Unmasking the 6,7,5-Tricarbocyclic Frame of [5 + 2]/[4 + 2] Pyrone−Alkene Cycloadducts

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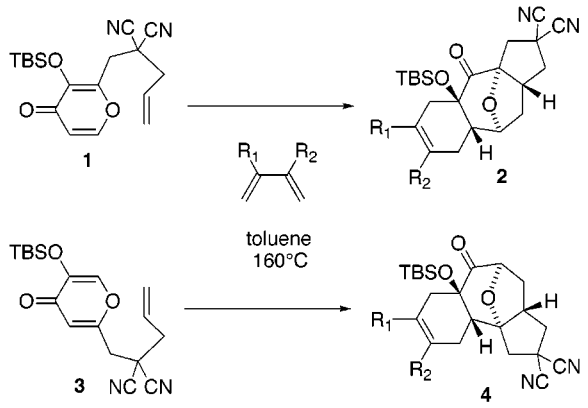
Opening of the bridging ether of 8-oxabicyclo[3.2.1]oct-6-ene systems 1,7-fused to a five-membered carbocycle that bears a double bond conjugated to that of the oxabicycle can be induced at low temperaure by the addition of an organolithium reagent. If this double bond is unsubstituted, the opening occurs via an anti-1,6-addition pathway, and if substituted it takes place by means of a more classical syn S_N2' addition.

Introduction

The enormous synthetic accomplishments of recent decades could certainly generate the impression that organic synthesis has reached such a degree of maturity that any compound, even the most complex, can be synthesized using the currently available methods. This is probably not far from the truth; however, much remains to be learned before such compounds can be assembled in a truly practical and efficient way.[1] One of the best ways to address this objective is to develop processes that afford a maximum increase in target-relevant molecular complexity at a minimal economical and ecological cost.[2] Among the transformations that best fit with this profile are cycloaddition reactions,[3] which create new rings by simple addition of two or more molecules, and tandem processes,[4] which integrate multistep processes in a single operation. We have recently reported the successful coupling of [5 + 2] and [4 + 2] cycloadditions in a one-pot process to obtain relatively complex, fused 6,7,5-tricarbocyclic systems from simple starting materials (Scheme 1).[5] The transformation occurs with complete atom economy[6] and creates four new carbon−carbon bonds and five new stereocenters.

Scheme 1



Since the tricarbocyclic core of the resulting adducts bears a marked similarity to the basic polycyclic skeleton of dolastane and spheroane diterpenes,[7] this tandem cycloaddition methodology might afford an immediate entry to these natural products provided the oxa-bridge on the seven-membered ring could be removed efficiently. Unfortunately, initial attempts to break this bridge in compounds **2** and **4** failed.[5] The precedents on reductive or nucleophilic opening of the bridging ether in simple 8-oxabicyclo[3.2.1]oct-6-ene systems[8] prompted us to investigate whether the introduction of a double bond in the tetrahydrofuran moiety of the central oxabicycle of our adducts might be a convenient solution to the problem. Herein we report the results of these studies, which led to the discovery of unprecedented bridge-opening pathways.

Results and Discussion

The required double-bond equipped adducts (**5**) should be easily obtainable using our thermal tandem

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(6) For a discussion on atom economy, see: (a) Trost, B. M. *Science* **1991**, *254*, 1471. (b) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259.

(7) For a detailed account of these natural products, see: Connolly, J. D.; Hill, R. A. *Dictionary of Terpenoids*; Chapman & Hall: New York, 1991; Vol. 2.

(8) An ample review of techniques for opening the oxa-bridge of oxabicyclic systems has recently appeared: (a) Chiu, P.; Lautens, M. In *Topics in Current Chemistry*; Springer-Verlag: Berlin, 1997; Vol. 190, p 1. See also: (b) Lautens, M. *Synlett* **1993**, 177. (c) Woo, S.; Keay, B. *Synthesis* **1996**, 669.

