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Generation and Reactions of Two New Functionalized Tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene Derivatives

Pelayo Camps,* M. Rosa Muñoz, and Santiago Vázquez*

Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmàcia, Universitat de Barcelona, Av. Diagonal 643, Barcelona, E-08028, Spain

camps@ub.edu; svazquez@ub.edu

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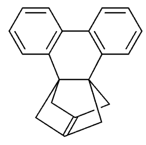

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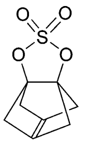

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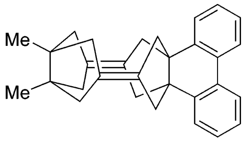

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The generation of the new functionalized and highly pyramidalized alkenes, 3,7-(2,2′-biphenylene)tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene (**20**) and 3,7-sulfonyldioxytricyclo[3.3.0.0^{3,7}]oct-1(5)-ene (**39**), and their trapping with 1,3-diphenylisobenzofuran and 11,12-dimethylene-9,10-dihydro-9,10-ethanoanthracene are described. While both alkenes **20** and **39** failed to give the expected cyclobutane or diene dimers, **20** was reacted with 3,7-dimethyltricyclo[3.3.0.0^{3,7}]oct-1(5)-ene (**1b**) to give the cross-coupled product 4,5-(2,2′)-biphenylene-10,11-dimethylpentacyclo[8.2.1.1^{2,5}.1^{4,7}.1^{8,11}]hexadeca-1,7-diene (**33**). DFT calculations [B3LYP/6-31G(d)] on compound **20** gave important parameters of this pyramidalized alkene, such as the pyramidalization angle (61.7°), the strain energy (72.9 kcal/mol), and the HOMO/LUMO gap (3.79 eV).

The study of the generation, structure, and reactivity of pyramidalized alkenes has been the subject of many publications in the past two decades.[1] Several years ago, we described the generation and several reactions of tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene (**1a**), the consummate member of the series of tricyclo[3.3.n.0^{3,7}]alk-1(5)-enes, and its 3,7-dimethyl derivative (**1b**) (Figure 1).[2]

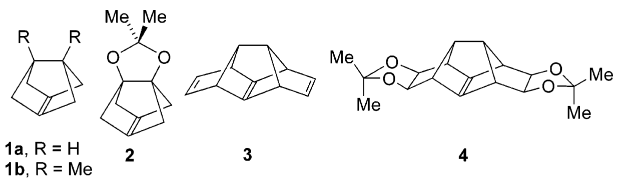

FIGURE 1. Tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene and derivatives.

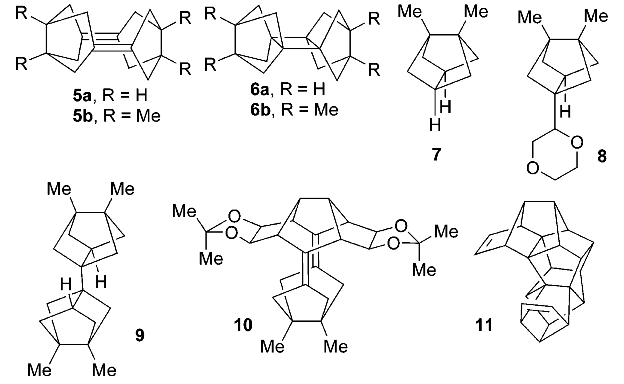

FIGURE 2. Products obtained from highly pyramidalized alkenes of Figure 1.

