JOC Article

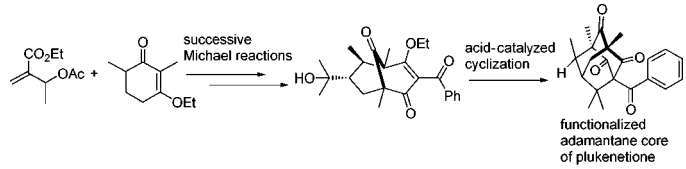
Construction of the Adamantane Core of Plukenetione-Type Polycyclic Polyprenylated Acylphloroglucinols

Ryukichi Takagi,* Yuta Inoue, and Katsuo Ohkata

Department of Chemistry, Graduate School of Science, Hiroshima University, 1-3-1 Kagamiyama, Higashi-Hiroshima 739-8526, Japan

rtakagi@hiroshima-u.ac.jp

Received July 18, 2008



The construction of a highly functionalized adamantane core of plukenetione-type polycyclic polyprenylated acylphloroglucinols (PPAPs) is described. The method features the construction of the bicyclo[3.3.1]nonane core (**3**) by successive Michael reactions and the construction of the adamantane core of plukenetione-type PPAPs by acid-catalyzed cyclization of a bicyclo[3.3.1]nonane precursor (**2**).

Introduction

Polycyclic polyprenylated acylphloroglucinols (PPAPs) are secondary metabolites isolated from Guttiferous plants and are biosynthetically generated from monocyclic polyprenylated acyphloroglucinols.[1] PPAPs feature a highly oxygenated and densely substituted bicyclo[3.3.1]nonane, bicyclo[3.2.1]octane, adamantane, or homoadamantane core. PPAPs are classified into three types (types A−C), depending on the relative position of the acyl group on the bicyclic core structure (Figure 1).[1a,2] The less common PPAPs bearing an adamantane core are also classified accordingly (Figure 2).[3]

PPAPs have attracted attention as synthetic targets due to their significant biological activity[1,4] and their synthetically challenging structure, and a number of synthetic efforts toward the bicyclo[3.3.1]nonane core have been reported.[5,6] We have recently developed a method for the construction of polyfunctionalized bicyclo[3.3.1]nonanes by successive Michael reactions of 2-cyclohexenone derivatives with acrylates.[7] In the course of the examination, we found that adamantane derivatives could be constructed by the one-pot reaction of ethyl 2,4-dioxocyclohexanecarboxylate with 2-phenylethyl 2-(acetoxymethyl)-acrylate or 2-(acetoxymethyl)-1-phenyl-2-propen-1-one via a domino reaction involving inter- and intramolecular Michael

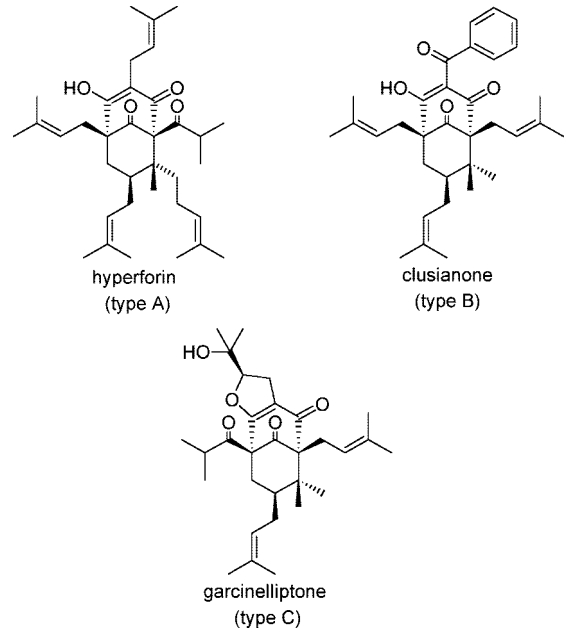


FIGURE 1. PPAPs with a bicyclo[3.3.1]nonane core.

* To whom correspondence should be addressed. Tel: +81-82-424-7434. Fax: +81-82-424-0727.

(1) (a) Ciochina, R.; Grossman, R. B. *Chem. Rev.* **2006**, *106*, 3963–3986. (b) Singh, I. P.; Bharate, S. B. *Nat. Prod. Rep.* **2006**, *23*, 558–591.

(2) Cuesta-Rubio, O.; Velez-Castro, H.; Frontana-Uribe, B. A.; Cárdenas, J. *Phytochemistry* **2001**, *57*, 279–283.

(3) (a) Henry, G. E.; Jacobs, H.; Carrington, C. M. S.; McLean, S.; Reynolds, W. F. *Tetrahedron Lett.* **1996**, *37*, 8663–8666. (b) Hu, L.-H.; Sim, K.-Y. *Tetrahedron Lett.* **1998**, *39*, 7999–8002. (c) Hu, L.-H.; Sim, K.-Y. *Tetrahedron Lett.* **1999**, *40*, 759–762. (d) Hu, L. H.; Sim, K. Y. *Org. Lett.* **1999**, *1*, 879–882. (e) Hu, L.-H.; Sim, K.-Y. *Tetrahedron* **2000**, *56*, 1379–1386. (f) Christian, O. E.; Henry, G. E.; Jacobs, H.; McLean, S.; Reynolds, W. F. *J. Nat. Prod.* **2001**, *64*, 23–25. (g) Tanaka, N.; Takaishi, Y.; Shikishima, Y.; Nakanishi, Y.; Bastow, K.; Lee, K.-H.; Honda, G.; Ito, M.; Takeda, Y.; Kodzhimatov, O. K.; Ashurmetov, O. *J. Nat. Prod.* **2004**, *67*, 1870–1875. (h) Teixeira, J. S. R.; Cruz, F. C. *Tetrahedron Lett.* **2005**, *46*, 2813–2816. (i) Řezanka, T.; Sigler, K. *Phytochemistry* **2007**, *68*, 1272–1276. (j) Xiao, Z. Y.; Mu, Q.; Shiu, W. K.-P.; Zeng, Y. H.; Gibbons, S. *J. Nat. Prod.* **2007**, *70*, 1779–1782.

