tained below 35° throughout the reaction. The resulting brown solution was diluted with tetrahydrofuran (10 ml) and cooled to 0° in an ice bath. A tetrahydrofuran solution of the methyl ketone **24** (152 mg, 0.56 mmol) was added dropwise with stirring. The mixture was stirred for 15 min at 0°, and then saturated ammonium chloride solution (25 ml) was added slowly. The mixture was extracted with ethyl ether (2 × 25 ml). The ether phase was washed with saturated sodium chloride solution and dried over anhydrous magnesium sulfate. Removal of the solvent left a yellow oil, which was immediately chromatographed on a thick layer silica gel plate, using 20% ether–petroleum ether as eluent (R_f 0.20). This gave 5-(5′-bromo-2′,6′,6′-trimethyl-1′-cyclohexen-1′-yl)-3-hydroxy-3-methyl-1-pentene: yield 154 mg (91%); ir ($CDCl_3$) 3550 sharp, 3420 broad, 1648, 1220, 910 cm^{-1}; NMR (220 MHz, CCl_4) δ 1.19 (s, 6 H), 1.30 (s, 3 H), 1.60 (s, 3 H), 4.22 (dd, J = 10, 4 Hz, 1 H), 5.02 (d, J = 11 Hz, 1 H), 5.18 (d, J = 18 Hz, 1 H), 5.85 (dd, J = 18, 11 Hz, 1 H); mass spectrum m/e (rel abundance) 302, 300 1:1 (M^+, 1.0) 284, 282 1:1 (2.0), 203 (10), 119 (100), 93 (83), 71 (89), 43 (89); high-resolution mass spectrum M^+ 300.1088 ($C_{15}H_{25}O^{79}Br$ requires 300.1089).

10-Bromo-α-chamigrene (1). The alcohol **25** (51 mg, 0.17 mmol) was dissolved in anhydrous benzene (10 ml). A few crystals of *p*-toluenesulfonic acid monohydrate were added and the mixture was heated to reflux for 15 min. Thin layer chromatography after this time showed no starting alcohol. The mixture was cooled and poured over saturated sodium carbonate (25 ml), then washed with saturated sodium chloride. The benzene layer was separated and dried over anhydrous magnesium sulfate. Most of the solvent was removed, and the black residue was put on a short silica gel column. Elution with ethyl ether gave 39 mg of a yellow oil. This material was purified by preparative thick layer chromatography on silica gel with hexane as an eluent to give a clear oil. The GLC on 3% SP2401 showed four components. The major component, with a retention time of 8.5 min, was 10-bromo-α-chamigrene, yield 26.5% (by GLC). The gas chromatograph–mass spectrum of this material was identical in every respect with that of another sample of 10-bromo-α-chamigrene prepared by an independent synthesis. Mass spectrum m/e (rel abundance) 284, 282 1:1 (M^+, 5.9) 216 (53), 214 (55), 203 (17), 202 (39), 187 (13), 173 (5.9), 161 (2.6), 159 (37.6), 147 (27), 145 (21), 135 (100), 119 (85), 105 (46), 91 (39), 81 (20), 79 (19), 77 (21), 69 (12), 67 (12), 45 (18), 43 (11); NMR (220 MHz, CCl_4) δ 0.95 (s, 3 H), 1.08 (s, 3 H), 1.65 (s, 6 H), 4.61 (dd, J = 4, 10 Hz, 1 H), 5.13 (broad, 1 H), 5.31 (broad, 1 H).

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Registry No.—**1**, 57473-87-7; **15**, 105-87-3; **19**, 57473-88-8; **20**, 57473-89-9; **21**, 57473-90-2; **22**, 3796-70-1; **23**, 57473-91-3; **24**, 57473-92-4; **25**, 57473-93-5.

