isolate of *A. flavus* used in this work (NRRL 6541) was obtained from the ARS culture collection of the USDA Northern Regional Research Center, Peoria, IL.

Hexane and $CHCl_3$ extracts of milled sclerotia (21.8 g) were subjected to reversed-phase flash chromatography followed by reversed-phase HPLC (5-μm C_{18} column, 250 × 10 mm, 70:30 MeOH-H_2O, 2.0 mL/min, monitored at 215 nm) to afford 1 (10.1 mg), **3** (7.1 mg), **4** (15.6 mg), and **5** (6.8 mg). Since some loss was involved, actual concentrations in the sclerotia were determined by direct HPLC quantitation of fresh sclerotial extracts.[4] Sclerotia from 10 other isolates of *A. flavus* and *A. parasiticus* contained comparable or higher concentrations of these compounds. Submerged shake cultures of NRRL 6541 grown in corn steep liquor or glucose-yeast extract media failed to produce sclerotia, and only traces of 1 and **3-5** (range, 0-80 μg/L) could be detected in these cultures by HPLC.

20,25-Dihydroxyaflavinine (1) was identified by analysis of spectral data and by comparison to an authentic sample. Earlier reports have not provided complete physical and spectral properties for 1, and this information is included here. Compound 1 (concentration in sclerotia, 470 ppm): mp 255-257 °C; $[\alpha]_D$ +22.9° (*c* 0.50, MeOH); HPLC retention time 14.4 min under the above conditions; UV (MeOH) 224 (ϵ 20190), 283 (3850), 291 nm (3670); ^1H NMR, Table I; ^{13}C NMR (CD_3OD) 138.5 (s), 137.7 (s), 129.9 (s), 128.4 (s), 123.2 (d), 122.2 (d), 120.0 (d), 119.6 (d), 118.0 (s), 112.2 (d), 72.6 (d), 71.0 (d), 67.3 (t), 49.9 (d), 45.9 (s), 44.7 (s), 40.4 (d), 35.9 (t), 32.5 (d), 31.3 (t), 31.2 (d), 28.6 (t), 23.1 (t), 22.8 (t), 20.1 (q), 19.6 (q), 15.6 (q), 13.6 ppm (q); EIMS (70 eV), 437 (M^+; relative intensity 12.5), 419 (3.5), 328 (3.0), 302 (5.4), 288 (5.4), 260 (18), 234 (31), 218 (44), 194 (47), 180 (45), 167 (49), 154 (30), 144 (40), 130 (100), 117 (85); HREIMS obsd 437.2931, calcd for $C_{28}H_{39}NO_3$ 437.2936.

20-Hydroxyaflavinine (3): concentration 1100 ppm; mp 174-176 °C dec; $[\alpha]_D$ +23.8° (*c* 0.56, MeOH); retention time 34.2 min; UV (MeOH) 224 (ϵ 14920), 283 (2760), 290 nm (2520); ^1H NMR, Table I; ^{13}C NMR (CD_3OD) 141.8 (s), 137.7 (s), 128.5 (s), 127.2 (s), 122.8 (d), 122.1 (d), 120.0 (d), 119.5 (d), 112.2 (d), 112.0 (s), 72.6 (d), 71.0 (d), 49.8 (d), 46.0 (s), 44.7 (s), 36.0 (t), 32.5 (d), 32.0 (d), 31.5 (t), 31.2 (d), 28.6 (t), 23.2 (t), 22.1 (t), 21.5 (q), 21.1 (q), 19.9 (q), 19.6 (q), 13.6 ppm (q); EIMS (70 eV), 421 (M^+; 20), 403 (2.0), 378 (3.1), 360 (3.1), 342 (4.3), 288 (4.4), 234 (12), 220 (26), 206 (22), 194 (35), 180 (28), 168 (62), 154 (25), 144 (26), 130 (100), 117 (50); HREIMS obsd 421.2981, calcd for $C_{28}H_{39}NO_2$ 421.2980.

24,25-Dehydro-10,11-dihydro-20-hydroxyaflavinine (4): concentration 440 ppm; mp 259-262 °C; $[\alpha]_D$ +0.9° (*c* 0.34, MeOH); retention time 25.8 min; UV (MeOH) 227 (ϵ 26260), 284 (6060), 291 nm (5720); ^1H NMR, Table I; ^{13}C NMR (CD_3OD) 151.7 (s), 137.7 (s), 128.6 (s), 124.6 (d), 122.0 (d), 119.3 (d), 118.7 (d), 116.2 (s), 112.3 (d), 111.6 (t), 72.6 (d), 69.1 (d), 47.4 (s), 45.5 (s), 44.8 (d), 39.5 (d), 38.9 (t), 35.7 (d), 32.6 (d), 32.3 (d), 31.1 (t), 29.2 (t), 28.5 (t), 25.8 (t), 23.1 (q), 19.7 (q), 18.4 (q), 13.8 ppm (q); EIMS (70 eV), 421 (M^+; 23), 406 (1.5), 403 (1.7), 388 (1.0), 330 (4.3), 302 (2.4), 288 (1.2), 248 (2.0), 220 (4.0), 210 (10), 196 (28), 184 (14), 168 (28), 143 (13), 130 (100), 117 (16); HREIMS obsd 421.2975, calcd for $C_{28}H_{39}NO_2$ 421.2980.

