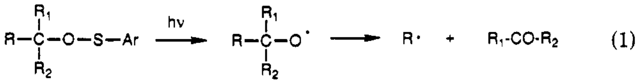
Table I. Relative Yields of Products Formed in the Irradiation of the 4-Nitrobenzenesulfenates

sulfenate	sulfide	alcohol	carbonyl compd	dimer
1a	1.00	0.87	0.1–1.2[a]	0.42
1b	1.00	0.87	0.1–1.3[a]	0.60
1c	1.00	–	–	0.42
6a	1.00	1.00	4.8	~0.05[b]
6b	1.00	–	–	–

[a] Yields vary widely. [b] Could not quantitatively determine the amount present.

the preparation of the necessary substituted systems. A potentially attractive route appeared to be the photoinduced homolytic cleavage of the S–O bond of a sulfenate followed by the β scission of the intermediate alkoxy radical (eq 1). A search of the literature revealed only two

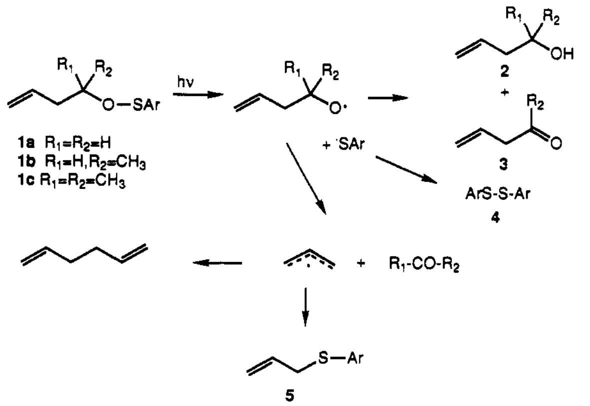


$$R{-}\underset{R_2}{\overset{R_1}{C}}{-}O{-}S{-}Ar \xrightarrow{h\nu} R{-}\underset{R_2}{\overset{R_1}{C}}{-}O^{\bullet} \longrightarrow R^{\bullet} + R_1\text{-CO-}R_2 \qquad (1)$$

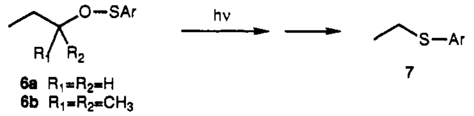
prior reports describing the photolytic cleavage of a sulfenate; one involving the photolytic cleavage of *tert*-butyl methanesulfenate by Kochi and co-workers,[1] the second the photolytic cleavage of a proposed, uncharacterized intermediate formed in the irradiation of a thiochromanone sulfoxide.[2] We report at this time the results of preliminary studies that show that the reaction illustrated in eq 1 is, in fact, an excellent method for the generation of free radicals.

Our initial attempts focused on the photoinduced homolytic cleavage of benzenesulfenates. Alkyl benzenesulfenates undergo photoinduced homolytic cleavage of the S–O bond followed by β scission to produce free radicals as illustrated in eq 1. The benzenesulfenates, however, proved to be somewhat thermally labile, undergoing extensive decomposition on chromatographic purification and on standing, and require light of <300 nm to induce the cleavage of the S–O bond. The 4-nitrobenzenesulfenates are considerably more thermally stable, can be conveniently purified by chromatography on silica gel,[3] and undergo photoinduced S–O bond cleavage by light of >300 nm (λ_{max} of the 4-nitrobenzenesulfenates, ~335 nm).

Irradiation of **1a** in benzene solution,[4] either by a sun lamp or in a Rayonet photochemical reactor, cleanly produces a mixture of the alcohol **2**,[5] carbonyl compound **3**, 1,5-hexadiene, formaldehyde, disulfide **4**,[6] and the allylic sulfide **5**. The relative yields of the products are given in Table I. Irradiation of **1b** produces **2**, **3**, 1,5-hexadiene, acetaldehyde, dissulfide **4**, and allylic sulfide **5**. Irradiation of **1c** produces 1,5-hexadiene, acetone, and **4** and **5** in quantitative yield. In this case the ratio of 1,5-hexadiene to **5** is 30:70.[7]



This procedure works equally well for the generation of saturated alkyl radicals. Irradiation of **6a** produces sulfide **7** and formaldehyde, along with propanol and propanal, and small amounts of butane and disulfide. Irradiation of **6b** cleanly produces only **7** and acetone in essentially quantitative yields.