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(18) **Note Added in Proof.** 10-Bromo-α-chamigrene (**1**) has recently been located in *Laurencia pacifica*.[15]

Nucleosides. XXXI.[1] Synthesis of 1-(2,6-Dideoxy-β-D-*arabino*-hexopyranosyl)cytosine, the Nucleoside Portion of Oxamicetin

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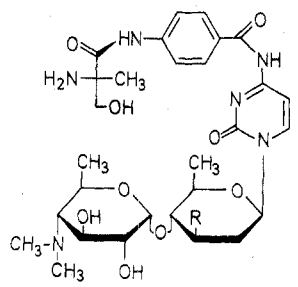
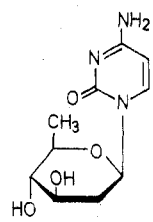
A synthesis of the nucleoside moiety of oxamicetin, 1-(2,6-dideoxy-β-D-*arabino*-hexosyl)cytosine (**3**), is described starting from the known 1-(2-deoxy-β-D-*arabino*-hexosyl)uracil (**7**). The synthetic sequence involved selective mesylation at the primary hydroxyl group, displacement by iodide, and reductive dehalogenation (**7** → **8** → **9** → **10**) followed by conversion of uracil nucleoside **10** into its cytosine analogue **3** by O-benzoylation, thiation, and ammonolysis. Structural and configurational assignments evolved from the mode of preparation as well as from spectroscopic data, a consideration of the circular dichroism Cotton effects indicating that the sugar-base conformation is strongly dependent on the nature of the 6′ substituent.

Oxamicetin (**1**), a new disaccharide nucleoside antibiotic isolated recently from the fermentation broth of *Arthrobacter oxamicetus*,[3,4] has been allotted[5] to the aminoacyl-4-aminohexosylcytosine group of protein biosynthesis inhibitors[6] on the basis of a close similarity to amicetin (**2**) in its gross antibacterial activity,[4] its inhibitory effect on the fragment reaction,[5] and its structural features,[7] differing from **2** only by an additional hydroxyl group in the disaccharide unit. The structural assignments within the nucleoside portion were mainly based on the isolation of 1-(2,6-dideoxy-β-D-*arabino*-hexopyranosyl)cytosine (**3**) on acid methanolysis, for which the alternate β-L-arabino configuration was excluded via the copper complex method.[7] This paper provides confirmatory evidence for the β-D-arabino configuration by an unequivocal synthesis of the nucleoside portion **3** and the proof of its identity with the oxamicetin derived product.

Of the several approaches conceivable for the synthesis of **3**, the utilization of the pyrimidinone nucleoside **4**, accessible from 3,4,6-tri-*O*-nitrobenzoyl-2-deoxy-α-D-*arabino*-hexosyl bromide and 2,4-diethoxypyrimidine in a remarkably stereoselective reaction,[8] was considered more propi-

