filtered. Concentration of organic solution yielded 1.17 g (5 mmol, 100% yield) of the Diels-Alder product.

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(6) Fellow of the Alfred P. Sloan Foundation, 1979-1981.

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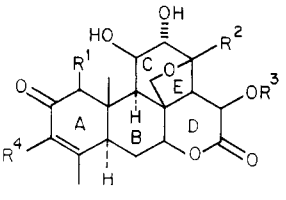
Model Studies for the Synthesis of Quassinoids. 1. Construction of the BCE Ring System

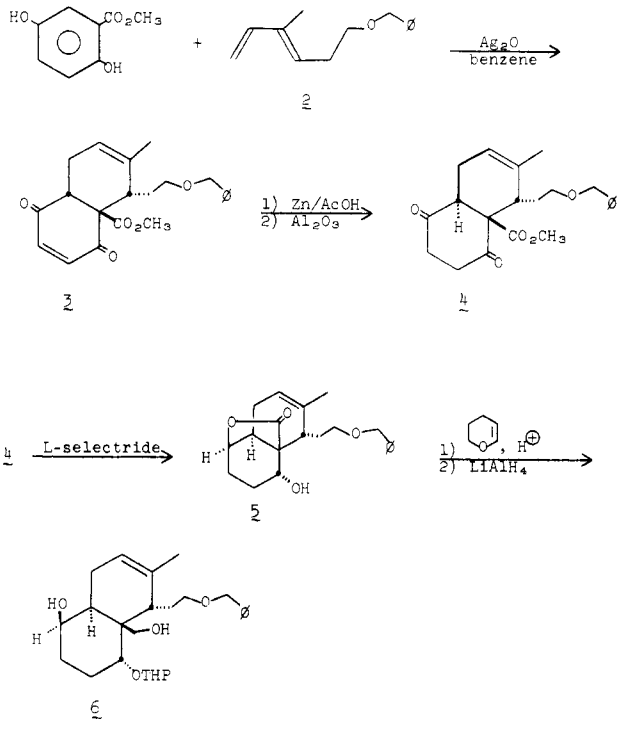
Summary: A tricyclic intermediate for the synthesis of quasimarin has been synthesized in 14 steps.

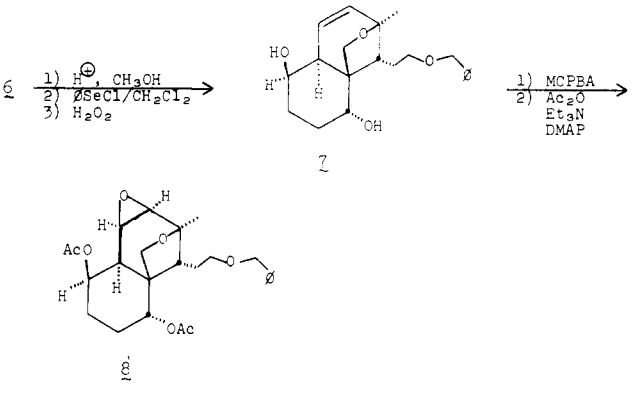
Sir: The structures of quasimarin (**1a**) and bruceantin (**1b**) were determined by Kupchan and co-workers.[1] Both their



1a, R^1 = OH; R^2 = CH_3; R^3 = $COC(OAc)(CH_3)Et$; R^4 = H
b, R^1 = H; R^2 = CO_2CH_3; R^3 = $COCH{=}C(CH_3)(i\text{-}Pr)$; R^4 = OH