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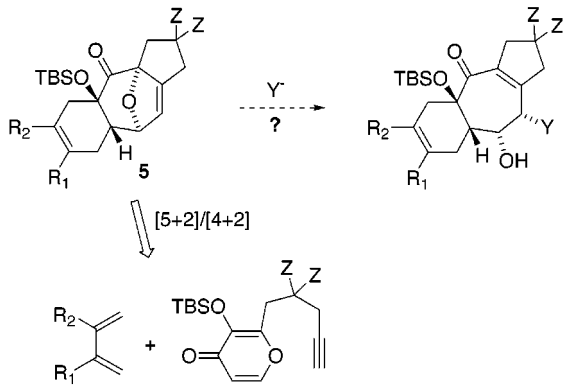
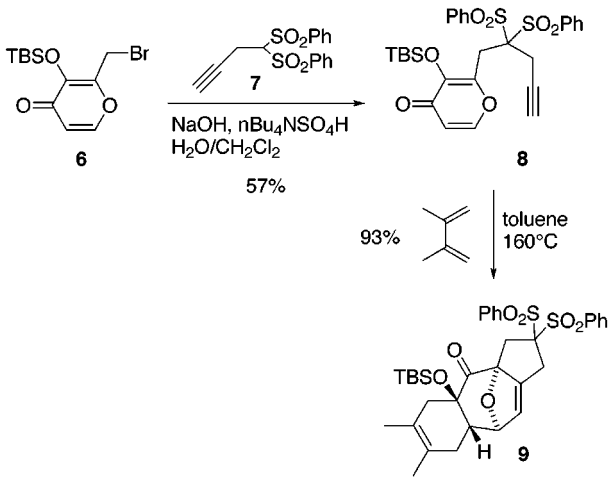
Scheme 2



Scheme 3



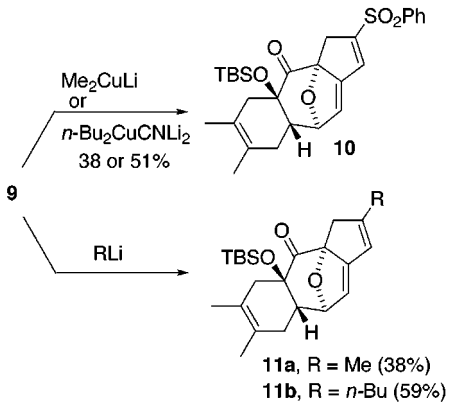
[5 + 2]/[4 + 2] cycloaddition methodology with an alkyne instead of an alkene as two-carbon partner in the first intramolecular cycloaddition (Scheme 2). Although it seemed reasonable to think that the hydro- or carbometalation methods that successfully open the bridging ether of oxabicyclic[3.2.1]oct-6-enes would also open compounds such as **5**, at the outset of this research it was not clear how the fused five-membered ring might influence the process.[9]

The tetracyclic adduct **9**, which bears a *gem*-disulfonyl group on the five-membered carbocycle, was readily assembled in just two steps from the known bromopyrone **6** (Scheme 3).[10] Reaction of **6** with the bis-sulfonyl butyne **7** under basic phase-transfer conditions gave the required cycloaddition precursor **8** in moderate yield (57%). When a solution of **8** in toluene was heated at 160 °C for 12 h in a sealed tube, in the presence of 5 equiv of 2,3-dimethylbutadiene, the expected tetracyclic compound **9** was obtained in 93% yield. Initial efforts to break the oxa-bridge of **9** were carried out using DIBAL-H for attempted reductive S_N2' ring opening.[8] Unfortunately, heating compound **9** with an excess of DIBAL-H in refluxing hexanes gave a relatively complex mixture of products, and NMR analysis of the reaction crude showed that in none of them was the ether bridge broken. Curiously, when **9** was treated with cuprates such as

(9) The presence of a third substituent at the double bond in 7-oxabicyclic [2.2.1] systems seems to impair the S_N2'-reactivity; see: Lautens, M.; Fillion, E. *J. Org. Chem.* **1998**, *63*, 647.

(10) Rumbo, A.; Castedo, L.; Mouriño, A.; Mascareñas, J. L. *J. Org. Chem.* **1993**, *58*, 5585.

