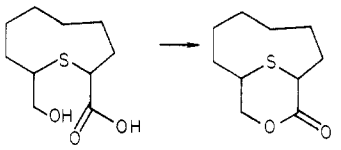
NaI–CH_3CN) followed by treatment with 2,6-lutidine (CH_3CN, reflux) affords the sulfur-bridged undecanolide **14**,[7] in 30% yield from **10** (iodide formation, cyclization to bicyclic salt **12**, rearrangement of ylide **13**). Although the yield is modest, it is nevertheless significant that bicyclic ylide **13** is capable of normal ring expansion. No products of competing Stevens rearrangement have been detected.

A closely parallel series of experiments has been performed with the sulfide lactone **17**, having one fewer methylene group in the side chain than in **10**. The acyclic precursor **16** can be prepared by the usual alkylation sequence starting from the iodide **15** (Scheme III). In this series, the yield of ring-expansion product from tetrahydropyranyl ether **17** to the sulfur-bridged decanolide **21**[8] is 33%. As in simpler, monocyclic systems, rearrangement via an ylide which incorporates a five-membered sulfur-containing ring leads to a ring-expansion product having a cis double bond.[1b] No isomeric products have been found.

The low material recovery from both of the bicyclic ylide rearrangements is probably due to the high reactivity of bridged sulfide lactones. This complication is also apparent in attempts to lactonize the monocyclic hydroxy acid **22**, available from **3** by saponification and reduction



22 **23**

with diimide. The Corey–Mukaiyama lactonization procedure[9] gives the lactone **23** under conditions of high dilution, which is identical with material prepared from **14** by diimide reduction, but the yield is only 56% after much effort. All of the classical lactonization procedures examined, including DCC/DMAP, afford only intractable materials assumed to be polyesters. Likewise, exposure of **23** to acid catalysts results in rapid degradation. The high reactivity of sulfur-bridged medium-ring lactones **14**, **21**, and **23** can be attributed to a combination of transannular effects and the inherent sensitivity of the six-membered sulfide lactone mentioned previously in connection with **10**.

We have shown that ring expansion can be achieved via monocyclic and bicyclic ylides originating from intramolecular S-alkylation. The technique has been used to prepare labile sulfur-bridged lactones **14** and **21**.[10] Subsequent publications will describe related applications for synthesis of medium-ring carbocycles.

Acknowledgment. This work was supported by a grant from the National Science Foundation (CHE-8113026).

(6) Hassner, A.; Alexanian, V. *Tetrahedron Lett.* **1978**, 4475.

(7) Characterization of **14**[10]: mp 87–88 °C (recrystallized from ether/hexane); IR ($CDCl_3$) 1712 (s), 1440 (m), 975 (m), 962 (m) cm^{-1}; NMR ($CDCl_3$) δ 5.8 (1 H, ddd, J = 16, 11, 6 Hz), 5.15 (1 H, ddd, J = 16, 11, 4 Hz), 4.85 (1 H, dd, J = 10.5, 2 Hz), 4.44 (1 H, dd, J = 10.5, 2 Hz), 3.92 (1 H, dd, J = 4.5, 2.5 Hz), 3.25 (1 H, d, J = 12.5 Hz), 2.65 (1 H, d, J = 12 Hz), 2.46 (1 H, m), 1.76 (6 H, m).

(8) Characterization of **21**:[10] oil after preparative TLC, silica gel; IR ($CHCl_3$) 1735, 1655, 1455, 915 cm^{-1}; NMR ($CDCl_3$) δ 6.04 (dt, J = 9.5, 7.6 Hz, 1 H), 5.59 (dt, J = 9.5, 7.9 Hz, 1 H), 4.62 (ABX, J_{AB} = 12.3 Hz, J_{AX} = 9.4 Hz, J_{BX} = 7.7 Hz, 2 H), 3.67 (t, J = 5.7 Hz, 1 H), 1.90 (m, 2 H).

(9) (a) Corey, E. J.; Nicolau, K. C. *J. Am. Chem. Soc.* **1974**, *96*, 5614. (b) Mukaiyama, T.; Matsueda, R.; Suzuki, M. *Tetrahedron Lett.* **1970**, 1901. (c) Mukaiyama, T.; Matsueda, R.; Marayma, H. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 1271. (d) Corey, E. J.; Brunelle, D. J. *Tetrahedron* Lett. **1976**, 3409.

