General Approach for the Synthesis of Polyquinenes via the Weiss Reaction. 14. Synthesis of Ellacene (1,10-Decanotriquinacene) and Studies of the Proposed Dimerization to a Substituted Dodecahedrane[1]

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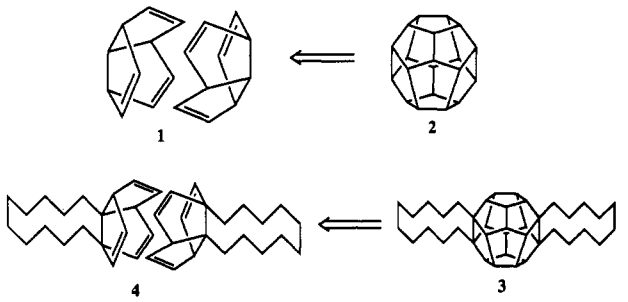
Received March 31, 1992

Ellacene 4, a tetracyclic 1,10-centrosubstituted triquinacene, has been synthesized via the Weiss reaction. The condensation of cyclododecane-1,2-dione (5) with di-*tert*-butyl 3-ketoglutarate (6) under aqueous alkaline conditions provided 13,15,16,18-tetrakis(*tert*-butoxycarbonyl)tricyclo[10.3.3.$0^{1,12}$]octadecane-14,17-dione in the bisenol form 7 in 85% yield. The bisenol ether 8 was regioselectively monoalkylated to furnish in 96% yield the monoallyl ester 9 which was hydrolyzed to provide 13-allyltricyclo[10.3.3.$0^{1,12}$]octadecane-14,17-dione (10). Intramolecular aldol reaction of the related diketo aldehyde 11 to furnish 17-hydroxytetracyclo[11.5.2.$0^{2,13}$.$0^{2,16}$]eicosane-15,19-dione (12) was carried out under aqueous acidic conditions. The Lewis acid mediated (BH_3/THF) reduction of the diketo alcohol provided the corresponding triol 13 in excellent yield. Conversion of the triol into the trisxanthate 21 followed by syn elimination (HMPA, 220 °C) provided the desired triene 4 in 91% yield. Attempted dimerization of 4 (ellacene) to a substituted dodecahedrane 3 under photochemical conditions and/or high pressure (130 kbar) has failed to generate 3 to date under conditions that did effect [2 + 2] dimerization of the parent, triquinacene.

Triquinacene 1, a $C_{10}H_{10}$ triquinane, was first prepared by Woodward et al. in 1964.[2a] The synthesis and chemistry of this molecule has been a topic of continuous interest. Several routes have been devised for the preparation of triquinacene[2] and substituted triquinacenes.[3] de Meijere et al. have detailed attempts to prepare the strained polyquinene acepentalene from triquinacene via dihydroacepentalenediide through an anion-mediated approach.[4] Triquinacene has also been of interest with regard to homoaromaticity. Experimental heats of hydrogenation for triquinacene compared to its dihydro, tetrahydro, and hexahydro derivatives by Liebman, Paquette, et al.[5] have suggested that the three double bonds provide 4.5 kcal/mol of resonance energy because of homoconjugation. However, these results are not in accord with the computations of Miller et al.[6] and Dewar et al.[7] who found no evidence for homoaromatic stabilization of the triquinacene system. Moreover, Woodward,[2a] Müller,[8] and Jacobson[9] have independently proposed triquinacene as an appropriate precursor for dimerization to dodecahedrane 2 (Scheme I). Attempts to dimerize triquinacene into dodecahedrane have been unsuccessful, to date, and have resulted either in products of [2 + 2] dimerization

Scheme I



or in no reaction at all.[10] Paquette et al.[11] and Prinzbach et al.[12a] have recently accomplished serial syntheses of dodecahedrane.[12]

To achieve the appropriate orbital alignment for dimerization into dodecahedrane, the two triquinacene units must be arranged in a concave–concave fashion. Although such dimerizations under photochemical conditions are allowed according to the Woodward–Hoffmann principles of orbital symmetry, the necessary orientation of the two molecules via their concave faces is not favorable. This steric factor combined with an unfavorable entropy has presumably hampered previous attempts to execute this convergent, reflexive synthesis and will likely pose difficulties in the related "aldol approach" recently proposed by Serratosa.[13]

In keeping with the interest in the preparation of polyquinenes and polyquinanes via the Weiss reaction,[14,15]

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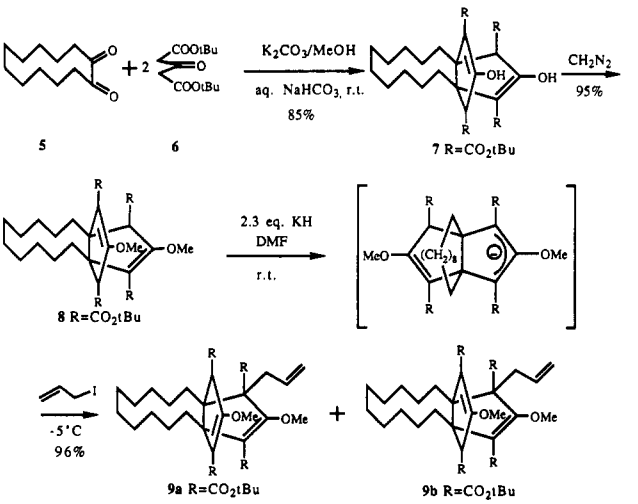
the synthesis of 1,2:16,17-bisdecanododecahedrane (3) was envisaged from ellacene (1,10-decanotriquinacene 4) by this convergent strategy (Scheme I). Since the 12-membered ring of ellacene would block the convex face of the triquinacene skeleton from self-condensation, presumably the opportunity would be increased for two molecules of the triene to react in the desired concave–concave fashion, photochemically, or through the aldol approach of Serratosa.[13] Moreover, the additional use of high pressure might force the two components into a proximity close enough to effect the intermolecular reaction between the concave faces via a symmetry-allowed process. In this paper, we report the successful synthesis of ellacene (tetracyclo-[11.5.2.0^{2,13}.0^{2,16}]eicosa-14,17,19-triene, 4) via the Weiss reaction and studies of the proposed dimerization of ellacene into 1,2:16,17-bisdecanododecahedrane (3).

The Weiss condensation[16] of dimethyl 3-ketoglutarate with 1,2-dicarbonyl compounds has been demonstrated as one of the more efficient methods for the synthesis of polyquinanes and polyquinenes.[17] From a retrosynthetic perspective, the third cyclopentanoid ring of the triquinacene skeleton could be built from the *cis*-bicyclo-[3.3.0]octane-3,7-dione unit by selective functionalization of position 2 followed by an intramolecular cyclization at position 8. Consequently, the key step in the generation of this functionalized triquinacene unit rests on regioselective monoalkylation of the *cis*-bicyclo[3.3.0]octane system, a process already reduced to practice in a related system.[18] The versatility of the Weiss reaction has, therefore, facilitated efficient incorporation of the 12-membered ring into the *cis*-1,5-bicyclo[3.3.0]octane-3,7-dione system by replacement of glyoxal with cyclododecane-1,2-dione in the condensation. This modification permitted extension of the chemistry developed in the synthesis of triquinacene[19] to other centrosubstituted triquinacenes including the target ellacene.

The preparation of cyclododecane-1,2-dione (5) was achieved on large scale from cyclododecene based on the procedure of Sharpless.[20] Condensation of 5 with 2 equiv of di-*tert*-butyl 3-ketoglutarate (6) under aqueous alkaline conditions at room temperature provided the tetra-*tert*-butyl carboxylate isolated as the bisenol 7 in 85% yield. The anti disposition of the two enolic double bonds of bisenol 7 correlate with that observed in another series.[21] This outcome was not surprising since the anti isomer has been found to be more stable than the corresponding syn bisenol.[22] Based on the ^{13}C- and ^{1}H-NMR spectra of tetraester 7, a C_2 symmetry exists in this molecule (see the

Scheme II



Experimental Section for details). The relative configuration on the carbon atoms bearing the ester functions was not assigned at this time, although it had been shown (NMR spectroscopy and X-ray crystallography)[23] that the *tert*-butyl carboxylates at positions C-4 and C-8 in the bisenols from either glyoxal or biacetyl exist with the exo configuration.