Scheme 4



Me_2CuLi (toluene, rt) or *n*-$Bu_2CuCNLi_2$ (THF/Et_2O, 0 °C), the major product isolated was the vinyl sulfone **10** (38% and 51%, respectively, Scheme 4), doubtless the result of a seemingly very easy phenyl sulfone elimination reaction.[11] On the other hand, treatment of **9** with 2.1 equiv of MeLi in THF at −78 °C, for 15 min, gave as major product the methylated derivative **11a**. We observed that this reaction proceeds via the intermediate **10**, suggesting the occurrence of a barely precedented geminal carbon−carbon coupling between the organolithium and this sulfone.[12] The same type of reaction occurred upon treatment of **9** with *n*-BuLi (Et_2O, −78 °C), the major product in this case being the *n*-butyl derivative **11b**.

The oxa bridge also resisted the action of oxophilic reagents used with a view to weakening the carbon−oxygen bond and so facilitating the operation of alternative carbocationic opening mechanisms. Hence, treatment of **9** with TMSI in CH_3CN or with $BF_3{\cdot}Et_2O$ in the presence of ethanedithiol or NaI led to complete recovery of the starting material, and reaction with BBr_3 gave a relatively complex mixture of secondary products. Since the presence of the *gem*-disulfone group seemed to introduce an unwanted side reactivity in the system which does not allow us to really evaluate the feasibility of inducing the desired nucleophilic type of oxa-bridge opening, we attempted to remove the sulfonyl groups by treatment of **9** with Na(Hg) (6% in MeOH/THF, rt, Scheme 5).[13] The major products of this reaction were the desulfonated derivatives **12** and **13** that could not be separated by silica gel flash chromatography (**12**/**13** 1.7:1 by ^{1}H NMR, 41% overall yield). Remarkably, treatment of this mixture with *t*-BuLi in Et_2O at −78 °C led to the instantaneous formation of the unbridged product **14** (87% yield from **12**), a compound that arises from an anti 1,6-addition of the organolithium reagent to the diene **12**, with compound **13** being almost completely recovered.[14] The stereochemistry of the tricycle **14** was inferred from the ^{1}H NMR coupling pattern for H-2, and particu-

(11) Simpkins, N. S. *Sulphones in Organic Synthesis*; Pergamon Press: Oxford, 1993; Chapter 7, p 262.

(12) There are precedents of the geminal alkylative desulfonation of vinyl sulfones using Grignard reagents and nickel or iron catalysts. See: Simpkins, N. S. *Sulphones in Organic Synthesis*; Pergamon Press: Oxford, 1993; Chapter 7, p 351.

(13) For a recent review on desulfonation reactions, see: Nájera, C.; Yus, M. *Tetrahedron* **1999**, *55*, 10547.

(14) It has been shown that generating an anion in an alkyl group attached to the double bond of 7-oxanorbornenes brings about ether bridge cleavage: (a) Arjona, O.; Conde, S.; Plumet, J. Viso, A. *Tetrahedron Lett.* **1995**, *36*, 6157. (b) Arjona, O.; Leon, M. L.; Plumet, J. *J. Org. Chem.* **1999**, *64*, 272.

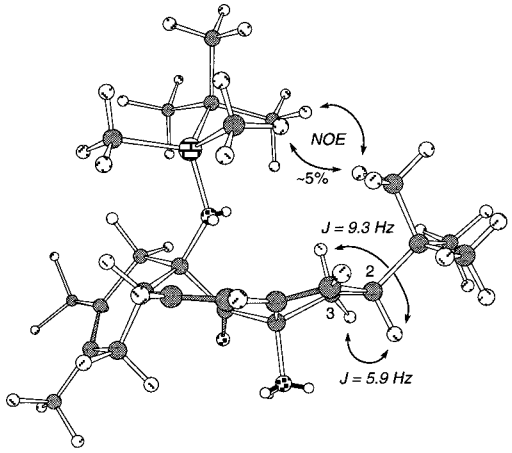
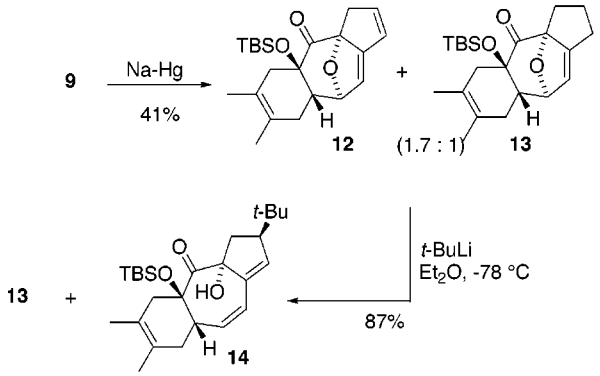


