dialdehyde and 0.55 g of diaza-18-crown-6 (Parish Chemical Co.). The product gave a negative Tollen's test, revealed no chain cleavage on SEC, and gave a nitrogen analysis of 1.02% (theoretical 0.8%). The yield was 96%.

**Kinetic Measurements.** Acetonitrile was dried by being stirred with calcium hydride until gas evolution ceased, fractionally distilled from diphosphorus pentoxide (5 g/L) in an all-glass apparatus, refluxed over calcium hydride (5 g/L) for at least 1 h, and slowly distilled (81.6 °C) from calcium hydride. The first 5% and the last 10% of the final distillate were discarded. Potassium acetate was dried at 90–100 °C for at least 2 days.

Dry acetonitrile (6 mL) was added to the PTA (0.2 or 0.4 g) and dry potassium acetate (6.67 g, 3.4 M) in a septum-topped Erlenmeyer flask. The heterogeneous system was stirred for 30 min before benzyl bromide (4 mL, 1.7 M) was added. Aliquots (0.2 mL) were withdrawn, diluted in acetonitrile (2 mL), and injected into the gas chromatograph. For PTA's of limited availability, a 5 mL total volume reaction was run (everything used in half the above amounts).

Results of the pseudo-first-order reaction were analyzed by plotting ln $(A_0/A_0 - x)$ vs. time (minutes) where $A_0$ is the initial reactant concentration (benzyl bromide) and $A_0 - x$ is the reactant concentration at time $t$. Duplicate reactions were normally followed through 3 half-lives and gave correlation coefficients better than 0.999.

**Extraction Studies.** The aqueous metal picrate solutions (0.0954 mM in potassium picrate or 0.085 mM in sodium picrate) were extracted with an equal volume of methylene chloride containing the PTA. The solutions were then analyzed by spectrophotometric analysis of the picrate absorptions at 357 nm in water ($\epsilon = 1.5 \times 10^4$ $M^{-1}$ $cm^{-1}$) and at 374 nm in $CH_2Cl_2$ ($\epsilon = 1.8 \times 10^4$ $M^{-1}$ $cm^{-1}$).

**Acknowledgment** is made to the National Aeronautics and Space Administration for partial support of this research (Grant No. NAS8-33978). We further gratefully acknowledge the many helpful comments of Dr. M. Yalpani and the assistance of Mr. K. Sharp in measuring the partitioning of labeled PEG.

**Registry No.** 1, 69496-25-9; 2, 83314-02-7; 3, 23978-55-4; poly(ethylene glycol), 25322-68-3; potassium picrate, 573-83-1; sodium picrate, 3324-58-1; PEG-3400 ditosylate, 35164-96-6; PEG-6800 dialdehyde, 83314-03-8; 18-crown-6, 17455-13-9; 15-crown-5, 33100-27-5; $CH_3COOK$, 127-08-2; $C_6H_5CH_2B$, 100-39-0.

## An Annulative Route to Enediones

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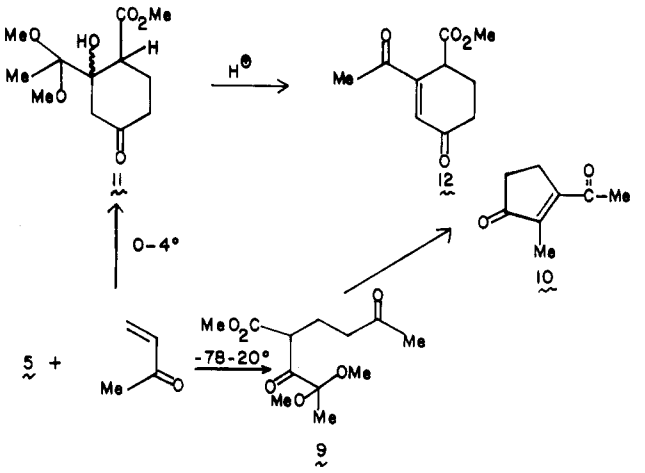
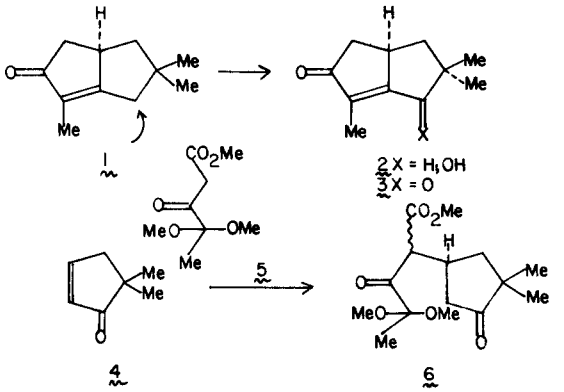
A central intermediate in our recent total synthesis of coriolin was the enedione **3**.[1,2] As a result of investigations which were directed toward the total synthesis and through follow-up studies,[3,4] we have developed the capability to introduce carbon functinality at either ethylenic carbon of enedione **1**.

