exhibiting similar TLC profiles were combined. A portion (2.5 g) of combined fractions 9–11 (16.45 g) was chromatographed on 40 g of thin layer mesh silica gel H using ether/hexane (5/95) as solvent and collecting 20-ml fractions. Dactylyne (175 mg) crystallized from the material obtained in fractions 18–20 (290 mg). Recrystallization from an ether/hexane mixture yielded large, colorless crystals roughly trapezoidal in shape which were utilized for x-ray crystallographic analysis.[2] After 29 fractions had been collected, one 250-ml fraction was collected and this yielded 170 mg of material, homogeneous by TLC. Chromatography of this fraction on thin-layer mesh silica gel gave 160 mg of isodactylyne (**2**). All attempts to crystallize isodactylyne were unsuccessful.

Isodactylyne had $[\alpha]^{24}D$ −8.06 ° (*c* 7.97, $CHCl_3$); R_f 0.46 (1:1 benzene/hexane, silica gel H); ir (neat) 3300, 3030, 2970, 2930, 2830, 2085 (weak), 1640, 1415, 1345, 1315, 1080 (br), 955, 870, 750, and 600 cm^{-1}; uv (isooctane) λ_{max} 224 nm (ϵ_{max} 15 500), with an inflection at 233 nm; 100-MHz NMR ($CDCl_3$), see Figure 1; mass spectrum (70 eV) *m/e* (rel intensity) M^+, 412 (3), 410 (4), 408 (2), 377 (1), 375 (2), 373 (1), 345 (2), 343 (3), 341 (2), 337 (7), 331 (16), 329 (10), 251 (3), 249 (5), 247 (1), 229 (3), 227 (4), 225 (1), 187 (5), 185 (10), 183 (10), 182 (8), 153 (15), 149 (24), 147 (28), 146 (15), 145 (14), 129 (11), 119 (29), 118 (18), 117 (51), 115 (14), 107 (11), 105 (20), 103 (31), 95 (11), 93 (10), 91 (34), 81 (23), 79 (30), 78 (18), 77 (19), 75 (10), 69 (13), 67 (65), 64 (100) base peak, 57 (15), 55 (18), 53 (27), 51 (12), 41 (40).

Pure dactylyne had mp 62.5–63.5 °C; $[\alpha]^{23}D$ −36.2° (*c* 15.2, $CHCl_3$); R_f 0.57 (1:1 benzene/hexane, silica gel H).

Octahydromonodebromodactylyne (3). A. From Dactylyne (1). To a stirred suspension of 30 ml of ethyl acetate containing a few milligrams of prereduced PtO_2 in a hydrogen atmosphere (1 atm) was added 105 mg of dactylyne dissolved in 10 ml of ethyl acetate. Hydrogenation was continued overnight, then the reaction mixture was filtered and the filtrate concentrated on a rotary evaporator to yield 77.8 mg (89.4%) of a clear, colorless oil which solidified after removal of the last traces of solvent under high vacuum. Recrystallization of the crude product from 95% ethanol yielded pure octahydromonodebromodactylyne (**3**), homogeneous by TLC: mp 51.4–52.5 °C; $[\alpha]D$ −0.90° (*c* 5.5 $CHCl_3$): ir ($CHCl_3$) 3000, 2960, 2860, 1450, 1415, 1370, 1345, 1310, and 1080 cm^{-1}; 60-MHz NMR[9] (CCl_4) δ 3.95 (m, 2 H, protons on the carbons bearing the halogens), 3.40, 320 (each 1 H, m, protons on carbons bearing oxygen), 2.67 (m, 2, methylene protons at C-4 of tetrahydropyran ring), 2.1–1.08 (m, 14 H), 0.95 (m, 6 H, terminal methyl group protons); mass spectrum (70 eV) *m/e* (rel intensity) 342 (2), 340 (6), 338 (5), 271 (14), 269 (53), 267 (37), 261 (4), 259 (10), 188 (16), 178 (13), 177 (20), 176 (15), 175 (59), 160 (10), 159 (9), 158 (24), 123 (97), 109 (13), 101 (37), 99 (19), 97 (33), 96 (42), 95 (16), 88 (22), 83 (93), 81 (88), 79 (12), 70 (40), 69 (55), 67 (84), 57 (25), 56 (32), 55 (100), 54 (22), 53 (25), 43 (76), 42 (20), 41 (94).