Replacement of the methyl ester functions in the original Weiss reaction with the *tert*-butyl ester groups provided several advantages for the synthesis of triquinacenes. It had been demonstrated that the large *tert*-butyl ester functions retard the rate of addition of electrophiles to the anion derived from the *cis*-bicyclo[3.3.0]octane-3,7-dione system.[18] Consequently, regioselective monoallylation could be accomplished in this system when the alkylation was carried out at −5 °C. Furthermore, hydrolysis and decarboxylation of the *tert*-butyl ester functions could be accomplished with relative ease in contrast to the conditions required for the same conversion in the methyl ester series.[24]

The hydroxyl groups of bisenol 7 were methylated with diazomethane, and dimethyl ether 8 was then monoallylated with allyl iodide at −5 °C. A mixture (1:1) of the syn (**9a**) and anti (**9b**) monoallyl isomers was isolated in 96% yield (Scheme II). No attempt to separate them at this stage was made since both ethers **9a** and **9b** provide the desired monoallyl [10.3.3]propellanedione **10** on hydrolysis. The monoallyl dione **10** was isolated from **8** in 80% overall yield as a mixture of endo (major) and exo (minor) stereoisomers. The ^{13}C-NMR spectrum of **10** clearly revealed two sets of carbonyl signals, which implied the presence of both stereoisomers. Ozonolysis at −78 °C, followed by reductive hydrolysis with dimethyl sulfide, produced a stereoisomeric mixture (endo:exo ca. 3:1) of diketo aldehydes **11** in 95% yield. This sequence could be scaled up to 10 g without difficulty. The aldehydic proton appeared as a singlet at δ 9.89 for the major isomer (**11a**) and at δ 9.87 for the minor one (**11b**).

It should be noted that substituents in the simple *cis*-bicyclo[3.3.0]octane-3,7-dione system usually prefer the thermodynamically favored exo configuration. On the other hand, only those substituents with the endo configuration can undergo cyclization to form a five-membered

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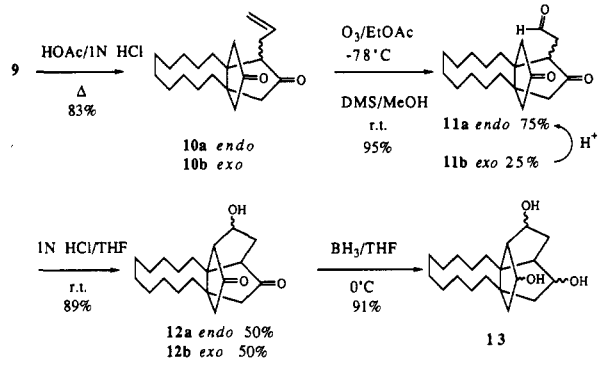
Scheme III



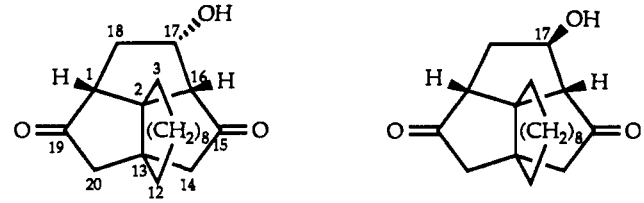
ring due to the topology of the *cis*-bicyclo[3.3.0]octane unit. In the case of keto aldehyde **11**, only the one (endo) isomer **11a** could cyclize to generate the triquinacene ring system **12**. It was, therefore, necessary to employ conditions that would permit epimerization of the exo isomer **11b** into the desired endo isomer **11a** preceding cyclization. Once the triquinane carbon–carbon bond was formed in **12**, the equilibrium could shift toward **11a** and eventually to **12**. The conversion of **11** into an (1:1) epimeric mixture (89%) of **12a** and **12b** was effected by intramolecular aldolization. The endo diketo alcohol **12a** crystallized from the mixture and was purified by recrystallization, but the exo isomer was obtained in only 85% purity.

The structures of **12a** and **12b** were assigned by NMR spectroscopy.[24a,b,25] The ^{1}H-NMR signals for the endo isomer **12a** were assigned based on 2D COSY experiments.[24b] Since the hydrogen atom at C-17 is the only one attached to an oxygen-substituted carbon nucleus, it appeared the furthest downfield (δ 4.47). Unequivocal assignment of this signal permitted identification of H-16 (δ 2.84), H-18$_{endo}$ (δ 2.07), and H-18$_{exo}$ (δ 2.22) by observation of the off-diagonal cross peaks between H-17 and those protons in the COSY spectrum. The complete assignments with coupling constants are summarized in Table I. The assignments for the exo isomer **12b** were based on a series of homonuclear decoupling experiments and are also depicted in Table I.[24b]

The relative stereochemistry of the hydroxyl group at C-17 was determined from the coupling constants of the two protons at C-18 of **12a** (see Table I).[24b] The presence of an intramolecular hydrogen bond was supported by FTIR, which revealed two absorptions for the endo isomer **12a** ($\Delta\nu$ = 7.5 cm^{-1}), whereas only one signal was observed for **12b** (Table II). All of these spectroscopic features are consistent with assignments reported for related systems[19,24a] and are summarized in Table II.

Due to the instability of the diketo alcohol in an alkaline medium (retro-aldol reaction),[26] the mixture of **12a** and **12b** was reduced with BH_3/THF. A mixture of diastereomeric triols (represented by **13**) was obtained in greater than 90% yield (Scheme III). The ^{13}C-NMR spectrum of this mixture clearly indicated the presence of at least three different triols. This result implies that the BH_3 reagent approaches the carbonyl groups from both the convex and concave faces of the polycyclic unit. This result is not surprising, since the convex face is shielded by a 12-membered ring, even though a similar reduction of the parent triquinacene diketo alcohol was found to occur solely from the convex face.[24a]

Table I. Proton Chemical Shifts and Coupling Constants for Monoalcohols 12a and 12b



proton[a]	chemical shift, δ (ppm)	coupling constants, J (Hz)	chemical shift, δ (ppm)	coupling constants, J (Hz)
H-17	4.47	J_{17-16} = 6.8 $J_{17-18exo}$ = 5.1 $J_{17-18endo}$ = 3.7 J_{17-OH} = 3.8	4.30	J_{17-16} = 3.4 $J_{17-18exo}$ = 5.2 $J_{17-18endo}$ = 5.2
H-16	2.84	J_{16-17} = 6.8 $J_{16-14exo}$ = 1.7 J_{16-OH} = 0.9	2.67	J_{16-17} = 3.4
H-1	2.58	$J_{1-18exo}$ = 9.1 $J_{1-18endo}$ = 3.5 $J_{1-20exo}$ 1.9	2.82	$J_{1-18exo}$ = 7.1 $J_{1-18endo}$ = 7.1 $J_{1-20exo}$ 1.9
H-14$_{exo}$	2.58	J_{gem} = 18.0 $J_{14exo-16}$ = 1.7	2.51	J_{gem} = 18.2 $J_{14exo-16}$ = 1.6
H-14$_{endo}$	2.35	J_{gem} = 18.1	2.19	J_{gem} = 18.1
H-20$_{exo}$	2.40	J_{gem} = 18.6 $J_{20exo-1}$ = 2.0	2.57	J_{gem} = 18.2 $J_{20exo-1}$ = 1.9
H-20$_{endo}$	2.69	J_{gem} = 18.6	2.20	J_{gem} = 18.1
H-18$_{exo}$	2.22	J_{gem} = 13.6 $J_{18exo-17}$ = 5.2 $J_{18exo-1}$ = 8.8	2.12	J_{gem} = 13.6 $J_{18exo-17}$ = 6.0 $J_{18exo-1}$ = 9.4
H-18$_{endo}$	2.07	J_{gem} = 13.8 $J_{18endo-17}$ = 3.7 $J_{18endo-1}$ = 3.7	1.99	J_{gem} = 13.7 $J_{18endo-17}$ = 5.6 $J_{18endo-1}$ = 5.7
OH	2.33	J_{OH-17} = 3.8 J_{OH-16} = 0.9		
1 H	1.75	m	1.85	m
2 H	1.65	m		
17 H	1.10–1.55	m		

[a] The proton signal assignments for **12a** were based on 2D-COSY experiments, while those for **12b** were based on homonuclear decoupling techniques.