Our initial approaches to **3** involved a variety of attempts to achieve, in essence, oxidation at the $\gamma$-carbon of enone **1**. A series of initiatives in this connection (attempted extended enol acetylation, attempted formation of the extended dienamine, attempted reaction with a Bredereck reagent at the $\gamma$-carbon) were unsuccessful, possibly as a consequence of steric resistance to attack at the neopentyl center. Unacceptably low yields (5–10%) of **2** and **3** were obtained by direct oxidation of **1** with selenium dioxide.[5]

Scheme I




Accordingly, a new annulation was developed to provide a route from **4** to **3**. The experimental details of the particular synthesis of compound **3** were published elsewhere.[2] Herein, we report our results on the scope and limitations of this type of annulation.[6]

The required $\beta$-keto ester **5**[2] was prepared by the carbomethoxylation of the readily available 3,3-dimethoxy-2-butanone.[7] Michael additions of **5** to cyclopentenone, cyclohexenone, and cycloheptenone were achieved. The reactions were carried out by using sodium methoxide (0.25 equiv) in methanol at room temperature. No attempt was made to separate the mixture of diastereomeric Michael products.

Cyclization to enediones **8**, as well as decarbomethoxylation could be achieved in one step by heating the adducts with *p*-TsOH in toluene or xylene for short periods of time. Serious difficulties were encountered only in the case of unsubstituted cyclopentenone (case **8c**). Here the yield of the Michael step was only 47%. Moreover, the quality of the decarbomethoxylation–cyclization step was undermined by difficulties in achieving complete cleavage of the ester. This was eventually accomplished through the action of HCl in aqueous dioxane though in poor yield.

(1) Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. chem. Soc.* **1980**, *102*, 2097.
(2) Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. chem. Soc.* **1981**, *103*, 3460.
(3) Danishefsky, S.; Kahn, M. *Tetrahedron Lett.* **1981**, 485.
(4) Danishefsky, S.; Kahn, M. *Tetrahedron Lett.* **1981**, 489.
(5) Kahn, M.; Etheredge, S. J. unpublished results.
(6) For examples of forming bicyclic systems in conceptually related ways see: Marfat, A.; Helquist, P. *Tetrahedron Lett.* **1978**, 4217. Abbot, R. E., Spencer, T. A. *J. Org. Chem.* **1980**, *45*, 5398. Knapp, S.; O'Connor, U.; Mobillo, D. *Tetrahedron Lett.* **1980**, *21*, 4557. Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1979**, *101*, 6429.
(7) Braude, E. A.; Timmons, C. *J. Chem. Soc.* **1953**, 3131.

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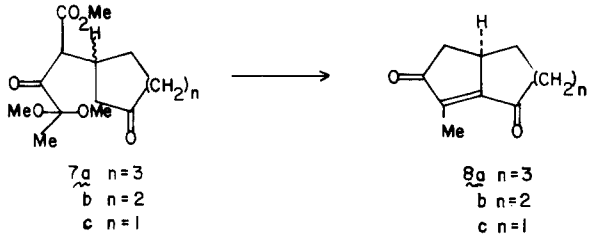
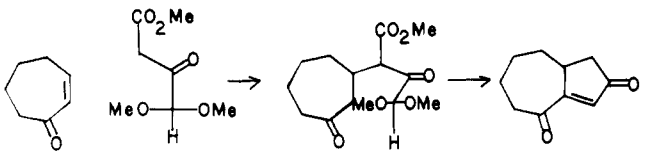