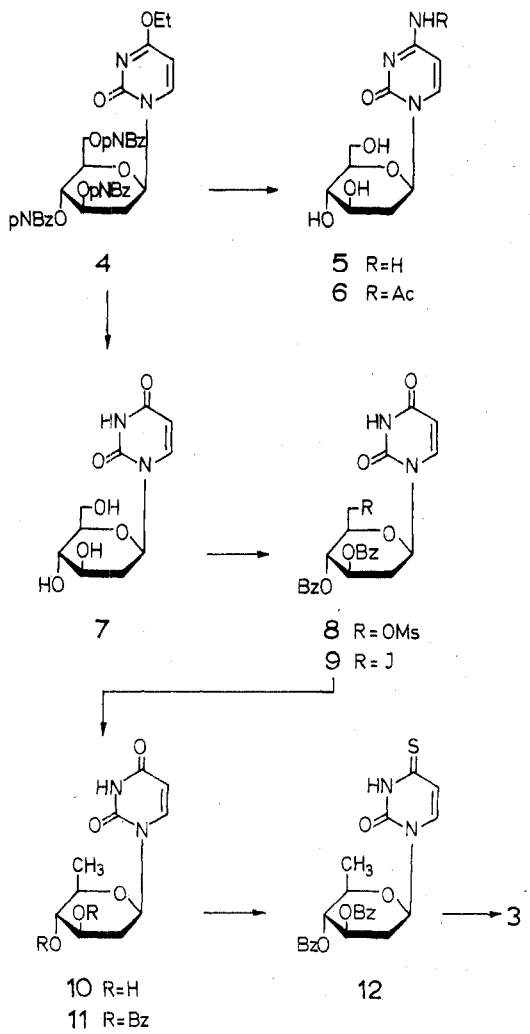


1 R=OH
2 R=H



3

tious than starting from the parent sugar[9] whose N-glycosidation was surmised to proceed much less stereoselectively owing to the absence of a hydroxy function at C-6. For conversion of **4** into **3**, the replacement of the primary hydroxyl group in the respective cytosine nucleoside **5**[8] would be the most direct route, yet reactions of **5** or its *N*-acetate **6** with sulfuryl bromide–hexamethylphosphoric triamide,[10] Rydon reagent,[11] or with triphenylphosphine–*N*-bromosuccinimide[12] failed or resulted in multicomponent mixtures under conditions that converted cytidine into its 5′-halide in yields of 50–60%. Similar difficulties were encountered with the corresponding 4-ethoxypyrimidinone nucleoside (**4**, H instead of pNBz), obtainable from **4** by deacylation with barium hydroxide in 50% ethanol–water[13] in low yield and, as yet, impure form. Thus, a more conventional approach was followed comprising a two-step halogenation of the uracil nucleoside **7** with subsequent elaboration of the cytosine nucleobase.



4
5 R=H
6 R=Ac
7
8 R=OMs
9 R=J
10 R=H
11 R=Bz
12

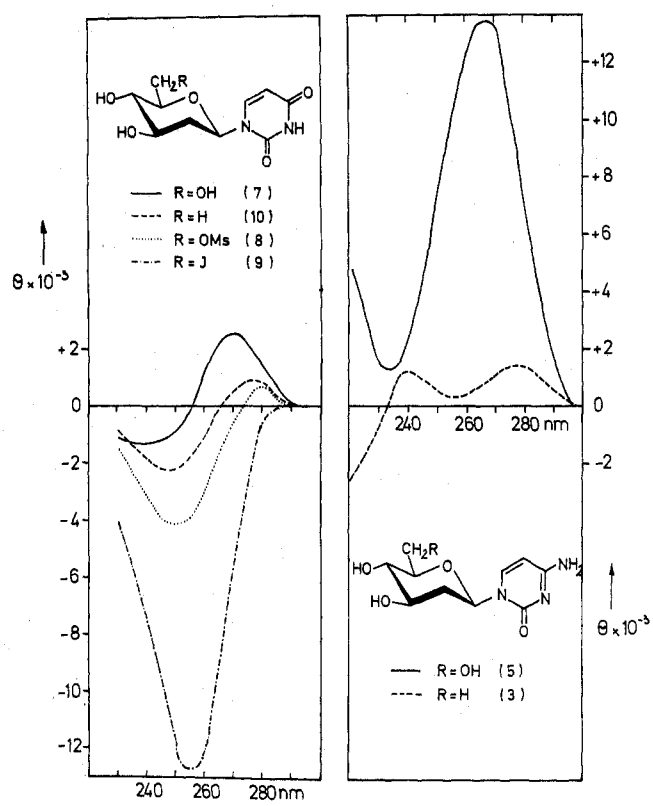


Figure 1. The circular dichroism curves of 1-(2-deoxy-β-D-*arabino*-hexopyranosyl)uracils **7–10** (left) and of cytosine analogues **3** and **5** (right) in water at pH 7.

The conversion of **4** into the uracil nucleoside **7**, previously effected by consecutive treatment with methanolic hydrogen chloride and sodium methoxide–methanol in 36% yield,[8] could readily be abridged into a single operation, stirring a suspension of **4** in aqueous barium hydroxide for 2 days, affording **7** in a yield of 85%. Subsequent selective mesylation of the primary hydroxyl group in **7** by treatment with methanesulfonyl chloride–pyridine yielded nucleoside **8** (51%). The primary mesyloxy group in **8** was then displaced with sodium iodide in dimethylformamide to give the corresponding 6′-iodonucleoside **9** (46%), which, in turn, was hydrogenated over 10% palladium on carbon, affording 1-(2,6-dideoxy-β-D-*arabino*-hexosyl)uracil (**10**) in 81% yield. The final transformation of the uracil moiety into the cytosine nucleobase (**10** → **3**) was effected in three steps, i.e., blocking of the hydroxyl groups in **10** by benzoylation to afford **11** (78%) followed by thiation with phosphorus pentasulfide–dioxane (58%) and subsequent treatment of the thionucleoside **12** with methanolic ammonia at 110° to give 1-(2,6-dideoxy-β-D-*arabino*-hexopyranosyl)cytosine (**3**) in 53% yield. All the physical constants of synthetic **3**, most notably the rotational and NMR spectroscopic data, were identical with those reported[7] for the oxamicetin derived **3**. Since well-defined synthetic procedures have been used throughout, structures and configurations of the newly synthesized nucleosides already followed from the mode of preparation. Sustaining evidence was furnished by NMR data exhibiting in all cases coupling patterns, particularly those arising from the 2′-CH_2 group, that are compatible with a $^4C_1$ conformation of the 2-deoxy sugar portion. The conformation of the planar pyrimidine ring with respect to the sugar, however, appears to be less uniform. As already indicated by the comparatively large differences in rotational values, e.g., −45.2° for the 6′-iodonucleoside **7** vs. +6.6° for the 6′-hydroxy analogue **5**, and more strikingly exposed in the circular dichroism spectra,