The configuration of these triols was not considered critical if an approach could be found to remove the endo and exo hydroxyl groups. In contrast to the reported HMPA-mediated dehydration of perhydrotriquinacenetriol to the desired triene,[19,24a] dehydration of triol **13** in HMPA provided only 14% of the triene as a mixture of the desired ellacene **4** and its bridgehead olefinic isomer **14** in the ratio of 8:2. The bridgehead isomer **14** was converted into the more stable ellacene (**4**) by an acid-catalyzed isomerization. The trace amounts of HCl present in commercial $CDCl_3$ is sufficient to effect this isomerization (Scheme IV).

The major products isolated from the HMPA-mediated reaction were ethers **15** and **16**, 38% combined yield. These two ethers were inseparable; however, their structures could be deduced by ^{1}H-NMR spectroscopy in component-enriched fractions. The more symmetrical ether **15** contained only five signals for the triquinacene ring skeleton. A singlet was observed at δ 2.39 (2 H) which exhibited cross peaks with the olefinic protons (δ 5.80, 2 H, t, J = 1.4 Hz) as well as H-15 and H-19 (δ 3.82, 2 H, s) in the COSY spectrum. Therefore, the signal at δ 2.39 was assigned to the bridgehead protons (H-1 and H-16); H-15 and H-19 were also coupled to two doublets at δ 1.68 (J = 11 Hz) and 1.83 (J = 11 Hz), respectively. Therefore,

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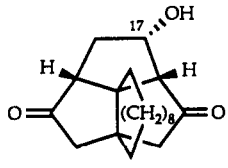
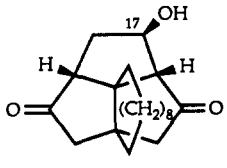
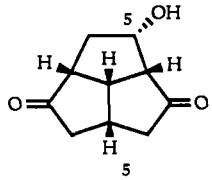
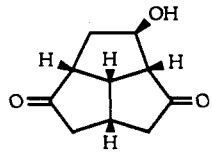
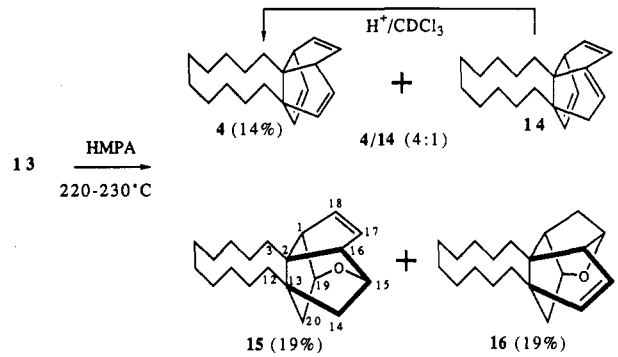
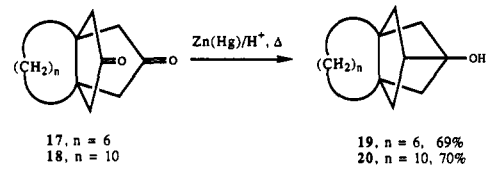
Table II. Diagnostic Signals Employed To Characterize the Diastereomeric Endo (12a) and Exo (12b) Monoalcohols

monol	^{1}H-NMR signals proton δ (ppm)	^{13}C-NMR signals carbon δ (ppm)	FTIR ν(C=O) (cm^{-1})
 12a	H-17, 4.47	C-17, 74.20	CCl_4: 1739.8 1732.3 Δ = 7.5 KBr: 1734.2 1724.2 Δ = 10.0
 12b	H-17, 4.30 Δ = 0.17	C-17, 77.50 Δ = 3.30	CCl_4: 1739.1, Δ=0 KBr: 1734.3, Δ=0
 5	H-5, 4.49	C-5, 74.74	neat: 1730.0 1705.0 Δ = 25.0
	H-5, 4.24 Δ = 0.25	C-5, 77.94 Δ = 3.20	KBr: 1735.0 1725.0 Δ = 10.0

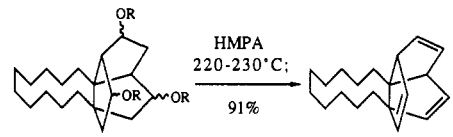
Scheme IV



Scheme V



Scheme VI



these two doublets were assigned to H-14 and H-20. Furthermore, only six carbon signals for the triquinacene ring unit were observed in the ^{13}C-NMR spectrum and at approximately double intensity as compared to signals for ether **16**. This feature is consistent with the structure of **15** as the more symmetrical of the two ethers.

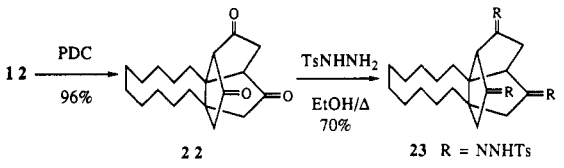
The ^{1}H-NMR spectrum for component **16** was more complex. However, the high-resolution spectrum (500 MHz) permitted the assignment of the signals in the mixture. Two downfield signals which were coupled to each other were assigned to the olefinic protons (δ 5.74, J = 5.7 Hz; and δ 5.36, dd, J = 5.7, 2.8 Hz) of ether **16**. The doublet of doublets exhibited a cross peak in the COSY spectrum with a singlet at δ 2.62, which correlated to H-1. Proton H-18 was correlated with H-1 and also with the protons (δ 2.01 and 1.82) at C-17. The other downfield signal (δ 4.15) was assigned to H-15 which was coupled to the bridgehead H-16 and the two protons at C-14 in the COSY spectrum.

The formation of both exo and endo hydroxyl groups in the carbonyl reduction coupled with buttressing by the 12-membered ring presumably produced ethers **15** and **16** in preference to the desired triene **4**. Buttressing by the 12-membered ring could force the cyclopentane rings into closer proximity, diminish the van der Waals distance between the hydroxyl groups, and facilitate ether formation between the five-membered rings. A buttressing effect in these systems was originally observed by Borden[27] in the case of 1,5-dimethyl-*cis*-bicyclo[3.3.0]octane-3,7-dione, and subsequently in a related system by Yang et al.,[27] as illustrated in Scheme V. It is important to note that *cis*-bicyclo[3.3.0]octane-3,7-dione, when heated under the conditions of Borden,[27] did not furnish any of the alcohol related to **19** or **20**.

In order to circumvent the difficulty in transforming triol **13** into triene **4**, a Chugaev approach[28] was successfully employed to obtain ellacene **4** in high yield. Trisxanthate **21** ultimately prepared in 99% yield was pyrolyzed at 230 °C (neat) to provide ellacene (**4**) in 54% yield, or at 220–230 °C in HMPA to furnish **4** in 91% yield (Scheme VI). The latter procedure was superior, probably because

(27) (a) Yang, D.; Cook, J. M. *J. Org. Chem.* **1976**, *41*, 1903. (b) Borden, W. T.; Ravindranathan, T. *J. Org. Chem.* **1971**, *36*, 4125.
(28) Nace, H. *Organic Reactions*; John Wiley: New York, 1962; Vol. 12, p 57.

Scheme VII



dilution of the desired triene limited intermolecular reactions that produce polymeric materials.

In the reported syntheses of triquinacene and cyclohexanotriquinacene,[19] isomeric olefins were observed from the HMPA-mediated dehydration of the corresponding triols, although these isomeric trienes could be isomerized to the desired triquinacene trienes. In contrast, the syn elimination of the trisxanthate **21** provided the desired triene **4** as the sole component in high yield. This sequence is of general interest for the preparation of polyquinenes especially for molecules that contain multiple olefinic bonds.