7a n=3
b n=2
c n=1

8a n=3
b n=2
c n=1

Some of the possibilities which might arise from the extension of this methodology to the case of acyclic enones are foreshadowed in the reaction of **5** with methyl vinyl ketone. The addition reaction was carried out in methanol from −78 to −20 °C by using Triton-B as the base. The Michael adduct, **9**, was indeed obtained in 81% yield (Scheme I). When this adduct was subjected to the usual cyclization conditions, there was obtained the enedione **10** (37%) as well as a small amount (6%) of the "Robinson annulation" type product, **12**. Interestingly, when the Michael reaction was conducted in sodium methoxide–methanol at 0–4 °C, there was obtained, in 74% yield, the ketol **11**. Subjection of the ketol to the usual acidic conditions gave a 73% yield of **12**. Thus, it appears that even in the acyclic cases, one can find conditions which favor either of the annulation products. The details would presumably have to be worked out on a case to case basis. Clearly cyclization to the β-ketol system **11** in the base-catalyzed step favors eventual formation of the "Robinson"-type product in the acid-induced process.

Very serious difficulties were encountered in attempting to use β-keto ester **13**[8] as the enedione annulation reagent. Michael addition to cycloheptenone gave epimer mixture **14** in 73% yield. However, in our hands, a wide range of



13 14 15

acidic conditions failed to give greater than a 9% yield of impure enedione **15**. Reactions were attended by serious decomposition. Unfortunately, we are unable to ascertain whether the major difficulty lies in unmasking of the α-keto aldehyde equivalent or in the aldolization step. For the moment at least, the failure in the aldehyde series must be regarded as a notable limitation of the method.

## Experimental Section[9]

**1,5,6,7,8,8a-Hexahydro-3-methyl-2,4-azulenedione (8a).** To a solution of 337 mg (3 mmol) of $\Delta^2$-cycloheptenone and 1.08 g (5.68 mmol) of methyl 4,4-dimethoxy-3-oxopentanoate (**5**) at 0 °C was added 3.3 mL of methanol containing 1 mmol of sodium methoxide. The reaction mixture was allowed to warm to room temperature and to stir for 44 h. It was poured into 100 mL of ether and 50 mL of saturated $NH_4Cl$. The organic layer was washed with water and with brine, dried ($MgSO_4$), and freed of solvent. Flash chromatography of the residual oil on silica gel and elution with 3:1 hexane/ethyl acetate afforded 703 mg (76%) of **7a** as a mixture of epimers: $^1H$ NMR ($CDCl_3$) δ 1.1–2.1 (m, 7), 1.33 (s, 3), 2.1–2.8 (m, 4), 3.20 (s, 6), 3.70 (s, 3), 3.76–3.97 (m, 1).

A solution of 457 mg (1.52 mmol) of **7a**, 0.6 mL of $H_2O$, and 230 mg of TsOH in 210 mL of toluene was heated at reflux for 18 h. Upon cooling, the reaction mixture was diluted with ether. The organic layer was washed with sodium bicarbonate solution followed by brine and dried ($MgSO_4$). Evaporation of the volatiles left a residue which upon flash chromatography on silica and elution with 4:1 hexane/ethyl acetate afforded 211 mg (78%) of **8a** as a yellow oil: IR ($CHCl_3$) $\nu_{max}$ 1706, 1679 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.1–3.2 (m), 1.68 (d, $J$ = 2 Hz); mass spectrum, $m/e$ 178 ($P^+$), 178.0984 (calcd for $C_{11}H_{14}O_2$ $m/e$ 178.0994 (parent)).

**5,6,7,7a-Tetrahydro-3-methyl-1*H*-indene-2,4-dione (8b).** To a solution of 1.30 g (6.84 mmol) of methyl 4,4-dimethoxy-3-oxopentanoate (**5**) and 574 mg (5.97 mmol) of $\Delta^2$-cyclohexenone at 0 °C was added in a rapid dropwise fashion 5.8 mL of methanol containing 2 mmol of sodium methoxide. The reaction mixture was allowed to warm to room temperature and to stir for 24 h. It was poured into 300 mL of ether and 100 mL of saturated $NH_4Cl$. The organic layer was washed with $H_2O$ and with brine, dried ($MgSO_4$), and freed of solvent. Flash chromatography of the ressidue on siica and elution with 3:1 hexane/ethyl acetate afforded 1.36 g (79%) of epimer mixture **7b** as a colorless oil: $^1H$ NMR ($CDCl_3$) δ 1.36 (s, 3), 1.38–2.8 (m, 9), 3.22 (s, 6), 3.66 and 3.70 (s, 3), 3.69–3.92 (m, 1).