10.1021/jo801595y CCC: $40.75
Published on Web 11/04/2008

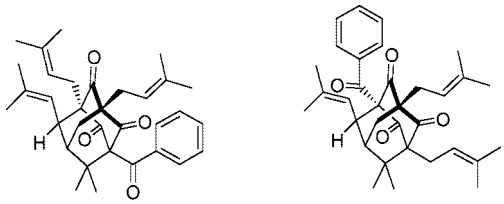
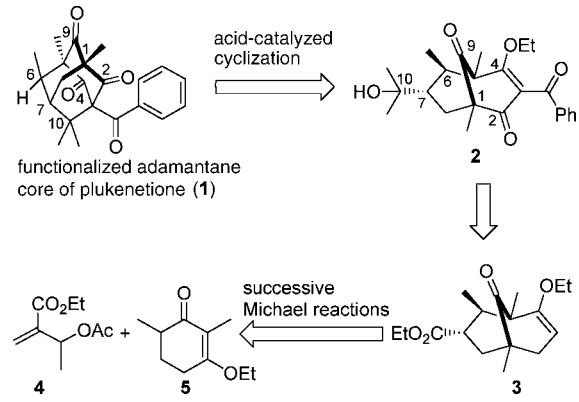


FIGURE 2. PPAPs with an adamantane core.

reactions and a Dieckmann condensation or an aldol-type reaction in succession.[8] Although the constructions of bicyclo[3.3.1]nonanes[9] and adamantanes[10] via Michael reactions have been reported, the Michael donors have mostly been limited to enamines derived from cyclohexanones. The method we developed using successive Michael reactions is able to directly afford poly functionalized bicyclo[3.3.1]nonenones and adamantanones from cyclohexenones. Porco and co-workers have recently reported a similar approach to properly functionalized clusianone-type bicyclo[3.3.1]nonanes via an alkylative dearomatization-annulation process involving acylphloroglucinols and in the course of their investigation, they found that a partially functionalized adamantane core for the type B hyperibone could also be prepared.[6h] However, probably due to the increased complexity accompanying adamantane cored PPAPs, so far, no total synthesis of adamantane cored natural PPAPs have been reported, and this is the only report we are aware of involving the synthesis of adamantanes with an advanced structure toward PPAP. We have succeeded in the construction of an advanced model compound of a type A adamantane cored PPAP, plukenetione. Our compound differs with the natural product only in the precise identity of three alkyl substituents (methyls in the place of prenyls). Herein we describe the synthetic details.

SCHEME 1. Synthetic Plan for the Model Adamantane Compound 1 of Plukenetione



Results and Discussion

The reports on both the construction of the adamantane skeleton from bicyclo[3.3.1]nonanes[8,11] and the speculated biosynthetic pathway of sampsoniones[3b−e] encouraged us to attempt the construction of adamantane **1**, as a highly functionalized model compound of plukenetione, by the acid-catalyzed cyclization of bicyclo[3.3.1]nonane **2** (Scheme 1).[12] We envisioned that bicyclo[3.3.1]nonane **3**, which was generated from

(4) For bioactivity of PPAPs in general, see, for example: (a) Gustafson, K. R.; Blunt, J. W.; Munro, M. H. G.; Fuller, R. W.; McKee, T. C.; Cardellina, J. H.; McMahon, J. B.; Cragg, G. M.; Boyd, M. R. *Tetrahedron* **1992**, *46*, 10093–10102. (b) Fukuyama, Y.; Kuwayama, A.; Minami, H. *Chem. Pharm. Bull.* **1997**, *45*, 947–949. (c) Roux, D.; Hadi, H. A.; Thoret, S.; Guénard, D.; Thoison, O.; Païs, M.; Sévenet, T. *J. Nat. Prod.* **2000**, *63*, 1070–1076. (d) Verotta, L. *Phytochem. Rev.* **2002**, *1*, 389–407. (e) Verotta, L.; Appendino, G.; Belloro, E.; Bianchi, F.; Sterner, O.; Lovati, M.; Bombardelli, E. *J. Nat. Prod.* **2002**, *65*, 433–438. (f) Šavikin-Fodulović, K.; Aljančić, I.; Vajs, V.; Menković, N.; Macura, S.; Gojgić, G.; Milosavljević, S. *J. Nat. Prod.* **2003**, *66*, 1236–1238. (g) Weng, J.-R.; Lin, C.-N.; Tsao, L.-T.; Wang, J.-P. *Chem. Eur. J.* **2003**, *9*, 1958–1963. (h) Baggett, S.; Protiva, P.; Mazzola, E. P.; Yang, H.; Ressler, E. T.; Basile, M. J.; Weinstein, I. B.; Kennelly, E. J. *J. Nat. Prod.* **2005**, *68*, 354–360. (i) Piccinelli, A. L.; Cuesta-Rubio, O.; Chica, M. B.; Mahmood, N.; Pagano, B.; Pavone, M.; Barone, V.; Rastrelli, L. *Tetrahedron* **2005**, *61*, 8206–8211. (j) Beerhues, L. *Phytochemistry* **2006**, *67*, 2201–2207. (k) Protiva, P.; Hopkins, M. E.; Baggett, S.; Yang, H.; Lipkin, M.; Holt, P. R.; Kennelly, E. J.; Bernard, W. I. *Int. J. Cancer* **2008**, *123*, 687–694, and references cited therein.

(5) For some recent synthetic studies toward the bicyclo[3.3.1]nonanone core of bicyclic PPAPs, see: (a) Usuda, H.; Kanai, M.; Shibasaski, M. *Tetrahedron Lett.* **2002**, *43*, 3621–3624. (b) Usuda, H.; Kanai, M.; Shibasaki, M. *Org. Lett.* **2002**, *4*, 859–862. (c) Spessard, S. J.; Stolz, B. M. *Org. Lett.* **2002**, *4*, 1943–1946. (d) Young, D. G.; Zeng, D. *J. Org. Chem.* **2002**, *67*, 3134–3137. (e) Kraus, G. A.; Nguyen, T. H.; Jeon, I. *Tetrahedron Lett.* **2003**, *44*, 659–661. (f) Klein, A.; Miesch, M. *Tetrahedron Lett.* **2003**, *44*, 4483–4485. (g) Kraus, G. A.; Dneprovskaia, E.; Nguyen, T. H.; Jeon, I. *Tetrahedron* **2003**, *59*, 8975–8978. (h) Ciochina, R.; Grossman, R. B. *Org. Lett.* **2003**, *5*, 4619–4621. (i) Mehta, G.; Bera, M. K. *Tetrahedron Lett.* **2004**, *45*, 1113–1116. (j) Ususa, H.; Kuramochi, A.; Kanai, M.; Shibasaki, M. *Org. Lett.* **2004**, *6*, 4387–4390. (k) Kraus, G. A.; Jeon, I. *Tetrahedron* **2005**, *61*, 2111–2116. (l) Nicolaou, K. C.; Carenzi, G. E. A.; Jeso, V. *Angew. Chem., Int. Ed.* **2005**, *44*, 3895–3899. (m) Mehta, G.; Bera, M. K. *Tetrahedron Lett.* **2006**, *47*, 689–692. (n) Shimizu, Y.; Kuramochi, A.; Usuda, H.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2007**, *48*, 4173–4177. (o) Kraus, G. A.; Jeon, I. *Tetrahedron Lett.* **2008**, *49*, 286–288. (p) Mehta, G.; Bera, M. K.; Chatterjee, S. *Tetrahedron Lett.* **2008**, *49*, 1121–1124. (q) Mehta, G.; Bera, M. K. *Tetrahedron Lett.* **2008**, *49*, 1417–1420. (r) Raikar, S. B.; Nuhant, P.; Delpech, B.; Marazano, C. *Eur. J. Org. Chem.* **2008**, *135*, 8–1369.