In a related approach, the monoalcohol **12** was oxidized with pyridinium dichromate (PDC) to the interesting trione **22**, which was converted into the tris(tosylhydrazone) **23** under standard conditions. The Shapiro approach[29] failed to convert the trishydrazone **23** into ellacene (**4**) (Scheme VII). However, trione **22** is closely related to the trione in the Serratosa aldol approach[13] to dodecahedrane derivatives and may be important in this context.

Ellacene, a molecule with unique topological features, has C_s symmetry, as evidenced by the appearance of only three olefinic carbon signals in the ^{13}C-NMR spectrum and five sets of signals in the ^1H-NMR spectrum of this centrosubstituted triquinacene. Its electronic character[30] and possible homoaromaticity[5-7] are of special interest. The large alicyclic ring on the convex face of the triene **4** might force the three double bonds in the polycyclopentanoid system into closer proximity (as suggested by the formation of ethers **15** and **16**). Consequently, molecules such as ellacene might be candidates for neutral homoaromaticity, if the prospects of such resonance are available in triquinacene. However, the UV spectra of both triquinacene (λ_{max} < 190 nm; lit.[31] λ_{max} = 187 nm) and ellacene (λ_{max} < 190 nm) indicate no enhanced delocalization in ellacene (**4**).

With gram quantities of ellacene in hand, our attempts next turned to its possible dimerization into a derivative (see **3**) of dodecahedrane. Initial attempts at the [6 + 6] dimerization of ellacene (**4**) were carried out by irradiation at λ_{max} = 254 nm and at 214 nm, at a pressure of 1 atm at 23 °C. However, no reaction occurred after exposure for 3 days. When ellacene was irradiated at high pressure (130 kbar), there was still no detectable reaction by GC/MS (although triquinacene undergoes [2 + 2] dimerization under the same conditions[10f]). Also ellacene was unchanged at 130 kbar in the absence of light, conditions known to give [2 + 2] dimerizations with triquinacene.[10f] Thus the 12-membered ring in ellacene has prevented, as desired, the convex face from undergoing a [2 + 2] cycloaddition; however, the desired [6 + 6] dimerization into dodecahedrane was also not effected. Further studies with ellacene are underway and will be reported in due course.

(29) (a) Shapiro, R. H.; Heath, M. J. *J. Am. Chem. Soc.* **1967**, *89*, 5737. Shapiro, R. H. *Organic Reactions*; John Wiley: New York, 1975; Vol. 23, p 405. (b) Adlington, R. M.; Barrett, A. G. M. *Acc. Chem. Res.* **1983**, *16*, 55.

(30) Bishof, P.; Bosse, D.; Gleiter, R.; Kukla, M. J.; de Meijere, A.; Paquette, L. A. *Chem. Ber.* **1975**, *108*, 1218.

(31) Paquette, L. A.; Kearney, F. R.; Drake, A. F.; Mason, S. F. *J. Am. Chem. Soc.* **1981**, *103*, 5064.

Experimental Section

The experimental details are analogous to those reported earlier.[19,22] All chemicals were purchased from Aldrich Chemical Co. unless otherwise stated. Cyclododecane-1,2-dione (**5**)[20] and di-*tert*-butyl β-ketoglutarate (**6**)[19] were prepared by literature procedures.

13,15,16,18-Tetrakis(*tert*-butoxycarbonyl)tricyclo[10.3.3.0^{1,12}]octadecane-14,17-dione (7). Di-*tert*-butyl 3-ketoglutarate (**6**, 54.5 g, 0.20 mol) was dissolved in distilled methanol (400 mL) followed by addition of aqueous 3% $NaHCO_3$ solution (130 mL). Anhydrous K_2CO_3 (43.0 g) was then added to the mixture with warming (using hot tap water at about 55 °C) until the solution became clear yellow. The mixture was allowed to cool to room temperature whereupon the solution became slightly turbid. A solution of cyclododecane-1,2-dione (**2**, 19.98 g, 0.10 mol) in methanol (40 mL) was added dropwise over 1 h with rapid stirring using an overhead stirrer. The orange solution that resulted was stirred at 25 °C and monitored by TLC (EtOAc/hexane, 1:9). Components active to $FeCl_3$ spray reagent were monitored until the TLC indicated the presence of only one major component (R_f = 0.6). **Note:** the reaction time ranges from 5 days to 3 weeks depending on the reaction scale. The precipitate that formed was filtered from the medium and washed with cold methanol and dried under vacuum. The filtrate was saved at this point. The orange precipitate that formed was dissolved in $CHCl_3$ (450 mL) and washed with cold aqueous HCl (1 N) until the aqueous layer became slightly acidic. The chloroform layer was separated and washed with water followed by brine. The organic layer was dried ($MgSO_4$) and concentrated to provide white crystalline **7** (34.6 g) in 51% yield. The filtrate from above was concentrated under reduced pressure and then cooled to 0 °C. The precipitate which formed was filtered under vacuum and treated in the same fashion as described above. The oil (29.3 g) that was isolated contained several components and was rich in the desired tetraester **7**, which was purified by flash chromatography (EtOAc/hexane, 1:15) to provide additional **7** (22.6 g). The combined yield was 85%. An analytical sample was obtained by recrystallization from MeOH to provide colorless crystals of **7**: mp 139.2–140.5 °C; FTIR (KBr) 1713, 1650 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.47 (18 H, s), 1.53 (18 H, s), 1.1–2.0 (20 H, m), 3.57 (2 H, s), 11.11 (2 H, s). **Note:** The integration of this latter singlet corresponded to only 1.1 protons when the routine proton NMR parameters (D5 = 1.0 s) were employed. However, the integration represented two protons with D5 = 4 s; ^{13}C NMR (125.75 MHz, $CDCl_3$) δ 25.1, 25.3, 27.8, 28.1, 28.5, 30.4, 58.2, 62.8, 81.7, 82.2, 108.8, 169.1, 169.5, 170.7; MS (EI) *m/z* (relative intensity) 564 (3.8), 508 (14.8), 490 (3.5), 452 (100.0), 434 (84.8), 416 (41.4). Anal. Calcd for $C_{38}H_{60}O_{10}$: C, 67.46; H, 8.88. Found: C, 67.69; H, 9.07.

13,15,16,18-Tetrakis(*tert*-butoxycarbonyl)-14,17-dimethoxytricyclo[10.3.3.0^{1,12}]octadeca-13,16-diene (8). An ethereal solution of diazomethane (0.3 mol) was prepared by addition of a solution of Diazald (64.2 g, 0.3 mol) in ether (400 mL) to a heated (70–80 °C), stirred mixture of 2-(2-ethoxyethoxy)ethanol (105 mL), potassium hydroxide (18 g, 0.32 mol), water (30 mL), and ether (40 mL). Tetraester (**7**, 47.5 g, 70.2 mmol) was added to the cold (−78 °C) ethereal diazomethane solution. The mixture that resulted was stirred at −78 °C for 1.5 h, followed by stirring at 0 °C for 5 h, and then allowed to warm to room temperature in a fume hood for 12 h. The solvent was removed under reduced pressure to leave a light yellow oil, which was purified by flash chromatography (EtOAc/hexane, 1:4) to afford pure bisenol ether (**8**, 47.2 g, 95%) as a white crystalline solid: mp 121.0–121.7 °C; FTIR (KBr) 1729, 1708, 1700, 1647, 1244 (broad strong) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.49 (18 H, s), 1.51 (18 H, s), 1.10–1.95 (20 H, m), 3.70 (2 H, s), 3.71 (6 H, s); ^{13}C NMR (62.86 MHz, $CDCl_3$) δ 25.1, 25.6, 27.7, 27.8, 28.0, 28.3, 30.9, 57.9, 59.7, 61.8, 80.6, 81.7, 114.3, 162.2, 164.2, 169.6; MS (EI) *m/z* (relative intensity) 704 (M^+, 6.6), 592 (37.2), 574 (74.4), 462 (52.5), 444 (100.0). Anal. Calcd for $C_{40}H_{64}O_{10}$: C, 68.18; H, 9.09. Found: C, 68.32; H, 9.08.