A solution of 672 mg (2.35 mmol) of **7b**, 1.2 mL of $H_2O$, and 495 mg of TsOH in 400 mL of toluene was heated under reflux for 18 h. Upon cooling, the reaction mixture was diluted with ether (250 mL), washed with dilute sodium bicarbonate solution and brine, dried ($MgSO_4$), and freed of solvent. Flash chromatography of the residue on silica and elution with 4:1 hexane/ethyl acetate afforded 186 mg (48%) of enedione **8b** as a yellow oil: IR ($CHCl_3$) $\nu_{max}$ 1706, 1692 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.33–3.26 (m), 1.90 (d, $J$ = 2 Hz); mass spectrum, $m/e$ 164.0841 (calcd for $C_{10}H_{12}O_2$, $m/e$ 164.0836 (parent)).

**1,5,6,6b-Tetrahydro-3-methylpentalene-2,4-dione (8c).** To a solution of 1.19 g (14.5 mmol) of $\Delta^2$-cyclopentenone and 3.3 g (17 mmol) of methyl 4,4-dimethoxy-3-oxopentanoate (5) under $N_2$ and at 0 °C was added in a rapid dropwise fashion 16 mL of a solution of methanol containing 4.8 mmol of sodium methoxide. The reaction mixture was allowed to warm to room temperature and to stir for 44 h. It was poured into 300 mL of ether and 50 mL of saturated $NH_4Cl$. The organic layer was washed with $H_2O$ and with brine, dried ($MgSO_4$), and freed of solvent. Flash chromatography of the residual oil on silica gel and elution with 3:1 hexane/ethyl acetate afforded 1.86 g (47%) of the epimeric Michael adducts **7c** as a crude white solid: $^1H$ NMR ($CDCl_3$) δ 1.37, 1.38 (s, 3), 1.1–3.1 (m, 7), 3.23 (s, 6), 3.70, 3.73 (s, 3), 3.8–4.2 (m, 1).

A solution of 546 mg (2.0 mmol) of **7c**, 0.5 mL of $H_2O$, and 120 mg of TsOH in 150 mL of xylene was prepared at room temperature. It was placed in an oil bath and heated from room temperature to reflux over 20 min. The solution was maintained at reflux for 1 h and 40 min. Upon cooling to room temperature, it was diluted with ether and washed with dilute sodium bicarbonate and brine. The *ether* was removed in vacuo. Flash chromatography of the remaining *xylene solution* on silica and elution with 4:1 hexane/ethyl acetate afforded 150 mg[10] of a yellow oil. From this there was obtained a pure sample of **8c** by further refluxing in 10 mL of dioxane and 10 mL of 1 N HCl for 1 h. After being cooled, the reaction mixture was diluted with ether, washed several times with $H_2O$ and finally with brine, and dried ($MgSO_4$). Flash chromatography as above gave a pure sample of **8c** as a yellow oil: IR ($CHCl_3$) $\nu_{max}$ 1707, 1722 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.2–3.4 (m), 2.0 (d, $J$ = 2 Hz); mass spectrum, $m/e$ 150.0682 (calcd for $C_9H_{10}O_2$, $m/e$ 150.0680 (parent)).

**2-Methyl-3-acetyl-2-cyclopentenone (10).** To a solution of 1.19 g (6.3 mmol) of methyl 4,4-dimethoxy-3-oxopentanoate (**5**) and 1.67 g (23.8 mmol) of methyl vinyl ketone in 6 mL of absolute MeOH at −78 °C and under $N_2$ was added in a rapid dropwise fashion 0.53 mL of a 40% solution of benzyltrimethylammonium hydroxide in methanol (1.3 mmol of base). The reaction mixture was stirred at −78 °C for 2 h and was maintained at −20 °C overnight. It was poured cold into 150 mL of saturated $NH_4Cl$ and extracted with water and ether. The organic extracts were

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(9) Infrared spectra were measured on a Nicolet Series 7000 Ft-IR spectrometer; low-resolution mass spectra were measured on a Hewlett-Packard 5985 GC/MS system, and NMR spectra were measured at 90 MHz in $CDCl_3$ solution with tetramethylsilane as internal standard on a Varian EM 390.

