in mineral oil, 70 mg, 1.7 mmol) in ether (7 mL) at 0 °C. The mixture was heated at reflux for 10 min and then cooled to 0 °C. Aldehyde **17** (247.4 mg, 0.870 mmol) in ether (10 mL) was added dropwise, and the resulting mixture was heated at reflux for 10 min. Water (8 mL) was added at room temperature, and the ether layer was separated and washed (bicarbonate, water, and brine). The combined aqueous layers were extracted with ether, and the combined ether layers were dried ($MgSO_4$) and concentrated to give a crude mixture of the expected *E* and *Z* isomers. Chromatotron purification (15% ether/hexanes) of the crude product afforded an initial set of fractions that contained 253.0 mg (79%) of the desired *E* ester: IR (film) 3090–3030, 2980–2850, 1710 (C=O), 1650 (C=C), 1450, 1365, 1280–1265, 1100–1075, 740, 700 cm^{-1}; ^1H NMR (200 MHz) δ 0.91 (s, 3 H, CCH_3), 0.86–0.97 (m, 1 H, ring CH CH_2CH_2), 1.01–1.10 (dd, J = 8.6 and 4.3 Hz, 1 H, $CHCH$=C), 1.27 (t, J = 7.0 Hz, 3 H, CH_3CH_2), 1.21–1.52 (m, 2 H, CH_2CH_2CH=C), 1.67–2.17 (m, 4 H, ring $CHCH_2CH_2$), 1.84 (d, J = 1.3 Hz, 3 H, CH_3C=CH), 2.26 (br q, J = 7.6 Hz, 2 H, CH_2CH=C), 3.90 (s, 2 H, CH=CCH_2O), 4.16 (q, J = 7.0 Hz, 2 H, CH_2CH_3), 4.42 (s, 2 H, PhCH_2O), 5.85 (br d, J = 4.3 Hz, 1 H, $CHCH$=C), 6.78 (tq, J = 7.6 and 1.3 Hz, 1 H, CH_2CH=C), 7.18–7.36 (m, 5 H, aromatic); ^{13}C NMR (50 MHz) δ 12.24 (CH_3C(R)=), 12.69 (CH_3C), 14.30 (CH_3CH_2), 17.33 (C-4 or C-5), 21.76 and 21.96 (C-1 and C-6), 23.61 (C-4 or C-5), 26.29 (CH_2C-H=), 28.62 (C-7), 41.46 (CCH_2CH_2), 60.26 (CH_3CH_2), 71.32 and 74.72 (CH_2OCH_2), 123.30 (C-2), 127.40 (CH_3C(R)= and *p*-aryl CH), 127.61 and 128.27 (aryl CH), 134.50 (C-3), 138.60 (quaternary aryl), 142.04 (CH_2CH=), 168.04 (CO_2); MS, *m/e* (percent) (no M^+), 260 (2), 186 (6), 159 (8), 158 (10), 146 (6), 141 (10), 133 (8), 128 (6), 119 (20), 115 (9), 105 (10), 99 (7), 95 (7), 92 (10), 91 (100), 79 (10), 77 (8). A second set of fractions contained a mixture of the *E* and *Z* isomers (7 mg, 2%). A third set of fractions contained 33.8 mg (11%) of the *Z* isomer: IR (film) 3090–3030, 2980–2850, 1710 (C=O), 1455, 1375, 1240, 1190, 1145, 1100–1070, 735, 700 cm^{-1}; ^1H NMR (200 MHz) δ 0.90 (s, 3 H, CCH_3), 0.90-0.99 (m, 1 H, ring $CHCH_2CH_2$), 1.03–1.12 (dd, J = 8.6 and 4.3 Hz, 1 H, $CHCH$=C), 1.15–1.50 (m, 2 H, CH_2CH_2CH=C), 1.31 (t, J = 7.2 Hz, 3 H, CH_3CH_2), 1.65–2.20 (m, 4 H, ring $CHCH_2CH_2$), 1.89 (d, J = 1.3 Hz, 3 H, CH_3C=CH), 2.56 (br q, J = 7.6 Hz, 2 H, CH_2CH=C), 3.91 (s, 2 H, CH=CCH_2O), 4.20 (q, J = 7.2 Hz, 2 H, CH_3CH_2), 4.43 (s, 2 H, PhCH_2O), 5.85 (m, 1 H, $CHCH$=C), 5.92 (tq, J = 7.6 and 1.3 Hz, 1 H, CH_2CH=C), 7.22–7.38 (m, 5 H, aromatic); ^{13}C NMR (50 MHz) δ 12.76 (CH_3C), 14.33 (CH_3CH_2), 17.37 (C-4 or C-5), 20.72 (CH_3C(R)=), 21.76 and 21.94 (C-1 and C-6), 23.65 (C-4 or C-5), 27.21 (CH_2CH=), 28.86 (C-7), 42.43 (CCH_2CH_2), 60.04 (CH_3CH_2), 71.29 and 74.84 (CH_2OCH_2), 123.70 (C-2), 126.92 (CH_3C(R)=), 127.45, 127.71, and 128.32 (aryl CH), 134.30 (C-3), 138.63 (quaternary aryl), 142.86 (CH_2CH=), 168.16 (CO_2).