Figure 1. MM-optimized conformation of **14**.[15]

Scheme 5



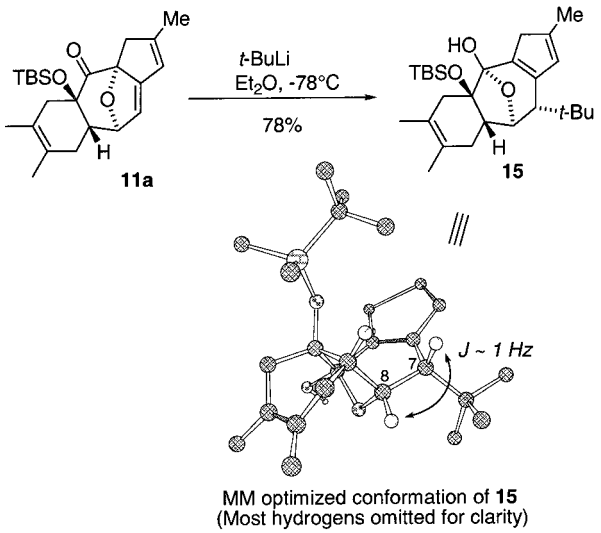
larly from the observation of NOE between the *tert*-butyl at C-2 and the methyl and *tert*-butyl groups of the TBS (Figure 1).[15]

Having discovered that the presence of a conjugated double bond in the ring adjacent to the central oxabicyclic-[3.2.1]octene unit of our tetracyclic adducts provides an excellent site for triggering the bridge-opening, we were curious about the reactivity of the methyl-substituted analogue **11**, for which the 1,6-pathway might be impaired. Quite surprisingly, diene **11a** reacted very rapidly with *t*-BuLi (Et_2O, −78 °C) to give the S_N2' ring-opened product arising from a syn attack of the organolithium to the less substituted position of the double bond (79% yield), with the resulting keto-alcohol existing almost completely in a closed hemiketal form (**15**, Scheme 6). Therefore it seems that the presence of a carbanion-stabilizing feature such as a conjugated double bond in the five-membered ring fused to the oxabicyclic alkene allows a standard S_N2' ring-opening process to occur, provided the alternative 1,6-addition mechanism is impeded. The stereochemistry of the tricycle **15** was easily deduced from the observation in the ^1H NMR spectrum of a almost negligible coupling (approx 1 Hz) between H-7 and H-8.

Conclusion

In summary, two unprecedented ways of opening the bridging ether of 8-oxabicyclo[3.2.1]oct-6-ene systems that are 1,7-fused to a five-membered carbocycle have been discovered. In both cases the success of the reaction depends on the five-membered ring possesing a double bond conjugated to that of the oxabicycle. This double bond either mediates a 1,6-addition reaction or stabilizes the carbanion resulting from carbometalation of the oxabicyclic alkene. As a result of these discoveries we can state that the way for applying the tandem [5 + 2]/[4 + 2] cycloaddition methodology to the synthesis of tricarbocyclic diterpenes is unblocked.

Scheme 6



MM optimized conformation of **15**
(Most hydrogens omitted for clarity)

Experimental Section

General Procedures. See ref 2.