the conformation about the glycosidic bond is dependent on the nature of the 6′ substituent.

As in uridine [14a] the B_{2u} and B_{1u} Cotton effects for the uracil nucleosides **7** and **10** are resolved with positive and negative signs, respectively (cf. Figure 1). Although the magnitudes of the former are reduced by factors of 3 and 10 attributable to a less restricted rotation about the glycosidic bond, these data suggest that the main rotameric component is in the anti conformation. In the 6′-mesylate **8** the B_{2u} CD maximum is still smaller in magnitude with concurrent increase of the negative B_{1u} minimum, while in the 6′-iodonucleoside **9** only one intense negative Cotton effect at 255 nm is observed, seemingly the B_{1u} band. Although it is difficult to rationalize this result in geometrical terms, the CD behavior of **9** is reminiscent of that observed for 2′,3′-*O*-isopropylidene-O^2,5′-cyclouridine[14b] and, hence, may indicate a shift in the sugar–base rotameric equilibrium toward the syn conformation.

A similar dependence of sugar–base conformation on the nature of the 6′ substituent appears to be operative in the respective cytosine nucleosides, as clearly evidenced by the drastic change in CD behavior when replacing the 6′-hydroxyl group in **5** by hydrogen, i.e., **3** (cf. Figure 1).

Experimental Section

Melting points were determined on a Bock Monoskop, and are uncorrected. Spectra were recorded on Perkin-Elmer 125 (ir), 137 (uv), 141 (rotations), Jasco J-25 (CD), and Varian A-60A and XL-100 (NMR) instruments. Thin layer chromatography (TLC) on Merck plastic sheets of Kieselgel F_{254} and cellulose was used to monitor the reactions and to ascertain the purity of the products. Developers employed for silica gel plates: (A) ethyl acetate–benzene (3:2); (B) chloroform–methanol (7:3); for TLC on cellulose (C) ethyl acetate–2-propanol–water (3:3:4) and (D) 1-butanol–water (5:1). The spots were visualized by uv light. Preparative separations (PLC) were performed on 20 × 40 cm plates coated with 2 mm layers of silica gel $PF_{254+366}$ (Merck, Darmstadt) and activated at 120° overnight.

1-(3,4,6-Tri-*O*-*p*-nitrobenzoyl-2-deoxy-β-D-*arabino*-hexopyranosyl)-4-ethoxy-2(1*H*)-pyrimidinone (4). 3,4,6-Tri-*O*-benzoyl-2-deoxy-α-D-*arabino*-hexopyranosyl bromide was treated with 2,4-diethoxypyrimidine in three- to fivefold extensions of the procedure given by Zorbach et al.,[8] affording **4** of mp 273–274° and $[\alpha]^{20}D$ +12° (*c* 0.5, CH_2Cl_2) in yields of up to 65% [reported[8] mp 271–272.5°, $[\alpha]^{20}D$ −6.6° (*c* 0.5, CH_2Cl_2)].

1-(2-Deoxy-β-D-*arabino*-hexopyranosyl)-N^4-acetylcytosine (6). A solution of 154 mg (0.6 mmol) 1-(2-deoxy-β-D-*arabino*-hexosyl)cytosine (**5**)[8] in methanol (50 ml) containing 1 ml of acetic anhydride was refluxed for 3 h, followed by concentration to dryness. Purification of the residue over a silica gel column by elution with 3:2 chloroform–methanol and evaporation of the eluate to dryness gave a crystalline residue that was recrystallized from ethanol–ether: 125 mg (71%), mp 168–170°; uv (H_2O) λ_{max} 297 nm (ε 8100) and 249 (16 550), λ_{min} 273 (5300) and 228 (6600).