10,11-Dihydro-11,12-dehydro-20-hydroxyaflavinine (5): concentration 530 ppm; mp 276-278 °C; $[\alpha]_D$ +1.7° (*c* 0.1, MeOH); retention time 35.5 min; UV (MeOH) 224 (ϵ 20030), 251 (3600), 285 nm (3380); ^1H NMR, Table I; ^{13}C NMR (CD_3OD) 144.7 (s), 137.5 (s), 129.5 (s), 124.5 (d), 122.2 (d), 121.6 (d), 120.0 (s), 119.6 (d), 118.3 (d), 112.3 (d), 73.1 (d), 70.7 (d), 46.1 (s), 44.9 (s), 40.1 (d), 37.9 (t), 37.1 (d), 31.5 (d), 31.4 (d), 30.9 (t), 30.2 (d), 29.0 (t), 28.7 (t), 23.4 (q), 21.1 (q), 19.7 (q), 17.9 (q), 13.6 ppm (q); EIMS (70 eV), 421 (M^+; 2.8), 403 (0.6), 388 (0.8), 342 (1.6), 274 (3.1), 260 (4.4), 246 (7.7), 232 (8.9), 220 (14), 210 (24), 196 (30), 180 (32), 168 (100), 143 (32), 130 (95), 117 (81); HREIMS obsd 421.2990, calcd for $C_{28}H_{39}NO_2$ 421.2980.

Activity against *C. hemipterus*. Antifeedant activity was measured by incorporating each metabolite into a plug of pinto bean diet and evaluating the extent of feeding by *C. hemipterus* after 7 days.[4] Compound 1 prevented any feeding damage to the plug when incorporated at 100 ppm. Compounds **3-5** were tested at their normal sclerotial concentrations. Compounds **4** and **5** allowed only slight penetration of the diet plug, while **3** permitted some penetration and fragmentation, but control plugs were completely pulverized by insect feeding.

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High Pressure Mediated Diels-Alder Reaction of Furan with Dialkyl (Acetoxymethylene)malonate

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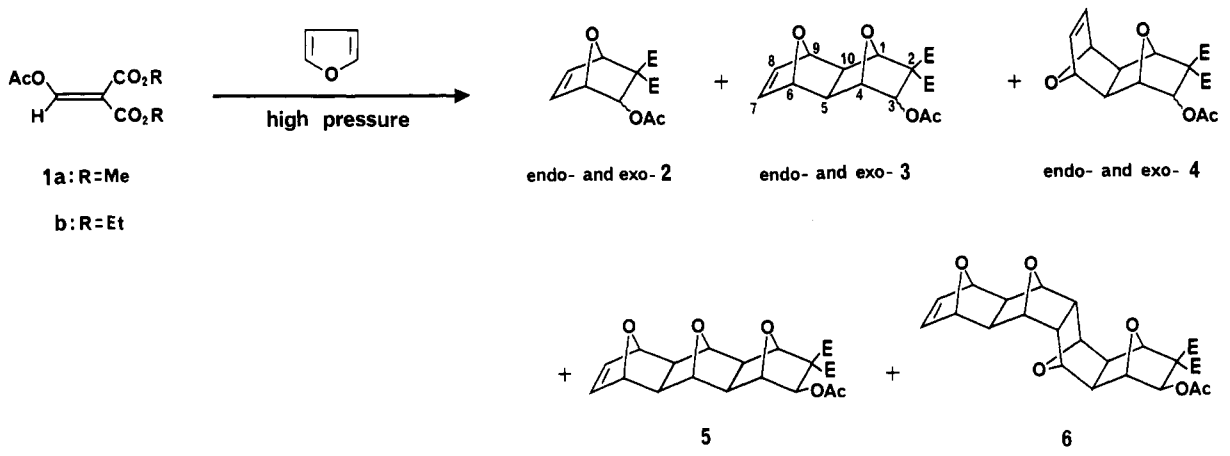
The Diels-Alder reaction of furan with dialkyl (acetoxymethylene)malonates 1 did not proceed even in the presence of Lewis acid catalysts under conventional conditions. However, the reaction under high pressure (1.1 GPa) gave the expected cycloadducts, dialkyl 3-acetoxy-7-oxabicyclo[2.2.1]hept-5-ene-2,2-dicarboxylates **2**. The bis-, tris-, and tetrakisadducts **3-6** were also produced in some amounts. Similar high-pressure reactions in the presence of zinc iodide as a catalyst yielded dialkyl 2-furfurylidenemalonate **8**, and none of the adducts were obtained.

Substituted 7-oxabicyclo[2.2.1]heptanes have been used as key intermediates in the syntheses of a variety of natural products.[1] Construction of a 7-oxabicyclo[2.2.1]hept-5-ene moiety should be achieved by the Diels-Alder reaction of furan with an appropriate dienophile. However, this strategy is in many cases not feasible because of the low reactivity of furan toward dienophiles, or thermal instability of adducts (retro Diels-Alder reactions). In fact, the reported Diels-Alder reactions of furan have been limited within those with very reactive dienophiles. In some instances, Lewis acid catalysts,[2] chelation by metal,[3] or high

(1) Warm, A.; Vogel, P. *J. Org. Chem.* **1986**, *51*, 5348 and references cited therein.

0022-3263/88/1953-5460$01.50/0

Scheme I[a]



[a] E = CO_2Et or CO_2Me.