4,4-Bis(phenylsulfonyl)-1-butyne (7). To a solution of bis-(phenylsulfonyl)methane (3.5 g, 11.8 mmol) in DMF (20 mL) was slowly added a suspension of NaH (520 mg, 13 mmol, 60% mineral oil,). After stirring for 5 min at room temperature and 10 min at 70 °C, propargyl bromide (1.4 mL, 12.5 mmol, 80wt % in toluene) was slowly added, and the resulting mixture was stirred at 70 °C for 5 min. The DMF was removed under vacuum and the residue partitioned between Et_2O and H_2O. The organic layer was washed with aqueous HCl (5%), dried, filtered, and concentrated. The residue was purified by silica gel flash chromatography (15−40% EtOAc/hexane) to give 3.615 g of **7** as a white solid [91%, R_f 0.68 (50% EtOAc/hexane), mp 96 °C]. ^1H NMR δ 7.99−7.54 (10H, m), 4.61 (1H, t, J = 6 Hz), 3.11 (2H, dd, J = 6 and 2.5 Hz), 1.92 (1H, br s).^{13}C NMR δ 138.0 (C), 135.3 (CH), 130.2 (CH), 129.6 (CH), 82.3 (CH), 77.2 (CH), 72.7 (C), 17.0 (CH_2).

3-(*tert*-Butyldimethylsilyloxy)-2-[2,2-bis(phenylsulfonyl)-4-pentynyl]-4*H*-4-pyranone (8). Bromopyrone **6**[10] (1 g, 3.13 mmol) and disulfone **7** (1.05 g, 3.14 mmol) were added to a suspension of NaOH (626 mg, 15.6 mmol) and n-Bu_4NHSO_4 (212 mg, 0.626 mmol) in CH_2Cl_2/H_2O (30 mL, 2:1). The mixture was vigorously stirred at room temperature for 12 h, poured into a saturated aqueous solution of NH_4Cl, and extracted with CH_2Cl_2. The organic extracts were dried, filtered, and concentrated to give a residue that was purified by silica gel flash chromatography (25−40% EtOAc/hexane), affording 1.02 g of compound **8** as a white solid [57%, R_f 0.44 (50% EtOAc/hexane), mp 175−177 °C]. ^1H NMR δ 8.01 (4H, brd, J = 7.3 Hz), 7.70−7.41 (m, 7H), 6.26 (1H, d, J = 5.5 Hz), 3.85 (2H, s), 3.48 (2H, d, J = 2.6 Hz), 2.06 (1H, t, J = 2.6 Hz), 0.90 (9H, s), 0.27 (6H, s); ^{13}C NMR δ 174.1 (C), 153.2 (CH), 150.2 (C), 144.5 (C), 136.8 (C), 135.4 (CH), 131.9 (CH), 129.6 (CH), 129.3 (CH), 116.0 (CH), 88.8 (C), 76.6 (CH), 75.0 (C), 27.3 (CH_2), 26.4 (CH_3), 22.8 (CH_2), 19.2 (C), −2.9 (CH_3).

(1*R,3*R**,8*S**,9*S**)-3-(*tert*-Butyldimethylsilyloxy)-5,6-dimethyl-13,13-bis(phenylsulfonyl)-15-oxatetracyclo-[7.5.1.0^{1,11}.0^{3,8}]pentadeca-5,10-dien-2-one (9).** A solution of

(15) MM minimization was carried out using MM2 as implemented in CS Chem 3D Pro (Cambridge Soft Corporation).

compound **8** (425 mg, 0.743 mmol) and 2,3-dimethylbutadiene (0.41 mL, 3.7 mmol) in toluene (25 mL) was heated at 160 °C in a sealed tube for 12 h. The solvent was evaporated, and the crude was purified by flash chromatography on silica gel (5−10% EtOAc/hexanes) to afford 452 mg of compound **9** as a white solid [93%, R_f 0.45 (25% EtOAc/hexanes), mp 206 °C]. ^{1}H NMR δ 8.11−7.97 (4H, m), 7.73−7.53 (6H, m), 5.80 (1H, d, J = 1.7 Hz), 4.47 (1H, d, J = 2.2 Hz), 3.42 (1H, d, J = 15.7 Hz), 3.11 (2H, s), 2.66 (1H, d, J = 15.7 Hz), 2.37 (1H, d, J = 16 Hz), 2.01 (1H, m), 1.95 (3H, m), 1.67 (3H, s), 1.63 (3H, s), 0.73 (9H, s), 0.06 (3H, s), −0.15 (3H, s). ^{13}C NMR δ 200.7 (C), 144.9 (C), 136.5 (C), 136.1 (C), 134.8 (CH), 134.6 (CH), 131.6 (CH), 131.4 (CH), 129.0 (CH), 128.9 (C), 128.6 (CH), 125.7 (C), 123.7 (C), 96.8 (C), 94.8 (C), 92.1 (CH), 81.7 (C), 48.0 (CH), 42.1 (CH_2), 35.4 (CH_2), 31.9 (CH_2), 30.6 (CH_2), 25.6 (CH_3), 19.0 (C), 18.8 (CH_3), 18.1 (C), −2.8 (CH_3), −3.4 (CH_3).