Anal. Calcd for $C_{12}H_{17}N_3O_6$: C, 48.16; H, 5.73; N, 14.04. Found: C, 48.06; H, 5.65; N, 13.88.

1-(2-Deoxy-β-D-*arabino*-hexopyranosyl)uracil (7). To a solution of barium hydroxide (21 g) in water (400 ml) was added 12.0 g (16 mmol) of ethoxynucleoside **4** followed by stirring of the resulting suspension at room temperature for 48 h. The insoluble material (ca. 5 g) was filtered off and washed three times with 15 ml of $Ba(OH)_2$ solution. To the combined washings and filtrate was added dry ice (CO_2) with vigorous stirring to obtain pH 7. The neutral mixture was filtered and evaporated to dryness in vacuo to give a residue which was extracted twice with 600 ml of boiling ethanol. Standing of the combined extracts at 0° overnight was followed by filtration, evaporation to dryness in vacuo and recrystallization of the residue from methanol–ether: 3.6 g (85%) of **7**, mp 156–159°, suitable for ensuing conversions. The analytical sample was obtained by another recrystallization from ethanol–ether: mp 161–163°; $[\alpha]^{20}D$ +6.6° (*c* 0.5, water) [reported[8] mp 168–169° and 196–197.5°; $[\alpha]^{20}D$ +5.6° (*c* 0.45, water)]; uv (H_2O) λ_{max} 261 nm, λ_{min} 230; (pH 12) λ_{max} 261, λ_{min} 242; CD (H_2O) θ −1300 (239 nm), +2600 (270); NMR (D_2O) δ 7.81 and 5.88 (two 1 H d, $J_{5,6}$ = 8 Hz, H-6 and H-5), 5.77 (q, 1, $J_{1',2'a}$ = 10 and $J_{1',2'e}$ = 2 Hz, H-1′), 3.45 (broad m, 5, H-3′–H-6′), 2.22 (octet, 1, $J_{2'e,2'a}$ = 11, $J_{2'e,3'}$ = 4 Hz, H-2′e), 1.90 (quintet, 1, $J_{2'a,3'}$ = 10 Hz, H-2′a).

1-(6-*O*-Mesyl-2-deoxy-β-D-*arabino*-hexopyranosyl)uracil (8). To a solution of uracil nucleoside **7** (2.5 g, 9.6 mmol) in 100 ml of dry pyridine was added 0.5 ml of methanesulfonyl chloride at 0° followed by stirring at this temperature for 30 min. Ice (35 g) was subsequently added with vigorous stirring and the mixture was then evaporated to dryness in vacuo. The syrupy residue was dissolved in methanol (20 ml) deposited on eight PLC plates and developed thrice with 7:3 chloroform–methanol. The main zone was removed and eluted with methanol (500 ml), followed by evaporation to dryness and extraction of the residue with ethanol (300 ml). Charcoal treatment of the extract and concentration in vacuo gave a residue, that crystallized on trituration with small amounts of aqueous ethanol: 1.67 g (51%) of 6′-*O*-mesylate **8**; mp 109–111°; uv (CH_3OH) λ_{max} 259 nm (ε 9940), λ_{min} 232 (2350); CD (H_2O) θ −4100 (250 nm), +700 (281); NMR (Me_2SO-d_6) δ 7.70 and 5.64 (two 8-Hz d, H-6 and H-5), 5.70 (H-1′ signal, multiplicity obscured by H-5), 3.16 (3 H s, OMs).

Anal. Calcd for $C_{11}H_{16}N_2O_8S$: C, 39.28; H, 4.80; N, 8.33. Found: C, 39.13; H, 4.73; N, 8.16.