Continuing investigations are being carried out on the use of this reaction for the generation of substituted allyl radicals and the study of the regioselectivity of their combination reactions and the study of the addition of the allyl and alkyl radicals generated in this photoinduced reaction to substituted alkenes and allenes.

Acknowledgment. This research has been supported by the National Science Foundation, grant no. CHE87-09725.

Supplementary Material Available: ^1H and ^{13}C NMR and mass spectra of all new compounds (17 pages). Ordering information is given on any current masthead page.

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(3) The benzene- and 4-nitrobenzenesulfenates are prepared by the reaction of 1 equiv of the alcohol with 1 equiv of benzene- or 4-nitrobenzenesulfenyl chloride in the presence of 2.3 equiv of triethylamine in methylene chloride at –40 °C (Reich, J. H.; Wollowitz, S. *J. Am. Chem. Soc.* **1982**, *104*, 7051). Small amounts of polar side reaction products are formed which can be readily removed from the sulfenate by quick chromatography on silica gel eluting with 3:1 Skelly solve B and methylene chloride. ^1H and ^{13}C NMR spectra and high-resolution EIMS have been obtained for all new compounds and are provided in the supplementary material.

(4) Solvents containing easily abstractable hydrogen or chlorine atoms cannot be used; the intermediate alkoxy radicals undergoing more rapid atom abstraction reactions that β scission.

(5) The yield of alcohol **2** varies widely (5–35%) for reasons that are not entirely clear. The relative yields of the other products remain remarkedly constant.

(6) The disulfide **4** precipitates from solution and its yield cannot be quantitatively determined.

(7) The greater tendency for the tertiary alkoxy radical to undergo β scission appears to be due to the more negative $\Delta G°_{(300)}$ for the cleavage of the tertiary alkoxy radical ($R_1 = R_2 = CH_3$, –49.33 kcal mol^{-1}) compared to that for cleavage of the secondary ($R_1 = H$, $R_2 = CH_3$, –27.68 kcal mol^{-1}) and primary ($R_1 = R_2 = H$, –2.5 kcal mol^{-1}) alkoxy radicals [calculated using group values for ΔH and ΔS of Benson (Benson, S. W. *Thermochemical Kinetics*; John Wiley: New York, 1976)].

Synthetic Studies on Quassinoids: Total Synthesis of (±)-Shinjulactone C

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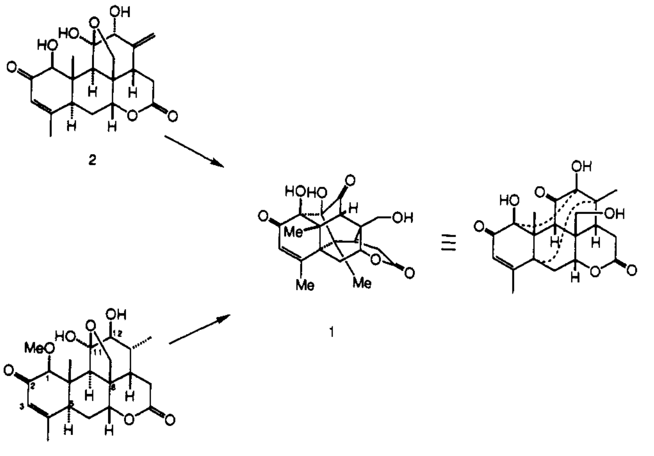
Summary: The total synthesis of the novel quassinoid Shinjulactone C (**1**) is detailed which proceeds via pentacyclic lactone **3** and features new protocols for elaboration of the ring A 1β-hydroxy-2-oxo-$\Delta^{3,4}$ olefin unit and the C(8), C(11) bridged hemiketal array which are present in **3** and common to numerous quassinoids.