cytotoxic activity and their challenging structures have prompted considerable synthetic interest.[2] Our approach has centered around the initial construction of a BC unit on which the A, D, and E rings can sequentially be appended. The requisite BC building block is efficiently assembled by the use of novel Diels-Alder reaction conditions described previously.[3] Diene **2**[4] is reacted with methyl gentisate in the presence of silver oxide to produce **3** in 95% yield. Reduction (Zn/HOAc) and epimerization (alumina chromatography)[6] afford diketone **4**[7] in 65-70% overall yield. L-Selectride reduction of **4** (THF, -78 °C, -25 °C for 12 h) provides lactone **5**,[8] whose structure is supported by IR absorptions at 3450 and 1770 cm^{-1} and the absence of ketone resonances in the ^{13}C NMR spectrum. The presence of only 19 ^{13}C NMR resonances presents strong evidence that hydroxy lactone **5** is stereochemically homogeneous. Protection of the hydroxyl group in **5** as the tetrahydropyranyl ether (THP) in quantitative yield by the method of Grieco[9] followed by lithium aluminum hydride reduction (1 equiv of LAH, Et_2O, 0 °C) affords diol **6** in 99% yield from **5**. Protection of the alcohol was necessary to avoid base-catalyzed fragmentation during the reduction. Ring E can now be introduced by the selenocyclization method developed by Nicolaou.[10]





We initially planned to construct the trans diaxial diol group in ring C by epoxide opening. Although this reaction is well precedented for simple unhindered systems, all attempts to open epoxide **8**[11] by external nucleophiles (H_2O, KO_2; $PhCH_2(N(CH_3)_3)OCHO$; $AcOH/Al_2O_3$) were unsuccessful. However, the sequence involving hydrogenolysis ($H_2/Pd/C$, MeOH), oxidation, and internal epoxide opening (CF_3CO_2H, CH_2Cl_2, 25 °C) to afford **9** provides an attractive solution to this difficulty. Infrared

(1) Bruceantin: Kupchan, S. M.; Britton, R. W.; Ziegler, M. F.; Siegel, C. W. *J. Org. Chem.* **1973**, *38*, 178. Quasimarin: Kupchan, S. M.; Streelman, D. R. *J. Org. Chem.* **1976**, *41*, 3481.

(2) Dias, J. R.; Ramachandra, R. *Tetrahedron Lett.* **1976**, 3685; *J. Org. Chem.* **1977**, *42*, 1613; *Synth. Commun.* **1977**, 293; *J. Org. Chem.*, **1977**, *42*, 3584. Snitman, D. L.; Tsai, M.-Y.; Watt, D. S. *Synth. Commun.* **1978**, 195.

(3) Kraus, G. A.; Taschner, M. J. *J. Org. Chem.*, previous paper in this issue.

(4) Diene **2** is prepared by deconjugation[5] of methyl 4-methyl-2,4-hexadienoate with lithium diisopropylamide, reduction with $LiAlH_4$, and protection of the alcohol with benzyl bromide.

(5) Torssell, K. *Tetrahedron Lett.* **1974**, 623.

(6) Ansell, M. F.; Lown, J. W.; Turner, D. W.; Wilson, D. A. *J. Chem. Soc.* **1963**, 3036.

(7) ^1H NMR δ 1.71 (3 H, br s), 2.6-3.5 (12 H, m), 3.70 (3 H, s), 4.42 (2 H, s), 5.28 (1 H, m), 7.33 (5 H, s); IR (film) 1740, 1720, 1215, 1090, 730, 690 cm^{-1}; mp 75-76 °C.

(8) ^1H NMR δ 1.72 (3 H, m), 3.56 (2 H, t, J = 5.5 Hz), 4.28 (1 H, d, J = 4 Hz), 4.52 (2 H, s), 5.26 (1 H, m), 7.3 (5 H, s); mp 105-106 °C.

(9) Miyashita, N.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.

(10) Nicolaou, K. C.; Lysenko, Z. *J. Am. Chem. Soc.* **1977**, *99*, 3185.

(11) ^1H NMR δ 1.48 (3 H, s), 2.00 (3 H, s), 2.20 (3 H, s), 2.90 (1 H, d, J = 4 Hz), 3.30 (1 H, dd), 3.61 (2 H, t, J = 5.7 Hz), 3.96 (1 H, d, J = 8 Hz), 4.61 (2 H, s), 4.61 (1 H, d, J = 8 Hz), 7.5 (5 H, s).