1-(2,6-Dideoxy-6-iodo-β-D-*arabino*-hexopyranosyl)uracil (9). To a solution of sodium iodide (10.3 g) in anhydrous dimethylformamide (75 ml) was added 1.5 g (4.5 mmol) of 6′-*O*-mesyl nucleoside **8** and the mixture was heated in an oil bath (140–150°) for 40 min, followed by evaporation to dryness in vacuo (1 Torr). The residue was purified by elution from a silica gel column (1.5 × 25 cm) with chloroform–methanol (4:1), followed by evaporation of the eluate and crystallization of the remaining syrup from acetone–methanol–ether: 0.74 g (46%) of **9** as needles: mp 213°; $[\alpha]^{20}D$ −45.2° (*c* 0.5, water); uv (H_2O) 259 nm (ε 13 020); λ_{min} 231 (3010); CD (H_2O) θ −12 700 (255 nm); NMR (Me_2SO-d_6) δ 7.61 and 5.64 (two 8-Hz d, H-6 and H-5), 5.73 (q, 1, $J_{1',2'a}$ = 10.5 and $J_{1',2'e}$ = 2.4 Hz, H-1′), 2.04 (octet, 1, $J_{2'e,2'a}$ = 12 and $J_{2'e,3'}$ = 4.8 Hz, H-2′e), 1.74 (quintet, 1, $J_{2'a,3'}$ = 10 Hz, H-2′a).

Anal. Calcd for $C_{10}H_{13}N_2O_5I$: C, 32.62; H, 3.56; N, 7.61. Found: C, 32.54; H, 3.45; N, 7.53.

1-(2,6-Dideoxy-β-D-*arabino*-hexopyranosyl)uracil (10). To the iodonucleoside **9** (0.75 g, 2.0 mmol) in 50% aqueous methanol (80 ml) was added 200 mg of 10% Pd/C catalyst, followed by vigorous agitation in an hydrogen atmosphere for 10 min at ambient temperature. Triethylamine (0.6 ml) was then added and agitation was continued for 2 h, whereafter TLC on cellulose (C) indicated absence of educt. The catalyst was removed by filtration, and the filtrate was evaporated in vacuo to a syrup, which was purified over a small Dowex 2 (HCO_3^-) column by elution with water. Evaporation of the eluate to dryness, followed by reevaporations from acetone and crystallization from acetone–ether, afforded 390 mg (81%) of the 2′,6′-dideoxynucleoside **10**: mp 199–200°; uv (pH 2–7) λ_{max} 259 nm (ε 8870), λ_{min} 230 (2930); (pH 12) λ_{max} 259 (6650) λ_{min} 242 (5480); CD (H_2O) θ −2140 (248 nm), +860 (278); NMR (D_2O) δ 7.75 and 5.87 (two 8-Hz d, H-6 and H-5), 5.74 (q, 1, $J_{1',2'a}$ = 10.5 and $J_{1',2'e}$ = 2.5 Hz, H-1′), 1.32 (d, 3, 6′-CH_3).

Anal. Calcd for $C_{10}H_{14}N_2O_5$: C, 49.58; H, 5.83; N, 11.57. Found: C, 49.50; H, 5.77; N, 11.47.

1-(3,4-Di-*O*-benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)uracil (11). To a solution of nucleoside **10** (350 mg, 1.5 mmol) in 15 ml of anhydrous pyridine was added dropwise with efficient stirring 0.9 ml of benzoyl chloride. The reaction mixture was kept at 55–60° for 20 hr, whereafter TLC (silica gel, solvents A, B) showed disappearance of the starting material. The reaction mixture was concentrated in vacuo to half of the volume, applied to four PLC plates, and developed four times with chloroform followed by elution of the main band (R_f 0.50) with chloroform. The eluate was evaporated to dryness in vacuo, codistilled with ethanol for crystallization, and recrystallized from ethanol: 510 mg (79%) of **11** as long needles; mp 188–190°; uv (ethanol) λ_{max} 235 nm (ε 24 680), inflection at 252 (18 680). The product was used directly for thiation.

1-(3,4-Di-*O*-benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-4-thiouracil (12). To a solution of 510 mg (0.9 mmol) of nucleoside **11** in dioxane (20 ml) was added 220 mg of phosphorus pentasulfide and the mixture was heated under reflux for 2.5 h. After concentration to about 5 ml, the suspension was filtered and the filtrate was applied to four PLC plates followed by development with chloroform–methanol (55:45). The main zone (R_f 0.43) was removed and eluted with chloroform, to give upon evaporation to dryness and trituration of the residue with ethanol 240 mg (58%), mp 220–222°, uv (ethanol) λ_{max} 328 nm (ε 8870).

Anal. Calcd for $C_{24}H_{22}O_6N_2S$: C, 61.80; H, 4.75; N, 6.01. Found: C, 61.65; H, 4.67; N, 5.95.