Anal. Calcd for $C_{15}H_{28}BrClO$: C, 52.87; H, 8.58; Br, 23.45; Cl, 10.40. Found: C, 53.47; H, 8.24; Br, 23.11; Cl, 10.09.

B. From Isodactylyne (2). Hydrogenation of 57.5 mg of **2** in the same manner as described above for **1** gave 36.7 mg (77.7%) of crude **3**. Recrystallization from 95% ethanol gave pure **3**, homogeneous by TLC: mp 51.0–52.5 °C; ir, NMR, and MS same as described in A above; mmp 51.5–53.3 °C; $[\alpha]D$ −0.90° (*c* 2.12, $CHCl_3$).

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Registry No.—**1**, 55306-12-2; **2**, 58001-90-4; **3**, 55229-33-9.

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(9) For NMR data at 100 MHz ($CDCl_3$) see ref 2.

Quassimarin, a New Antileukemic Quassinoid from *Quassia amara*[1,2]

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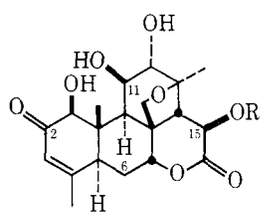
In the course of a continuing search for tumor inhibitors of plant origin, the sap of *Quassia amara* L.[3] (Simaroubaceae) was found to show significant activity in vivo against the P-388 lymphocytic leukemia in mice (PS) and in vitro against cells derived from human carcinoma of the nasopharynx (KB).[4] We report herein the fractionation of an active extract of *Q. amara* and the isolation and structural elucidation of a new antileukemic quassinoid,[5] quassimarin (**1**), and the companion quassinoid, simalikalactone D (**2**).



1, R = $COC(OAc)(CH_3)C_2H_5$
2, R = $COCH(CH_3)C_2H_5$

Fractionation of the dried sap, guided by assay against the KB and PS systems, revealed that the inhibitory activity was concentrated, successively, in the ethyl acetate layer of an ethyl acetate–water partition, the aqueous methanol layer of a 10% aqueous methanol–petroleum ether partition, and in the aqueous methanol layer of a 20% aqueous methanol–carbon tetrachloride partition. Column chromatography of the final aqueous methanol soluble material on SilicAR CC-7 yielded KB- and PS-active fraction D upon elution with 2% methanol in chloroform. Rechromatography of fraction D, first on silica gel 60 with isopropyl alcohol in dichloromethane as eluent, then on SilicAR CC-7 with acetone in hexane as eluent, gave quassimarin (**1**) and simalikalactone D (**2**).[6]

Elemental analysis and high-resolution mass spectrometry established a molecular formula of $C_{27}H_{36}O_{11}$ for quassimarin (**1**). The presence of an α-acetoxy-α-methylbutyrate ester was indicated by peaks in the mass spectrum at *m/e* 143 $[CO\text{-}C(OAc)(CH_3)C_2H_5]\cdot^+$, 115 $[C(OAc)(CH_3)C_2H_5]\cdot^+$, and 83 $[COC(CH_3)=CHCH_3]\cdot^+$, and by a dominant high mass fragment ion at *m/e* 358 corresponding to $M^+ - H_2O -$ HOOC-$C(OAc)(CH_3)C_2H_5$. Furthermore, the NMR spectrum contained signals for primary, tertiary, and acetate methyl groups assignable to the ester. Lithium aluminum hydride reduction of **1** afforded 2-methyl-1,2-butanediol. A one-proton doublet at τ 3.52 (J = 14 Hz) in the NMR spectrum of **1** confirmed the point of ester attachment to be at C-15.[7]

Irradiation of the C-15 proton doublet at τ 3.52 led to the

assignment of the doublet of doublets at τ 7.66 (J = 14, 2 Hz) to the C-14 proton. Then irradiation of the latter peaks caused not only the collapse of the doublet at τ 3.52, but also sharpening of a broad singlet at τ 6.18 assigned to the C-12 proton. The long-range coupling between the C-12 and C-14 protons is in accord with an α configuration for the C-12 hydroxyl. The small coupling between the C-11 and C-12 protons suggests a β stereochemistry for the C-11 hydroxyl, since any flattening of the ring to relieve the strain caused by two axial hydroxyls could cause the dihedral angle between the C-11 and C-12 protons to approximate 90°.