(1*R,3*R**,8*S**,9*S**)-3-(*tert*-Butyldimethylsilyloxy)-5,6-dimethyl-13-(phenylsulfonyl)-15-oxatetracyclo-[7.5.1.0^{1,11}.0^{3,8}]pentadeca-5,10,12-trien-2-one (10).** *n*-BuLi (0.383 mL, 0.91 mmol, 2.4 M in hexanes) was added to a cooled (−78 °C) solution of CuCN (45 mg, 0.50 mmol) in THF/Et_2O (10 mL, 1:1). The reaction mixture was allowed to reach room temperature and recooled at 0 °C. To the resulting suspension was added a solution of **9** (100 mg, 0.153 mmol) in THF/Et_2O (3 mL, 1:1). The mixture was stirred at room temperature for 1 h, poured into brine, and extracted with Et_2O. Drying, filtering, and concentration gave a residue that was purified by silica gel flash chromatography (5−10% EtOAc/hexane) to afford 40 mg of **10** as a white solid [51%, R_f 0.6 (25% EtOAc/hexanes), mp 110 °C]. ^{1}H NMR δ 7.88 (2H, m), 7.75−7.56 (3H, m), 6.92 (1H, s), 6.36 (1H, s), 4.92 (1H, s), 2.98 (1H, d, J = 15 Hz), 2.61 (1H, d, J = 15 Hz), 2.29 (2H, m), 2.02 (3H, m), 1.69 (3H, s), 1.61 (3H, s), 0.73 (9H, s), 0.08 (3H, s), −0.20 (3H, s). ^{13}C NMR δ 200.5 (C), 153.7 (C), 149.4 (C), 139.0 (C), 134.3 (CH), 130.2 (CH), 129.7 (CH), 129.6 (CH), 128.4 (CH), 126.8 (C), 124.1 (C), 97.0 (C), 94.3 (CH), 81.8 (C), 47.9 (CH), 42.5 (CH_2), 36.1 (CH_2), 32.6 (CH_2), 26.0 (CH_3), 19.3 (CH_3), 19.2 (CH_3), 18.6 (C), −2.3 (CH_3), −3.2 (CH_3).

(1*R,3*R**,8*S**,9*S**)-3-(*tert*-Butyldimethylsilyloxy)-5,6,-13-trimethyl-15-oxatetracyclo[7.5.1.0^{1,11}.0^{3,8}]pentadeca-5,-10,12-trien-2-one (11a).** MeLi (0.62 mL, 0.93 mmol, 1.5 M in Et_2O) was added to a solution of **9** (300 mg, 0.458 mmol) in THF (10 mL) cooled at −78 °C. The reaction mixture was stirred at that temperature for 15 min, poured in brine, and extracted with Et_2O. Drying, filtering, and concentration of the organic extracts led to a residue that was purified by silica gel flash chromatography to afford 69 mg of compound **11a** as a viscous colorless oil [38%, R_f 0.66 (10% EtOAc/hexanes)]. ^{1}H NMR δ 5.75 (1H, s), 5.70 (1H, br s), 4.82 (1H, d, J = 2.1 Hz), 2.69 (1H, d, J = 16.6 Hz), 2.38−2.23 (3H, m), 2.13−1.98 (3H, m), 1.93 (3H, s), 1.73 (3H, s), 1.66 (3H, s), 0.78 (9H, s), 0.12 (3H, s), −0.12 (3H, s). ^{13}C NMR δ 203.6 (C), 156.9 (C), 153.3 (C), 125.4 (C), 123.9 (C), 117.7 (CH), 117.5 (CH), 97.7 (C), 93.1 (CH), 81.8 (C), 48.2 (CH), 43.1 (CH_2), 38.2 (CH_2), 35.5 (CH_2), 25.7 (CH_3), 19.1 (C), 18.9 (CH_3), 18.3 (CH_3), 18.2 (CH_3), −2.9 (CH_3), −3.2 (CH_3).