(12) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

(13) Lindgren, B. O.; Nilsson, T. *Acta Chem. Scand.* **1973**, *27*, 888. Our modification used 2-methyl-2-butene as the chlorine scavenger.

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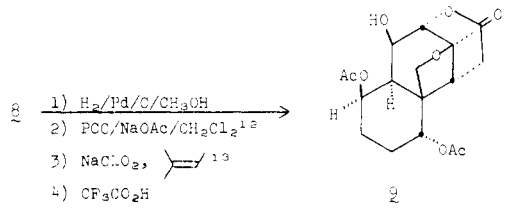

absorptions at 3510 and 1730 cm^{-1} and ^1H NMR absorptions at δ 1.51, 2.06, and 2.10 support the assignment of structure **9**.

Structure **9** contains seven contiguous asymmetric centers found in quasimarin and is available in 13% yield from **2**. We expect that this compound will serve as a key intermediate for the synthesis of quasimarin.

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Registry No. **2**, 72827-04-4; **3**, 72826-90-5; **4**, 72844-64-5; **5**, 72844-65-6; **6**, 72844-66-7; **7**, 72844-67-8; **8**, 72844-68-9; **9**, 72844-69-0; methyl gentisate, 2150-46-1.

(14) Fellow of the Alfred P. Sloan Foundation, 1979–1981.
(15) Compounds **4**, **5**, **6**, **7**, **8**, and **9** exhibited satisfactory high-resolution mass spectra and combustion analyses.

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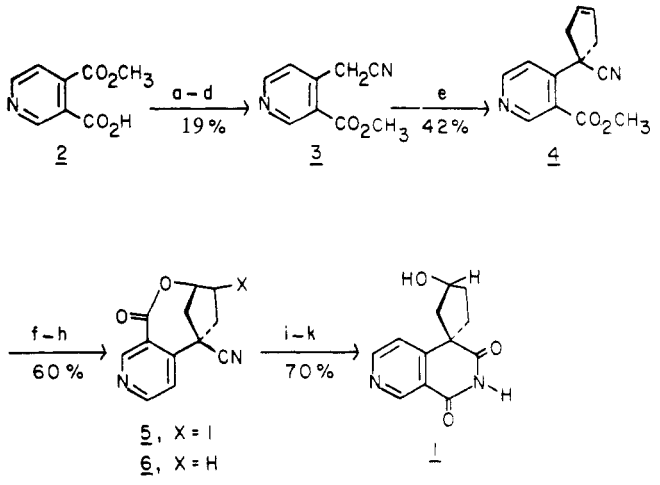
Total Synthesis of Racemic Sesbanine

Summary: A stereospecific total synthesis of racemic sesbanine (**1**) from 4-(methoxycarbonyl)nicotinic acid is described.

Sir: Powell and co-workers have reported antileukemic activity associated with extracts from seeds of *Sesbania drummondii*, a native plant with a history of toxicity to livestock.[1] Extensive purification procedures, guided by in vivo (P388 leukemia) and in vitro (KB cell culture) bioassays, ultimately resulted in isolation of sesbanine (**1**), a new spirocyclic structure based on the 2,7-naphthyridine nucleus; the structure of **1** was established by X-ray crystallography.[2]

In view of the unusual structure of **1** and the possibility that potent antileukemic activity might be associated with such a structure, we have developed a stereospecific synthesis of racemic **1** as outlined in Scheme I. 4-(Methoxycarbonyl)nicotinic acid (**2**),[3] available from methanolysis of 3,4-pyridinedicarboxylic anhydride, reduced with $LiAlH_4$ to afford 4-(hydroxymethyl)nicotinic acid, an unstable substance with a propensity to lactonize. The crude hydroxymethyl acid was converted to cyano ester

Scheme I[a]



[a] (a) $LiAlH_4$, THF; (b) PCl_5, CH_2Cl_2; (c) CH_3OH; (d) NaCN, Aliquat 336, CH_2Cl_2; (e) (*Z*)-1,4-dichlorobut-2-ene, NaH, THF; (f) NaOH, H_2O/THF; (g) I_2, KI, $NaHCO_3$, H_2O/CH_2Cl_2; (h) *n*-Bu_3SnH, AIBN, C_6H_6; (i) NH_3, CH_3OH; (j) NaH, *i*-PrOH; (k) H_3O^+.