(6) Total synthesis of PPAPs with a bicyclic core: (a) Kuramochi, A.; Usuda, H.; Yamatsugu, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 14200–14201. (b) Siegel, D. R.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2006**, *128*, 1048–1049. (c) Rodeschini, V.; Ahmad, N. M.; Simpkins, N. S. *Org. Lett.* **2006**, *8*, 5283–5285. (d) Nuhant, P.; David, M.; Pouplin, T.; Delpech, B.; Marazano, C. *Org. Lett.* **2007**, *9*, 287–289. (e) Rodeschini, V.; Simpkins, N. S.; Wilson, C. *J. Org. Chem.* **2007**, *72*, 4265–4267. (f) Ahmad, N. M.; Rodeschini, V.; Simpkins, N. S.; Ward, S. E.; Blake, A. J. *J. Org. Chem.* **2007**, *72*, 4803–4815. (g) Tsukano, C.; Siegel, D. R.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 8840–8844. (h) Qi, J.; Porco, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 12682–12683.

(7) (a) Takagi, R.; Nerio, T.; Miwa, Y.; Matsumura, S.; Ohkata, K. *Tetrahedron Lett.* **2004**, *45*, 7401–7405. (b) Takagi, R.; Miwa, Y.; Nerio, T.; Inoue, Y.; Matsumura, S.; Ohkata, K. *Org. Biomol. Chem.* **2007**, *5*, 286–300.

(8) Takagi, R.; Miwa, Y.; Matsumura, S.; Ohkata, K. *J. Org. Chem.* **2005**, *70*, 8587–8589.

(9) (a) Nelson, R. P.; Lawton, R. G. *J. Am. Chem. Soc.* **1966**, *88*, 3884–3885. (b) Nelson, R. P.; McEuen, J. M.; Lawton, R. G. *J. Org. Chem.* **1969**, *34*, 1225–1229. (c) McEuen, J. M.; Nelson, R. P.; Lawton, R. G. *J. Org. Chem.* **1970**, *35*, 690–696. (d) Frontier, A. J.; Danishefsky, S. J.; Koppel, G. A.; Meng, D. *Tetrahedron* **1998**, *54*, 12721–12736.

(10) (a) Stetter, H.; Thomas, H. G. *Angew. Chem., Int. Ed.* **1967**, *6*, 554–555. (b) Stetter, H.; Thomas, H. G. *Chem. Ber.* **1968**, *101*, 1115–1119. (c) Stetter, H.; Thomas, H. G.; Meyer, K. *Chem. Ber.* **1970**, *103*, 863–867. (d) Hickmott, P. W.; Suschitzky, H.; Urbani, R. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2063–2064. (e) Stetter, H.; Elfert, K. *Synthesis* **1974**, 36–37. (f) Hickmott, P. W.; Ahmed, M. G.; Ahmed, S. A.; Wood, S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2559–2571. (g) Huque, A. K. M. F.; Mosihuzzaman, M.; Ahmed, S. A.; Ahmed, M. G.; Andersson, R. *J. Chem. Res., Synop.* **1987**, 214. (h) Ahmed, M. G.; Huque, A. K. M. F.; Ahmed, S. A.; Mosihuzzaman, M.; Andersson, R. *J. Chem. Res., Synop.* **1988**, 362–363. (i) Ahmed, M. G.; Moeiz, S. M. I.; Ahmed, S. A.; Kiuchi, F.; Tsuda, Y.; Sampsom, P. *J. Chem. Res., Synop.* **1999**, 316–317. (j) Ahmed, M. G.; Moeiz, S. M. I.; Ahmed, S. A.; Kiuchi, F.; Tsuda, Y. *Tetrahedron* **2001**, *57*, 3143–3150. (k) Ahmed, M. G.; Ahmed, S. A.; Akhter, K.; Moeiz, S. M. I.; Tsuda, Y.; Kiuchi, F.; Hossain, M. M.; Forsterling, F. H. *J. Chem. Res.* **2005**, 293–298.

(11) (a) Denmark, S. E.; Henke, B. R. *J. Am. Chem. Soc.* **1989**, *111*, 8032–8034. (b) Ayres, F. D.; Khan, S. I.; Chapman, O. L.; Kaganove, S. N. *Tetrahedron Lett.* **1994**, *35*, 7151–7154. (c) Bhat, J. I.; Clegg, W.; Maskill, H.; Elsegood, M. R. J.; Menneer, I. D.; Miatt, P. C. *J. Chem. Soc., Perkin Trans 2* **2000**, 1435–1446. (d) Itoh, H.; Kato, I.; Unoura, K.; Senda, Y. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 339–345. (e) Shibuya, M.; Taniguchi, T.; Takahashi, M.; Ogasawara, K. *Tetrahedron Lett.* **2002**, *43*, 4145–4147.

(12) The atomic numbering is based on the bicylo[3.3.1]non-3-en-2-one core.

(13) (a) Barrack, S. A.; Okamura, W. H. *J. Org. Chem.* **1986**, *51*, 3201–3206. (b) Miyaura, N.; Satoh, Y.; Hara, S.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2029–2031.

SCHEME 2. Successive Michael Reactions of 4 with 5

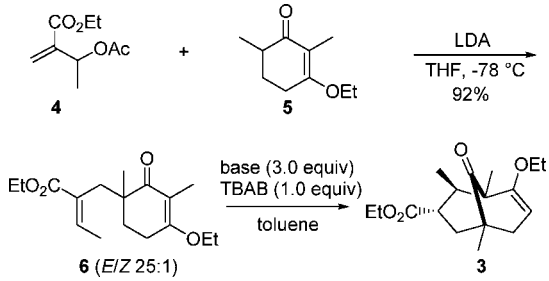
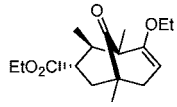
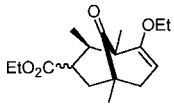
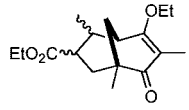
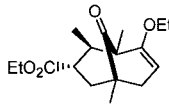
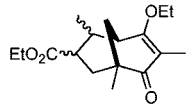


TABLE 1. Optimization of the Intramolecular Michael Reaction of 6

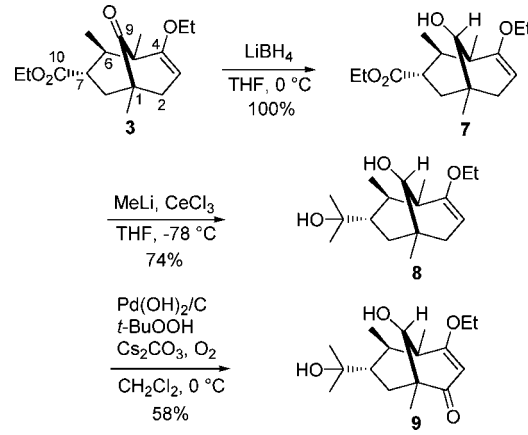
entry	conditions	products
1	K_2CO_3, 90 °C, 3 days	 **3**: 41%
2	Cs_2CO_3, 90 °C, 23 h	 **3**: 29%  γ-**3**: 7%
3	K_2CO_3, 110 °C, 31 h	 **3**: 55%  γ-**3**: 25%

successive Michael reactions of cyclohexenone **5**[13] with acrylate **4**,[14] would serve as a moderately substituted synthetic intermediate for adamantane **1**.