(*E*)-2-Methyl-5-{(1α,6α,7α)-3-[(benzyloxy)methyl]-7-methylbicyclo[4.1.0]hept-2-en-7-yl}-2-penten-1-ol. A solution of DIBAL-H (Aldrich, 1.0 M in hexane, 1.9 mL, 1.9 mmol) was added to a solution of the ester prepared above (236.4 mg, 0.641 mmol) in ether at 0 °C. The mixture was stirred for 1 h at 0 °C. The reaction was quenched by dropwise addition of acid. The organic layer was washed (acid, bicarbonate, and brine), dried ($MgSO_4$), and concentrated to give a clear, colorless oil. Chromatotron purification furnished 192.2 mg (92%) of alcohol: IR (film) 3380 (br, OH), 3090–3030, 2990–2850, 1455, 1070, 735, 700 cm^{-1}; ^1H NMR (200 MHz) δ 0.90 (s, 3 H, CCH_3), 0.85–0.95 (m, 1 H, ring $CHCH_2CH_2$), 1.02–1.09 (dd, J = 8.6 and 4.3 Hz, 1 H, $CHCH$=C), 1.13–1.44 (m, 2 H, CH_2CH_2CH=C), 1.65 (s, 3 H, CH_3C=CH), 1.60–2.05 (m, 4 H, ring $CHCH_2CH_2$), 2.12 (m, 2 H, CH_2CH=C), 2.35 (br s, 1 H, O*H*), 3.90 (s, 2 H, CH=CCH_2O) and 3.92 (s, 2 H, CH=CCH_2O), 4.42 (s, 2 H, PhCH_2O), 5.37 (br t, J = 7.0 Hz, 1 H, CH_2CH=C), 5.86 (br d, J = 4.3 Hz, 1 H, $CHCH$=C), 7.18–7.35 (m, 5 H, aromatic); ^{13}C NMR (50 MHz) δ 12.81 (CH_3C), 13.54 (CH_3C(R)=), 17.39 (C-4 or C-5), 21.72 and 21.89 (C-1 and C-6), 23.62 (C-4 or C-5), 25.11 (CH_2CH=), 28.94 (C-7), 42.59 (CCH_2CH_2), 68.62 (CH_2OH), 71.18 and 74.74 (CH_2-OCH_2), 123.80 (C-2), 125.96 (CH_2CH=), 127.43, 127.68, and 128.27 (aryl CH), 134.09 and 134.44 (C-3 and CH_3C(R)=), 138.46 (quaternary aryl).