Table I. ^1H NMR Data for Biscycloadducts[a]

	endo-3b	*exo*-3b	*endo*-4b	*exo*-4b
H_1	5.01	5.07	4.45	4.74
H_3	5.84 (d, $J_{3,4}$ = 5.0)	5.60	5.73 (d, $J_{3,4}$ = 5.5)	5.54
H_4	4.82 (d)	4.44	4.47 (d)	4.04
H_5	3.03 (d, $J_{5,10}$ = 7.0)	1.60 (d, $J_{5,10}$ = 6.0)	3.54 (dd, $J_{5,6}$ = 5.0, $J_{5,10}$ = 8.0)	2.24 (dd, $J_{5,6}$ = 5.0, $J_{5,10}$ = 8.0)
H_6	4.90	4.95	4.89[b] (d)	4.89[b] (br d)
H_7	6.41	6.35	6.26	6.24[c] (dd, $J_{6,7}$ = 1.5, $J_{7,8}$ = 6.0)
H_8	6.41	6.35	6.26	6.28 (dd, $J_{8,9}$ = 1.5)
H_9	4.90	4.95	5.01[d] (d, $J_{9,10}$ = 5.0)	4.94[d] (br d, $J_{9,10}$ = 4.5)
H_{10}	2.13 (d)	1.99 (d)	2.79 (dd)	2.58 (dd)

[a] Chemical shifts in parts per million and coupling constants (J) in hertz. [b] Tentatively assigned to H_6. [c] Tentatively assigned to H_7. [d] Tentatively assigned to H_9.

pressure[4] was employed to overcome low reactivity of the Diels–Alder reactions of furan. Synthesis of C-nucleosides by means of the Diels–Alder reactions of furan is of continuing interest, and methyl 3-nitroacrylate,[5] dimethyl acetylenedicarboxylate,[6] tetrachlorocyclopropene,[7] and 1,3-bis(ethoxycarbonyl)allene[8] have been employed as tailored dienophiles.

Recently, a new dienophile, dialkyl (acetoxymethylene)malonate **1**, was developed by Katagiri, Kaneko, and their co-workers.[9] An advantage of this dienophile is that the C–C bonds originated from the dienophile in the cycloadducts can be cleaved under mild conditions ($NaBH_4$–K_2CO_3/MeOH) to give a C-glycoside with the desired stereochemistry. Thus a lyxopyranosyl C-glycoside was synthesized stereospecifically from the cycloadduct of 3,4-dialkoxyfuran with **1a**.[10] Unfortunately, a Diels–Alder reaction of **1** with furan itself did not yield the desired cycloadduct, from which one can expect to synthesize C-ribonucleosides stereospecifically.[11] This paper concerns the high pressure mediated Diels–Alder reaction of furan with dialkyl (acetoxymethylene)malonate.

Results and Discussion

Dialkyl (acetoxymethylene)malonate **1** was developed as a versatile dienophile to produce bicyclo[2.2.1]heptene derivatives by Diels–Alder reactions with cyclic dienes.[9] Thus the reaction of **1a** with cyclopentadiene yielded dimethyl 3-acetoxybicyclo[2.2.1]hept-5-ene-2,2-dicarboxylate in good yield, from which a carbocyclic analogue of a C-nucleoside was synthesized.[12] Unfortunately, **1** did not react with furan under conventional Diels–Alder reaction conditions. Generally, cycloaddition reactions are characterized by the property of having negative values of activation volume,[13] and the use of high pressure for preparative Diels–Alder reactions has been well explored.[4] Accordingly, the reaction of **1** with furan was examined under high pressure.

A reaction of **1b** with furan (furan:**1b** = 6.9, without an additional solvent[14]) was carried out under 1.1 GPa at ambient temperature for 9 days to give a mixture of cycloadducts. Separation of the mixture by means of repeated column chromatography afforded the desired ad-

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(13) Asano, T.; Le Noble, W. J. *Chem. Rev.* **1978**, *78*, 407.

(14) High-pressure reactions (1 GPa) of **1b** with furan in tetrahydrofuran or dichloromethane for 10 days gave **2b** in unexpectedly low yields: less than 1% and 16%, respectively.

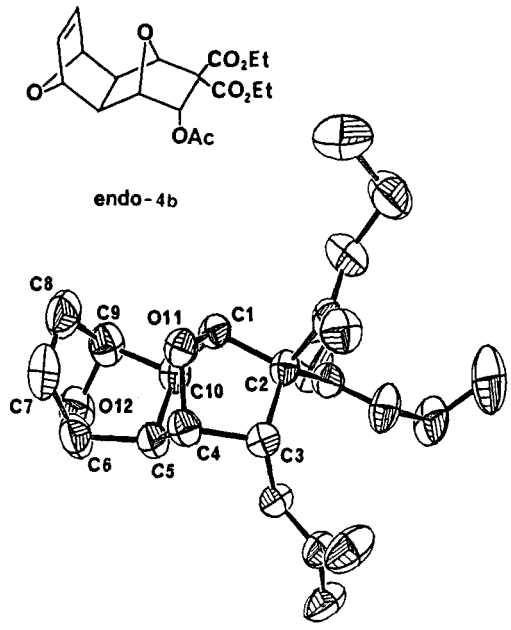


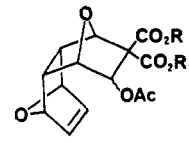
Figure 1. A computer-generated drawing of *endo*-**4b** derived from the X-ray coordinates with hydrogen atoms omitted for clarity.