13,15,16,18-Tetrakis(*tert*-butoxycarbonyl)-14,17-dimethoxy-13-allyltricyclo[10.3.3.0^{1,12}]octadeca-13,16-diene (9). A

suspension of KH in mineral oil was added to a 500-mL round-bottom flask and washed twice with dry hexane. The hexane was decanted off under an atmosphere of argon. The residual hexane was flushed off with argon. The weight of pure KH was then determined (1.46 g, 36.0 mmol), after which dry DMF (20 mL) was added via syringe under argon. The tetra-*tert*-butyl ester bisenol ether (**8**, 11.53 g, 16.38 mmol) was dissolved in dry DMF (200 mL) and then added to the above mixture containing KH via a double-ended transfer needle (under argon). The clear yellow solution was stirred at room temperature for 2 h and cooled to −5 °C by stirring in an ice–salt bath. Allyl iodide (6.1 g, 36 mmol) was added to the solution and the mixture was stirred for 6 h at 0 °C. The reaction mixture was quenched by the addition of cold aqueous HCl (1 N, 130 mL). The solution was allowed to warm to room temperature and extracted with EtOAc (4 × 150 mL). The combined organic layers were washed with water (3 × 50 mL) and brine and dried ($MgSO_4$). The solvent was removed under reduced pressure to provide a 1:1 mixture of isomers (**9a,b**, 11.7 g, 96.0%) as a light yellow-colored oil. This material was employed in the next step without further purification. Analytical samples of **9a** and **9b** were obtained by preparative TLC (EtOAc/hexane, 18:82).

9a: R_f = 0.65 (EtOAc/hexane, 18:82); FTIR (KBr) 1731, 1702, 1663 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.46 (9 H, s), 1.47 (9 H, s), 1.49 (18 H, s), 1.2–2.0 (19 H, m), 2.21 (1 H, m), 2.71 (2 H, m), 3.59 (1 H, s), 3.72 (3 H, s), 3.75 (3 H, s), 4.90 (1 H, dd, J = 10.0, 1.0 Hz), 4.96 (1 H, dd, J = 16.6, 1.0 Hz), 5.87 (1 H, m); ^{13}C NMR (125.75 MHz, $CDCl_3$) δ 22.3, 23.7, 23.8, 24.2, 24.9, 27.7, 28.3, 28.4, 28.6, 29.3, 31.6, 40.3, 56.5, 59.2, 60.5, 60.9, 65.0, 63.4, 80.6, 81.3, 81.7, 112.1, 115.9, 135.6, 165.4, 165.9, 170.6, 171.1; MS (EI, 15 eV) m/z (relative intensity) 688 (14.7), 687 (34.3), 502 (83.2), 501 (53.8), 470 (55.9), 459 (100). Anal. Calcd for $C_{43}H_{68}O_{10}$: C, 69.35; H, 9.14. Found: C, 69.71; H, 9.32.

9b: R_f = 0.48 (EtOAc/hexane, 18:82); FTIR (KBr) 1729, 1701, 1652, 1637 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.45 (9 H, s), 1.47 (9 H, s), 1.48 (9 H, s), 1.51 (9 H, s), 1.10–1.90 (18 H, m), 2.05–2.27 (2 H, m), 2.56 (1 H, dd, J = 14.8, 7.1 Hz), 2.75 (1 H, dd, J = 14.8, 6.5 Hz), 3.68 (3 H, s), 3.70 (1 H, s), 3.73 (3 H, s), 4.81 (1 H, dd, J = 10.5, 1.0 Hz), 4.90 (1 H, dd, J = 16.9, 1.1 Hz), 5.72 (1 H, m); ^{13}C NMR (125.75 MHz, $CDCl_3$) δ 25.1, 25.6, 25.9, 27.4, 27.5, 27.6, 27.9, 28.0, 32.1, 32.3, 38.5, 57.7, 59.1, 60.5, 61.3, 63.9, 68.3, 80.2, 81.2, 81.3, 81.8, 113.7, 113.8, 115.4, 135.7, 163.3, 163.4, 164.6, 165.1, 169.7, 171.5; MS (EI, 15 eV) m/z (relative intensity) 744 (M^+, 6.2), 632 (40.8), 502 (98.6), 426 (96.5), 378 (72.4), 377 (74.7), 321 (100.0). Anal. Calcd for $C_{43}H_{68}O_{10}$: C, 69.35; H, 9.14. Found: C, 68.87; H, 9.13.

13-Allyltricyclo[10.3.3.0^{1,12}]octadecane-14,17-dione (10). To a stirred solution of glacial acetic acid (150 mL) and aqueous HCl (1 N, 150 mL) was added the monoalkylated tetraester (**9**, 11.0 g, 14.8 mmol). The mixture was heated to reflux (oil bath temperature 125 °C) for 5 h and then allowed to cool to 25 °C. The reaction mixture was diluted by addition of water (200 mL) and extracted with $CHCl_3$ (4 × 200 mL). The combined chloroform fractions were washed with water (3 × 50 mL) and saturated aqueous $NaHCO_3$ solution until the organic layer was alkaline to pH paper. The solution was dried ($MgSO_4$) and the solvent removed under reduced pressure to provide a viscous oil. The crude oil was purified by flash chromatography (EtOAc/hexane, 1:4) to furnish the pure monoallyl diones (**10a,b**, 3.87 g, 83%) as a mixture of endo and exo stereoisomers: FTIR (film) 1748 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.00–1.90 (21 H, m), 2.00–2.60 (9 H, m), 4.95 (1 H, d, J = 10 Hz), 5.04 (1 H, d, J = 16 Hz), 5.90 (1 H, m); ^{13}C NMR (62.86 MHz, $CDCl_3$) δ major isomer 21.1, 22.9, 23.1, 23.7, 24.1, 26.5, 26.8, 26.9, 27.2, 31.4, 33.6, 34.7, 47.5, 47.9 48.8, 53.3, 54.4, 116.2, 136.5, 216.0, 217.7; minor isomer (only the signals from the carbonyl and double bonds could be easily identified) 117.3, 136.1, 205.8, 217.3; MS (EI, 70 eV) m/z (relative intensity) 316 (M^+, 93.4), 275 (38.7), 273 (47.5), 219 (100); HRMS calcd for $C_{21}H_{32}O_2$ 316.2403, found 316.2394.

13-(2′-Oxoethyl)tricyclo[10.3.3.0^{1,12}]octadecane-14,17-dione (11a,b). Monoallyltricyclo[10.3.3.0^{1,12}]octadecane-14,17-dione (**10a,b**, 3.80 g, 12.0 mmol) was dissolved in EtOAc (400 mL) in a 1-L three-neck flask equipped with a magnetic stirrer and a low-temperature thermometer. The flask was placed into a dry ice–EtOAc cooling bath and the temperature was allowed to drop to −78 °C. Ozone was generated (O_3 flow, 3.5–4 L/min, 110–120 VAC; O_2 pressure 6–7 psi) and bubbled through the cold solution until it took on a light blue coloration. Excess ozone was purged from the reaction medium with dry nitrogen. Methanol (100 mL) and dimethyl sulfide (100 mL) were added to the cold solution. The mixture was then stirred and allowed to slowly warm to 23 °C. The reaction progress was monitored by TLC (EtOAc/hexane, 1:1). After 16 h the spot corresponding to the ozonide had disappeared and was replaced by a 2,4-DNP active component of slightly lower R_f. The solvent was removed under reduced pressure in a fume hood, and the residue was carefully flash evaporated with toluene (3 × 50 mL) under vacuum. The residual DMSO present in the crude mixture was removed by Kuglerohr distillation [50 °C (1.5 mmHg)] to provide a viscous oil. The oily residue was purified by a wash column (silica gel) with EtOAc to afford a mixture of **11a,b** (3.62 g, 95%) as a colorless oil: IR (film) 1715 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) **11a** (endo isomer, ca 75%) δ 1.10–1.75 (19 H, m), 1.82 (1 H, m), 2.05–3.05 (8 H, m), 3.25 (1 H, m), 9.89 (1 H, s); **11b** (exo isomer ca. 25%). A singlet for the aldehydic proton appeared in the proton NMR spectrum at δ 9.87, while the other signals overlapped with those of the major isomer. ^{13}C NMR (62.86 MHz, $CDCl_3$) δ 21.0, 22.4, 22.9, 23.5, 23.9, 26.2, 26.6, 26.8, 33.3, 34.4, 40.2, 40.8, 47.8, 48.4, 48.7, 50.2, 52.5, 199.5, 215.5, 216.1; MS (EI) m/z (relative intensity) 318 (M^+, 100.0), 300 (72.3), 233 (98.1), 220 (73.4); HRMS calcd for $C_{20}H_{30}O_3$ 318.2195, found 318.2187.