Our synthetic effort commenced with successive Michael reactions of cyclohexenone **5** with acrylate **4** (Scheme 2). The annulation precursor **6** was obtained in 92% yield by the intermolecular Michael reaction of cyclohexenone **5** with acrylate **4** (*E*/*Z* 25:1).[15] The stereoselectivity in the intermolecular Michael reaction was similar to that observed by Buchholz and Hoffmann.[16] Results of the optimization of the intramolecular Michael reaction of **6** are summarized in Table 1. Treatment of the annulation precursor **6** with K_2CO_3 (3.0 equiv) and tetrabutylammonium bromide (TBAB) (1.0 equiv) at 90 °C for 3 days gave α-annulation product **3** in 41% yield (entry 1).[7b] When Cs_2CO_3 was used as the base instead of K_2CO_3, a diastereomeric mixture of α-annulation product **3** and γ-annulation product γ-**3** was obtained (entry 2). This result suggested that decomposition and/or isomerization of the annulation products under the reaction conditions had occurred. When the reaction was carried out at 110 °C for 31 h, the yield of the annulation products improved (**3**: 55% plus a diastereomeric mixture of the γ-annulation product γ-**3**: 25%, entry 3).

The introduction of the C10-*gem*-dimethyl groups and the C2-carbonyl group to bicyclo[3.3.1]nonane **3** is depicted in

SCHEME 3. Introduction of the C10-*gem*-Dimethyl Groups and the C2-Carbonyl Group



Scheme 3. To prevent nucleophilic attack during introduction of the C10-*gem*-dimethyl groups, the C9-carbonyl group was reduced with $LiBH_4$ to give **7** as a single isomer (100%). The product stereochemistry of **7** was determined on the basis of ^{1}H NMR dif-NOE experiments, in which NOE enhancement between H2 and H9 was observed (Figure 3). The steric hindrance of the pseudoaxial C6-methyl group probably played an important role in bringing about the high stereoselectivity.[17] The C10-*gem*-dimethyl groups were introduced by the reaction of **7** with MeLi in the presence of $CeCl_3$ (74%).[18,19] The X-ray structure of **8** confirmed the stereochemical assignment in the reduction of **3**. The C2-carbonyl group was introduced by the $Pd(OH)_2$/C-catalyzed allylic oxidation of **8**.[20] Compared with typical literature conditions, a large amount of base and/or catalyst and long reaction time were necessary for optimum yields [$Pd(OH)_2$/C (5 mol%), Cs_2CO_3 (10 equiv), 0 °C, 1 week: 60%; $Pd(OH)_2$/C (5 mol%), Cs_2CO_3 (5.0 equiv), 0 °C, 1.5 days then $Pd(OH)_2$/C (5 mol%), 0 °C, 1.5 days: 58%].

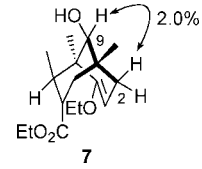


FIGURE 3. ^{1}H NMR NOE experiment of **7**.

With bicyclo[3.3.1]nonane **9** in hand, we shifted our attention to the introduction of the C3-benzoyl group. We initially planned the introduction of the C3 benzoyl group via diketone **10**[6d,21] and attempted acid-catalyzed deprotection of ethyl enol ether **9** with concd HCl (10 equiv) in THF at 40 °C. However, dehydration product **11** and adamantane **12** were obtained

(14) (a) Hayashi, N.; Yanagihara, K.; Tsuboi, S. *Tetrahedron: Asymmetry* **1998**, *9*, 3825–3830. (b) Trost, B. M.; Machacek, M. R.; Tsui, H. C. *J. Am. Chem. Soc.* **2005**, *127*, 7014–7024.

(15) The diastereomer mixture was used for the next intramolecular Michael reaction without separation.

(16) (a) Buchholz, R.; Hoffmann, H. M. R. *Helv. Chim. Acta* **1991**, *74*, 1213–1220. (b) Ayed, T. B.; Amri, H.; Gaied, M. M. E. *Tetrahedron* **1991**, *47*, 9621–9628. (c) Das, B.; Banerjee, J.; Ravindranath, N. *Tetrahedron* **2004**, *60*, 8357–8361. (d) Chandrasekhar, S.; Chandrashekar, G.; Vijeender, K.; Reddy, M. S. *Tetrahedron Lett.* **2006**, *47*, 3475–3478.

(17) In the reduction of 7-*endo*-*tert*-butoxycarbonyl-1,5-dimethylbicyclo[3.3.1]-non-2-en-9-one with $NaBH_4$, practically no diastereoselectivity was observed (dr 44:56).

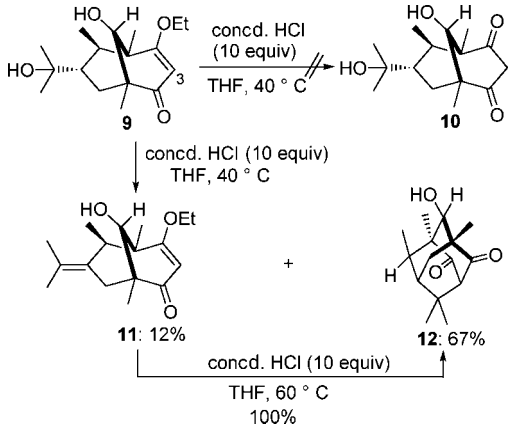
(18) (a) Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904–3912. (b) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392–4398.

(19) In initial studies, the C7-*tert*-butoxy ester was used as the substituent. However, the organocerium reaction did not proceed with this ester. Therefore, the less bulky ethyl ester **3** was used instead for the ensuing synthetic studies.

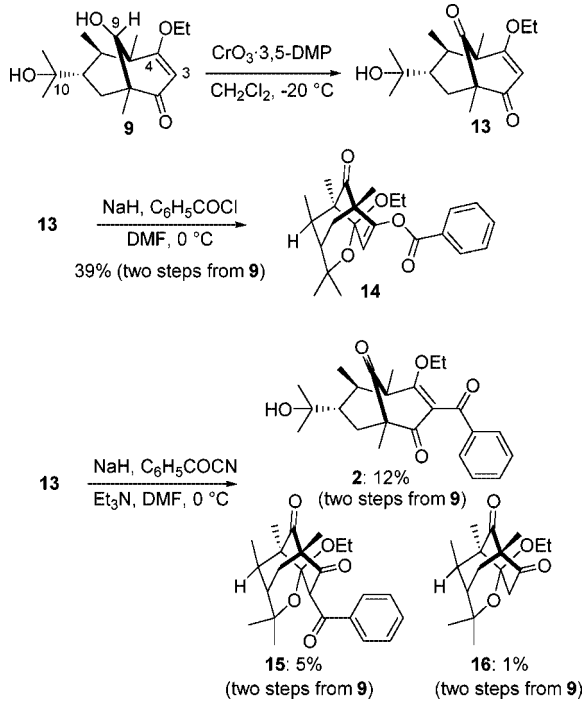
(20) (a) Yu, J.-Q.; Corey, E. J. *Org. Lett.* **2002**, *4*, 2727–2730. (b) Yu, J.-Q.; Corey, E. J. *J. Am. Chem. Soc.* **2003**, *125*, 3232–3233. (c) Yu, J.-Q.; Wu, H.-C.; Corey, E. J. *Org. Lett.* **2005**, *7*, 1415–1417.