Examination of the bitter principles of Simaroubaceous plants, in particular, *Ailanthus altissima* Swingle led to the discovery in 1983 of an intriguing quassinoid, Shinjulactone C (1), possessing a modified picrasane skeleton.[1] During the structure elucidation of 1, the chemical conversion of the naturally occurring quassinoid, ailanthone 2, into shinjulactone C (1) was reported.[2] We detail below the first total synthesis of (±)-shinjulactone C (1) which proceeds via the intermediacy of pentacyclic lactone 3 and features new protocols for the elaboration of the ring A 1β-hydroxy-2-oxo-$\Delta^{3,4}$ olefin unit[3] and the C(8), C(11) bridged hemiketal array[4] which are present in 3 and common to a large number of quassinoids.[5]



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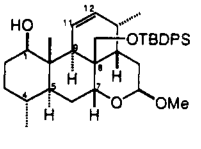
3

The synthesis of 1 starts with the known tetracyclic alcohol 4[6] prepared previously in our laboratory in connection with a total synthesis of racemic chaparrinone (5).



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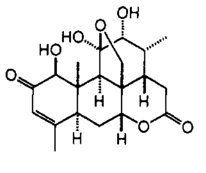

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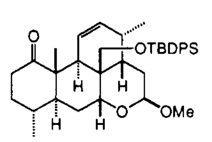
That tetracyclic alcohol 4 possesses the wrong configuration at C(9) is of no consequence, since the synthesis requires the eventual introduction of a ketone at C(11) which will permit the necessary inversion of configuration in the penultimate step of the synthesis. Oxidation (PCC, NaOAc, CH_2Cl_2) of 4 provided crystalline tetracyclic ketone 6, mp 176.5–178.0 °C, in quantitative yield. Osmylation of the C(11), C(12) olefin in 6 followed by acetonide formation ($Me_2C(OMe)_2$, CSA) afforded 7 in 81% overall yield. Tetracyclic ketone 7 was transformed (78% overall yield) into 8, mp 187.5–189.0 °C, via a three-step sequence [1. LDA, THF, HMPA, -78 °C → 0 °C; Me_2SO_4; 2. B_2H_6, THF; NaOH, H_2O_2; 3. PCC, NaOAc, CH_2Cl_2] involving hydroboration of the methyl enol ether derived from 7 and subsequent oxidation. Introduction of an olefin into the C(3), C(4) position of 8 was realized via a Saegusa reaction [$Pd(OAc)_2$, Na_2CO_3, CH_3CN, CH_2Cl_2, 48 °C][7] on the $\Delta^{2,3}$-silyl enol ether derived from 8. The overall yield for the formation of 9 was 82%.



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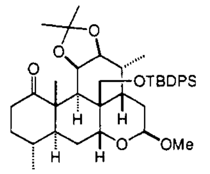

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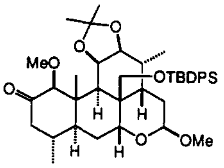

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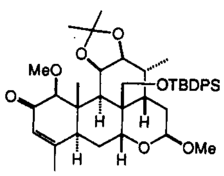

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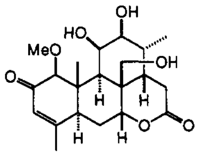
Prior to manipulation of the protected glycol in tetracyclic compound 9, the protected lactol was hydrolyzed (10% HCl, THF), and the resulting lactol was oxidized (PCC, NaOAc, CH_2Cl_2), giving rise (75%) to the corresponding δ-lactone which upon exposure to boron trifluoride etherate in acetonitrile very nicely cleaved, in 75% overall yield, the *tert*-butyldiphenylsilyl ether and the C(11), C(12) acetonide. The hydroxymethyl group and the hydroxyl at C(12) in triol 10 were selectively acetylated (Ac_2O, py, DMAP), providing (87%) after Collins oxidation at C(11) tetracyclic enedione 11, mp 278–279 °C. Hydrolysis (K_2CO_3, MeOH, CH_2Cl_2) of the C(12) acetoxy and the C(8) acetoxy methyl groups in 11 gave rise (82%) to pentacyclic alcohol 3, mp 248–250 °C. The formation of the C(8), C(11) bridged hemiketal during the hydrolysis of 11 serves to protect the C(8) hydroxymethyl group while leaving the C(12) hydroxyl exposed for subsequent oxidation.