ducts, *endo*-**2b** in 36.4% yield and *exo*-**2b** in 4.1% yield. In the other high-pressure reaction (furan:**1b** = 2.8, 1.1 GPa, 10 days), **2b** was obtained in an increased yield (56%, endo:exo = 2.1). The major isomer (*endo*-**2b**) showed a characteristic ^{1}H NMR signal of an *exo*-H_3 at 6.05 ppm as a doublet with J = 4.4 Hz, whereas the minor isomer (*exo*-**2b**) showed an *endo*-H_3 signal at 5.55 ppm as a singlet. During a separation procedure by silica gel chromatography, or during heating in solvents, these two adducts reverted slowly to the starting compounds at atmospheric pressure. The retro Diels–Alder reactions of **2b** were followed by means of ^{1}H NMR, and the first-order rate constants of the reactions were found to be 6.1×10^{-5}/s for *endo*-**2b** and 2.9×10^{-5}/s for *exo*-**2b** at 71.2 °C, respectively. In the presence of zinc iodide, the retro Diels–Alder reaction of **2b** was completed within a few minutes at room temperature to give **1b** in 69% yield.

In addition to the expected adducts, four biscycloadducts, 3-*endo*- and 3-*exo*-acetoxy syn-joined bisadducts[15] (*endo*- and *exo*-**3b**) and 3-*endo*- and 3-*exo*-acetoxy anti-joined bisadducts[15] (*endo*- and *exo*-**4b**) were obtained in 5.6, 5.1, 6.8, and 5.9% yields, respectively. Their structures were elucidated as depicted in Scheme I on the basis of ^{1}H NMR (Table I) and other spectral data. A characteristic feature in ^{1}H NMR spectrum was that the H_5 signal of the syn-bisadducts appeared as a doublet, whereas that of the anti-bisadducts appeared as a double doublet. Characterization of the C_3 endo and exo isomers was made by inspecting the shape of the H_3 and H_4 signals, the H_3 and H_4 of the endo isomers being doublets, and those of the exo isomers being singlets. The structure of *endo*-**4b** was further confirmed by an X-ray structure determination as depicted in Figure 1. The calculated dihedral angles for *endo*-**4b** ($\angle H_3,C_3,C_4,H_4$ = 32.7°; $\angle H_4,C_4,C_5,H_5$ = 82.8°; $\angle H_5,C_5,C_6,H_6$ = 28.7°; $\angle H_5,C_5,C_{10},H_{10}$ = 0.3°; $\angle H_9,C_9,C_{10},H_{10}$ = 35.4°; $\angle H_1,C_1,C_{10},H_{10}$ = 82.9°) accorded well with the observed values of the coupling constants.

Okamoto[16] reported that the high-pressure Diels–Alder reaction of furan with dichloromaleic anhydride afforded

Scheme II



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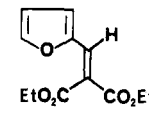

8

only one anti-bisadduct corresponding to 4. No syn-bisadduct like 3 was isolated, and a steric disadvantage was suggested for them because of supposed nonbonding interaction between the two oxygen bridges located in close proximity. In the present high-pressure reaction, however, all of the four possible bisadducts (*endo*- and *exo*-**3b** and *endo*- and *exo*-**4b**) having an exo-joined additional dihydrofuran ring to the original 7-oxabicyclo[2.2.1]heptane structure were produced in almost equal amounts. Although pressure has been known to favor formation of sterically congested products, no bisadduct was isolated in which an additional dihydrofuran ring was joined in an endo direction to the original bicyclic framework like 7 (Scheme II) even under a high pressure of 1 GPa.

In addition to the bisadducts, small amounts of a syn,syn-trisadduct **5** and an anti,anti,syn-tetrakisadduct **6** were also isolated by further chromatography. The other tris- and tetrakisadducts may exist in the reaction mixture; however, these were not isolated as yet.

High-pressure cycloaddition of dimethyl (acetoxymethylene)malonate (**1a**) with furan also proceeded well under similar conditions to give *endo*-**2a** and *exo*-**2a** in satisfactory yields (see Experimental Section).

A high-pressure reaction of furan with **1b** was also examined in the presence of zinc iodide as a catalyst. The reaction gave no cycloadducts at all; instead, diethyl 2-furfurylidenemalonate (**8**) was isolated as the sole product. This compound was also detected in a trace amount in a noncatalyzed reaction of furan with **1b** (in benzene, under reflux).[10] Formation of **8** can be rationalized by a formal Michael-type addition of furan to **1b** followed by elimination of acetic acid. This type of reaction has been familiar in pyrrole chemistry,[17] but examples with furan are rather rare.

Experimental Section

Infrared spectra were recorded on a JASCO IRA-3 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM FX-90Q, PS-100, and GX-500 spectrometers. Chemical shifts are given in parts per million downfield from internal tetramethylsilane. Mass spectra were recorded on ESCO EMD-05A and JEOL DX-303 spectrometers. Melting points were measured on a micro hot plate apparatus and are uncorrected. High-pressure reactions were carried out by using an ordinary high-pressure apparatus.

Benzene, dichloromethane, and furan were distilled from calcium hydride prior to use. Tetrahydrofuran was dried over lithium aluminum hydride and distilled.