(10) Correct high-resolution m/e values were obtained for all sulfur heterocycles.

Registry No. **1**, 79815-75-1; **2**, 79827-16-0; **3**, 79815-76-2; **4**, 79815-77-3; **5**, 79815-78-4; **6**, 79815-79-5; **7**, 79815-80-8; **8**, 79815-81-9; **9**, 79815-82-0; **10**, 79815-83-1; **11**, 79815-84-2; **12**, 79815-85-3; **13**, 79815-86-4; **14**, 79815-87-5; **15**, 79815-88-6; **16**, 79815-89-7; **17**, 79815-90-0; **18**, 79815-91-1; **19**, 79815-92-2; **20**, 79815-93-3; **21**, 79815-94-4; **22**, 79815-95-5; **23**, 79815-96-6.

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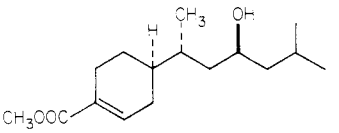
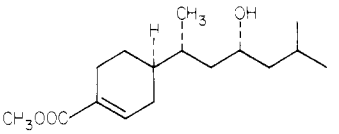
A Synthesis of the Juvabiols

Summary: Synthetic studies utilizing condensations of α-sulfinyl carbanions, have provided (+)-juvabiol and its analogous diastereoisomers.

Sir: Throughout the last several years, new synthetic methodologies have been developed and illustrated by preparation of (±)-juvabione and (±)-epijuvabione.[1] The wood of balsam fir (*Abies balsamea* (L.) Mill.) also contains a mixture of alcohols identified as (+)-juvabiol (**1**) and (+)-isojuvabiol (**2**), whereas alpine fir produces (+)-juvabiol (**1**) and (+)-epijuvabiol (**3**).[2] All of these constituents demonstrate insect juvenile hormone activity. The remaining isomer, (+)-isoepijuvabiol (**4**), is recognized as a reduction product from (+)-epijuvabione. These alcohols have identical ^1H NMR, IR, mass spectra, and chromatographic properties, complicating the analysis of unresolved mixtures. However, ^{13}C NMR information is advantageous for recognition of each of the diastereoisomers.[2a]



1



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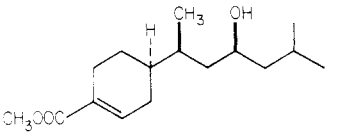

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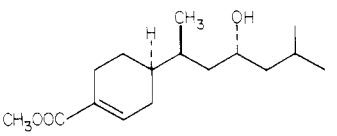

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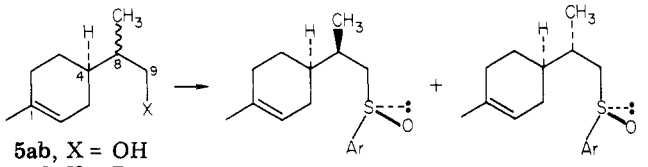
(1) For some leading references, see the following: Evans, D. A.; Nelson, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 774. Trost, B. M.; Tamaru, Y. *Ibid.* **1977**, *99*, 3101. Ficini, J.; d'Angelo, J.; Noire, J. *Ibid.* **1974**, *96*, 1213.

(2) (a) Manville, J. F.; Kriz, C. D. *Can. J. Chem.* **1977**, *55*, *2547*. (b) Manville, J. F. *Ibid.* **1976**, *54*, 2365.

0022-3263/81/1946-5452$01.25/0

Recently we have explored condensations of asymmetric α-lithiosulfinyl carbanions with aldehydes to construct 1,3 stereochemical relationships in acyclic systems.[3] Owing to the difficulties of providing unambiguous 1,3 stereochemical assignments in related systems, supportive evidence was sought by application of our methodology to afford a synthesis of individual juvabiol diastereomers 1–4.