(10) This material contained approximately 18% of a contaminant containing a methyl ester as estimated from its NMR spectrum.

washed with brine, dried ($MgSO_4$), and freed of solvent. The residual oil, when subjected to flash chromatography on silica gel with 3:1 hexane/ethyl acetate for elution, afforded 1.32 g (81%) of **9** as a colorless oil: $^1H$ NMR ($CDCl_3$) $\delta$ 1.40 (s, 3), 1.83–2.33 (m, 2), 2.17 (s, 3), 2.53 (t, $J$ = 8 Hz, 2), 3.21, 3.23 (s, 6), 3.70 (s, 3), 3.88 (t, $J$ = 8 Hz, 1).

A solution of 534 mg (2.0 mmol) of **9**, 1 mL of $H_2O$, and 100 mg of TsOH in 300 mL of toluene was heated at reflux for 12 h. Upon cooling, it was diluted with ether, washed with diluted $NaHCO_3$ and brine; dried ($MgSO_4$) and concentrated to 5 – 10 mL volume. Flash chromatography on silica after elution with 6:1 hexane:ethyl acetate afforded 106 mg (37%) of **10** as a light yellow oil: IR ($CHCl_3$) $\nu_{max}$ 1707, 1689, 1675, 1600 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.01 (t, $J$ = 2 Hz, 3), 2.45–2.76 (m, 2), 2.48 (s, 3), 2.67–2.90 (m, 2); mass spectrum, $m/e$ 138.0703 (calcd for $C_8H_{10}O_2$, 138.0680 (parent)). Continued elution with 4:1 hexane/ethyl acetate afforded 25 mg (6%) of **12** whose spectral characteristics are described in the next experiment.

**Methyl 2-Acetyl-4-oxo-2-cyclohexene-1-carboxylate (12).** To a solution of 914 mg (48 mmol) of methyl 4,4-dimethoxy-3-oxopentanoate (**5**) and 608 mg (8.7 mmol) of methyl vinyl ketone at 0 °C was added, in rapid dropwise fashion, 3 mL of methanol containing 1.2 mmol of sodium methoxide. The reaction mixture was maintained at 4 °C overnight and was poured into 200 mL of ether and 100 mL of saturated $NH_4Cl$. The organic layer was washed with brine, dried ($MgSO_4$), and freed of solvent. Flash chromatography of the residual oil on silica gel and elution with 3:1 hexane/ethyl acetate afforded 42 mg (3.3%) of **9**. Further elution with 2:1 hexane/ethyl acetate afforded 934 mg (74%) of the $\beta$-ketol epimers **11** as a colorless oil: $^1H$ NMR ($CDCl_3$) $\delta$ 1.4 (s), 1.9–2.6 (m) 3.28 (s), 3.32 (s), 3.40–3.65 (m), 3.97–4.24 (m).

A solution of 195 mg of the ketol **11**, 0.1 mL of $H_2O$, and 43 mg of TsOH in 50 mL of toluene was heated at reflux for 2.5 h. Upon cooling, the reaction mixture was diluted with ether, washed with diluted $NaHCO_3$ and brine, dried ($MgSO_4$), and freed of solvent to afford 107 mg (73%) of **12**: IR ($CHCl_3$) 1733, 1684, 1602 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.0–2.7 (m, 4), 2.44 (s, 3), 3.73 (s, 3) 3.7–3.9 (m, 1), 6.63 (s, 1); mass spectrum, $m/e$ 196.0747 (calcd for $C_{10}H_{12}O_4$, 196.0734 (parent)).

**Acknowledgment.** This research was supported by a grant from the National Institutes of Health (CA 28824).

**Registry No.** **5**, 62759-83-5; **7a** (isomer 1), 83220-21-7; **7a** (isomer 2), 83220-22-8; **7b** (isomer 1), 83220-23-9; **7b** (isomer 2), 83220-24-0; **7c** (isomer 1), 83220-25-1; **7c** (isomer 2), 83220-26-2; **8a**, 83220-27-3; **8b**, 83220-28-4; **8c**, 83220-29-5; **9**, 83220-30-8; **10**, 83220-31-9; *cis*-**11**, 83220-32-0; *trans*-**11**, 83232-00-2; **12**, 83220-33-1; methyl vinyl ketone, 78-94-4; $\Delta^2$-cycloheptanone, 1121-66-0; $\Delta^2$-cyclohexenone, 930-68-7; $\Delta^2$-cyclopentenone, 930-30-3; coriolin, 33404-85-2.