High-Pressure Reactions of Furan with Diethyl (Acetoxymethylene)malonate (1b). A mixture of 2.305 g (10 mmol) of diethyl (acetoxymethylene)malonate (**1b**)[9,11] and 4.707 g (69 mmol) of furan was placed in a Teflon tube plugged at both ends with Teflon stoppers. The tube was placed in a high-pressure reactor and pressurized to 1.1 GPa. After 9 days, the pressure was released and the reaction mixture was evaporated under reduced pressure to remove remaining furan. The resulting oil (3.63 g) was chromatographed on silica gel successively with benzene and benzene–ether to afford 1.088 g (36.4%) of *endo*-**2b**, 0.123 g (4.1%) of *exo*-**2b**, and 0.151 g of the starting compound

(15) Stereochemistry of the ring junction is given as syn or anti with respect to the two oxygen bridges.

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(17) Bosshard, P.; Eugster, C. H. *Adv. Heterocycl. Chem.* **1966**, *7*, 377.

(**1b**). A following elution with acetone gave 0.247 g (6.8%) of *endo*-**4b**. A mixture of adducts (1.92 g) was obtained by a final elution with ethanol. This mixture was again subjected to silica gel column chromatography (benzene–ethyl acetate and ethyl acetate) to give 0.496 g of a mixture consisting of *endo*-**3b** and *exo*-**4b** (1:1) and 0.186 g of pure *exo*-**3b** (5.1%). Specimens of pure *endo*-**3b** and *exo*-**4b** were obtained by a further chromatography eluted with hexane–acetone (2:1). From the second chromatography, 0.020 g (0.5%) of **5b**, 0.020 g (0.4%) of **6b**, and 0.375 g of a mixture consisting of tris- and tetrakisadducts were also obtained. Further isolation of the mixture was not carried out.

A similar reaction was carried out by the use of 4.314 g of **1b** and 3.59 g of furan at 1.1 GPa for 10 days, and 38% of *endo*-**2b** and 18% of *exo*-**2b** (total 56% yield) were obtained. Isolation of the other adducts was not carried out.

Diethyl 3-*endo*-Acetoxy-7-oxabicyclo[2.2.1]hept-5-ene-2,2-dicarboxylate (*endo*-2b): colorless crystals from hexane; mp 87 °C; IR (KBr disk) 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.87 (dd, J = 2.0, 5.7 Hz, 1 H), 6.37 (dd, J = 1.6, 5.7 Hz, 1 H), 6.05 (d, J = 4.4 Hz, 1 H), 5.23 (br s, 1 H), 5.22 (dd, J = 1.6, 4.4 Hz, 1 H), 4.29 (q, J = 7.1 Hz, 1 H), 4.27 (q, J = 7.1 Hz, 1 H), 4.14 (q, J = 7.1 Hz, 2 H), 1.96 (s, 3 H), 1.29 (t, J = 7.1 Hz, 3 H), 1.22 (t, J = 7.1 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 169.49, 167.90, 166.20, 137.40, 133.74, 84.09, 79.51, 75.04, 65.32, 62.34, 61.53, 20.57, 14.07, 13.99; EIMS, m/z 238 (M^+ – 60), 210, 193, 187. Anal. Calcd for $C_{14}H_{18}O_7$: C, 56.37; H, 6.08. Found: C, 56.44; H, 6.17.

Diethyl 3-*exo*-Acetoxy-7-oxabicyclo[2.2.1]hept-5-ene-2,2-dicarboxylate (*exo*-2b): colorless crystals from hexane; mp 98–99 °C; IR (KBr disk) 1750–1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.55 (dd, J = 1.7, 5.9 Hz, 1 H), 6.38 (dd, J = 1.5, 5.9 Hz, 1 H), 5.55 (s, 1 H), 5.41 (br t, J = 1.5 Hz, 1 H), 4.93 (br t, J = 1.7 Hz, 1 H), 4.24 (q, J = 7.1 Hz, 2 H), 4.18 (q, J = 7.1 Hz, 2 H), 2.07 (s, 3 H), 1.28 (t, J = 7.1 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 169.79, 166.89, 166.81, 136.34, 83.30, 81.52, 76.75, 63.75, 61.82, 20.81, 14.07, 13.88; EIMS, m/z 238 (M^+ – 60), 210, 193, 187. Anal. Calcd for $C_{14}H_{18}O_7$: C, 56.37; H, 6.08. Found: C, 56.42; H, 6.10.

Diethyl 3-*endo*-Acetoxy-*syn*-11,12-dioxatetracyclo-[6.2.1.1^{5,10}.0^{6,9}]dodec-7-ene-2,2-dicarboxylate (*endo*-3b): colorless crystals from hexane–acetone (2:1); mp 127 °C; IR (KBr disk) 1765, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.41 (s, 2 H), 5.84 (d, J = 5.0 Hz, 1 H), 5.01 (s, 1 H), 4.90 (s, 2 H), 4.82 (d, J = 5.0 Hz, 1 H), 4.24 (q, J = 7.0 Hz, 2 H), 4.17 (q, J = 7.0 Hz, 2 H), 3.03 (d, J = 7.0 Hz, 1 H), 2.13 (d, J = 7.0 Hz, 1 H), 2.04 (s, 3 H), 1.27 (t, J = 7.0 Hz, 3 H), 1.23 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 169.32, 167.84, 165.91, 137.44, 137.14, 84.41, 81.41, 80.73, 80.27, 75.15, 65.42, 62.50, 61.52, 43.31, 41.83, 20.76, 14.11, 14.06; EIMS, m/z 366, 298, 238, 231, 193, 187. Anal. Calcd for $C_{18}H_{22}O_8$: C, 59.01; H, 6.05. Found: C, 58.83; H, 5.85.