(21) (a) Montes, I. F.; Burger, U. *Tetrahedron Lett.* **1996**, *37*, 1007–1010. (b) Tang, Q.; Sen, S. E. *Tetrahedron Lett.* **1998**, *39*, 2249–2252.

SCHEME 4. Attempted Acid-Catalyzed Deprotection of the Ethoxy Enol Ether



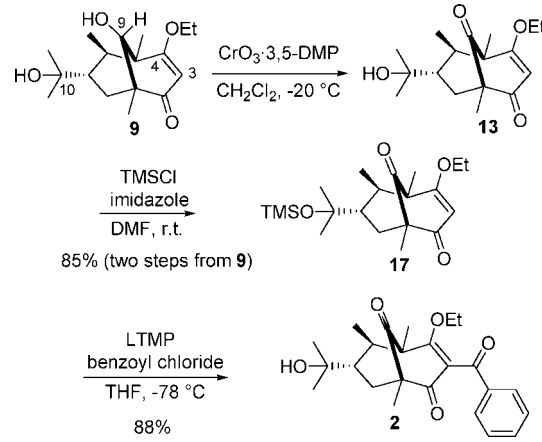
SCHEME 5. Attempted C3-Benzoylation via an Intramolecular Hetero-Michael Reaction



instead of diketone **10** (Scheme 4). The adamantane skeleton of **12** was confirmed by X-ray structural analysis. Treatment of **11** with concd HCl in THF at 60 °C quantitatively gave adamantane **12**. Thus, deprotection of the enol ether and cyclization to the adamantane skeleton could be achieved in an elegant tandem manner by acid catalysis. Unfortunately, introduction of the C3-benzoyl group to adamantane **12** could not be effected in spite of extensive efforts and we had to abandon this route.

Since C3-benzoylation had to be carried out before the formation of the adamantane framework, we decided to attempt C3-benzoylation by reacting the enolate involving C3 position generated by the intramolecular hetero-Michael addition of the oxide from the C10-alcohol to the C4 position (Scheme 5). This strategy seemed favorable since the C10-alcohol could also be protected during the process. Before carrying out the intramolecular hetero-Michael reaction, the C9-carbonyl group was regenerated by the oxidation of **9** with CrO_3·3,5-dimethylpyrazole (3,5-DMP).[22,23] Exposure of **9** to Swern oxidation conditions was unsatisfactory, furnishing a complex mixture also containing **11** and **12** among others. The benzoylation of **13** with benzoyl chloride via the intramolecular hetero-Michael reaction gave *O*-benzoylation product **14** (39%, two steps). Attempted cyanide catalyzed isomerization of **14** to *C*-benzoylation product **2** with KCN and Et_3N failed.[21a,24] A switch to benzoyl cyanide[25] for the reaction with **13** enabled us to obtain *C*-benzoylation products **2** (12%, two steps) and **15** (5%, two steps) along with protonated product **16** (1%, two steps). However, the separation of the products **2**, **15**, and **16** proved to be troublesome.

SCHEME 6. C3-Benzoylation via a Vinyl Anion



Although **2** and **15** could be envisioned as precursors to the benzoylated adamantane product, the total yield of the two was not acceptable. Thus, in order to develop a more practical method, C3-benzoylation via the vinyl anion was examined (Scheme 6).[6c,e,f] To prevent the hetero-Michael pathway, the C10-alcohol of **9** was protected with a trimethylsilyl (TMS) group (85%, two steps from **9**). Treatment of **17** with lithium 2,2,6,6-tetramethylpiperidide (LTMP), followed by benzoyl chloride gave C3-benzoylation product **2**, in which the TMS group incidentally hydrolyzed off during workup (88%).

The acid-catalyzed cyclization of **2** is summarized in Scheme 7. In the acid-catalyzed cyclization of **9**, decomposition of THF by acids had been observed to accompany adamantane formation (Scheme 4). Therefore, to overcome this side reaction, several acidic reaction conditions were examined for the cyclization of **2**. The attempted acid-catalyzed cyclization of **2** in DMSO and toluene accompanied decomposition of the solvent (entries 1−3).[26] However, when **2** was treated with TfOH (1.0 equiv) in CH_2Cl_2, decomposition of the solvent could be avoided and adamantane **2** was obtained in 59% yield (entry 4).

In summary, we have developed an efficient method for the construction of the adamantane core of plukenetione-type PPAPs. The method features the construction of bicyclo[3.3.1]nonane **3** by successive Michael reactions and the construction of the adamantane core by acid-catalyzed cyclization of bicyclo[3.3.1]nonane **2**. This report is the first on the cons-

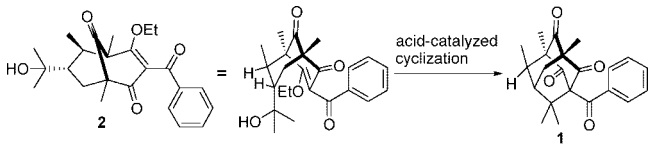
(22) Salmond, W. G.; Barta, M. A.; Havens, J. L. *J. Org. Chem.* **1978**, *43*, 2057–2059.

(23) The product could not be freed of small quanitities of impurities upon purification. Therefore, the product was used for the next reaction after only simple purification.

(24) Tabuchi, H.; Hamamoto, T.; Ichihara, A. *Synlett* **1993**, 651–652.

(25) Wiles, C.; Watts, P.; Haswell, S. J.; Pombo-Villar, E. *Tetrahedron Lett.* **2002**, *43*, 2945–2948.

SCHEME 7. Acid-Catalyzed Cyclization of 2 to the Adamantane Core of Plukenetione



entry	reagent	conditions	1
1	concd. HCl (20 equiv)	DMSO 120 °C, 23 h	trace
2	*p*-TsOH·H_2O (10 equiv)	toluene 100 °C, 8 h	43%
3	TfOH (1.5 equiv)	toluene 100 °C, 15 h	decomposed
4	TfOH (1.0 equiv)	CH_2Cl_2 reflux, 5.5 h	59%

truction of the adamantane core of plukenetione and the product differs with the actual natural product only in the exact identity of three alkyl groups (methyls in the place of prenyls). Synthetic studies toward plukenetione A using the newly developed methodology are now in progress.