(1*R,3*R**,8*S**,9*S**)-13-Butyl-3-(*tert*-Butyldimethylsilyl-oxy)-5,6-dimethyl-15-oxatetracyclo[7.5.1.0^{1,11}.0^{3,8}]penta-deca-5,10,12-trien-2-one (11b).** *n*-BuLi (0.2 mL, 0.5 mmol, 2.5 M in hexane) was added to a solution of **9** (105 mg, 0.16 mmol) in Et_2O (8 mL) cooled at −78 °C. The mixture was allowed to reach room temperature, poured into brine, and extracted with Et_2O. Drying and concentration of the organic extracts led to a residue that was purified by silica gel flash chromatography to afford 41 mg of compound **11b** as a viscous colorless oil [59%, R_f 0.87 (25% EtOAc/hexanes)]. ^{1}H NMR δ 5.81 (1H, s), 5.75 (1H, br s), 4.79 (1H, br s), 2.65 (1H, d, J = 16.3 Hz), 2.36−1.95 (8H, m), 2.13−1.98 (3H, m), 1.69 (3H, s), 1.62 (3H, s), 1.51−1.20 (4H, m), 0.86 (3H, t, J = 6.6 Hz), 0.76 (9H, s), 0.11 (3H, s), −0.16 (3H, s). ^{13}C NMR δ 203.7 (C), 162.0 (C), 153.5 (C), 126.1 (C), 124.4 (C), 117.9 (CH), 116.8 (CH), 97.8 (C), 93.7 (CH), 82.1 (C), 48.7 (CH), 43.5 (CH_2), 37.0 (CH_2), 36.0 (CH_2), 32.5 (CH_2), 29.6 (CH_2), 26.1 (CH_3), 22.7 (CH_2), 19.6 (CH_3), 19.3 (CH_3), 18.7 (C), 14.2 (CH_3), −2.5 (CH_3), −3.3 (CH_3).

(1*R,3*R**,8*S**,9*S**)-3-(*tert*-Butyldimethylsilyloxy)-5,6-dimethyl-15-oxatetracyclo[7.5.1.0^{1,11}.0^{3,8}]pentadeca-5,10,12-trien-2-one (12) and (1*R**,3*R**,8*S**,9*S**)-3-(*tert*-Butyldimethylsilyloxy)-5,6-dimethyl-15-oxatetracyclo-[7.5.1.0^{1,11}.0^{3,8}]pentadeca-5,10-dien-2-one (13).** Freshly prepared Na(Hg) (1.8 g, 6% in Na) was added to a solution of **9** (400 mg, 0.611 mmol) in THF/MeOH (30 mL, 1:1). The resulting suspension was stirred for 30 min at room temperature and filtered through a short path of Celite with MeOH washings. The filtrate was concentrated, poured into brine, and extracted with Et_2O. Drying, filtering, and concentration of the organic extracts led to a residue that was purified by silica gel flash chromatography to afford 88 mg of a mixture of compounds **12** and **13** (approximately 1.7:1). [41%, R_f 0.69 (12% EtOAc/hexanes)]. ^{1}H NMR of the mixture: δ 6.32 (br s), 6.03 (br s), 5.90 (s), 5.83 (s), 4.84 (br s), 4.68 (br s), 2.83 (d, J = 16.2 Hz), 2.44−2.19 (m), 2.10−1.90 (m), 1.73 (s), 1.62 (s), 1.58 (s), 0.73 (br s), 0.10 (br s), −0.10 (s), −0.18 (s).