Diethyl 3-*exo*-Acetoxy-*syn*-11,12-dioxatetracyclo-[6.2.1.1^{5,10}.0^{6,9}]dodec-7-ene-2,2-dicarboxylate (*exo*-3b): colorless crystals from benzene; mp 206–209 °C; IR (KBr disk) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.35 (s, 2 H), 5.60 (s, 1 H), 5.07 (s, 1 H), 4.95 (s, 2 H), 4.44 (s, 1 H), 3.9–4.5 (m, 4 H), 2.03 (s, 3 H), 1.99 (d, J = 6.0 Hz, 1 H), 1.60 (d, J = 6.0 Hz, 1 H), 1.25 (t, J = 7.3 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 169.79, 167.49, 165.95, 137.37, 137.10, 83.41, 81.43, 80.70, 80.46, 79.75, 69.60, 62.15, 61.74, 44.90, 43.89, 20.87, 14.15, 13.99; EIMS, m/z 366, 298, 238, 231, 193, 187. Anal. Calcd for $C_{18}H_{22}O_8$: C, 59.01; H, 6.05. Found: C, 59.08; H, 6.08.

Diethyl 3-*endo*-Acetoxy-*anti*-11,12-dioxatetracyclo-[6.2.1.1^{5,10}.0^{6,9}]dodec-7-ene-2,2-dicarboxylate (*endo*-4b): colorless crystals from chloroform–ether; mp 164–165 °C; IR (KBr disk) 1760, 1740, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.26 (br s, 2 H), 5.73 (d, J = 5.5 Hz, 1 H), 5.01 (br d, J = 5.0 Hz, 1 H), 4.89 (br d, J = 5.0 Hz, 1 H), 4.47 (d, J = 5.5 Hz, 1 H), 4.45 (s, 1 H), 4.18 (q, J = 7.1 Hz, 4 H), 3.54 (dd, J = 5.0, 8.0 Hz, 1 H), 2.79 (dd, J = 5.0, 8.0 Hz, 1 H), 2.06 (s, 3 H), 1.24 (t, J = 7.1 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 169.30, 167.76, 165.38, 134.34, 133.77, 80.49, 79.54, 79.32, 76.45, 74.96, 65.26, 62.34, 61.36, 43.03, 41.45, 20.60, 14.02, 13.88; EIMS, m/z 366, 298, 238, 193, 187. Anal. Calcd for $C_{18}H_{22}O_8$: C, 59.01; H, 6.05. Found: C, 58.96; H, 6.12.

Single crystals for X-ray analysis were prepared by crystallization from chloroform–ether in a refrigerator. Intensities were measured up to 2θ = 55.0° on a Rigaku AFC-5 four-circle automatic diffractometer with Mo Kα radiation. The structure was solved by the direct method and refined by the block-diagonal least-squares method to R = 0.064 (R_w = 0.0578).

Crystal data: $C_{18}H_{22}O_8$, monoclinic, space group $P2_1/c$; Z = 4, a = 11.365 (1) Å, b = 8.626 (1) Å, c = 18.680 (4) Å, β = 99.72 (2); V = 1804.9 Å^3; D_{measd} = 1.351 g cm^{-3}, D_{calcd} = 1.349 g cm^{-3}.

Diethyl 3-*exo*-Acetoxy-*anti*-11,12-dioxatetracyclo-[6.2.1.1^{5,10}.0^{6,9}]dodec-7-ene-2,2-dicarboxylate (*exo*-4b): colorless crystals from hexane–acetone (2:1); mp 148–150 °C; IR (KBr disk) 1750, 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.29 (dd, J = 1.5, 9 Hz, 1 H), 6.24 (dd, J = 1.5, 9 Hz, 1 H), 5.54 (s, 1 H), 4.94 (br d, J = 4.5 Hz, 1 H), 4.89 (br d, J = 5.0 Hz, 1 H), 4.74 (s, 1 H), 4.5–4.1 (m, 4 H), 4.04 (s, 1 H), 2.57 (dd, J = 4.5, 8.0 Hz, 1 H), 2.25 (dd, J = 5.0, 8.0 Hz, 1 H), 1.99 (s, 3 H), 1.29 (t, J = 7.0 Hz, 3 H), 1.24 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 169.68, 167.08, 166.08, 134.09, 133.36, 80.19, 79.89, 79.48, 79.43, 77.99, 70.06, 62.26, 61.82, 44.62, 43.43, 20.79, 14.18, 14.07; EIMS, m/z 366, 298, 238, 193, 187. Anal. Calcd for $C_{18}H_{22}O_8$: C, 59.01; H, 6.05. Found: C, 59.07; H, 6.16.

Diethyl 3-*exo*-Acetoxy-*syn*,*syn*-15,16,17-trioxahexacyclo[10.2.1.1^{6,13}.1^{8,11}.0^{5,14}.0^{7,12}]heptadec-9-ene-2,2-dicarboxylate (5b): colorless crystals; mp 212–215 °C; IR (KBr disk) 1755, 1740, 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.30 (br s, 2 H), 5.54 (s, 1 H), 5.03 (s, 1 H), 4.86 (br s, 2 H), 4.48 (br s, 2 H), 4.42 (s, 1 H), 4.4–4.0 (m, 4 H), 2.04 (d, J = 6.6 Hz, 1 H), 2.01 (s, 3 H), 1.74, 1.71 (AB q, J = 6.2 Hz, 2 H), 1.63 (d, J = 6.6 Hz, 1 H), 1.27 (t, J = 7.0 Hz, 3 H), 1.24 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 169.79, 167.59, 165.84, 137.07, 84.34, 82.24, 80.76, 80.49, 80.39, 80.34, 79.44, 69.52, 62.18, 61.79, 49.36, 48.60, 48.28, 47.58, 20.86, 14.18, 14.09; EIMS, m/z 434, 366, 298, 238, 231, 193, 187.