Experimental Section

3-Ethoxy-6-(2′-ethoxycarbonyl-2′*Z*-butenyl)-2,6-dimethyl-2-cyclohexenone (6). To a stirred solution of LDA, prepared from *i*-Pr_2NH (2.10 mL, 16.0 mmol) in THF (13 mL) and *n*-BuLi (1.60 M in hexane, 8.20 mL, 13.1 mmol), was added a solution of cyclohexenone **5** (1.44 g, 8.59 mmol) in THF (3.0 mL) at −78 °C. After 30 min, a solution of acrylate **4** (1.85 g, 9.94 mmol) in THF (3.0 mL) was added. The mixture was stirred at −78 °C for 4 h and quenched with satd NH_4Cl. The resulting mixture was extracted with Et_2O. The combined organic layer was washed with water and brine, dried over Na_2SO_4, and evaporated. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc 5:1) to give a mixture of *E*- and *Z*-**6** (2.33 g, 92%, *E*/*Z* 25:1) as a yellow oil. *E*-**6**: IR (thin film) 2981, 2938, 1709, 1618, 1449, 1381, 1256, 1052, 1025 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.94 (q, J = 7.2 Hz, 1 H), 4.19−4.12 (m, 2 H), 4.06 (q, J = 6.9 Hz, 2 H), 2.80 (d, J = 13.8 Hz, 1 H), 2.78−2.69 (m, 1 H), 2.55−2.42 (m, 1 H), 2.52 (d, J = 13.8 Hz, 1 H), 1.84 (dt, J = 13.9, 5.8 Hz, 1 H), 1.79 (d, J = 7.2 Hz, 3 H), 1.75−1.67 (m, 1 H), 1.69 (t, J = 1.6 Hz, 3 H), 1.35 (t, J = 6.9 Hz, 3 H), 1.28 (t, J = 7.2 Hz, 3 H), 1.00 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 169.2, 168.8, 139.8, 130.2, 113.2, 63.1, 60.4, 43.9, 32.5, 32.0, 22.2, 22.3, 15.3, 15.2, 14.2, 8.0; EI-HRMS *m*/*z* calcd for $C_{17}H_{26}O_4$ [M^+] 294.1831, found 294.1819. Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.07; H, 9.16.

2-Ethoxy-7-*endo*-ethoxycarbonyl-1,5,8-*exo*-trimethylbicyclo[3.3.1]non-2-en-9-one (3). To a solution of **6** (101.0 mg, 0.34 mmol, *E*/*Z* 25:1) in toluene (1.5 mL) were added K_2CO_3 (142.2 mg, 1.03 mmol) and TBAB (111.0 mg, 0.34 mmol). The resulting mixture was stirred at 110 °C for 31 h. The mixture was quenched with satd. NH_4Cl and extracted with CH_2Cl_2. The combined organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and evaporated. The resulting residue was purified by preparative TLC (silica gel, hexane/EtOAc 10:1) to give **3** (55.7 mg, 55%) as a yellow oil and γ-**3** (25.3 mg, 25%) as a white solid. **3**: mp 73−75 °C; IR (thin film) 2973, 2943, 1714, 1665, 1455, 1369, 1232, 1207, 1144, 1033 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.41 (dd, J = 4.8, 2.0 Hz, 1 H), 4.16 (dq, J = 10.7, 7.2 Hz, 1 H), 4.03 (dq, J = 10.7, 7.16 Hz, 1 H), 3.57−3.50 (m, 2 H), 3.14 (qt, J = 7.4, 1.7 Hz, 1 H), 2.66 (dt, J = 14.5, 1.7 Hz, 1 H), 2.52 (dd, J = 16.2, 4.8 Hz, 1 H), 2.24 (dt, J = 7.4, 1.7 Hz, 1 H), 2.12 (dt, J = 16.2, 2.0 Hz, 1 H), 1.89 (ddd, J = 14.5, 7.4, 2.0 Hz, 1 H), 1.30 (t, J = 7.2 Hz, 3 H), 1.28 (t, J = 7.0 Hz, 3 H), 1.12 (s, 3 H), 1.02 (s, 3 H), 0.92 (d, J = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 214.0, 173.1, 154.9, 94.2, 62.6, 60.6, 52.9, 45.4, 44.5, 42.4, 38.1, 37.8, 23.8, 16.1, 15.3, 14.5, 14.1; EI-HRMS *m*/*z* calcd for $C_{17}H_{26}O_4$ [M^+] 294.1831, found 294.1838. Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.40; H, 8.60.

2-Ethoxy-7-*endo*-ethoxycarbonyl-9-hydroxy-1,5,8-*exo*-trimethylbicyclo[3.3.1]non-2-ene (7). To a solution of **3** (123.3 mg, 0.42 mmol) at 0 °C was added $LiBH_4$ (27.4 mg, 1.26 mmol). After the mixture was stirred at 0 °C for 3.5 h, the reaction was quenched with satd NH_4Cl, and the mixture was extracted with CH_2Cl_2. The combined organic layer was washed with H_2O and brine, dried over Na_2SO_4, and evaporated. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc 5:1) to give **7** (130.2 mg, 100%) as a yellow oil: ^1H NMR (500 MHz, C_6D_6) δ 4.14 (dd, J = 4.9, 2.3 Hz, 1 H), 3.99 (dq, J = 10.8, 7.2 Hz, 1 H), 3.83 (dq, J = 10.8, 7.2 Hz, 1 H), 3.39−3.32 (m, 2 H), 3.08 (s, 1 H), 2.90 (q, J = 7.6 Hz, 1 H), 2.31 (dd, J = 16.2, 4.9 Hz, 1 H), 2.27 (dt, J = 7.0, 2.4 Hz, 1 H), 2.12 (ddt, J = 14.0, 2.4, 1.0 Hz, 1 H), 1.92 (ddd, J = 16.2, 2.3, 1.4 Hz, 1 H), 1.88 (ddd, J = 14.0, 7.0, 1.4 Hz, 1 H), 1.31 (s, 3 H), 1.27 (d, J = 7.6 Hz, 3 H), 1.18 (t, J = 7.0 Hz, 3 H), 1.01 (t, J = 7.2 Hz, 3 H), 0.93 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 174.1, 157.6, 92.8, 79.4, 62.1, 60.0, 46.0, 42.3, 36.9, 34.9, 33.7, 28.9, 27.8, 19.3, 18.2, 14.8, 14.2; EI-HRMS *m*/*z* calcd for $C_{17}H_{28}O_4$ [M^+] 296.1988, found 296.2000.