(±)-Sirenin, (*E*)-2-Methyl-5-{(1α,6α,7α)-3-(hydroxymethyl)-7-methylbicyclo[4.1.0]hept-2-en-7-yl}-2-penten-1-ol (1). To 10 mL of liquid NH_3 (distilled from a solution of lithium metal in liquid NH_3) was added 5 mg of lithium metal ($^1/_4$-in. wire). The initial blue color slowly disappeared to produce a cloudy white solution.[20] The monobenzyl ether described above (36.8 mg, 0.113 mmol) was introduced as a solution in THF (2 mL). Small pieces of lithium (2-3 mg) were added until the blue color persisted for at least 15 min (total lithium: 17 mg, 2.4 mmol). Solid NH_4Cl was added, the solution was diluted with ether, and the mixture was stirred without a condenser until the NH_3 had evaporated. The ether solution was washed (saturated NH_4Cl and brine), dried ($MgSO_4$), and concentrated. Purification by column chromatography (60% ether/hexanes) gave 24.4 mg (92%) of sirenin (**1**) as a viscous, colorless oil. Microdistillation (0.07 mm/140–145 °C) provided samples for biological analysis. All spectral values were in excellent agreement with those previously reported:[3a,b,g,i,j,o] IR (film) 3340 (br, OH), 2990, 2920, 2860, 1665, 1450, 1385, 1065, 1020–990 (br), 910, 735 cm^{-1}; ^1H NMR (200 MHz) δ 0.87 (s, 3 H, CCH_3), 0.88–0.96 (m, 1 H, ring $CHCH_2CH_2$), 1.00–1.08 (dd, J = 8.5 and 4.3 Hz, 1 H, ring $CHCH$=C), 1.13–1.44 (m, 2 H, CH_2CH_2CH=C), 1.67 (s, 3 H, CH_3C=CH), 1.68–2.05 (m, 6 H, ring CH_2CH_2 and hydroxyls), 2.12 (br q, J = 7.6 Hz, 2 H, CH_2CH=C), 3.98 (s, 2 H, CH_2OH) and 4.00 (s, 2 H, CH_2OH), 5.40 (tq, J = 7.3 and 1.2 Hz, 1 H, CH_2CH=C), 5.84 (br d, J = 4.3 Hz, 1 H, $CHCH$=C); ^{13}C NMR (50 MHz) δ 12.68 (CH_3C) 13.59 (CH_3C(R)=), 17.49 (C-4 or C-5), 21.63 and 21.68 (C-1 and C-6), 23.40 (C-4 or C-5), 25.13 (CH_2CH=), 28.84 (C-7), 42.56 (CCH_2-CH_2), 67.40 and 68.84 (two CH_2OH), 121.31 (C-2), 126.24 (CH_2CH=), 134.42 and 137.12 (two C=CH); MS, *m/e* (percent) (no M^+), 218 (4), 200 (5), 187 (8), 148 (47), 135 (47), 133 (34), 131 (47), 119 (44), 117 (23), 109 (26), 107 (48), 105 (67), 93 (44), 91 (100), 81 (42), 79 (85), 77 (47), 67 (61); accurate mass calcd for $C_{15}H_{22}O$ ($M^+ - H_2O$) 218.16706, found 218.16764; accurate mass calcd for $C_{15}H_{20}$ ($M^+ - 2H_2O$) 200.15650, found 200.15685.

Acknowledgment. We thank the Robert A. Welch Foundation (Grant A-442) for support of this research. Initial studies were funded by a NIH Biomedical Sciences Support Grant through Texas A & M University.

(20) Although the ammonia had been redistilled and all normal measures for keeping the reaction free of water had been taken, it is obvious that quenching of lithium by water was taking place in this reaction.

On the Structure of Isobongkrekic Acid, a Novel Δ^2-*E* Isomer of the Antibiotic Bongkrekic Acid

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Bongkrekic acid (BA, Ia) is a toxic antibiotic produced by the microorganism *Pseudomonas cocovenenans* and was found responsible for the fatal food poisoning that used to frequently occur in Indonesia after consumption of an infected coconut product "bongkrek".[1] The high toxicity of bongkrekic acid has been attributed to its affinity for the ATP/ADP translocator protein residing in the mitochondrial inner membrane, thus preventing oxidative phosphorylation.[2]

(1) (a) Isolation: Lijmbach, G. W. M.; Cox, H. C.; Berends, W. *Tetrahedron* **1970**, *26*, 5993. (b) Structure elucidation: Lijmbach, G. W. M.; Cox, H. C.; Berends, W. *Ibid.* **1971**, *27*, 1839. Bruijn, J. de., Frost, D. J.; Nugteren, D. H.; Gaudemer, A.; Lijmbach, G. W. M.; Cox, H. C.; Berends, W. *Ibid.* **1973**, *29*, 1541. (c) Synthesis: Corey, E. J.; Tramontano, A. *J. Am. Chem. Soc.* **1984**, *106*, 462.

(2) van Veen, A. G.; Mertens, W. K. *Recl. Trav. Chim. Pays-Bas* **1934**, *53*, 257.