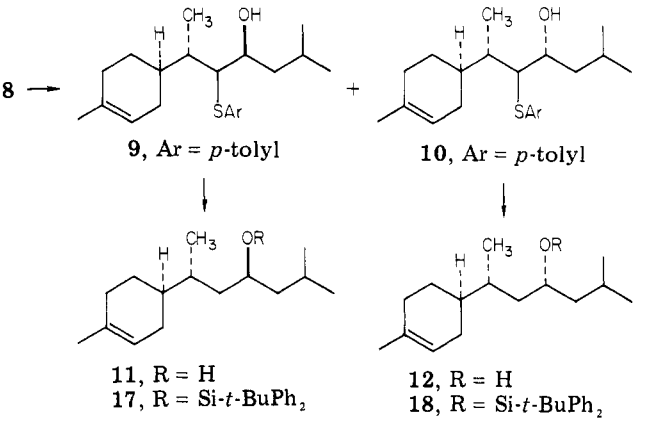
Hydroboration of *R*-(+)-limonene with disiamylborane, as previously described, afforded a 3:2 mixture of *p*-menth-1-en-9-ols **5a** (4*R*,8*R*) and **5b** (4*R*,8*S*).[4] Transformation to the corresponding bromides **6** proceeded in two steps (68% overall), using methanesulfonyl chloride (1.1 equiv, Et_3N, CH_2Cl_2, 0 °C) followed by displacement (LiBr, 2 equiv, dry THF, 60 °C, 16 h). Conversion of purified bromides [bp 68–72 °C (1.5 mm)] to the corresponding Grignard reagent was achieved under conditions to minimize facile formation of dimer resulting from Wurtz coupling,[5] and reaction with (–)-menthyl *p*-toluenesulfinate at 0 °C gave diastereomeric sulfoxides **7** and **8** (73%), which were easily separated by column chromatography (silica gel).[6]



5ab, X = OH
6, X = Br

7, Ar = *p*-tolyl **8**, Ar = *p*-tolyl

Deprotonation of the minor sulfoxide **8** (mp 67–69 °C; $[\alpha]^{23}_D$ +210.8° (*c* 1.08, EtOH), using lithium diisopropylamide (THF, –90 °C, 1 min, argon), and addition of 3-methylbutanal provided instantaneous formation of two sulfoxide adducts in a 3:2 ratio (87%). Direct reduction of the mixture with acetyl bromide (2.1 equiv, 0 °C, 10 min) in methylene chloride solution containing 2-methyl-1-butene (15 equiv) afforded the corresponding sulfides **9** and **10** (94%), which were readily separable (silica gel). Although magnetic resonance studies of these samples displayed distinctive chemical shifts and coupling patterns, stereochemical assignments along the acyclic carbon chain were not convincingly feasible. Conversions to the natural products established the identity of 1,3 stereochemical relationships at C-8 and C-10. Thus, reduction of each sulfide **9** and **10** with Raney nickel in ethanol (0 °C, 30 min) gave the 4*R*,8*R*,10*R* alcohol **11**, and the 4*R*,8*R*,10*S* isomer **12**, respectively (65%).[7]