Diethyl 3-*exo*-Acetoxy-*anti*,*anti*,*syn*-19,20,21,22-tetraoxaoctacyclo[14.2.1.1^{6,17}.1^{8,15}.1^{10,13}.0^{5,18}.0^{7,16}.0^{9,14}]docos-11-ene-2,2-dicarboxylate (6b): colorless crystals; ^1H NMR ($CDCl_3$) δ 6.32 (s, 2 H), 5.55 (s, 1 H), 4.88 (s, 1 H), 4.76 (s, 2 H), 4.43 (d, J = 6.3 Hz, 1 H), 4.41 (d, J = 6.3 Hz, 1 H), 4.34 (d, J = 6.3 Hz, 1 H), 4.31–4.13 (m, 6 H), 2.58 (dd, J = 5.8, 8.9 Hz, 1 H), 2.43 (dd, J = 5.8, 8.9 Hz, 1 H), 2.42 (dd, J = 5.8, 8.9 Hz, 1 H), 2.08 (dd, J = 5.8, 8.9 Hz, 1 H), 2.04 (s, 3 H), 1.94, 1.93 (AB q, J = 6.6 Hz, 2 H), 1.26 (t, J = 7.0 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 169.77, 167.17, 166.03, 137.04, 80.78, 80.19, 79.92, 78.26, 76.42, 69.33, 62.31, 61.96, 49.63, 48.47, 47.93, 45.79, 20.84, 14.18, 14.02; EIMS, m/z 502, 434, 366, 298, 238, 231, 193, 187; HRMS calcd for $C_{26}H_{30}O_{10}$ 502.1827, found 502.1839.

High-Pressure Reaction of Furan with Dimethyl (Acetoxymethylene)malonate (1a). A mixture of 4.24 g (21 mmol) of **1a**[9,11] and 2.63 g (39 mmol) of furan was allowed to react as described above at 1.0 GPa for 10 days. A similar workup of the resulting adduct mixture by silica gel chromatography (benzene–diethyl ether) afforded mixtures of **1a** and *endo*-**2a** as a colorless oil (1.504 g, **1a**:*endo*-**2a** = 3) and a solid (1.817 g, **1a**:*endo*-**2a** = 1:3), an endo–exo mixture of **2a** as a colorless oil (0.620 g, endo:exo = 3:2), and pure *exo*-**2a** as crystals (0.554 g). An authentic specimen of *endo*-**2a** was obtained by crystallization of the **1a**–*endo*-**2a** mixture.

Dimethyl 3-*endo*-Acetoxy-7-oxabicyclo[2.2.1]hept-5-ene-2,2-dicarboxylate (*endo*-2a): colorless crystals from diethyl ether; mp 90–91 °C; IR (KBr disk) 1738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.86 (dd, J = 1.8, 5.8 Hz, 1 H), 6.38 (dd, J = 1.4, 5.8 Hz, 1 H), 6.07 (d, J = 4.4 Hz, 1 H), 5.27 (br s, 1 H), 5.20 (br d, J = 4.4 Hz, 1 H), 3.82 (s, 3 H), 3.68 (s, 3 H), 1.96 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 169.34, 168.26, 166.63, 137.16, 133.77, 83.93, 79.28, 74.75, 65.05, 53.27, 52.35, 20.39; EIMS, m/z 210 (M^+ – 60), 179, 160, 159, 129. Anal. Calcd for $C_{12}H_{14}O_7$: C, 53.33; H, 5.22. Found: C, 53.37; H, 5.16.

Dimethyl 3-*exo*-Acetoxy-7-oxabicyclo[2.2.1]hept-5-ene-2,2-dicarboxylate (*exo*-2a): colorless crystals from diethyl ether; mp 80–81 °C; IR (KBr disk) 1748, 1738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.54 (dd, J = 1.8, 5.7 Hz, 1 H), 6.34 (dd, J = 1.8, 5.7 Hz, 1 H), 5.56 (s, 1 H), 5.41 (br s, 1 H), 4.93 (br s, 1 H), 3.78 (s, 3 H), 3.71 (s, 3 H), 2.07 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 169.85, 167.54, 167.35, 136.53, 83.41, 81.62, 76.88, 63.96, 53.02, 52.97, 20.95; EIMS, m/z 210 (M^+ – 60), 179, 160, 159, 129. Anal. Calcd for $C_{12}H_{14}O_7$: C, 53.33; H, 5.22. Found: C, 53.39; H, 5.29.