0022-3263/88/1953-4883$01.50/0

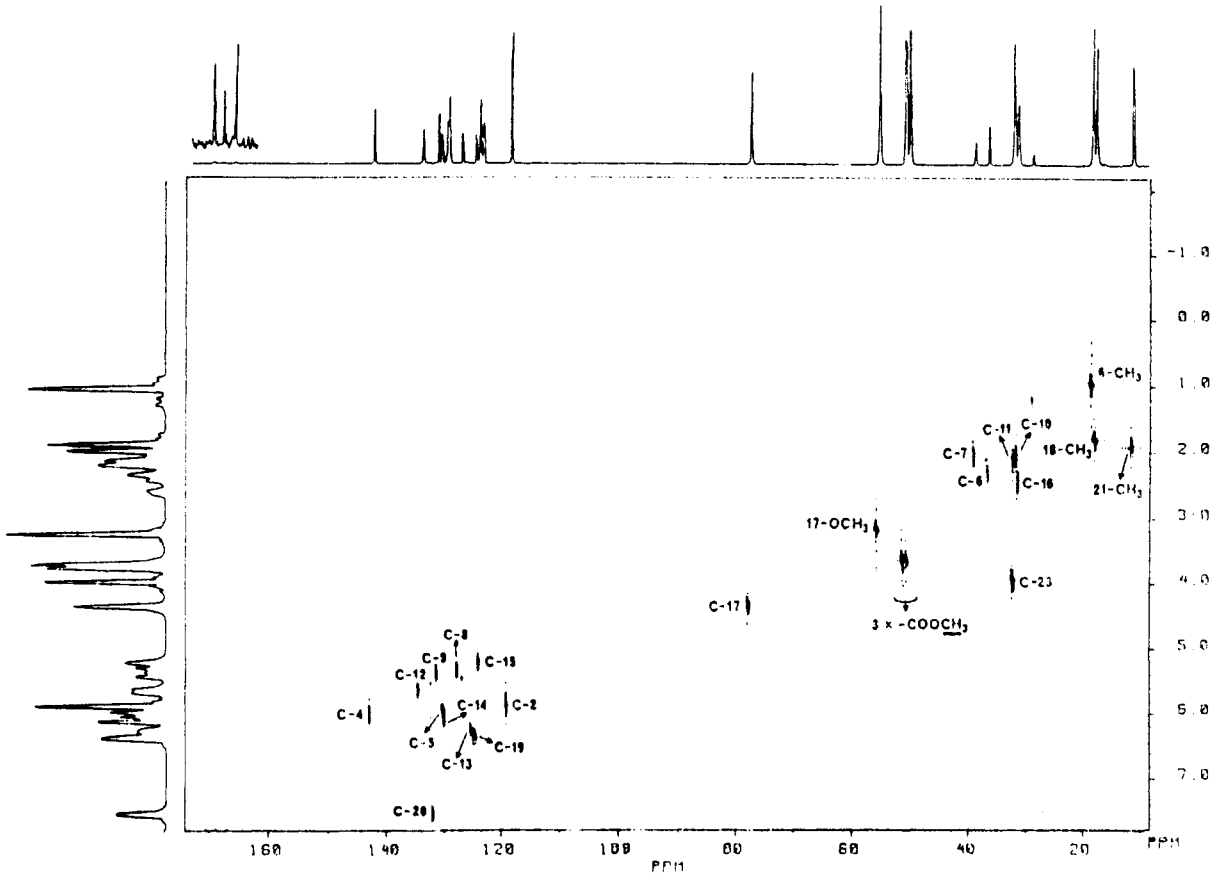
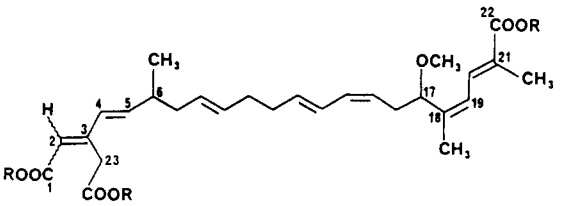


Figure 1. ^{13}C–^{1}H COSY spectrum of $IBAMe_3$ (IIb) (350 mM in $CDCl_3$).

During the course of our screening program for new antifungal secondary metabolites, we isolated a compound bearing physicochemical and spectral properties strikingly similar to those of bongkrekic acid with, however, tangible differences. We named this compound isobongkrekic acid (IBA, IIa) after isolating it from the fermentation of an unidentified eubacterium, culture number HIL Y-84,0700.[3] Successive bioassay-guided (*Aspergillus niger*) chromatographies on Diaion HP-20,[4] silica, reverse-phase silica, and Sephadex G-10[4] afforded isobongkrekic acid as a water-soluble white powder:[5] mp 190 °C dec; $[\alpha]^{20}_D$ +93.75° (*c* 0.016, 40% aqueous MeOH), FAB-MS (glycerol matrix), MH^+ at *m/z* 487.[6,7] The UV absorption maxima in aqueous MeOH at 234 and 268 nm (254 nm with NaOH) indicated conjugated diene and α,β-unsaturated COOH moieties, respectively.