The pyramidalization angle of alkene **1a** (61.9°) is among the highest so far described.[3] The less pyramidalized members of this series could be observed by IR on an Ar matrix at 10 K,[4] or by ^{13}C NMR spectroscopy,[5] or trapped as Pt complexes,[6] which has not been possible with the more highly pyramidalized alkenes.[7] Pyramidalized alkenes **1a**,**b**, generated from 1,5-diiodotricyclo[3.3.0.0^{3,7}]octane or its 3,7-dimethyl derivative by reaction with *t*-BuLi in THF in the presence of reactive dienes, provided the corresponding Diels−Alder adducts in good yields. When alkenes **1a**,**b** were generated from the above diiodides by reaction with molten sodium in boiling dioxane in the absence of a trapping agent, they gave diene dimers (**5a**,**b**) via cyclobutane products (**6a**,**b**) (Figure 2). Moreover, the formation of the reduction product **7**, the addition product of **1b** to 1,4-dioxane (**8**), and dihydrodimer **9** was observed. The above reactions of alkenes **1a**,**b** reflect their diradical character, which was calculated to be around 11% using the TCSCF calculations (Figure 2).[8] Later on, in connection with the preparation of polyquinanes, we generated and reacted functionalized pyramidalized alkenes, such as **2**−**4** (Figure 1), and carried out for the first time the cross-coupling of two different pyramidalized alkenes, obtaining cross-coupled products such as **10** (Figure 2).[9] Worthy of note, when pyramidalized alkene **3** was generated in the

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* Corresponding author. Phone: +34 934024536. Fax: 34 934035941.

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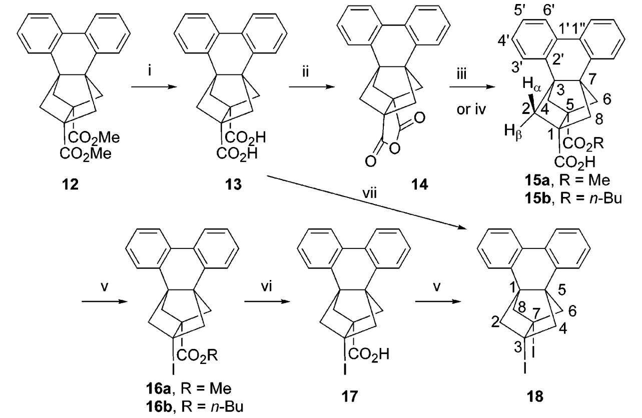
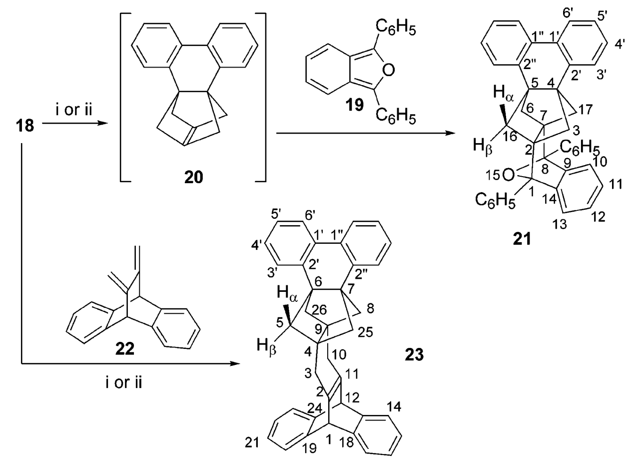
SCHEME 1. Synthesis of Diiodide 18[a]



[a] Key: (i) KOH/MeOH, then 10% HCl, 98%; (ii) Ac_2O, Δ, quant yield; (iii) NaOMe, MeOH, Δ, then 10% HCl, quant yield; (iv) NaOBu-*n*, *n*-BuOH, Δ, then 10% HCl, 36%; (v) IBDA, I_2, benzene, *hν*, 59.5% for **16a**, 81% for **16b**, 87% for **18**; (vi) KOH/MeOH, then 10% HCl, 92% from **16a**, 93% from **16b**; (vii) IBDA, I_2, CH_3CN, *hν*, 61%.