17-Hydroxytetracyclo[11.5.2.0^{2,13}.0^{2,16}]eicosane-15,19-dione (12a,b). A mixture of the endo and exo diketo aldehydes (**11a,b**, 3.59 g, 11.3 mmol) was dissolved in freshly distilled THF (250 mL). Aqueous HCl (25 mL, 1 N) was added, and the mixture was stirred at 23 °C under nitrogen. The reaction progress was monitored by TLC (EtOAc/hexane, 1:1). After 5 days, the reaction was quenched by the addition of solid $NaHCO_3$ to neutralize the excess acid. The mixture was concentrated under reduced pressure and extracted with EtOAc (4 × 100 mL). The combined organic layers were washed with water and dried ($MgSO_4$). The solvent was removed under reduced pressure to afford a brown, viscous oil. The crude reaction product was purified by flash chromatography (EtOAc/hexane, 1:1). The initial fractions contained unreacted diketo aldehyde (0.62 g, 17%). The major product (2.65 g, 89% based on the reacted diketo aldehyde) was a mixture (ca. 1:1) of endo and exo tetracyclic diketo alcohols **12a,b**. The endo isomer **12a** crystallized from the mixture upon standing. A pure sample of **12a** was obtained by recrystallization from EtOAc/hexane.

12a (endo): FTIR (KBr) 3459, 1734, 1724 cm^{-1}; (CCl_4) 3593, 1740, 1732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.10–1.55 (17 H, m), 1.65 (2 H, m), 1.75 (1 H, m), 2.07 (1 H, dt, J = 13.81, 3.68 Hz), 2.22 (1 H, ddd, J = 13.64, 8.83, 5.21 Hz), 2.35 (1 H, d, J = 18.05 Hz), 2.40 (1 H, dd, J = 18.56, 2.01 Hz), 2.58 (1 H, dd, J = 18.0, 1.68 Hz), 2.58 (1 H, ddd, J = 9.05, 3.53, 1.93 Hz), 2.69 (1 H, d, J = 18.59 Hz), 2.84 (1 H, d, J = 6.82 Hz), 4.47 (1 H, dddd, J = 6.82, 5.10, 3.68, 3.79 Hz); ^{13}C NMR (62.86 MHz, $CDCl_3$) δ 22.5 (1 C, t), 22.7 (1 C, t), 23.1 (1 C, t), 23.5 (1 C, t), 25.9 (1 C, t), 26.3 (1 C, t), 26.9 (1 C, t), 27.5 (1 C, t), 33.3 (1 C, t), 35.1 (1 C, t), 42.2 (1 C, t), 47.2 (1 C, s), 50.9 (1 C, t), 54.2 (1 C, t), 57.2 (1 C, d), 60.7 (1 C, s), 65.5 (1 C, d), 74.2 (1 C, d), 218.4 (1 C, s), 220.3 (1 C, s); MS (EI, 15 eV) m/z (relative intensity) 318 (M^+, 78.1), 300 (75.0), 233 (100). Anal. Calcd for $C_{20}H_{30}O_3$: C, 75.47; H, 9.43. Found: C, 75.73; H, 9.79.

The exo isomer was obtained in 85% purity (^1H-NMR integration of signals corresponding to the H-17 proton of both isomers) as a colorless oil. **12b**: FTIR (KBr) 3438, 1734 cm^{-1}; (CCl_4) 3625, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.10–1.70 (19 H, m), 1.86 (1 H, m), 1.99 (1 H, dt, J = 13.69, 5.57 Hz), 2.12 (1 H, ddd, J = 13.59, 9.35, 5.96 Hz), 2.19 (1 H, d, J = 18.07 Hz), 2.20 (1 H, d, J = 18.12 Hz), 2.51 (1 H, dd, J = 18.08, 1.58 Hz), 2.57 (1 H, dd, J = 18.18, 1.92 Hz), 2.67 (1 H, d, J = 3.43 Hz), 2.82 (1 H, t, J = 7.05 Hz), 4.30 (1 H, ddd, J = 5.24, 5.15, 4.18 Hz); ^{13}C NMR (62.86 MHz, $CDCl_3$) δ 22.8 (1 C, t), 23.1 (1 C, t), 23.2 (1 C, t), 23.6 (1 C, t), 25.7 (1 C, t), 26.6 (1 C, t), 26.9 (1 C, t), 27.5 (1 C, t), 34.1 (1 C, t), 34.8 (1 C, t), 40.0 (1 C, t), 47.0 (1 C, s), 52.0 (2 C, t), 57.6 (1 C, d), 60.9 (1 C, s), 67.5 (1 C, d), 77.5 (1 C, d), 217.8 (1 C, s), 219.3 (1 C, s); MS (EI, 15 eV) m/z (relative intensity) 318 (M^+, 78.1), 300 (75.0); HRMS calcd for $C_{20}H_{30}O_3$ 318.2195, found 318.2190. Anal. Calcd for $C_{20}H_{30}O_3$: C, 75.47; H, 9.43. Found: C, 76.06; H, 9.40.

Tetracyclo[11.5.2.0^{2,13}.0^{2,16}]eicosane-15,17,19-triol (13). The mixture of endo and exo hydroxy diketones (**12a,b**, 2.97 g, 9.34 mmol) was dissolved in dry THF (120 mL) and cooled to 0 °C by stirring in an ice bath under nitrogen. A solution of borane–THF (26 mL, 1 M) was then added to the above mixture. The reaction was allowed to stir at 0 °C for 24 h, after which methanol (10 mL) was added to quench the unreacted borane. The solvent was removed under reduced pressure, and methanol was added (4 × 100 mL), followed by repeated flash evaporation with methanol under vacuum to remove the residual trimethoxyborane. The crude solid **13** was further purified by flash chromatography (gradient elution: 75% EtOAc/hexane to 8% methanol/EtOAc) to provide a mixture of diastereomeric triols as a white crystalline solid (2.73 g, 91%). **13**: FTIR (KBr) 3310 (br s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95–2.36 (31 H, m), 2.85–4.60 (3 H, m); ^{13}C NMR (125.75 MHz, $CDCl_3$) δ 22.2, 22.5, 22.6, 23.4, 23.5, 23.7, 23.9, 24.5, 24.7, 25.2, 27.4, 27.5, 27.7, 27.8, 29.8, 33.8, 35.9, 36.4, 36.5, 36.8, 42.8, 42.9, 43.3, 44.2, 45.1, 45.3, 45.8, 45.9, 48.1, 48.7, 50.8, 54.3, 57.1, 59.8, 61.5, 62.7, 62.7, 62.8, 63.2, 66.4, 70.9, 72.4, 72.8, 73.3, 73.4, 74.2, 74.5, 74.6; MS (EI) m/z (relative intensity) 305 (22.6), 304 (M$^+$ – H_2O, 100.0), 286 (98.1). Anal. Calcd for $C_{20}H_{34}O_3$: C, 74.53; H, 10.56. Found: C, 74.12; H, 10.64.