Isobongkrekic acid was unstable and was converted into a trimethyl ester ($IBAMe_3$, IIb) by CH_2N_2. The IR spectrum of $IBAMe_3$ bore copybook similarity to the reported IR spectrum of the trimethyl ester of bongkrekic acid ($BAMe_3$, Ib).[1b] The ^1H NMR spectrum of $IBAMe_3$ in $CDCl_3$ was also identical with the reported spectrum of $BAMe_3$ in most areas with, however, remarkable differences for the C-4 H and C-23 H_2 resonances.[1b] These appeared at δ 6.09 (d, J = 16 Hz) and 3.96 (pair of doublets), respectively, as compared to δ 7.51 and 3.31 for $BAMe_3$. NOE difference spectra at 500 MHz indicated a signal enhancement of C-4 H by ca. 3.9% on irradiation of the C-2H (δ 5.90, s) and a signal enhancement of C-2H by ca. 4.55% on irradiation of C-4 H. No NOE could be seen between C-2H and C-23H_2 in sharp contrast to the reported 15% NOE enhancement for these two singlets in the case of $BAMe_3$.[1b]



Ia : R = H , Δ^2–Z (COOR and CH_2COOR trans)
Ib : R = CH_3, Δ^2–Z
IIa : R = H , Δ^2–E (COOR and CH_2COOR cis)
IIb : R = CH_3, Δ^2–E

All these observations can be interpreted in terms of a Δ^2-*E* stereochemistry in $IBAMe_3$ as against the Δ^2-*Z* stereochemistry for $BAMe_3$. Further support for the stereochemistry of this element is found in the ^1H NMR data of the *E* (IIIa) and *Z* (IIIb) isomers of dimethyl 3-

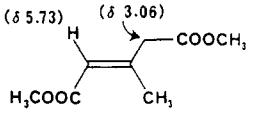
(3) The strain has been deposited at the Deutsches Sammlung von Mikroorganism, Gottingen, F.R.G., where it has been assigned the number DSM 4305.
(4) Diaion HP-20 is supplied by Mitshubishi Chemical Industries Limited, Japan, and Sephadex G-10 by Pharmacia Chemical Industries Limited, Sweden.
(5) Bongkrekic acid has been reported to be a colorless oil, which solidifies on drying to a white solid with a melting traject of 50–60 °C, $[\alpha]^{25}_D$ +162.5°.[1a]
(6) FAB-MS also shows cluster ions $(M + Na)^+$, $(M + 2Na - H)^+$, $(M + 3Na - 2H)^+$, and $(M + 4Na - 3H)^+$ at *m/z* 509, 531, 553, and 575, respectively. Similar ion clusters have been reported in the FAB-MS spectra of polyunsaturated fatty acids using matrices saturated with alkali metal halides, see for example: Adams, J.; Gross, M. J. *Anal. Chem.* **1987**, *59*, 1576.
(7) We could not get a reliable combustion analysis for isobongkrekic acid presumably due to its instability. Bongkrekic acid has also been reported by Corey et al. to be unstable in the neat form.[1c] The corresponding trimethyl ester $IBAMe_3$, however, gave satisfactory elemental analysis.