2-Ethoxy-7-*endo*-(2′-hydroxy-2′-propyl)-9-hydroxy-1,5,8-*exo*-trimethylbicyclo[3.3.1]non-2-ene (8). THF (2.0 mL) was added to anhydrous $CeCl_3$ (256.3 mg, 1.04 mmol), and the mixture was stirred at room temperature for 11 h. To the mixture at −78 °C was added MeLi (1.20 M in Et_2O, 0.90 mL, 1.08 mmol) and stirring was continued at the same temperature for 1.5 h. A solution of **7** (34.4 mg, 0.12 mmol) in THF (1.0 mL) was added to the reaction mixture. After the resulting mixture was stirred at −78 °C to room temperature for 7 h, the reaction was quenched with satd NH_4Cl and extracted with EtOAc. The combined organic layer was washed with H_2O and brine, dried over Na_2SO_4, and evaporated. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc 3:1) to give **8** (21.6 mg, 74%) as a white solid: mp 116−119 °C; IR (thin film) 3475, 3348, 2974, 2933, 2881, 1705, 1643, 1454, 1370, 1264, 1215, 1174, 1060 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 4.19 (dd, J = 5.9, 1.7 Hz, 1 H), 3.48−3.35 (m, 2 H), 2.99 (d, J = 4.3 Hz, 1 H), 2.11 (dq, J = 7.5, 7.0 Hz, 1 H), 1.89 (dt, J = 12.0, 7.5 Hz, 1 H), 1.83 (dd, J = 15.6, 1.7 Hz, 1 H), 1.70 (d, J = 15.6, 5.9 Hz, 1 H), 1.52 (dd, J = 14.1, 7.5 Hz, 1 H), 1.46 (d, J = 7.0 Hz, 3 H), 1.41 (dd, J = 14.1, 12.0 Hz, 1 H), 1.38 (s, 3 H), 1.11 (s, 3 H), 1.09 (s, 3 H), 1.08 (t, J = 7.0 Hz, 3 H), 0.99 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 161.6, 90.8, 81.9, 62.4, 48.8, 43.8, 41.2, 34.8, 34.1, 33.3, 29.8, 26.9, 26.7, 21.9, 21.5, 20.0, 14.7; EI-HRMS *m*/*z* calcd for $C_{17}H_{30}O_3$ [M^+] 282.2195, found 282.2204. Anal. Calcd for $C_{17}H_{30}O_3$: C, 72.30; H, 10.71. Found: C, 72.37; H, 10.59.

4-Ethoxy-7-*endo*-(2′-hydroxy-2′-propyl)-9-hydroxy-1,5,6-*exo*-trimethylbicyclo[3.3.1]non-3-en-2-one (9). To a solution of **8** (51.4 mg, 0.18 mmol) in CH_2Cl_2 (1.8 mL) at 0 °C were added $Pd(OH)_2$/C (20 wt % Pd on C, 6.39 mg, 0.91 mmol), Cs_2CO_3 (296.7 mg, 0.91 mmol), and *tert*-butyl hydroperoxide (70 wt % in H_2O, 0.12 mL, 0.91 mmol). The resulting mixture was vigorously stirred at 0 °C under an oxygen atmosphere. After 1.5 days, additional $Pd(OH)_2$/C (20 wt % Pd on C, 6.45 mg, 0.93 mmol) was added, and the mixture was stirred for an additional 1.5 days under the same conditions. The reaction was quenched with satd NH_4Cl and the mixture was extracted with CH_2Cl_2. The combined organic layer was washed with H_2O and brine, dried over Na_2SO_4, and evaporated. The resulting residue was purified by recrystallization from MeOH to give **9** (31.4 mg, 58%) as a white solid: mp 182−183 °C; IR (thin film) 3326, 3267, 2986, 2968, 2936, 2887, 2473, 2429, 1627, 1598,

(26) When DMSO was used as a solvent, the stench like Me_2S occurred and a large amount of concd HCl and long reaction time were required. In the ^1H NMR of the crude product, which was obtained from the reaction in toluene, some complicated signals were observed in the aromatic region.

1464, 1375, 1241, 1227, 1167, 1067 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 5.16 (s, 1 H), 3.96−3.82 (m, 2 H), 3.42 (s, 1 H), 1.92 (ddd, J = 11.0, 6.6, 5.2 Hz, 1 H), 1.83 (dq, J = 7.0, 6.2 Hz, 1 H), 1.66 (dd, J = 15.2, 11.0 Hz, 1 H), 1.40 (dd, J = 15.2, 6.6 Hz, 1 H), 1.37 (t, J = 7.1 Hz, 3 H), 1.27 (s, 3 H), 1.25 (d, J = 7.0 Hz, 3 H), 1.12 (s, 3 H), 1.02 (s, 3 H), 0.99 (s, 3 H); ^{13}C NMR (125 MHz, CD_3OD) δ 206.3, 184.0, 101.1, 78.4, 74.7, 66.1, 50.1, 46.6, 45.2, 32.5, 31.2, 28.3, 26.4, 22.6, 21.4, 20.6, 14.4; EI-HRMS *m/z* calcd for $C_{17}H_{28}O_4$ [M^+] 296.1988, found 296.2005. Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 69.16; H, 9.37.

4-Ethoxy-7-*endo*-(2′-hydroxy-2′-propyl)-1,5,6-*exo*-trimethylbicyclo[3.3.1]non-3-ene-2,9-dione (13). To a solution of CrO_3 (159.1 mg, 1.59 mmol) in CH_2Cl_2 (0.7 mL) at −20 °C was added 3,5-dimethylpyrazole (3,5-DMP) (153.4 mg, 1.60 mmol). After the reaction mixture was stirred for 20 min, a solution of **9** (47.1 mg, 0.16 mmol) in CH_2Cl_2 (0.8 mL) was added, and stirring was continued at −20 °C for 2 h. The mixture was then diluted with Et_2O and passed through a pad of Celite. The filtrate was washed with 1 M HCl, H_2O, and brine, dried over Na_2SO_4, and evaporated. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc 1:1) to provide **13** (49.9 mg) as a yellow oil with a small quantity of impurities. The product was used for the next reaction without further purification: IR (thin film) 3534, 2984, 2933, 2895, 1719, 1666, 1597, 1478, 1454, 1372, 1249, 1218, 1162, 1024 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 5.39 (s, 1 H), 4.07−4.01 (m, 2 H), 2.62 (dq, J = 7.1, 6.9 Hz, 1 H), 2.46 (dd, J = 14.6, 11.7 Hz, 1 H), 1.92 (dd, J = 14.6, 7.7 Hz, 1 H), 1.52 (ddd, J = 11.7, 7.7, 7.1 Hz, 1 H), 1.41 (t, J = 7.0 Hz, 3 H), 1.18 (s, 3 H), 1.15 (s, 3 H), 1.13 (s, 3 H), 1.12 (s, 3 H), 1.02 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, CD_3OD) δ 211.5, 199.3, 182.0, 100.2, 73.4, 67.1, 59.2, 55.0, 50.2, 44.1, 41.7, 28.7, 26.3, 20.7, 16.8, 16.1, 14.3; EI-HRMS *m/z* calcd for $C_{17}H_{26}O_4$ [M^+] 294.1831, found 294.1830. Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.14; H, 8.83.