Lewis Acid Catalyzed High-Pressure Reactions of Furan with 1b. ZnI_2 as a Catalyst. A solution of 0.516 g (2.24 mmol) of **1b**, 0.700 g (11.2 mmol) of furan, and 0.113 g (0.35 mmol) of zinc iodide in 0.5 mL of tetrahydrofuran was pressurized to 1.0 GPa for 2 days. After the solvent and remaining furan were removed under reduced pressure, the resulting mixture was

chromatographed on a silica gel column with benzene–hexane as an eluent to afford 0.285 g (54%) of 8[18] as a colorless oil: IR 1740, 1640, 1260, 1230 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50 (br d, J = 1.8 Hz, 1 H), 7.45 (s, 1 H), 6.75 (d, J = 3.6 Hz, 1 H), 6.50 (dd, J = 1.8, 3.6 Hz, 1 H), 4.40 (q, J = 7.2 Hz, 2 H), 4.27 (q, J = 7.2 Hz, 2 H), 1.36 (t, J = 7.2 Hz, 3 H), 1.30 (t, J = 7.2 Hz, 3 H).

A titanium tetrachloride catalyzed reaction of **1b** with furan in dichloromethane at 0 °C at atmospheric pressure also afforded 8 in 35% yield.

Yb(fod)$_3$ as a Catalyst. To a solution of 0.502 g (2.2 mmol) of **1b** and 0.07 g (10.4 mmol) of furan in dichloromethane was added 0.024 g of tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)ytterbium (Yb(fod)$_3$). The solution was pressurized to 1.0 GPa for 5 days. Working up of the reaction mixture as mentioned above gave 0.203 g (39%) of 8.

Thermal Retro Diels–Alder Reactions of 2b. A solution containing *endo*-**2b** (66.9 mg; 0.224 mmol) and *exo*-**2b** (29.7 mg; 0.1 mmol) in 1.0 mL of benzene-d_6 was sealed in an NMR tube, and the tube was immersed in a constant temperature bath maintained at 71.2 °C. The reactions were monitored by a 100-MHz NMR spectrometer. The decomposition rates of *endo*-**2b** and *exo*-**2b** were calculated by the intensity change of the acetoxy methyl signals of the reactants and **1b**, and the ring hydrogens of furan as well. The reactions were found to be very clean, and no other product signals were detected.

Lewis Acid Catalyzed Retro Diels–Alder Reactions of *endo*-2b. ZnI$_2$ as a Catalyst. A solution of *endo*-**2b** (59.5 mg; 0.2 mmol) and zinc iodide (75.7 mg; 0.2 mmol) in 5 mL of tetrahydrofuran was stirred for 5 min at 20 °C. The solution was evaporated, and to the residue was added 10 mL of benzene. Then the mixture was washed with saturated aqueous sodium hydrogen carbonate and water, and the organic layer was dried over sodium sulfate. After removal of the solvent under reduced pressure, 31.9 mg (69%) of **1b** was obtained as a colorless oil.

Yb(fod)$_3$ as a Catalyst. A solution of *endo*-**2b** (59.5 mg; 0.2 mmol) and Yb(fod)$_3$ (20.3 mg; 0.19 mmol) in 5 mL of tetrahydrofuran was stirred for 30 min at 20 °C. Working up of the reaction mixture as described above afforded 32.8 mg (71%) of **1b** as the sole product.

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Highly Stereoselective Total Synthesis of β-Ribofuranosylmalonate

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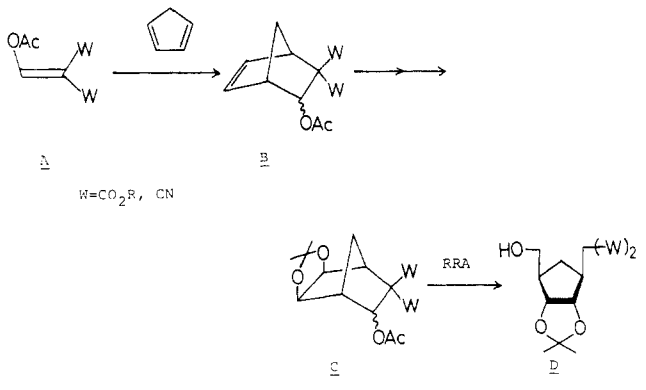
β-Ribofuranosylmalonates, prospective synthons for a variety of C-nucleosides, have been synthesized stereoselectively through the high-pressure Diels–Alder reaction of furan with dialkyl (acetoxymethylene)malonate, followed by reductive retrograde aldol C–C bond fission of the diol derived from the adduct.

Previously, we have established a facile method for the synthesis of the carbocyclic analogues D (Scheme I) of β-ribofuranosylmalonate and demonstrated their usefulness by their conversion to a variety of carbocyclic analogues of C-nucleosides (e.g., carbocyclic pyrimidine C-nucleosides[1] and carbocyclic oxazinomycins[2]). Although our method follows the general strategy for the construction of the bicyclo[2.2.1]heptene framework B using the Diels–Alder reaction of cyclopentadiene with acrylate derivatives,[3,4] the novelty of this method is the use of 3-acetoxyacrylate derivatives having a strong electron-withdrawing substituent at the 2-position (A: W = CO_2R, CN), which permits not only ready access of the cycloadduct B but also stereoselective cleavage of the C–C bond

Scheme I[a]



[a] RRA: reductive retrograde aldol reaction (K_2CO_3–$NaBH_4$–MeOH, room temperature).

of the dihydroxylated derivative C by reductive retrograde aldol reaction. We hereafter term this reaction as the RRA reaction.

Recently, we have found that the use of di-*l*-menthyl (acetoxymethylene)malonate (A: W = CO_2-*l*-menthyl) in the titanium tetrachloride catalyzed Diels–Alder reaction affords the corresponding adduct (chiral B) in high diastereomeric excess (de, ≥90%) and hence accomplished

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