Table I

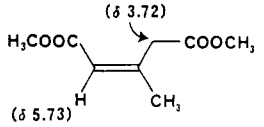
position no.	δ_c in ppm of $IBAMe_3$[a]	δ_H in ppm (multiplicity, coupling constant) $IBAMe_3$	$BAMe_3$[b]
1, 22, 24[c]	170.34, 168.67, 166.70		
2[d]	119.21	5.90 (s)	5.69 (s)
3	147.94		
4[d]	142.96	6.09 (d, 16 Hz)	7.51 (d, 16 Hz)
5	130.28	6.01 (dd, 7.5, 16 Hz)	6.04 (dd, 7.5, 16 Hz)
6	37.04	2.29 (septet)	ca. 2.3 (septet)
6-CH_3	19.02	0.94 (s)	1.01 (s)
7	39.40	1.88 (m)	1.95–2.2 (complex)
8	127.80	5.35 (ddd, 7, 7, 15 Hz)	5.37 (complex)
9	131.84	5.41 (dt, 7, 15 Hz)	5.37 (complex)
10	31.80	1.94 (m)	1.95–2.2 (complex)
11	32.55	2.11 (m)	1.95–2.2 (complex)
12	134.53	5.67 (dt, 7, 14.8 Hz)	5.67 (dt, 7, 14.5 Hz)
13	125.41	6.27 (dd, 11, 16 Hz)	6.26 (dd, 11, 14.5 Hz)
14	130.02	5.99 (t, 11 Hz)	5.99 (t, 11 Hz)
15	124.09	5.22 (dt, 7, 11 Hz)	5.21 (dt, 7, 10.5 Hz)
16	32.00	2.57 (ddd, 7.8, 7.8, 15 Hz)	2.57 (dt, 15.7 Hz)
		2.37 (ddd, 7.8, 7.8, 15 Hz)	2.35 (complex)
17	78.11	4.35 (t, 7 Hz)	4.35 (t, 7 Hz)
17-OCH_3	56.03	3.20 (s)	3.20 (s)
18	126.09		
18-CH_3	18.37	1.85 (s)	1.83 (s)
19	124.63	6.35 (d, 12 Hz)	6.35 (d, 12 Hz)
20	131.35	7.50 (d, 12 Hz)	7.50 (d, 12 Hz)
21	145.29		
21-CH_3	11.98	1.90 (s)	1.93 (s)
23[d]	32.75	3.94 (d, 16.9 Hz), 3.99 (d, 16.9 Hz)	3.31 (s)
3 × $COOCH_3$[c]	51.65, 51.47, 50.83	3.75 (s), 3.70 (s), 3.67 (s)	3.75 (s), 3.70 (s), 3.67 (s)

[a] Determined from HC shift correlation data. [b] Values from ref 1b. [c] Assignments were not made. [d] Chemical shift differences at these positions are remarkable.

methylglutaconate, the downfield shift of the carboxymethylene protons in the *Z* isomer being attributed to the magnetic anisotropy of the COOMe group.[8a]



IIIa (E)



IIIb (Z)

The structure of $IBAMe_3$ in the C-5 to C-22 fragment was found to be identical with that reported for $BAMe_3$. HH shift correlation spectroscopy at 500 MHz indicated all the proton couplings, which in turn established the assignments of carbon resonances of $IBAMe_3$ as revealed from the HC correlation data (Figure 1). HH 2D *J*-resolved spectra of $IBAMe_3$ further clarified the multiplicity patterns of the proton resonances and supported the structural assignments. Long-range couplings of the order of 1–2 Hz could be seen for the H-12, H-13, H-16, H-19, and H-20 protons and also for the 21- and 18-methyls. Structure of $IBAMe_3$ was thus conclusively established to be the trimethyl ester of 3-(carboxymethyl)-17-methoxy-6,18,21-trimethyldocosa-2(*E*),4(*E*),8(*E*),12(*E*),14(*Z*),18(*Z*),20(*E*)-heptaene-1,22-dioic acid. The absolute stereochemistries at C-6 and C-17 remain to be established. Table I gives the ^{13}C and ^{1}H shift assignments of $IBAMe_3$ (500 MHz for ^{1}H; 125 MHz for ^{13}C; $CDCl_3$ solvent).

Isobongkrekic acid thus differs from bongkrekic acid *in only one (C2-C3) out of the seven double bonds being isomeric.* When a sample of IBA dissolved in D_2O was treated with DCl and then extracted into $CDCl_3$, the resulting ^{1}H NMR spectrum was identical with that reported for BA.[1b] To rule out the possibility of isomerization of BA to IBA during the isolation and esterification process, we extracted the crude antibiotic into $CHCl_3$ at pH 6–7 and at pH 2 (with HCl). Esterification with CH_2N_2 and purification showed a ≥98:2 ratio (determined by the intensity ratios of the δ 3.96 and 3.31 resonance for the 23-H_2 protons) of the Δ^2 *E*/*Z* isomers in the former case and an approximately 50:50 mixture of the two isomers in the latter case. These results clearly indicate that IBA is configurationally unstable to acid across the Δ^2 bond. The corresponding ester, $IBAMe_3$, however, shows no evidence of stereochemical scrambling on treatment with HCl even for 24 h. Although the mechanism of such selective isomerization in the presence of acid is not clear, the driving force may be the release of steric compression between the COOH and the CH_2COOH groups in going from the Δ^2 *E* isomer in IBA to Δ^2 *Z* isomer in BA. It is interesting to note in this context that 3-methylglutaconic acid (III) has also been reported to undergo acid-induced isomerization albeit under more vigorous condition (20% HCl, 100 °C) with the *Z* isomer (IIIb), having the COOH and CH_2COOH groups in the cis orientation, predominating in the mixture.[8b]