SCHEME 2. Generation and Chemical Trapping of the Highly Pyramidalized Alkene 20[a]



[a] Key: (i) *t*-BuLi, THF, −78 °C, 68% of **21**, 75% of **23**; (ii) ~0.45% Na(Hg), 1,4-dioxane, rt, 68% of **21**, 73% of **23**.

absence of a trapping agent, dimer **11** was isolated in 24% yield (Figure 2).[10]

In this paper, we describe the generation and particular reactivity of two new functionalized tricyclo[3.3.0.$0^{3,7}$]oct-1(5)-ene derivatives, 3,7-(2,2′-biphenylene)tricyclo[3.3.0.$0^{3,7}$]oct-1(5)-ene (**20**) and 3,7-sulfonyldioxytricyclo[3.3.0.$0^{3,7}$]oct-1(5)-ene (**39**), which required an improvement of the usual conditions of bis-iododecarboxylation utilized for the preparation of the corresponding *vic*-diiodo precursors (**18** and **38**, respectively).

Initial attempts to prepare diiodide **18** from the known[11] diester **12** were not too promising (Scheme 1). Bis-iododecarboxylation of diacid **13**, obtained in good yield by saponification of diester **12**, using iodosobenzene diacetate (IBDA) under the standard conditions[12a,b] (benzene or dichloromethane solution) gave the expected diiodide **18** in low yield (20% in benzene and 33% in CH_2Cl_2), most of the starting diacid being recovered unchanged. This result was ascribed to the low solubility of diacid **13** in both solvents. As an alternative, a stepwise iododecarboxylation was planned. To this end, diacid **13** was quantitatively transformed into anhydride **14** by reaction with acetic anhydride, which on reaction with sodium methoxide in anhydrous methanol gave quantitatively methyl hemiester **15a**. Iododecarboxylation of **15a** in benzene solution using the standard conditions provided iodo ester **16a** in 59.5% yield. When iodo acid **17**, obtained in 92% yield by saponification of **16a**, was submitted to iododecarboxylation under the conditions used to prepare iodo ester **16a**, diiodo derivative **18** was obtained in 87% yield. With the aim of improving the yield of the first iododecarboxylation step we prepare butyl hemiester **15b**, which was expected to be more soluble under the reaction conditions.

However, although the yield of iododecarboxylation of **15b** was improved to 81% and its saponification to **16b** took place in 93% yield, the reaction of anhydride **14** with sodium butoxide in anhydrous butanol always gave a low yield (36%) of hemiester **15b**. Unsatisfied with this lengthy and medium yield synthesis of diiodide **18**, we undertook a screening of the bis-iododecarboxylation of diacid **13** using different solvents. From this study, acetonitrile was shown to be the solvent of choice. Moreover, the excess of IBDA could be greatly reduced from 120 to 35%. Under the optimized conditions (see the Supporting Information), diiodide **18** was obtained from diacid **13** in 61% yield.

We had no problems in trapping the highly pyramidalized alkene **20**, generated by reaction of **18** with *t*-BuLi in THF solution at −78 °C, with reactive dienes, such as 1,3-diphenylisobenzofuran (**19**) or 11,12-dimethylene-9,10-dihydro-9,10-ethanoanthracene (**22**), isolating the corresponding Diels−Alder adducts **21** and **23**, respectively, in good yields (Scheme 2). Alternatively, these adducts were obtained in good yields when the pyramidalized alkene **20** was generated from diiodide **18** by reaction with sodium amalgam (~0.45%).

However, contrary to our expectations, reaction of diiodide **18** with molten sodium in boiling dioxane or with *t*-BuLi in anhydrous THF did not give any of the expected diene or cyclobutane dimers (**24** or **25**) (Scheme 3). Sublimation of the reaction mixture obtained from **18** and molten sodium in boiling dioxane allowed us to isolate the reduction product **26** in only 10% yield. GC/MS analysis of the reaction mixture from another run showed the presence of **26** (87% relative area) and a minor component, whose MS spectrum suggests it to be **27**, an addition product of the pyramidalized alkene **18** and the solvent. A similar compound (**8**, Figure 2), derived from a related pyramidalized alkene (**1b**, Figure 1), has been previously isolated and fully characterized.[9a] The low isolated yield of **26** compared with its high relative area by GC/MS is indicative of the formation of non volatile compounds. MS (MALDI-TOF) analysis of a fraction of