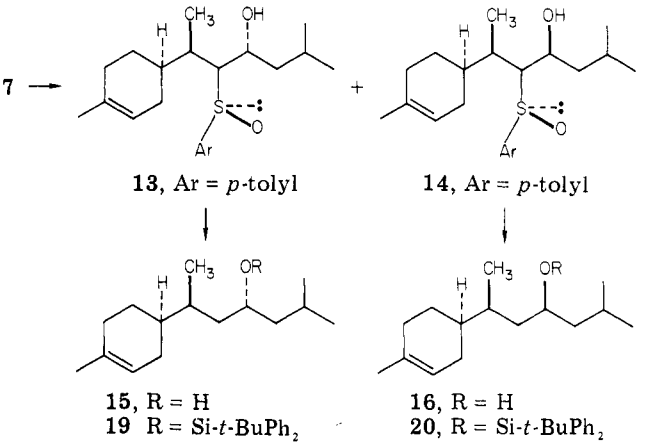


9, Ar = *p*-tolyl **10**, Ar = *p*-tolyl

11, R = H
17, R = Si-*t*-$BuPh_2$

12, R = H
18, R = Si-*t*-$BuPh_2$

In similar fashion, the α-lithiosulfinyl carbanion derived from diastereomeric sulfoxide **7** (mp 58–60 °C: $[\alpha]^{24}_D$ +136.4° (*c* 1.66, EtOH)) was condensed with 3-methylbutanal, affording a 3:2 ratio of two major sulfoxide adducts **13** and **14** in 78% isolated yield after silica gel chromatography. The reaction additionally produced a small amount (10%) of the other two possible diastereoisomers, isolated in more polar fractions; however, these sulfoxide adducts were not cleanly separated. Individual reductions of the major sulfoxides **13** (mp 70–72 °C) and **14** (mp 93–95 °C; Raney nickel, EtOH, 0 °C) gave the pure 4*R*,8*S*,10*R* alcohol **15** and the 4*R*,8*S*,10*S* isomer **16**, respectively (67%).[7]



13, Ar = *p*-tolyl **14**, Ar = *p*-tolyl

15, R = H
19 R = Si-*t*-$BuPh_2$

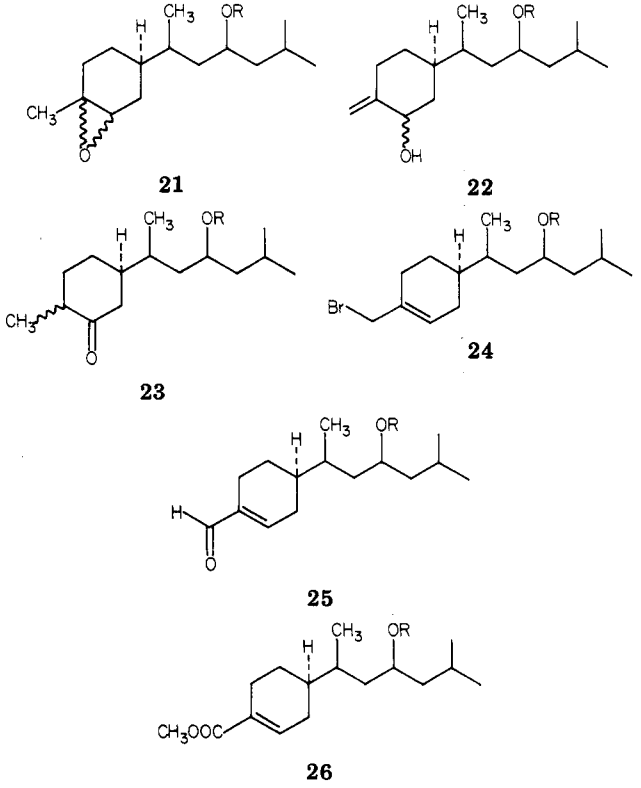
16, R = H
20, R = Si-*t*-$BuPh_2$

All four diastereomeric alcohols **11**, **12**, and **15**, **16** were more conveniently characterized as their *tert*-butyldiphenylsilyl ethers **17**, **18**, **19**, and **20**,[8] since ^1H NMR spectra clearly distinguished epimeric ethers **17** from **18** and, likewise, **19** from **20**,[7] and transformation of the vinylic methyl group (C-7) into a methyl ester was accomplished by the following sequence. Treatment with *m*-chloroperbenzoic acid (CH_2Cl_2, 0 °C, 30 min) gave a mixture of epoxides **21** (90%), and ring opening with diethylaluminum 2,2,6,6-tetramethylpiperidide (DATMP) in benzene (0 °C, 3 h) afforded the desired allylic alcohols **22** (92%).[9] Use of lithium diethylamide in ether, or in the presence of HMPA,[10] produced cyclohexanone derivatives **23** (30%) as well as small amounts of alternative allylic alcohols.