Isobongkrekic acid showed strong inhibitory activity especially against phytopathogenic fungi, the minimum inhibitory concentrations (MIC) being in the range of 7.8–125 μg/mL. Its LD_{50} value in Swiss mice was 4.5 mg/kg body weight when administered subcutaneously. The antibiotic activity of isobongkrekic acid is slightly less than that reported for bongkrekic acid.[9] The trimethyl ester $IBAMe_3$ however did not exhibit any antibiotic property.

Experimental Section

Melting points were determined with a Bristoline instrument and are uncorrected. UV spectra were recorded on a Uvikon 810 double-beam spectrometer. IR spectra were recorded on a Per-

(8) (a) Jackman, L. M.; Wiley, R. H. *J. Chem. Soc.* **1960**, 2886. (b) Cawley, J. *J. Am. Chem. Soc.* **1955**, *77*, 4125.

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kin-Elmer 782 spectrophotometer, and optical rotations were measured on Perkin-Elmer 141 and 241 polarimeters. Mass spectra were recorded on a Kratos MS 80 RFA instrument. NMR spectra including the 2D experiments were recorded on a Bruker AM-500 FT NMR spectrometer interfaced with an Aspect 3000 computer. Standard pulse sequences were used for proton–proton[10] and proton–carbon[11] cosy spectra. 2D *J*-resolved[12] NMR experiment was carried out using the pulse sequence RD – $\pi/2$ – $t_1/2$ – π – $t_1/2$ – FID.

Isolation of Isobongkrekic Acid (IIa). Approximately 250 L of the clarified broth filtrate (pH 7.3) was passed through a column of 8 L of Diaion HP-20. The column was first washed with demineralized water and then eluted with 40 L of 50% aqueous MeOH. Concentration in vacuo followed by lyophilization gave 670 g of the crude antibiotic as a dark brown mass. This was subjected to medium-pressure liquid chromatography (MPLC) over SiO_2 (230–400 mesh, 3 kg), and the antibiotic was eluted with 10 L of 5:95 MeOH–$CHCl_3$ at a flow rate of 150 mL min^{-1}. Concentration gave 100 g of a dark brown oil, which on repeated trituration with petroleum ether (60–80 °C) gave 16 g of a brown powder. This was subjected to three MPLC's over dimethyl octadecylsilyl SiO_2 (RP 18) with aqueous MeOH as the eluant. The antibiotic eluted out with 30% aqueous MeOH in the first case, 40% aqueous MeOH in the second case, and with 50% aqueous MeOH in the third column. Concentration followed by lyophilization gave 1.0 g of a very pale yellowish powder. Final purification on Sephadex G-10 column using double-distilled water afforded isobongkrekic acid as a white powder: HPLC retention time 1.8 min on a 4 × 120 mm ODS-hypersil (5 μm) column, eluant 30% aqueous MeOH, flow rate 0.5 mL min^{-1}, detection at 268 nm; FAB-MS 487 $(M + H)^+$; UV λ_{max} (aqueous MeOH) 234, 268 (254 with alkali) nm; IR (KBr) 3400, 3200, 1670–1560 (broad), 1400, 1345, 1090, 980, 945, 770 cm^{-1}; ^{13}C NMR (D_2O) δ 183.13 (s), 180.83 (s), 179.12 (s), 143.95 (s), 143.80 (d), 143.57 (s), 139.17 (d), 136.11 (s), 134.64 (d), 133.72 (d), 132.16 (d), 131.15 (d), 129.02 (d), 128.41 (d), 128.26 (d), 127.96 (d), 127.38 (d), 81.34 (d), 58.39 (q), 46.06 (t), 42.12 (t), 39.71 (d), 34.81 (t), 34.30 (t), 34.11 (t), 21.62 (q), 20.24 (q), 15.77 (q); ^1H NMR (D_2O, DSS) δ 7.26 (1 H, d, J = 12 Hz), 6.92 (1 H, d, J = 16 Hz), 6.47 (1 H, d, J = 12 Hz), 6.42 (1 H, dd, J = 11, 16 Hz), 6.09 (1 H, t, J = 11 Hz), 5.92 (1 H, dd, J = 7.5, 16 Hz), 5.81 (1 H, dt, J = 16, 7 Hz), 5.71 (1 H, s), 5.55 (2 H, m), 5.30 (1 H, dt, J = 11, 7 Hz), 4.58 (1 H, t, J = 7.9 Hz), 3.25 (3 H, s), 3.15 (2 H, s), 2.65–2.40 (2 H, ddd, J = 6, 8, 16 Hz), 2.32 (1 H, septet, J = 6 Hz), 2.38–1.98 (6 H, m), 1.90 (3 H, s), 1.80 (3 H, s), 1.05 (3 H, s).