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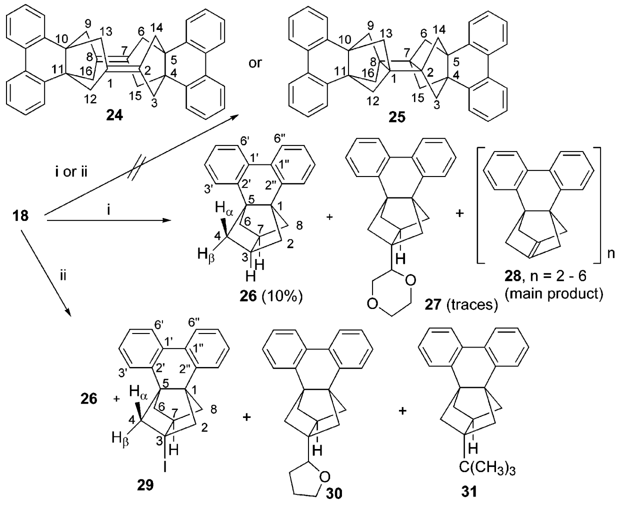
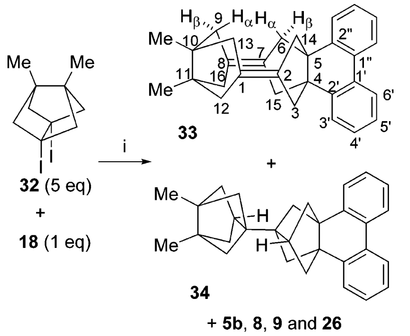
SCHEME 3. Attempts to Dimerize the Highly Pyramidalized Alkene 20[a]



[a] Key: (i) Na, 1,4-dioxane, Δ; (ii) *t*-BuLi, THF, −78 °C. Relative areas by GC/MS of the crude product: **26**, 30%; **29**, 7%; **30**, 14%; **31**, 31%.

SCHEME 4. Cross-Coupling of the Highly Pyramidalized Alkenes 1b and 20[a]



[a] Key: (i) Na, 1,4-dioxane, Δ. Relative area by GC/MS of the crude product: **33**, 23.6% (17% isolated yield); **5b**, 39%; **8**, 6.7%; **9**, 20.2%; **26**, 7.1%; **34**, 3.3%.

the above reaction mixture (the diethyl ether soluble part, 70% of the total amount) showed the presence of peak groups around $m/z = 256n + 1$, being $2 \leq n \leq 6$, suggesting the presence of oligomers (**28**) of the pyramidalized alkene **20**. In a similar way, reaction of diiodide **18** with *t*-BuLi in anhydrous THF at −78 °C gave a complex mixture which when analyzed by GC/MS showed the presence of the reduction product **26** (30% relative area), monoiodo derivative **29** (7% relative area), a compound which could be isolated and fully characterized in very low yield, two products which could not be isolated, whose MS spectra suggest them to be **30** (14% relative area) and **31** (31% relative area), derived from the reaction of pyramidalized alkene **20** and the solvent or *t*-BuLi, respectively. The formation of compound **30** may be explained on the basis of the diradical character of pyramidalized alkenes,[8] by hydrogen abstraction from THF followed by coupling of the thus formed radicals. The formation of **31** may be easily explained by addition of *tert*-butyllithium to **20** followed by protonation during the work up. Products similar to **30** and **31**, derived from different pyramidalized alkenes, have been previously observed.[3b−d,9a,b,13,14]

Worthy of note, when a mixture of diiodides **18** (1 equiv) and 1,5-diiodo-3,7-dimethyl tricyclo[3.3.0.0^{3,7}]-octane (**32**) (5 equiv) was reacted with molten sodium in boiling dioxane, the cross diene product **33** could be isolated in 17% yield (Scheme 4). GC/MS analysis of the crude reaction mixture showed in order of elution the following compounds (relative areas), most of them previously characterized: **8** (6.7%),[9a] **9** (20.2%),[9a] **5b** (39.0%),[2a] **26** (7.1%), a product whose molecular ion suggests it to be **34** (3.3%), and **33** (23.6%).