4-Ethoxy-7-*endo*-(2′-trimethylsilyloxy-2′-propyl)-1,5,6-*exo*-trimethylbicyclo[3.3.1]non-3-ene-2,9-dione (17). To a solution of **13** (51.7 mg, 0.18 mmol) in DMF (1.7 mL) at room temperature were added imidazole (108.3 mg, 1.59 mmol) and TMSCl (70.0 μL, 0.55 mmol). After the mixture was stirred at room temperature for 2 h, the reaction was quenched with H_2O, and the mixture was extracted with Et_2O. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc 1:1) to give **17** (54.8 mg, 85% from **9**) as a white solid: mp 51−52 °C; IR (thin film) 2976, 2931, 1727, 1676, 1591, 1460, 1378, 1250, 1218, 1250, 1161 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 5.38 (s, 1 H), 4.09−3.97 (m, 2 H), 2.62 (quin, J = 7.0 Hz, 1 H), 2.51 (dd, J = 14.5, 12.2 Hz, 1 H), 1.89 (dd, J = 14.5, 7.5 Hz, 1 H), 1.46 (ddd, J = 12.2, 7.3, 7.0 Hz, 1 H), 1.41 (t, J = 7.0 Hz, 3 H), 1.21 (s, 3 H), 1.17 (s, 6 H), 1.15 (s, 3 H), 0.99 (d, J = 7.0 Hz, 3 H), 0.11 (s, 9 H); ^{13}C NMR (125 MHz, CD_3OD) δ 211.6, 199.4, 182.0, 99.9, 77.2, 67.1, 59.1, 55.1, 51.1, 44.1, 41.2, 29.7, 27.3, 20.9, 17.0, 16.1, 14.4, 2.6 (×3); EI-HRMS *m/z* calcd for $C_{20}H_{34}O_4Si$ [M^+] 366.2266, found 366.2206. Anal. Calcd for $C_{20}H_{34}O_4Si$: C, 65.53; H, 9.35. Found: C, 65.41; H, 9.30.

3-Benzoyl-4-ethoxy-7-*endo*-(2′-hydroxy-2′-propyl)-1,5,6-*exo*-trimethylbicyclo[3.3.1]non-3-ene-2,9-dione (2). To a solution of **17** (40.3 mg, 0.11 mmol) in THF (1.1 mL) at −78 °C was added lithium 2,2,6,6-tetramethylpiperidide (LTMP) (0.50 M in THF, 0.50 mL, 0.25 mmol), prepared from *n*-BuLi and 2,2,6,6-tetramethylpiperidine in THF at −78 °C. After the reaction mixture was stirred for 30 min, a solution of benzoyl chloride (40 μL, 0.35 mmol) in THF (1.1 mL) was added to the mixture at −78 °C. After the mixture was stirred at −78 °C for 2.5 h, the reaction was quenched with satd NH_4Cl. The mixture was extracted with CH_2Cl_2. The combined organic layer was washed with H_2O and brine, dried over Na_2SO_4, and evaporated. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc 2:1) to give **2** (44.5 mg, 86%) as a yellow oil: IR (thin film) 3521, 2981, 2937, 1731, 1708, 1673, 1659, 1574, 1450, 1373, 1314, 1294, 1237, 1171, 1015 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 7.91−7.88 (m, 2 H), 7.64−7.59 (m, 1 H), 7.52−7.47 (m, 2 H), 3.94−3.84 (m, 2 H), 2.95 (dd, J = 14.6, 12.5 Hz, 1 H), 2.81 (dq, J = 7.4, 6.9 Hz, 1 H), 2.01 (dd, J = 14.6, 7.4 Hz, 1 H), 1.55 (dt, J = 12.5, 7.4 Hz, 1 H), 1.31 (s, 3 H), 1.26 (t, J = 6.9 Hz, 3 H), 1.24 (s, 3 H), 1.23 (s, 3 H), 1.15 (s, 3 H), 1.05 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, CD_3OD) δ 210.2, 197.8, 196.8, 180.5, 139.3, 135.0, 130.2 (×2), 130.0 (×2), 127.6, 73.1, 71.7, 60.0, 57.0, 50.0, 43.5, 41.8, 29.0, 27.1, 20.5, 17.2, 16.0, 15.3; EI-HRMS *m/z* calcd for $C_{24}H_{30}O_5$ [M^+] 398.2093, found 398.2089.

3-Benzoyl-1,5,6-*exo*-10,10-pentamethyltricyclo[3.3.1.1^{3,7}]deca-2,4,9-trione (1). A solution of TfOH (0.1 M in CH_2Cl_2, 0.63 mL, 0.063 mmol) in CH_2Cl_2 was added to **2** (29.6 mg, 63.0 μmol), and the reaction mixture was refluxed for 5.5 h. After the reaction mixture was cooled to room temperature, the reaction was quenched with satd K_2CO_3. The mixture was extracted with CH_2Cl_2. The combined organic layer was washed with H_2O and brine, dried over Na_2SO_4, and evaporated. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc 5:1) to give **1** (13.2 mg, 59%) as a white solid: mp 240−241 °C; IR (thin film) 2985, 2936, 1741, 1701, 1596, 1455, 1442, 1393, 1375, 1270, 1237, 1163, 1149, 1018, 1001 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.44−7.40 (m, 1 H), 7.31−7.27 (m, 2 H), 7.17−7.14 (m, 2 H), 2.92−2.86 (m, 1 H), 2.53 (dt, J = 13.8, 2.7 Hz, 1 H), 2.47 (dd, J = 13.8, 2.7 Hz, 1 H), 1.58 (q, J = 2.7 Hz, 1 H), 1.49 (s, 3 H), 1.48 (s, 3 H), 1.30 (s, 3 H), 1.27 (s, 3 H), 1.08 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.7, 202.5, 202.4, 193.1, 135.0, 132.4, 128.8 (x2), 128.1 (x2), 81.6, 69.1, 65.0, 55.3, 49.1, 49.0, 41.8, 23.7, 23.1, 15.0, 14.8, 12.9; EI-HRMS *m/z* calcd for $C_{22}H_{24}O_4$ [M^+] 352.1675, found 352.1689. Anal. Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 74.92; H, 6.60.

Acknowledgment. This work was partly supported by a Grant-in-Aid for Scientific Research on Priority Areas (No. 17035055) from the Ministry of Education, Culture, Sports, Science and Technology (MEXT). NMR, MS, and elemental analysis measurements were made at the Natural Science Center for Basic Research and Development (N-BARD), Hiroshima University. We express our gratitude toward Dr. Yoshikazu Hiraga for NMR measurements at the Hiroshima Prefectural Institute of Science and Technology. We thank Dr. Satoshi Kojima for crystallographic analysis and suggestions. We thank Dr. Manabu Abe for his helpful discussions.

Supporting Information Available: General experimental methods, characterization data of γ-**3**, **11**, **12**, and **14**−**16**, copies of NMR spectra of new compounds, and X-ray crystallographic files (CIF) for compounds **8** and **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO801595Y