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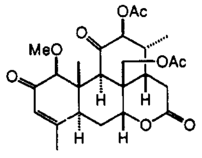

11

Completion of the synthesis of shinjulactone C requires (1) oxidation at C(12), (2) cleavage of the methyl ether and oxidation at C(1), and (3) inversion of configuration at C(9) followed by intramolecular ring closure leading to 1. Toward this end, pentacyclic alcohol 3 was subjected to Swern oxidation conditions, and the resulting ketone upon treatment with acetic anhydride in pyridine containing 4-(dimethylamino)pyridine afforded tetracyclic compound 12 (R = Me), mp 272–273 °C, in 61% overall yield. The methyl ether in 12 (R = Me) was cleaved with 10 equiv of boron tribromide in methylene chloride at -45 °C, giving

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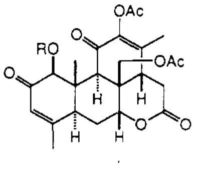
(8) Crystalline compounds have been fully characterized by IR, ^1H NMR, and combustion analyses.

rise to 12 (R = H), mp 214-216 °C, in 82% yield. Jones oxidation of 12 (R = H) provided (74%) the α-diketone



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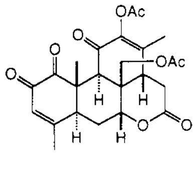

13

13, which upon heating in pyridine at reflux gave rise in ca. 20% yield to the C(12), C(20) diacetate of shinjulactone C. Hydrolysis (KOMe, MeOH) of the acetates gave rise to crystalline (±)-shinjulactone C, mp 242.5–244.0 °C dec, whose ^{1}H NMR spectrum was not in complete agreement with the ^{1}H NMR data recorded in the literature.[1,9] That the structure of synthetic (±)-shinjulactone C was correct was unambiguously established by single-crystal X-ray analysis.

Acknowledgment. Generous support for this work from the National Cancer Institute, National Institutes of Health (Grant CA 28865), is gratefully acknowledged. The 500-MHz NMR instrument (Bruker 500) used in the above studies was purchased in part with funds provided by the National Institutes of Health (RR 02858) and the National Science Foundation (CHE 85-13707).

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[9] During the tabulation of the ^{1}H NMR data for shinjulactone C,[1] the coupling constants for $J_{6\alpha,7}$ and $J_{6\beta,7}$ were interchanged. The C(6) α proton which appears as a doublet of doublets at δ 2.40 has coupling constants of 15.5 and 5.0 Hz, whereas the C(6) β proton (δ 2.70, dd) possesses J values of 15.5 and 10.0 Hz.

The Total Synthesis of Nikkomycin B

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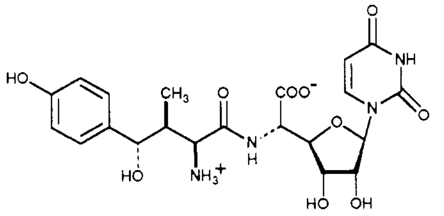
Received August 16, 1990

Summary: A highly stereoselective and general synthesis of the γ-hydroxy-β-methyl-α-aminobutanoic acid moiety, a common feature of the nikkomycin N-terminal amino acid is described and utilized in the total synthesis of nikkomycin B.

The nikkomycins[2] (neopolyoxins)[3] are a unique class of nucleoside peptide antibiotics isolated from the culture broths of *Streptomyces tendae* and *S. cacaoi* ssp. *asoensis*. Especially noteworthy is their effectiveness against the medically important human pathogen *Candida albicans*.[3b,c] This class of compounds has been shown to possess antifungal, insecticidal, and acaricidal activity[2-4] which render them particularly significant synthetic targets. Concurrent with the isolation and structure elucidation, König[2b,5] reported a nonstereoselective synthesis of the N-terminal amino acid residue of nikkomycin B (1) and B_x (2). More recently, they have reported the total syntheses of nikkomycin B_x (2) and related analogues.[6] Other syntheses of similar γ-hydroxy amino acid derivatives have been described in the literature.[5,7-9] We report a highly diastereo- and enantioselective synthesis of the N-terminal γ-hydroxy amino acid unit (3)[2b,5a,10] and the subsequent coupling to the C-terminal amino acid unit (4),[11] culminating in the total synthesis of nikkomycin B (1).



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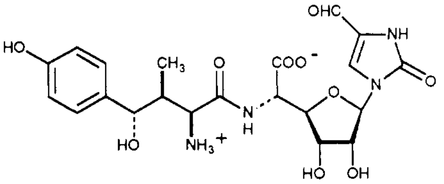

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Recently a high degree of stereoselectivity has been achieved in the synthesis of β-methyl homoallylic alcohols

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[1] Address correspondences to the author at Colorado State University, Fort Collins, CO 80523.

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