Conversion to bromides **24** was affected with phosphorous tribromide (THF, 0 °C, 50–65% yields), and direct oxidation to the α,β-unsaturated aldehydes **25** was most cleanly accomplished in 88% yield, using 2-nitropropane and potassium hydroxide in aqueous tetrahydrofuran–2-

(3) Williams, D. R.; Phillips, J. G. *J. Org. Chem.* **1981**, *46*, 4101.
(4) Pawson, P. A.; Cheung, H.-C.; Gurbaxani, S.; Saucy, G. *J. Am. Chem. Soc.* **1970**, *92*, 336.
(5) A flask, containing dry ether and a small amount of Mg turnings, was fitted with a glass column packed with Mg turnings and equipped with a condenser and dropping funnel. Solvent was heated to reflux, and an ethereal solution of bromide was slowly added dropwise onto the column under argon.
(6) Mislow, K.; Green, M. M.; Laur, P.; Melillo, J. T.; Simmons, T.; Ternay, A. L. *J. Am. Chem. Soc.* **1965**, *87*, 1958.
(7) All compounds showed ^1H NMR, ^{13}C NMR, IR, and mass spectra consistent with assigned structures. Partial characterization for selected intermediates is as follows. NMR spectra were recorded on 220- and 270-MHz instruments in $CDCl_3$ (0.1% Me_4Si). **11**: ^{13}C NMR δ 16.8, 22.0, 23.4, 23.7, 24.7, 25.0, 29.5, 31.0, 34.0, 38.4, 42.9, 47.0, 68.8, 121.1, 134.0. **12**: ^{13}C NMR δ 16.1, 22.3, 23.38, 23.42, 24.8, 25.7, 29.2, 30.9, 33.3, 39.4, 42.5, 48.0, 67.9, 121.0, 134.0. **15**: ^{13}C NMR δ 16.4, 22.1, 23.5, 23.7, 24.7, 27.0, 27.4, 31.1, 34.1, 37.9, 43.1, 47.1, 68.5, 120.9, 134.1. **16**: ^{13}C NMR δ 15.7, 22.3, 23.4, 23.5, 24.8, 26.9, 27.9, 31.0, 33.4, 39.3, 42.8, 48.0, 67.8, 121.0, 134.0. **17**: $[\alpha]^{23}_D$ +66.6° (*c* 1.16, EtOH). **18**: $[\alpha]^{23}_D$ +16.6° (*c* 1.43, EtOH). **19**: $[\alpha]^{23}_D$ –12° (*c* 0.94, EtOH). **20**: $[\alpha]^{23}_D$ +27.9° (*c* 1.3, EtOH). The diastereomeric silyl ethers **17** through **26** displayed highly characteristic ^1H chemical shift patterns for the isopropyl moiety (C-13, C-14) and the methyl at C-8 (C-15). For example, compounds **17** and **19** showed δ 0.70 (t, *J* = 8 Hz, 6 H), 0.52 (d, *J* = 7 Hz, 3 H), whereas **18** and **20** gave δ 0.68 (d, *J* = 7 Hz, 3 H), 0.57 (t, *J* = 8 Hz, 6 H). Proton spectra of isomeric alcohols were essentially superimposable.
(8) Hanession, S.; Lavallee, P. *Can. J. Chem.* **1977**, *55*, 562.
(9) Yasuda, A.; Tanaka, S.; Oshimi, K.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 6513.
(10) Apparu, M.; Barrelle, M. *Tetrahedron* **1978**, *34*, 1541.

propanol (1:2:2 by volume) by dropwise addition of the bromides in THF at 22 °C followed by warming (40–50 °C, 1 h).[11] Finally oxidation to the methyl esters **26** was achieved with manganese dioxide in the presence of sodium cyanide–acetic acid (22 °C, 12 h, 87%),[12] and desilylation with tetra-*n*-butylammonium fluoride (dry THF at reflux, 7 h, 88%) afforded the natural products.[13]



21 **22** **23** **24** **25** **26**

Thus, the major adducts from condensation of sulfoxides **7** and **8** each display the 1,3-substituents in an anti relationship (as illustrated in the extended conformations). Sulfide **9** led to synthesis of (+)-juvabiol (**1**) and minor adduct **10** gave (+)-isojuvabiol (**2**), whereas (+)-epijuvabiol (**3**) was obtained from sulfoxide **14** and (+)-isoepijuvabiol (**4**) from **13**. We anticipate the feasibility of significant improvement of stereoselectivity in α-sulfinyl carbanion condensations. Further studies are underway.