(2*R,3a*R**,4a*R**,8a*S**)-2-*tert*-Butyl-4a-(*tert*-butyldimethylsilyloxy)-3a-hydroxy-6,7-dimethyl-2,3,3a,4,4a,5,8,8a-octahydrobenzo[*f*]azulen-4-one (14).** *t*-BuLi (0.32 mL, 0.512 mmol, 1.6 M in pentanes) was added to a solution of the previously obtained 1.7:1 mixture of **12** and **13** (37 mg, approx 0.1 mmol) in Et_2O (6 mL) cooled at −78 °C. After 2 min, the reaction mixture was poured into brine and extracted with Et_2O. Drying and concentration of the organic extracts led to a residue that was purified by silica gel flash chromatography to afford 24 mg of **14** as a white solid [87%, R_f 0.65 (12% EtOAc/hexanes), mp 85 °C] and 11 mg of **13**. ^{1}H NMR δ 6.24 (1H, d, J = 11.7 Hz), 5.97 (1H, s), 5.51 (1H, dd, J = 6.7 and 11.7 Hz), 2.82 (2H, m), 2.55 (1H, d, J = 16.2 Hz), 2.13 (2H, m), 2.01 (1H, dd, J = 12.6 and 5.9 Hz), 1.99 (1H, m), 1.83 (1H, dd, J = 12.7 and 9.3 Hz), 1.66 (3H, s), 1.54 (3H, s), 0.88 (9H, s), 0.80 (9H, s), 0.12 (3H, s), 0.05 (3H, s); ^{13}C NMR δ 207.2 (C), 141.8 (C), 139.0 (CH), 128.8 (CH), 124.8 (C), 124.7 (CH), 123.8 (C), 87.7 (C), 83.3 (C), 52.8 (CH), 44.9 (CH), 43.6 (CH_2), 42.4 (CH_2), 37.4 (CH_2), 31.7 (C), 27.8 (CH_3), 26.0 (CH_3) 18.7 (CH_3), 18.4 (C), 18.1 (CH_3), −2.1 (CH_3), −2.6 (CH_3). ^{1}H NMR of **13**: δ 5.90 (1H, s), 4.68 (1H, br s), 2.45−1.81 (8H, m), 1.73 (3H, s), 1.62 (3H, s), 1.52 (m, 2H), 0.73 (9H, s), 0.10 (3H, s), −0.10 (3H, s).

(1*R,7*S**,8*S**,9*S**, 14*R**)-7-*tert*-Butyl-14-(*tert*-butyldimethylsilyloxy)-4,11,12-trimethyl-15-oxatetracyclo-[6.6.1.0^{2,6}.0^{9,14}]pentadeca-2(6),4,11-trien-1-ol (15).** *t*-BuLi (0.30 mL, 0.48 mmol, 1.6 M in pentanes) was added to a solution of diene **11a** (40 mg, 0.103 mmol) in Et_2O (5 mL) cooled at −78 °C. After 5 min the reaction mixture was poured into brine and extracted with Et_2O. Drying, filtering, and concentration of the organic extracts led to a residue that was purified by silica gel flash chromatography to afford 36 mg of **15** as a viscous colorless oil [79%, R_f 0.44 (10% EtOAc/hexanes)]. ^{1}H NMR δ 6.07 (1H, s), 3.88 (1H, br s), 3.10 (2H, m), 2.75 (1H, br s), 2.45 (2H, m), 2.04 (4H, m), 1.93 (2H, m), 1.87 (3H, s), 1.78 (3H, s), 0.99 (9H, s), 0.79 (9H, s), −0.08 (3H, s), −0.3 (3H, s). ^{13}C NMR δ 143.3 (C), 142.6 (C), 140.2 (C), 130.4 (CH), 125.9 (C), 123.9 (C), 103.7 (C), 88.8 (C), 82.0 (CH), 60.3 (C), 53.8 (CH), 49.3 (CH), 43.6 (CH_2), 39.0 (CH_2), 35.6 (CH_2), 34.0 (C), 29.4 (CH_3), 26.1 (CH_3), 19.5 (CH_3), 18.2 (CH_3), 16.1 (C), 14.1 (CH_3), −2.5 (CH_3), −2.8 (CH_3).

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Supporting Information Available: Copies of ^{1}H, ^{13}C NMR, and HMBC, HMQC, and NOE spectra of selected products, and full lists of mass spectral data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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