19, 2.29 Hz.), 6.39 (dd, 1H, J = 10.18, 2.07 Hz.), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 144.2, 143.9, 140.6, 135.3, 129.7, 128.7, 128.1, 127.9, 127.1, 124.4, 113.4, 53.8, 21.6. The imine carbon (146.2 ppm) is 3.98-fold enhanced relative to the normal signal. FAB mass spectrometry: ^{13}C enhancement is 6.55 ± 0.98%.

Decomposition of the Lithium Salt of *1*-^{13}*C*-4,4-Diphenyl-2,5-cyclohexadienone Tosylhydrazone (27). The title tosylhydrazone (**27**) (0.94 g, 2.27 mmol), THF (20 mL), and a magnetic stir bar were placed in a 100 mL three-necked, round-bottom flask. The flask was fitted with a nitrogen inlet, septum, and glass stopper. The nitrogen flow was started, and the stirring was turned on. Upon mixing, the tosylhydrazone (**27**) dissolved, and a light yellow solution remained. The solution allowed to stir for 30 min. A 5 cm^3 Leur tip syringe was flushed with dry nitrogen and used to transfer 2 mL of methyllithium (1.4 M in Et_2O, 2.8 mmol) to the round-bottom flask. After about 1 min, the yellow solution became cloudy and a white precipitate started to form. After 5 min of stirring, additional methyllithium (0.2 mL) was added. A deep gold color appeared at the top of the mixture, showing evidence of dianion formation. The mixture was then stirred for 2 h. At that time the flask was opened and the THF blown out with a stream of dry nitrogen. The rest of the THF was removed by pumping on the flask for 2 h at 0.8 Torr. A white solid coating was left on the walls and bottom of the flask. This was gently scraped off the sides with a microspatula and broken up into smaller pieces. A glass decomposition apparatus was then set up consisting of the original round-bottom flask fitted with a gas outlet and two ground glass stoppers. The gas outlet was fitted with a 8 in. length of Tygon tubing that was attached to a glass trap cooled in dry ice/ethyl alcohol. Another 8 in. length of Tygon tubing was attached from the first trap to a second. An outlet tube from the second trap was attached to a mineral oil bubbler. The round-bottom flask was placed in an oil bath, and the lithium salt was heated to 175 °C. Nitrogen evolution was observed at about 130 °C and was complete by 140 °C. The material was heated at 175 °C for 10 min, and then the oil bath was removed and the brown-orange residue was allowed to cool to room temperature. Chloroform (50 mL) was added first to the flask and then the contents were transferred to a separatory funnel. The chloroform layer was washed with water (3 × 60 mL). The aqueous layer was washed with chloroform (1 × 50 mL). The combined chloroform layers were washed with saturated NaCl (1 × 50 mL) and then dried overnight over sodium sulfate. The dark orange solution was then filtered by vacuum filtration and concentrated by rotary evaporation. A dark orange oil (0.72 g) was collected.

Separation and Analysis of *o*-Terphenyl (12). The oil from the tosylhydrazone decomposition was brought up in dichloromethane (2 mL) and then chromatographed using flash chromatography techniques[25] on a 2.5 cm diameter × 20 cm silica gel column (Aldrich chemical silica gel, Merck, grade 60, 70−230 mesh, 60 Å) eluting with straight dichloromethane until 19 25 mL test tubes of solution had been collected. The final polar band was eluted from the column with MeOH. Analytical thin-layer chromatography (TLC) of each fraction using Spectrum precoated silica gel 60 F_{254} and dichloromethane solvent gave the appearance of four bands in fractions 3, 4, and 5 (R_f values 0.20, 0.37, 0.49, and 0.80 respectively), one band in fractions 6−12 (R_f 0.20), and one band in fractions 13−15 (R_f 0.00). The last four fractions contained the polar residue from the MeOH wash. Capillary gas chromatography (Varian instruments 3400 gas chromatograph fitted with a SE-54 30m capillary column; initial temperature 140 °C for 1 min and then ramped at 10 °C/min to 240 °C and held for 10 min, He carrier gas−head pressure 10 psi) was used to identify some of the products in the silica gel fractions. *o*-Terphenyl, *p*-terphenyl, and biphenyl were identified as three of the six major peaks in fractions 3−5 by coinjection with known standards and comparison of retention times (10.280, 13.940, and 4.774 min, respectively). *o*-Terphenyl was separated by preparative gas chromatography (Varian 3700 gas chromatograph fitted with a 3/8 in. 10% OV-17 + 10% SE-30 on Chromosorb W 45/60 mesh, 3 m column, He carrier gas 40 mL/min) by collecting the peak at retention time 7.30 min with a glass collection tube cooled in dry ice/2-propanol. The *o*-terphenyl was washed from the collection tube with a small amount of dichloromethane and then analyzed via capillary GC as described above. The impurities in each sample were held at 10% or below. If the amount was greater, the mixture was separated via preparative GC again. The separation was complicated by the fact that there was an impurity that coeluted with almost exactly the same retention time as *o*-terphenyl. This impurity was minimized by collecting

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only the front portion of the *o*-terphenyl peak. A final ^{13}C NMR (400 MHz, $CDCl_3$) spectrum was gathered by a Brüker am400 spectrometer fitted with a Nalorac 3 mm microprobe. ^{13}C NMR: δ 141.5, 140.6, 130.6, 129.9, 127.9, 127.5, 126.4. The aromatic carbon 4 of the central ring (127.5 ppm) is 4.07-fold enhanced relative to the normal signal.

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