Since the biphenylene substituent of **20** seems to be compatible with the pyramidalized alkene, we do not understand why this alkene, generated by reaction of a 1,2-diiodo precursor (**18**) with molten sodium, does not dimerize to a diene or cyclobutane product, as it has been always the case in related pyramidalized alkenes. This is especially so, when its generation on reaction with *t*-BuLi, sodium amalgam or molten sodium is clear from the isolation of Diels−Alder adducts and even of a cross-coupling product with another pyramidalized alkene.

To better understand this behavior, we have performed density functional theory (DFT) calculations using the B3LYP/6-31G(d) method that is very successful in modeling pyramidalized alkenes.[8,15] We used this method, as implemented in Gaussian 98, to calculate the structure of **20**.[16] While the values for the pyramidalization angle ($\Phi = 61.7°$), the carbon−carbon double bond length (1.381 Å), the heat of hydrogenation of the pyramidalized double bond (−96.8 kcal/mol), the olefin strain energy (72.9 kcal/mol) and the ^{13}C NMR chemical shift of the olefinic carbon atom (δ = 191.4 ppm) of **20** are very similar to the previously calculated for **1a** and **1b**,[8,17] interestingly, the HOMO/LUMO energy gap on alkene **20** is lower ($\Delta E_{\mathrm{HOMO-LUMO}}$: 3.79 eV) than in the related alkenes **1a** ($\Delta E_{\mathrm{HOMO-LUMO}}$: 4.17 eV) and **1b** ($\Delta E_{\mathrm{HOMO-LUMO}}$: 4.21 eV). This fact could facilitate the transfer of one electron from molten sodium to the pyramidalized alkene to give a species (radical anion) unable to give the expected diene dimer, although able to give the reduction product **26** or to polymerize. In the same way, Borden has also suggested that *t*-BuLi may transfer one electron into the very low-lying LUMO of highly pyramidalized alkenes leading to reduction products.[18]

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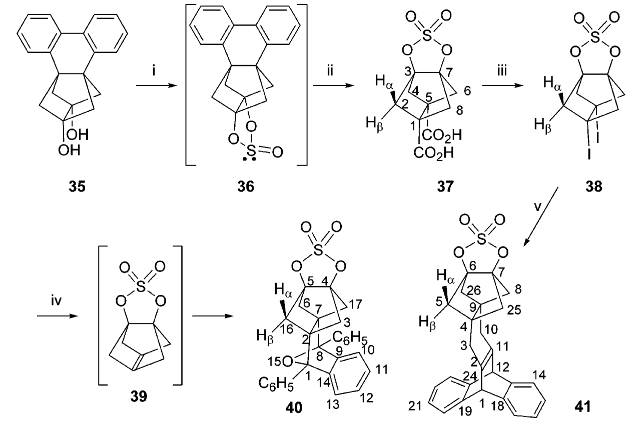
SCHEME 5. Generation and Trapping of the Highly Pyramidalized Alkene 39[a]



[a] Key: (i) Cl_2SO/Et_3N, CH_2Cl_2; (ii) $RuCl_3{\cdot}H_2O$, NaClO, $CH_3CN/CH_2Cl_2/H_2O$, 38% from **35**; (iii) IBDA, I_2, *hν*, CH_3CN, 34%; (iv) **19**, *t*-BuLi, THF, −78 °C, 29%; (v) **22**, *t*-BuLi, THF, −78 °C, 16%.