Preparation of Trimethyl Ester of Isobongkrekic Acid (IIb). IBA (IIa, 100 mg) was esterified with 4–5-fold excess of CH_2N_2 in a mixture of MeOH, diethyl ether, and water at 0 °C for 1 h. The crude ester was purified by preparative TLC (20 × 20 cm SiO_2 plates; 0.5 mm thickness; solvent for developing 1.5% MeOH in $CHCl_3$; solvent for elution 5% MeOH in $CHCl_3$). The ester was obtained as a colorless oil (IIb, 59 mg): R_f 0.54 (SiO_2, 1.5% MeOH in $CHCl_3$); $[\alpha]^{20}_D$ +27.78° (*c* 1.4, $CHCl_3$); EIMS, m/z 528 (M^+); UV λ_{max} (MeOH) 236, 268 (no alkali shift) nm; IR (neat) 3020, 2950, 2920, 2840, 1745, 1715, 1635, 1615, 1435, 1380, 1320, 1260, 1190, 1160, 1110, 1020, 970, 945, 915, 870, 830, 780, 750 cm^{-1}. Anal. Found: C, 69.95; H, 8.50. Calcd for $C_{31}H_{44}O_7$: C, 70.45; H, 8.33.

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Stereospecific Syntheses of (*E*)-1,3-Disubstituted Dienes

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(*E*)-1,3-dienes, unlike the *Z* isomers, are useful components in Diels–Alder reactions.[2,3] We have found a straightforward method for stereospecific preparation of (*E*)-1,3-dialkyl-substituted 1,3-dienes from allylic acetates and describe herein our findings.

Tsuji and co-workers[4] have reported that treatment of allylic acetates with triphenylphosphine and a catalytic amount of palladium acetate in refluxing dioxane or toluene furnishes *E,Z* mixtures of 1,3-dienes. Although a variety of allylic acetates were examined in that study, none of the starting materials had a substitution pattern that would lead to 1,3-disubstituted 1,3-dienes.

Our interest in the use of dienes such as **2a** and **2b** as intermediates to 1,4(*H*)-naphthalenones led us to explore the palladium-catalyzed elimination of **1a** and **1b**. Under the Tsuji conditions, the allylic acetates[5] **1a** and **1b** were converted exclusively to the (*E*)-dienes **2a** and **2b** in 91 and 96% yield, respectively. Since the stereochemical result was unexpected and the procedure appeared especially promising as a method for stereospecific synthesis of (*E*)-1,3-disubstituted 1,3-dienes, additional examples were performed, and these are shown in Scheme I.

Stereospecific conversion of **1c** and **1d** to the (*E*)-1,3-dienes **2c** and **2d** established that the oxygens in the acetal were not a factor in the stereochemical outcome. Moreover, the fact that conversion of **1e** and **1f** to the (*E*)-1,3-dienes **2e** and **2f** proceeded without isomerization to the conjugated compound indicated that subsequent isomerization of the initially formed diene was probably not occurring. Finally, in order to establish the compatibility of other functionality in the reaction, the conversion of allylic acetates with terminal thiophenyl groups was examined. Here again we observed that **1g** and **1h** produced the (*E*)-1,3-dienes **2g** and **2h** exclusively. In all cases, yields were uniformly very good to excellent.

It is well known that palladium(II) acetate reacts with triphenylphosphine to give a palladium(0) complex.[6] In a subsequent step, the palladium(0) species displaces the acetate group to furnish a π-allyl intermediate, which is in equilibrium with the σ-bonded species.[7] Although it is unknown whether the π-allyl or the σ-bonded intermediate is the species undergoing reaction or whether the elimination step is a syn or anti process, *it is clear that the transition state is highly ordered and that the 2-alkyl substituent on the vinyl moiety is a controlling feature, since systems devoid of this group furnish E,Z mixtures.*[3,4]

In summary, the palladium-catalyzed conversion of allyl acetates with a 2-alkyl group on the vinyl moiety provides

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