3[4] by reaction with PCl_5 to afford the chloromethyl acyl chloride, methanolysis of the acyl chloride, and displacement of the primary chloride by CN^-. The intermediate chloro derivatives are too reactive for purification. Cyclization of **3** with (*Z*)-1,4-dichlorobut-2-ene afforded **4** (85% pure) that contained a small amount of the corresponding vinyl cyclopropyl derivative.[5] Purification of **4**[4] by chromatography on silica gel was useful for characterization, but crude **4** was satisfactory for further transformations.

Stereospecific introduction of the hydroxyl group was effected by the iodolactonization reaction. Ester **4** was saponified as indicated in Scheme I, $I_2/KI/HCO_3^-$ in H_2O/CH_2Cl_2 was added to the saponification mixture, and the two-phase mixture was stirred in the dark for 4 days to afford iodo lactone lactone **5** as a light-sensitive substance that was reduced to lactone **6**[4] with *n*-Bu_3SnH. Aminolysis of lactone **6**, intramolecular addition of the amide anion to the nitrile group, and hydrolysis to the imide by workup with aqueous acid afforded racemic **1**.[4,6]

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(1) Powell, R. G.; Smith, C. R.; Madrigal, R. V. *Planta Med.* **1976**, *30*, 1–8.
(2) Powell, R. G.; Smith, C. R.; Weisleder, D.; Muthard, D. A.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 2784–5.
(3) Dimitrijević, D. M.; Tadić, Ž. D.; Mišic-Vuković, M. M.; Muškatirovic, M. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1051–5. Thunus, L.; Dejardin-Duchene, M. *J. Pharm. Belg.* **1969**, *24*, 3–21. A. Kirpal *Monatsh. Chem.* **1902**, *23*, 929–35 and references cited therein.
(4) Satisfactory analytical data (combustion and high-resolution mass spectrum) have been obtained for **1**, **3**, **4**, and **6**. High-resolution mass spectra were provided by the facility supported by National Institutes of Health Grant RR00317 (principal investigator, Professor K. Biemann) from the Biotechnology Resources Branch, Division of Research Resources. For **3**: mp 100–101 °C; IR (CCl_4) 2250, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.11 (s, 3 H, OCH_3), 4.42 (s, 2 H, CH_2CN), 7.79 (d, 1 H, J = 5 Hz, py H_5), 8.96 (d, 1 H, J = 5 Hz, py H_6), 9.39 (s, 1 H, py H_2). For **4**: IR (CCl_4) 2240, 1730 cm^{-1}; ^1H NMR δ 2.16 (br s, 4 H, allylic H), 3.94 (s, 3 H, OCH_3), 5.79 (br s, 2 H, vinyl H), 7.25 (d, 1 H, J = 5 Hz, py H_5), 8.58 (d, 1 H, J = 5 Hz, py H_6), 8.80 (s, 1 H, py H_2). For **6**: mp 210–212 °C; IR ($CHCl_3$) 2250, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.8–2.8 (m, 6 H, aliphatic H), 5.20 (m, 1 H, OCH<), 7.76 (d, 1 H, J = 5 Hz, py H_5), 8.80 (d, 1 H, J = 5 Hz, py H_6), 9.51 (s, 1 H, py H_2).
(5) Schmid, G. H.; Wolkoff, A. W. *J. Org. Chem.* **1967**, *32*, 254.
(6) The IR (KBr), mass, and ^{13}C NMR spectra (Me_2SO-d_6) of synthetic **1** (mp 239–241 °C) were identical with those of the natural material except that, whereas C-5 and C-8a gave overlapping signals in the ^{13}C NMR spectrum of the natural material,[2] we observed separate signals at 119.7 (C-8a) and 121.8 (C-5) ppm. We thank Dr. R. G. Powell for providing authentic spectral data.

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