1-(2,6-Dideoxy-β-D-*arabino*-hexopyranosyl)cytosine (3). A solution of 175 mg (0.38 mmol) of thionucleoside **10** in anhydrous methanol (25 ml) was placed in a glass sealing tube (50 ml) an which after saturation with ammonia at 0° was sealed and heated at 110–120° for 20 h. The tube was cooled and opened and its contents were evaporated to dryness. The residue, already homogeneous by TLC in A and C, was purified by PLC on cellulose plates (Machery and Nagel 300–50 with 0.5-mm coatings) with 2-propanol–concentrated ammonia–water (7:1:2). Elution of the main zone (R_f 0.71) with water, evaporation of the eluate to dryness, and trituration with methanol–acetone afforded 51 mg (53%) of **3** as fine crystals of mp 135–140° after softening from 120° on and $[\alpha]^{25}D$ −4.3° (*c* 0.55, H_2O) [reported[7] mp 137–140° and $[\alpha]^{25}D$ −4° (*c* 0.38, H_2O)]; CD (H_2O) θ +1200 (240 nm), +1300 (278), cf. Figure 1. The uv data in 0.1 N HCl and 0.1 N NaOH were identical, i.e. ϵ_{max} (pH 13)/ϵ_{max} (pH 1) 0.68; the NMR spectrum in D_2O was superimposable on that reported[7] for oxamicetin derived **3**.

Acknowledgment. We express our appreciation with thanks to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for generously supporting this investigation.

Registry No.—**3**, 52598-18-2; **4**, 6067-28-3; **5**, 6027-64-1; **6**, 57459-51-5; **7**, 5139-56-0; **8**, 57459-52-6; **9**, 57459-53-7; **10**, 57459-54-8; **11**, 57459-55-9; **12**, 57459-56-0; acetic acid, 108-24-7; methanesulfonyl chloride, 124-63-0; benzoyl chloride, 98-88-4.

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Regiospecificity of the 1,4 Cycloaddition of 2-Methyl-1-penten-3-one to Methyl Crotonate and to Methyl Methacrylate

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The thermal cycloaddition of 2-methyl-1-penten-3-one (**6**) to methyl methacrylate (**2**) gave 3,6-dimethyl-2-ethyl-1-oxacyclohex-2-ene-6-carboxylic acid methyl ester (**12**), and subsequent reduction of the ester group and acid-catalyzed cyclization gave 1,4-dimethyl-5-ethyl-6,8-dioxabicyclo[3.2.1]octane (**14**). In contrast to this result, the addition of **6** to methyl crotonate (**7**) gave 3,6-dimethyl-2-ethyl-1-oxacyclohex-2-ene-5-carboxylic acid methyl ester (**10**), and reduction and cyclization gave 3,7-dimethyl-1-ethyl-2,6-dioxabicyclo[2.2.2]octane (**11**). A dimer of **6**, 3,6-dimethyl-2-ethyl-6-propanoyl-1-oxacyclohex-2-ene (**16**), was formed in both thermal addition reactions, and the dimerization of **2** to yield 2-methyl-5-methylene-1,6-hexanedioic acid dimethyl ester (**18**) co-occurred with the addition of **6** to **2**.

Brevicomin (**5**),[1] frontalin (**4**),[2] and multistriatin (**9**)[3] are related bicyclic ketal structures that are components of the aggregation pheromones of three bark beetle species, *Dendroctonus brevicomis, Dendroctonus frontalis,* and *Scolytus multistriatus.* The aggregation pheromones of these insects are potentially useful agents for survey and control of insect populations. These compounds have been synthesized by different routes,[4–6] one of which utilized the cycloaddition of an α,β-unsaturated ketone to an α,β-unsaturated ester.[7]

Mundy and coworkers synthesized **4** via the cycloaddition of methyl vinyl ketone (**1**) to methyl methacrylate (**2**).[7] The cycloaddition product (**3**) was subsequently reduced and cyclized to yield **4.** One critical feature of this synthetic approach is the regiospecificity of the 1,4-cycloaddition reaction. Mundy's synthesis was based on earlier work of Smith and coworkers,[8] and in both studies addition proceeded via path a and not b. Furthermore, cycloadditions with dienophiles such as α,β-unsaturated nitriles, al-