HMPA-Mediated Dehydration of the Diastereomeric Tetracyclic Triols 13 To Provide Tetracyclo-[11.5.2.0^{2,13}.0^{2,16}]eicosa-14,17,19-triene (4). The mixture of dry epimeric triols (**13**, 0.43 g, 1.3 mmol) was dissolved in dry HMPA (25 mL) and transferred into a custom-built one-piece reflux apparatus equipped with a cold finger condenser (dry ice–EtOAc). The mixture was heated (oil bath) at reflux (ca. 230 °C) for 24 h under an atmosphere of argon. The mixture was allowed to cool to 23 °C. Water (100 mL) was added to the apparatus, and the diluted reaction mixture was transferred to a separatory funnel. The apparatus was washed with pentane (3 × 50 mL), and the washes were added to the funnel as the extraction solvent. The aqueous layer was further extracted with fresh pentane (4 × 75 mL). The combined organic layers were washed with water (3 × 50 mL) and brine and dried ($MgSO_4$). Capillary gas chromatography (isothermal at 200 °C) of the pentane extracts indicated the presence of a mixture of three products: the desired triene **4** (t_R = 6.29 min, 30.7%), accompanied by its bridgehead olefinic isomer **14** (t_R = 6.58 min, 7.8%), and a peak at t_R = 12.78 min (61.6%) which represented the ethers **15** and **16**. It was not possible to separate **15** from **16** under a variety of conditions. Removal of solvent (pentane) under reduced pressure provided the crude mixture. The mixture was separated by flash chromatography with hexane to provide a mixture of the desired triene **4** and its olefinic isomer **14** (total yield was 50.0 mg, 14%). Elution with 20% EtOAc in hexane yielded the ethers (**15** and **16**, 140 mg, 38%). When the mixture of **4** and the olefinic isomer **14** was stirred in commercial $CDCl_3$, the mixture was converted into pure **4**.

Ellacene **4** (colorless oil): FTIR (film) 3044, 2924, 2861, 1469, 1441 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37–1.40 (18 H, m), 1.66 (1 H, m), 1.73 (1 H, m), 3.33 (2 H, s), 5.46 (2 H, dd, J = 5.80, 1.69 Hz), 5.50 (2 H, dd, J = 5.70, 2.22 Hz), 5.57 (2 H, s); ^{13}C NMR (125.75 MHz, $CDCl_3$) δ 22.8 (1 C, t), 23.8 (1 C, t), 24.1 (1 C, t), 24.3 (1 C, t), 25.7 (1 C, t), 26.9 (1 C, t), 27.5 (1 C, t), 28.0 (1 C, t), 33.3 (1 C, t), 35.8 (1 C, t), 63.4 (1 C, s), 63.8 (2 C, d), 68.2 (1 C, s), 129.7 (2 C, d), 132.2 (2 C, d), 138.0 (2 C, d); MS (EI, 15 eV) m/z (relative intensity) 268 (M$^+$, 100.0); HRMS calcd for $C_{20}H_{28}$ 268.2191, found 268.2178.

15 and **16**: FTIR (film) 2931, 2861, 1469, 1096, cm^{-1}. The ^{1}H-NMR signals were assigned by 2D COSY experiments, and the ^{13}C NMR of the triquinacene ring system by off-resonance experiments and relative intensities. **15** (15,19-epoxytetracyclo-[11.5.2.0^{2,13}.0^{2,16}]eicos-17-ene): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30–1.60 (20 H, m) 1.68 (2 H, d, J = 11.3 Hz), 1.83 (2 H, d, J = 11.3 Hz), 2.39 (2 H, s), 3.82 (2 H, s), 5.80 (2 H, t, J = 1.4 Hz); ^{13}C NMR (125.75 MHz, $CDCl_3$) δ 45.8 (s), 48.9 (t), 59.2 (s), 59.6 (d), 74.2 (d), 128.6 (d). **16** (17,19-epoxytetracyclo-[11.5.2.0^{2,13}.0^{2,16}]eicos-14-ene): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30–1.60 (21 H, m), 1.82 (1 H, d, J = 12.5 Hz), 1.90 (1 H, d, 13.0 Hz), 2.01 (2 H, dt, J = 10.2, 1.9 Hz), 2.30 (1 H, s), 2.62 (1 H, s), 4.07 (1 H, s), 4.15 (1 H, t, J = 2.7 Hz), 5.36 (1 H, dd, J = 5.7, 2.8 Hz), 5.74 (1 H, d, J = 5.7 Hz); ^{13}C NMR (125.75 MHz, $CDCl_3$) δ 40.6 (t), 45.7 (t), 52.3 (d), 62.1 (s), 64.6 (d), 67.6 (s), 78.7 (d), 82.8 (d), 124.5 (d), 142.4 (d). The unassigned signals (in the mixture) for the 12-membered rings of **15** and **16**: 22.8, 23.8, 24.0, 24.1, 24.2, 24.3, 24.5, 26.1, 26.2, 26.9, 27.4, 27.6, 27.7, 27.8, 28.3, 29.4, 33.2, 34.7. MS (EI, 15 eV) m/z (relative intensity) 286 (M$^+$, 7.5), 268 (30.5), 153 (100.0), 126 (35.0); HRMS calcd for $C_{20}H_{30}O$ 286.2297, found 286.2285.

Synthesis of Tetracyclo[11.5.2.0^{2,13}.0^{2,16}]eicosane-15,17,19-triol Tris(methyl xanthate) (21) To Provide Tetracyclo-[11.5.2.0^{2,13}.0^{2,16}]eicosa-14,17,19-triene (4). A suspension of NaH in mineral oil was added to a preweighed 100-mL two-neck round-bottom flask, and the solid was washed with dry hexane (3 × 25 mL). The hexane was decanted off or removed by pipette under nitrogen. The residual hexane was flushed out with nitrogen. The weight of pure NaH was then determined (104 mg, 4.3 mmol), and CS_2 (8.0 mL) was added via syringe. The mixture of diastereomeric tetracyclic triols represented by **13** (100 mg, 0.31 mmol) was dissolved in dry THF (2 mL) and transferred into the above slurry via a syringe. The mixture which resulted [if a white precipitate (triols) was observed, an additional 1 or 2 mL of dry THF was added] was allowed to stir at 25 °C for 24 h under an atmosphere of nitrogen. Iodomethane (0.3 mL, 0.684 g, 4.8 mmol) was injected into the reaction mixture, and stirring was continued at 25 °C for an additional 24 h. The unreacted NaH was quenched by careful addition of methanol (1 mL), and the solution was diluted with ether (50 mL). The organic mixture was then washed with water (15 mL) and brine and dried ($MgSO_4$). The organic layer was concentrated in vacuo to provide a yellow-colored oil. A diastereomeric mixture of trisxanthates (**21**, 182 mg, 99%) was obtained by flash chromatography with hexane (to remove an initial yellow band) and 30% EtOAc in hexane. **21**: ^{1}H NMR (250 MHz, $CDCl_3$) SCH_3 singlets at δ 2.572, 2.551, 2.535, 2.518, 2.504, 2.497, 2.490, 2.483, 2.472 (these signals indicated that there were at least three epimeric trisxanthates); MS (EI) m/z (relative intensity) 592 (M$^+$, 4.4), 409 (23.5), 269 (100.0). This material was used directly in the next experiment.

Pyrolysis of the Mixture of Trisxanthates 21. A mixture of the trisxanthates (**21**, 118 mg, 0.2 mmol) was heated (neat) to 230 °C for 3 h (TLC indicated the major component was ellacene **4** at this time). Pentane (50 mL) was added to the mixture, and the pentane solution was passed through a short column of silica gel. The mixture was separated by flash chromatography to provide pure ellacene (**4**) (29 mg, 54%). Gas chromatography of the product indicated the presence of only one isomer, ellacene (t_R = 6.67 min, at 200 °C), which was identical with the authentic sample prepared in a previous experiment (TLC/GC/MS).

Pyrolysis of the Mixture of Trisxanthates 21 in Refluxing HMPA. The mixture of dry epimeric trisxanthates (**21**, 182 mg, 0.31 mmol) was dissolved in dry HMPA (20 mL) and transferred into a custom-built one-piece reflux apparatus equipped with a cold finger condenser (dry ice–EtOAc). The mixture was heated (oil bath) at reflux (ca. 230 °C) for 9 h under an atmosphere of argon. The mixture was allowed to cool to 23 °C and diluted with pentane (150 mL). The apparatus was then washed with water (4 × 25 mL). The pentane extracts/washes were combined, dried ($MgSO_4$), and passed through a short wash column of silica gel. Removal of the solvent under reduced pressure at less than 25 °C provided the crude triene. The crude material was purified by flash chromatography with pentane to provide ellacene (**4**) (75 mg) in 91% yield. The properties of this material were identical (GC, ^{1}H NMR, ^{13}C NMR) to those of an authentic sample prepared above.