A broad multiplet at τ 5.3, superimposed on two other proton resonances, was assigned to the C-11 proton. Addition of benzene to the chloroform solution of 1 resolved the three resonances into the C-11 proton multiplet, a doublet (J = 8 Hz) coupled with a broadened doublet at τ 6.43, both assigned to the C-30 protons, and a triplet (J = 3 Hz) assigned to the C-7 proton. Irradiation of the C-11 proton multiplet caused the collapse of an OH doublet (J = 7 Hz) at τ 6.82 as well as change in a signal at τ 7.8. The latter signal was assigned to the C-9 proton.

The uv spectrum and characteristic fragment ion[8] at m/e 151 in the mass spectrum of quassimarin (1) supported the formulation of the A-ring portion as shown. In addition, the NMR spectrum of 1 contained signals for a vinyl proton and a vinyl methyl as well as a sharp singlet at τ 5.83 assignable to the C-1 proton. The detection of a 6% nuclear Overhauser effect between the C-1 and C-9 protons confirmed the β stereochemistry of the C-1 hydroxyl.

Experimental Section

General. Melting points were determined on a Mettler Model FP2 hot stage and are uncorrected. Ultraviolet absorption spectra were determined on a Beckman Model DK-2A recording spectrophotometer. Infrared spectra were determined on Perkin-Elmer Model 257 and Model 337 recording spectrophotometers. Nuclear magnetic resonance spectra were determined on a Varian HA-100 spectrometer or a JEOL PS-100 pulsed FT NMR spectrometer interfaced to a Texas Instrument JEOL 980A computer, with tetramethylsilane as an internal standard. Mass spectra were determined on Hitachi Perkin-Elmer Model RMU-6E and AEI Model MS-902 spectrometers. Values of $[\alpha]$D were determined on a Perkin-Elmer Model 141 automatic polarimeter. Gas–liquid chromatography was carried out on a Varian Aerograph Model 1800 gas chromatograph equipped with a 9-ft column, packed with 18% QF on Chromosorb W, at a column temperature of 80 °C with helium as carrier gas. Microanalyses were carried out by Spang Microanalytical Laboratory, Ann Arbor, Mich. Petroleum ether refers to the fraction of bp 60–68 °C. All thin layer chromatography was carried out on ChromAR 7GF precoated glass plates (Mallinckrodt). Visualization of TLC was effected with short-wavelength uv and concentrated sulfuric acid–vanillin–ethanol (20:1:3) spray.

Extraction and Preliminary Fractionation. The dried sap (2 kg) of *Q. amara* was partitioned between water (12 l.) and ethyl acetate (3 × 8 l.). The combined ethyl acetate layers were evaporated to give a dark brown residue (A, 80 g). Fraction A was partitioned between 10% aqueous methanol (0.5 l.) and petroleum ether (5 × 0.3 l.). The aqueous methanol layer and combined petroleum ether layers were evaporated to give B (77 g) and C (3 g), respectively. Further partitioning of fraction B between 20% aqueous methanol (0.6 l.) and carbon tetrachloride (3 × 0.3 l.) afforded, after evaporation, fractions D (65 g) and E (12 g).

Fraction D was subjected to column chromatography (SilicAR CC-7, 1500 g) with chloroform followed by chloroform containing increasing amounts of methanol as eluents. Elution with 2% methanol in chloroform gave fraction F (6.1 g) which was further fractionated by column chromatography on silica gel 60 (500 g). Elution with 4% isopropyl alcohol in dichloromethane yielded fraction G (1.9 g). Fraction G was submitted to further column chromatography on SilicAR CC-7 (120 g). Elution with 25% acetone in hexane gave fractions H (0.33 g) and I (0.49 g).