## 1-Phenyl-3,4:5,6-dibenzocycloheptatrienyl Anion. A Stable Antiaromatic Carbanion

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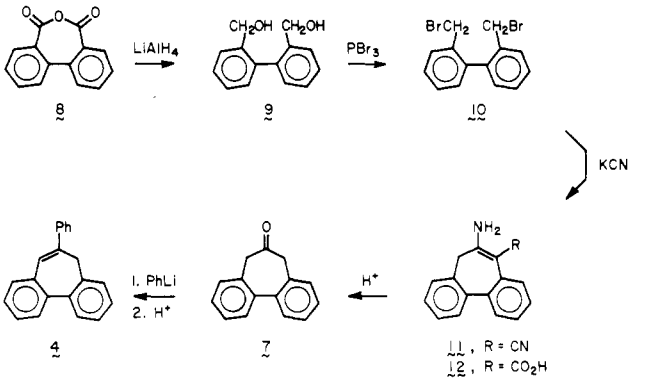
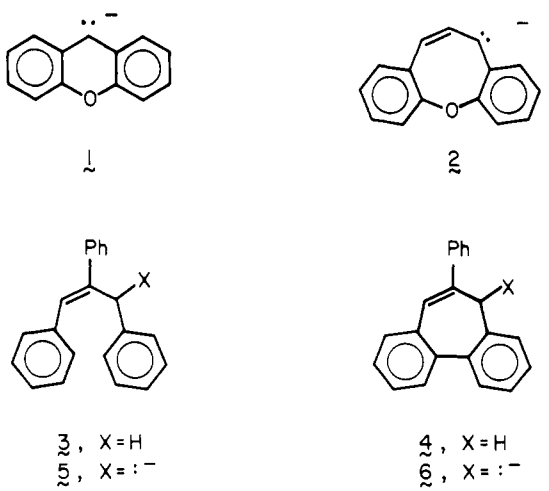
A major hindrance to the study of antiaromatic anions is the lack of stable examples that can be studied by conventional techniques. Staley has studied the 8-$\pi$-electron cycloheptatrienyl anion, for instance, and noted its instability and propensity for undergoing addition reactions.[1a] Its benzo analogue, moreover, has been studied by NMR techniques and exhibits decidedly paratropic behavior.[1b] Anastassiou has reported on the paratropic properties of the formally 8-$\pi$-electron xanthenyl anion (**1**),[2] which is in marked contrast to the potentially but apparently *not* aromatic dibenzo[*b*,*g*]oxocinide anion **2**.[3] Since the imponderables associated with electronegativity may obscure the effects of antiaromaticity for the former anion, we chose to investigate a carbocyclic analogue stabilized as in **1** and **2** by benzo groups. In the course of our photochemical studies of carbanions[4] we had occasion to synthesize 1,2,3-triphenylpropene (**3**) and its cyclic analogue, 1-phenyl-3,4:5,6-dibenzocycloheptatriene (**4**). This allowed us to investigate not only paratropic effects but also the potential destabilization induced by cyclization of an eight-electron system. In contrast to the conjugate base **5** of the former, the anion **6** derived from the latter showed definite paratropic behavior and other evidence of antiaromaticity in a system not encumbered by heteroatoms.

Scheme I. Synthesis of Dibenzocycloheptatriene 4.




1-Phenyl-3,4:5,6-dibenzocyclohepta-1,3,5-triene (**4**), mp 92–94 °C, was synthesized by phenyllithium addition to the known 3,4:5,6-dibenzocyclohepta-3,5-dien-1-one (**7**)[5] followed by dehydration in acetic acid/sulfuric acid. Ketone **7** itself was achieved in overall 43% yield through an improvement on the literature[4] procedure with use of more readily available starting materials (see Scheme I). Thus, lithium aluminum hydride reduction of diphenic anhydride (**8**) yielded [1,1′-biphenyl]-2,2′-dimethanol (**9**),

(1) (a) Staley, S. W.; Orvedal, A. W. *J. Am. Chem. Soc.* **1974**, *96*, 1618. (b) *Ibid.* **1973**, *95*, 3382.

(2) Anastassiou, A. G.; Kasmai, H. S. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 43.

(3) (a) Anastassiou, A. G.; Kasmai, H. S. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 393. (b) Kasmai, H. S.; Whitlock, H. W., Jr. *J. Org. Chem.* **1972**, *37*, 2161.

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