Acknowledgment. We are most grateful to John F. Manville, Centre de Recherche Forestierte du Pacifique, Victoria, Canada, for samples of (+)-juvabione, (+)-juvabiol, and (+)-isojuvabiol. Acknowledgement is made to donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(11) Montavon, M.; Lindlar, H.; Marbet, R.; Rüegg, R.; Ryser, G.; Saucy, G.; Zeller, P.; Isler, O. *Helv. Chim. Acta* **1957**, *40*, 1250.

(12) Corey, E. J.; Gilman, N. W.; Ganem, B. E. *J. Am. Chem. Soc.* **1968**, *90*, 5616.

(13) The synthetic substances **1** and **2** were identical in all respects, including ^{13}C NMR, by comparison to samples of (+)-juvabiol and (+)-isojuvabiol. Data for compounds **3** and **4** were identical with spectroscopic information published for (+)-epijuvabiol and (+)-isoepijuvabiol, respectively (see ref 2). Juvabiol (**1**): $[\alpha]^{23}_D$ +50.0° (*c* 0.15, EtOH). Isojuvabiol (**2**): $[\alpha]^{23}_D$ +41.5° (*c* 0.137, EtOH). Epijuvabiol (**3**): $[\alpha]^{23}_D$ +24.0° (*c* 0.25, EtOH). Isoepijuvabiol (**4**): $[\alpha]^{23}_D$ +45.6° (*c* 0.16, EtOH).

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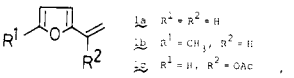
High-Pressure Diels–Alder Reactions of Vinylfurans[1]

Summary: The Diels–Alder reactions of vinylfurans with dimethyl acetylenedicarboxylate and dimethyl maleate very nicely proceed under the conditions of 15 kbar and 30 °C in dichloromethane.

Sir: 2-Vinylfuran has two alternative diene systems, and it is known that the conjugated system involving the exocyclic double bond is more reactive than the furan ring system itself (Scheme I).[2] Under conventional conditions, however, the reported yields of the adducts are extremely poor even after long reaction times.[3,4]

One of the most powerful features of high-pressure reactions is to highly accelerate the rate of reactions having a large negative activation volume under thermally mild conditions (usually at *room temperature*).[5] So we have investigated the Diels–Alder reactions of vinylfurans (**1**)



with dimethyl acetylenedicarboxylate (**2**) and dimethyl maleate (**3**) at 15 kbar and 30 °C in dichloromethane and found that the yields are considerably improved.[6] The results are summarized in Table I.[7]

In all of the reactions with **2**, benzofurans, which would be formed by the aromatization of the intermediate cycloadducts, were obtained as main products without being accompanied by 7-oxabicyclo[2.2.1]hepta-2,5-diene deriv-

(1) High-Pressure Organic Chemistry. 6. Part 4: Kotsuki, H.; Nishizawa, H. *Heterocycles* **1981**, *16*, 1287. Part 5: Kotsuki, H.; Nishizawa, H.; Ochi, M.; Matsuoka, K. *Bull. Chem. Soc. Jpn.*, in press.

(2) Acheson, R. M. "An Introduction to the Chemistry of Heterocyclic Compounds", 3rd ed.; Wiley: New York, 1976; p 136.

(3) Davidson, W. J.; Elix, J. A. *Aust. J. Chem.* **1973**, *26*, 1059 and references cited therein. For instance, the reported yield of the adduct **4** from **1a** and **2** is 5% in the reaction at 80 °C for 24 h or at room temperature for 4 days.

(4) For our intramolecular approach to this chemistry, see: Kotsuki, H.; Kawamura, A.; Ochi, M.; Tokoroyama, T. *Chem. Lett.* **1981**, 917.

(5) For recent reviews, see: Asano, T.; le Noble, W. J. *Chem. Rev.* **1978**, *78*, 407. Osugi, J., et al. *Kagaku Sosetsu* **1979**, *No. 22*, 157. Matsumoto, K.; Uchida, T.; Acheson, R. M. *Heterocycles* **1981**, *16*, 1367. Isaacs, N. S. "Liquid Phase High Pressure Chemistry"; Wiley: New York, 1981.