Simalikalactone D (2). Fraction H was purified by preparative TLC on ChromAR using ethyl acetate–cyclohexane (2:1). Elution of the major uv-active band afforded a residue which gave needles upon crystallization from ethyl acetate–hexane (**2**, 0.089 g, 0.005%). The material was identified by comparison of its melting point, $[\alpha]$D, and uv and NMR spectra with those reported for simalikalactone D,[6] and by comparison of its TLC and ir and mass spectra with those of an authentic sample.[9]

Quassimarin (1). Preparative TLC of fraction I on ChromAR using ethyl acetate–cyclohexane (2:1), followed by elution of the major uv-active band, gave a residue which crystallized as needles from ethyl acetate–hexane (**1**, 0.06 g, 0.003%): mp 237.5–238.5 °C dec; $[\alpha]^{26}$D +22.4° (c 0.29, $CHCl_3$); uv max (EtOH) λ (ϵ) 239 nm (10 800); ir ($CHCl_3$) 2.82, 5.71, 5.99, 7.93, 9.01, 9.43, 9.76 μ; NMR ($CDCl_3$) τ 8.95 (3 H, t, J = 7 Hz, CH_2CH_3), 8.80 (3 H, s, 10-CH_3), 8.45 (3 H, s, 13-CH_3), 8.38 (3 H, s, 2′-CH_3), 8.05 (3 H, s, 4-CH_3), 7.92 [3 H, s, C(=O)-CH_3], 7.66 (1 H, dd, J = 14 and 2 Hz, 14-H), 6.82 (1 H, d, J = 7 Hz, 11-OH), 6.43, 5.31 (each 1 H, d, J = 8 Hz, CH_2O), 6.18 (1 H, s, 12-H), 5.83 (1 H, s, 1-H), 5.6 (1 H, br s, OH), 5.35 (1 H, t, J = 3 Hz, 7-H), 5.3 (1 H, m, 11-H), 3.89 (1 H, br s, 3-H), 3.52 (1 H, d, J = 14 Hz, 15-H); mass spectrum m/e 536.2257 (M^+, calcd for $C_{27}H_{36}O_{11}$, 536.2258), 518, 358.1407 (calcd for $C_{20}H_{22}O_6$, 358.1416), 340, 301, 165, 151, 143.0707 (calcd for $C_7H_{11}O_3$, 143.0708), 115, 83.

Anal. Calcd for $C_{27}H_{36}O_{11}$: C, 60.44; H, 6.76. Found: C, 60.54; H, 6.88.

2-Methyl-1,2-butanediol from Quassimarin (1). A suspension of lithium aluminim hydride (7.0 mg, 0.18 mmol) and quassimarin (**1**, 9.7 mg, 0.018 mmol) in ether (1.5 ml) was stirred at room temperature for 4 h. Excess reagent was decomposed with saturated sodium potassium tartrate solution, the precipitate was removed, and the filtrate was concentrated at reduced pressure. Preparative GC afforded 2-methyl-1,2-butanediol which was shown to be identical (NMR, mass spectra, mixture GC analysis) with a sample prepared by conventional methods.[10]

Registry No.—**1**, 59938-97-5; **2**, 35321-80-3.

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A Convenient Preparation of Methyl (*E*)- and (*Z*)-4,4-Dimethoxy-2-butenoates by Electrolyses of Furfuryl Alcohol, Furfural, and 2-Furoic Acid

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Alkyl 4,4-dialkoxy-2-butenoates have been recognized as powerful Michael acceptors in the syntheses of the plant antitumor agent camptothecin[1] and of 11-oxoprostaglandins[2] and also as an unusual Diels–Alder dienophile.[3] Several efforts to obtain 4,4-dialkoxy-2-butenoates by the ozonolysis of 1,3-dienoates and subsequent acetalization, giving the *E* isomer,[3] by the alcoholysis of 4-ethoxy-2-butenolide derived