In connection with the generation of another functionalized tricyclo[3.3.0.$0^{3,7}$]oct-1(5)-ene derivative, the known pinacol **35**[19] was reacted with thionyl chloride and the sulfinyldioxy product (**36**) thus obtained was directly oxidized with ruthenium tetraoxide, generated from a catalytic amount of $RuCl_3{\cdot}H_2O$ and an excess of bleach in a biphasic system containing acetonitrile, CH_2Cl_2 and water, to give diacid **37** in 38% overall yield (Scheme 5). As can be seen, under these conditions not only the sulfinyldioxy group of **36** is oxidized to sulfonyldioxy but, as previously described in related cases,[9c,11] the biphenylene substituent is converted into two carboxyl groups. Bisiododecarboxylation of diacid **37** using the standard conditions in benzene as solvent gave **38** in only 8% yield.[12] When this reaction was carried out in CH_2Cl_2, **38** was obtained in 5% yield. The low yield in these cases is most probably due to the insolubility of diacid **37** in the used solvent. Fortunately, the improved procedure, working in acetonitrile, allowed us to obtain **38** in 34% yield.

Not unexpectedly, the sulfonyldioxy group was not compatible with molten sodium or sodium amalgam, but it partially survived reaction with *t*-BuLi in the presence of dienes **19** and **22** which allowed us to obtain the corresponding Diels−Alder adducts derived from the highly pyramidalized and funtionalized alkene **39** in low yields [**40** (29%) and **41** (16%), respectively]. Reaction of **38** with (a) molten sodium in boiling 1,4-dioxane, (b) 2% sodium amalgam in the same solvent, or (c) *t*-BuLi in THF led to very complex mixtures in which dimers derived from **39**, analogues to **5** or **6**, could not be detected.

In conclusion, we have been able to generate two new highly pyramidalized alkenes, which were trapped as Diels−Alder adducts. Although the sulfonyldioxy substituent of diiodide **38** was not compatible with several conditions used to generate the highly pyramidalized alkenes (molten sodium or sodium amalgam), pyramidalized alkene **39** could be obtained by reaction of diiodide **38** with *t*-BuLi and trapped with reactive dienes. Contrary to our expectations, pyramidalized alkene **20**, generated by reaction of diiodide **18** with molten sodium did not give any diene or cyclobutane dimer, although it could be cross coupled with another pyramidalized alkene to give a cross diene product (**33**). Work is in progress to use the dimerization of functionalized alkenes for the preparation of more complex cage compounds.