(6) For a description of our high-pressure apparatus and general procedure for high-pressure reactions, see: Kotsuki, H.; Nishizawa, H.; Kitagawa, S.; Ochi, M.; Yamasaki, N.; Matsuoka, K.; Tokoroyama, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 544.

(7) Physical and spectral data are as follows. **4**: mp 66–67 °C (lit.[3] mp 64–66 °C). **5**: mp 71–73 °C; ν_{max} ($CHCl_3$) 1720, 1600 cm^{-1}; λ_{max} (EtOH) 229 nm (ϵ 19600), 252 (5400), 306 (3100). ^1H NMR ($CDCl_3$) δ 2.45, 3.86, 3.90 (each 3 H, s), 6.58 (1 H, br s), 7.41, 7.58 (each 1 H, d, J = 9 Hz). **6**: mp 85–87 °C; ν_{max} ($CHCl_3$) 1775, 1730 (sh), 1630, 1600 cm^{-1}; λ_{max} (EtOH) 224 nm (ϵ 30900), 258 (7500), 296 (3800); ^1H NMR (CCl_4) δ 2.36, 3.84, 3.87 (each 3 H, s), 7.00 (1 H, d, J = 2 Hz), 7.43 (1 H, s), 7.66 (1 H, d, J = 2 Hz). **7**: mp 89–90 °C; ν_{max} ($CHCl_3$) 1720, 1620, 1545 cm^{-1}; λ_{max} (EtOH) 220 nm (ϵ 27000), 238 (21000), 299 (18000); ^1H NMR (CCl_4) δ 3.77, 3.87 (each 3 H, s), 3.89 (6 H, s), 6.91 (1 H, s), 6.95 (1 H, d, J = 2 Hz), 7.65 (1 H, s), 7.75 (1 H, d, J = 2 Hz). **8** (as a tetrahydro derivative): mp 51–52 °C; ν_{max} ($CHCl_3$) 1740 cm^{-1}, ^1H NMR (CCl_4) δ 0.96 (3 H, t, J = 8 Hz), 1.2–1.9 (4 H, m), 1.74 (2 H, q, J = 8 Hz), 2.81, 3.05 (each 1 H, d, J = 10 Hz), 3.54, 3.56 (each 3 H, s), 4.92 (1 H, d, J = 4 Hz). **9** (X = OOH): mp 92–95 °C; ν_{max} ($CHCl_3$) 3400, 1740, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.44 (1 H, ddd, J = 14, 12.5, 4 Hz), 2.81 (1 H, ddd, J = 14, 3, 2 Hz), 3.17 (1 H, ddd, J = 12.5, 6, 3 Hz), 3.66, 3.72 (each 3 H, s), 4.07 (1 H, d, J = 6 Hz), 5.08 (1 H, dd, J = 4, 2 Hz), 6.40 (1 H, d, J = 2 Hz), 7.37 (1 H, d, J = 2 Hz), 8.26 (1 H, s). **10**: mp 68–72 °C; ν_{max} ($CHCl_3$) 1730, 1665, 1570 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.85 (3 H, dd, J = 3, 1.5 Hz), 2.1–2.9 (4 H, m), 3.51 (1 H, dd, J = 6, 3 Hz), 3.61, 3.69 (each 3 H, s), 4.87 (1 H, m), 5.09 (1 H, ddd, J = 7, 3.5, 1.5 Hz). **12**: oil; ν_{max} (film) 1740, 1440, 1200 cm^{-1}; ^1H NMR(CCl_4) δ 2.08 (3 H, s), 3.26 (1 H, d, J = 10 Hz), 3.7–3.5 (1 H, m), 3.54, 3.56 (each 3 H, s), 5.01 (1 H, m), 5.05, 5.21 (each 1 H, d, J = 2 Hz), 6.41 (1 H, dd, J = 6, 2 Hz), 6.50 (1 H, d, J = 6 Hz). **13**: oil; ν_{max} (film) 1740, 1440, 1200 cm^{-1}; ^1H NMR (CCl_4) δ 2.12 (3 H, s), 2.67, 2.94 (each 1 H, d, J = 9 Hz), 3.52, 3.59 (each 3 H, s), 5.27 (2 H, s), 5.33 (1 H, br s), 6.41 (2 H, s).

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