Tetracyclo[11.5.2.0^{2,13}.0^{2,16}]eicosane-15,17,19-trione (22). The mixture of endo and exo hydroxy diketones (**12a,b**, 0.320 g, 1.0 mmol) was dissolved in dry CH_2Cl_2 (20 mL). To this solution were added Celite powder (0.5 g) and PDC (0.80 g, mmol) under argon. The mixture was allowed to stir at 23 °C for 18 h. The suspension which resulted was filtered and washed with CH_2Cl_2 (4 × 20 mL). The filtrate and washes were combined and concentrated under reduced pressure to provide a brown oil. The crude material was separated by flash chromatography with EtOAc/hexane (36:64) to provide the trione (0.249 g, 96% based on recovered starting material) as a white solid and recovered diketo monol (**12a,b**, 60 mg). **22**: mp 112–112.5 °C; FTIR (KBr) 1770, 1754, 1723 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.20–1.50 (16 H, m), 1.65 (1 H, m), 1.73 (1 H, m), 1.80 (1 H, m), 1.89 (1 H, m), 2.09 (1 H, d, J = 18.07 Hz), 2.26 (1 H, d, J = 16.69 Hz), 2.48 (1 H, dd, J = 18.2, 1.2 Hz),

2.54 (1 H, dd, J = 19.65, 5.36 Hz), 2.66 (1 H, d, J = 16.38 Hz), 2.70 (1 H, dd, J = 19.58, 11.64 Hz), 2.89 (1 H, dd, J = 11.81, 4.76 Hz), 3.15 (1 H, s); ^{13}C NMR (125.75 MHz, $CDCl_3$) δ 22.5 (1 C, t), 22.8 (1 C, t), 23.1 (1 C, t), 23.3 (1 C, t), 25.6 (1 C, t), 25.9 (1 C, t), 26.7 (1 C, t), 27.1 (1 C, t), 34.1 (1 C, t), 34.3 (1 C, t), 40.6 (1 C, t), 47.2 (1 C, s), 50.1 (1 C, t), 50.8 (1 C, t), 53.0 (1 C, d), 57.4 (1 C, s), 69.2 (1 C, d), 205.0 (1 C, s), 206.2 (1 C, s), 215.4 (1 C, s); MS (EI, 15 eV) m/z (relative intensity) 316 (M^+, 69.4), 273 (100.0).

Tetracyclo[11.5.2.0^{2,13}.0^{2,16}]eicosane-15,17,19-trione Tris(tosylhydrazone) (23). The trione (22, 22 mg, 0.07 mmol) and tosylhydrazine (64 mg, 0.35 mmol) were dissolved in anhydrous ethanol (3 mL) which contained 2 drops of concentrated HCl. The mixture which resulted was allowed to heat at reflux. The reaction progress was monitored by TLC (EtOAc/hexane, 3:2) on silica gel. After 4 h, examination of the reaction mixture by TLC indicated the presence of a new component and the absence of starting material. The reaction mixture was allowed to cool to 25 °C, and the ethanol was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (100 mL), washed with water and brine, and dried ($MgSO_4$). The solvent was removed in vacuo to provide a crude solid which was chromatographed (EtOAc/hexane, 2:3) to provide tris(tosylhydrazone) (40 mg, 70%) 23: FTIR (KBr) 1650 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.42 (3 H, s, CH_3), 2.43 (6 H, s, 2 CH_3), 1.20–3.50 (28 H, m), 7.20–8.05 (12 H, m).

Attempted Preparation of 1,2:16,17-Bisdecanododecahedrane (3) via the Photodimerization of Ellacene (4). Ellacene (4, 30 mg, 0.11 mmol) was dissolved in pentane (0.1 mL) and transferred into a quartz tube (2-mm diameter) with a NMR cap. Argon was carefully bubbled into the solution for 5 min, and then it was placed in a photochemical apparatus (low-pressure Hg lamp with λ = 254 nm). The reaction progress was monitored by GC/MS (temperature 200 °C; initial time, 2 min; program rate, 10 °C/min; final temperature 260 °C; final time, 5 min). The GC/MS results suggested no change over a 3-day period [t_R(4) = 7.0 min]. The reaction was worked up, and the NMR (^{1}H, ^{13}C) spectrum of the entire mixture was identical to that of authentic ellacene. The same reaction was repeated with a light source at 214 nm for 24 h; GC/MS of the reaction mixture indicated no change of the starting triene. The starting ellacene was recovered and found to be identical with an authentic sample of ellacene, 4 (^{1}H NMR, TLC).

Attempted Preparation of 1,2:16,17-Bisdecanododecahedrane (3) via High-Pressure Dimerization of 1,10-Decanotriquinacene (4, Ellacene). High pressure was generated in a gasketed diamond anvil cell, and ellacene was directly introduced via a syringe into the gasket hole, which also contained a ruby chip for pressure calibration. After each high-pressure experiment, the contents of the cell were removed with ca. 2–4 μL of benzene and analyzed by GC/MS on a Finnigan 8230 mass spectrometer using on-columm injection of the entire sample. The GC/MS results indicated that pressurization of ellacene to nearly 20 GPa (1 GPa = 10 kbar) and/or exposure to 308-nm ultraviolet radiation at 5 GPa failed to produce any detectable products except the starting ellacene. Only starting ellacene was obtained. Under the same conditions triquinacene underwent [2 + 2] dimerization.[10f]

Acknowledgment. We wish to thank the NSF (CHE 9111392) and donors of the Petroleum Research Fund, administered by the American Chemical Society, for generous financial support of this research. Technical assistance and helpful discussions by Professor Mark Steinmetz of Marquette University (photochemical reactions of ellacene) and Dr. Steven Bertz[10f] of Bell Laboratories (high-pressure experiments with ellacene) are gratefully acknowledged.

Supplementary Material Available: NMR spectra of 4, 15/16, and 22 (5 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

2-Iminooxetane Chemistry. 3. Synthesis of β-Hydroxy Amides[1,2]

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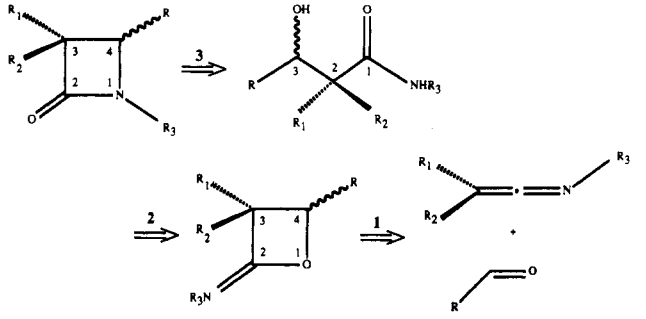
Received October 15, 1991 (Revised Manuscript Received April 13, 1992)

β-Hydroxy amides were synthesized by hydrolysis of the corresponding 2-iminooxetanes, which were prepared in a very simple step by lanthanide-catalyzed cycloaddition of aldehydes to ketene imines. The stereochemical outcome of the hydrolysis, performed under neutral ($DMSO/H_2O$) or acidic (H_2SO_4/H_2O) conditions, depends on the steric and electronic nature of the substituents, which play a crucial role in the ring-opening mechanism. Experiments done with ^{18}O-labeled water showed that two alternatives are possible: one involving ring opening of the oxetane at the C4–O bond, the other involving ring opening at the C2–O bond.

Introduction

We have recently reported the synthesis of 2-iminooxetanes[2] via a heterocycloaddition route. In a preliminary study, it was found[3] that 2-(*N*-*p*-tolylimino)-4-phenyloxetane could be transformed, through medium-controlled ring opening, into the corresponding β-hydroxy amide, β-keto amide, γ-amino alcohol, and β-lactam. This variety of products demonstrates the utility of 2-iminooxetanes for the introduction of functionalized C_2, C_3, and C_4 units into organic compounds. In particular, the possible use of hydrolytic ring opening to obtain β-hydroxy amides

Scheme I



(1) Presented in part at the *Fifth European Symposium on Organic Chemistry*, Jerusalem, Israel, Aug–Sept, 1987.
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0022-3263/92/1957-5128$03.00/0 © 1992 American Chemical Society