Experimental Section

4,5-(2,2′)-Biphenylene-10,11-dimethylpentacyclo[8.2.1.$1^{2,5}$.$1^{4,7}$.$1^{8,11}$]hexadeca-1,7-diene (33). A mixture of diiodide **18** (150 mg, 0.29 mmol) and 3,7-dimethyl-1,5-diiodotricyclo[3.3.0.$0^{3,7}$]octane (**32**, 560 mg, 1.44 mmol) was added at once under argon to molten sodium (320 mg, 14 mmol) in boiling 1,4-dioxane (3 mL), and the mixture was heated under reflux for 3.5 h. The reaction mixture was allowed to cool to room temperature and filtered through Celite, the solid being washed with diethyl ether (3 × 7 mL). The sodium on the Celite was destroyed with a small amount of water, and it was washed with CH_2Cl_2 (3 × 3 mL). The combined filtrate and washings were concentrated in vacuo to give a light yellow residue (290 mg), which on GC/MS analysis (conditions A) showed the presence of the known compounds: **8** ($M^{\bullet+}$ = 222, 6.7% relative area, rt 15.05 min),[9a] **9** ($M^{\bullet+}$ = 270, 20.2% relative area, rt 17.51 min),[9a] **5b** ($M^{\bullet+}$ = 268, 39.0% relative area, rt 20.46 min),[2a] **26** ($M^{\bullet+}$ = 258, 7.1% relative area, rt 24.03 min), a product that could be 3,7-(2″,2‴-biphenylene)-3′,7′-dimethylbi(tricyclo[3.3.0.$0^{3,7}$]oct-1-yl) (**34**) ($M^{\bullet+}$ = 392, 3.3% relative area, rt 31.56 min), and **33** ($M^{\bullet+}$ = 290, 23.6% relative area, rt 34.32). The above residue was submitted to column chromatography [flash silica gel (9 g), hexane/EtOAc mixtures]. On elution with hexane, compounds **5b** (50 mg), **26** (30 mg), and **33** (20 mg, 17% yield) were successively eluted. The analytical sample of **33** was obtained as a white solid by crystallization from CH_2Cl_2/*n*-pentane in the ratio of 1:1: mp 202−204 °C; IR (KBr) no significant bands; ^1H NMR δ 1.16 [s, 6H, 10(11)-CH_3], 2.12 [broad d, J = 13.0 Hz, 4H, 9(12,13,16)-H_α], 2.44 [broad d, J = 13.0 Hz, 4H, 3(6,14,15)-H_α], 2.67 [d, J = 13.0 Hz, 4H, 9(12,13,16)-H_β], 3.16 [d, J = 13.0 Hz, 4H, 3(6,14,15)-H_β], 7.24 [dt, J = 1.5 Hz, J' = 7.5 Hz, 2H, 4′(4″)-H], 7.29 [dt, J = 1.5 Hz, J' = 7.5 Hz, 2H, 5′(5″)-H], 7.36 [dd, J = 1.5 Hz, J' = 7.5 Hz, 2H, 3′(3″)-H], 7.97 [dd, J = 1.5 Hz, J' = 7.5 Hz, 2H, 6′(6″)-H]; ^{13}C NMR δ 24.9 [CH_3, 10(11)-CH_3], 42.2 [C, C10(11)], 45.3 [C, C4(5)], 48.7 [CH_2, C9(12,13,16)], 50.7 [CH_2, C3(6,14,15)], 122.4 [CH, C6′(6″)], 126.1 [CH, C4′(4″)], 127.3 [C, C2(7)], 127.9 [CH, C3′(3″)], 128.2 [CH, C5′(5″)] 128.5 [C, C1(8)], 132.7 [C, C1′(1″)], 144.6 [C, C2′(2″)]; MS (EI) *m/z* 391 (31), 390 ($M^{\bullet+}$, 100), 321 (54), 309 (36), 308 (37), 256 (47), 241 (32), 239 (25), 217 (23), 216 (57), 215 (62), 159 (22), 135 (40), 119 (26), 117 (23), 107 (20), 105 (32), 91 (50), 79 (29), 77 (24), 55 (21). MS (EI) spectrum of **34** *m/z* 392 ($M^{\bullet+}$, 5), 350 [$(M - C_3H_6)^{\bullet+}$, 21] 256 (13), 217 (31), 216 (100), 215 (29), 207 (38), 135 (31), 95 (24), 93 (25), 91 (23), 73 (34). Anal. Calcd for $C_{30}H_{30}{\cdot}0.4\ H_2O$ (397.77): C, 90.59; H, 7.80. Found: C, 90.60; H, 7.70.

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Supporting Information Available: Experimental procedures and characterization data for the rest of the new compounds, including copies of the NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) The calculated values for **1a** and **1b** are: pyramidalization angle, Φ = 61.9° (**1a**), 61.7° (**1b**); carbon−carbon double bond length, 1.380 Å (**1a** and **1b**); heat of hydrogenation of the double bond, −99.1 kcal/mol (**1a**), −96.5 kcal/mol (**1b**); olefin strain energy, 74.7 kcal/mol (**1a**), 74.2 kcal/mol (**1b**); ^{13}C NMR chemical shift of the olefinic carbon atom, δ = 201.2 ppm (**1a**), 192.5 (**1b**). See also: Vázquez, S. *J. Chem. Soc., Perkin Trans. 2* **2002**, 2100−2103.

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