Table I. Amino Acids Formed upon Hydrolysis of the Products of the Reaction of Carbon Vapor with Ammonia

	amino acid yield, mmol		
amino acid formed	reaction a[a]	reaction b[b]	reaction c[c]
glycine	6.0×10^{-2}	1.0×10^{-1}	3.0
alanine	1.6×10^{-2}	8.6×10^{-3}	1.8×10^{-1}
β-alanine	2.0×10^{-3}	7.5×10^{-3}	1.7×10^{-1}
N-methylglycine	4.8×10^{-2}	1.1×10^{-2}	2.4×10^{-1}
serine		1.1×10^{-2}	5.9×10^{-2}
aspartic acid	4.4×10^{-5}	2.6×10^{-3}	1.4×10^{-1}

[a] Reactants: carbon (73.7 mmol) and NH_3 (89.1 mmol). Hydrogen cyanide (7.2×10^{-1} mmol) was detected by infrared analysis of the volatile products of this reaction. [b] Reactants: carbon (64.2 mmol), NH_3 (100.7 mmol), and H_2O (55.5 mmol). [c] Reactants: carbon (79.6 mmol), NH_3 (104.2 mmol), H_2O (55.5 mmol), and HCN (31.0 mmol).

the proton NMR spectrum of the products prior to hydrolysis reveals the presence of **3** (1.6×10^{-2} mmol). This mechanism is consistent with the fact that inclusion of HCN among the reactants increases the yield of glycine. The yield of the other amino acids also increases when HCN is added (Table I).

Although evidence regarding the mechanism of formation of the remaining amino acids or their precursors is lacking, it is obvious that a number of reactions must occur subsequent to the initial encounter between carbon and ammonia. These reactions take place in the condensed phase on the walls of a reactor that is immersed in liquid nitrogen.[8] However, this surface is also exposed to thermal and electromagnetic radiation from the carbon arc, and it is reasonable to suppose that various reactive intermediates may be generated and possess mobility under these conditions. These include CH_2, formed by hydrogen abstraction by C_1,[9] and various species formed by the reactions of C_2. The major reaction that has been reported for C_2 is hydrogen abstraction to generate acetylene.[1,10] Skell and Plonka[11] have shown that this reaction involves an intramolecular pathway with vinylidene (**4**) as an intermediate and an intermolecular route involving ethynyl radicals (**5**). If these pathways are operative in

$$C_2 + NH_3 \rightarrow :NH + \underset{\mathbf{4}}{H_2C{=}C:} \rightarrow C_2H_2$$

$$C_2 + NH_3 \rightarrow H_2N\cdot + \underset{\mathbf{5}}{\cdot C{\equiv}CH} \xrightarrow{NH_3} H\text{-}C{\equiv}C\text{-}H + \cdot NH_2$$

the reaction of C_2 with ammonia, it is reasonable to assume that such reactive species as **4**, **5**, :NH, and $\cdot NH_2$ are present. Since there are many reactions possible when energetic species such as these are generated in NH_3 containing C_2H_2 and HCN, it is premature to speculate on detailed reaction mechanisms.

It may be that some of the observed amino acids arise not from monomeric precursors but from hydrolysis of a polymeric material produced under the reaction conditions. In particular, the hydrolysis of HCN polymers and oligomers has been shown to generate amino acids.[12] Control experiments demonstrate that HCN is not polymerized when condensed with an excess of NH_3 and warmed to 25 °C. An additional control involved striking the carbon arc in the presence of HCN coated on the reactor walls at −196 °C. Hydrolysis of the residue from this reaction gave only traces of glycine and β-alanine but none of the other amino acids in Table I. However, neither of these controls rule out a polymerization of HCN induced under the reaction conditions. That glycine does not arise solely by hydrolysis of a polymer is demonstrated by the fact that **3**, a monomeric precursor to glycine, is detected prior to hydrolysis. We are currently developing analytical methods that may allow the detection of monomeric precursors of other amino acids.

Although the mechanisms of formation of amino acid precursors in these systems are unclear, the results demonstrate that amino acids can be formed in systems in which carbon vapor is the only source of carbon. It is possible that reactions similar to those reported here may play a role in the formation of extraterrestrial amino acids such as those which have been detected in meteorites[13] and lunar samples.[14] Since ammonia,[15] water,[15] C_1,[16] and C_2[17] have all been detected as extraterrestrial species, the experiments described here may mimic those reactions which occur when interstellar carbon vapor condenses on a cold surface containing solid ammonia and water or in interstellar clouds containing these species.

Acknowledgment. We thank H. Daron and J. H. Hargis for helpful and perceptive comments. Support by the National Science Foundation under Grant CHE 77-24624 is gratefully acknowledged.

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Facile Regio- and Stereoselective Total Synthesis of Racemic Aklavinone[†]

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We have previously described[1] the development of a convergent strategy for the regiospecific construction of the aklavinone (I) skeleton. Aklavinone[2] is the aglycon of aclacinomycin A,[3] which is a highly promising chemotherapeutic agent for the treatment of a wide spectrum of cancers, including acute leukemia,[4] and has been reported to possess lower cardiotoxicity than the existing antineoplastic anthracycline antibiotics, adriamycin and daunomycin.[5] In recent years, its total synthesis has attracted the

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[§] Shanghai Institute of Organic Chemistry, People's Republic of China. Syntex Postdoctoral Fellow, 1980–present.

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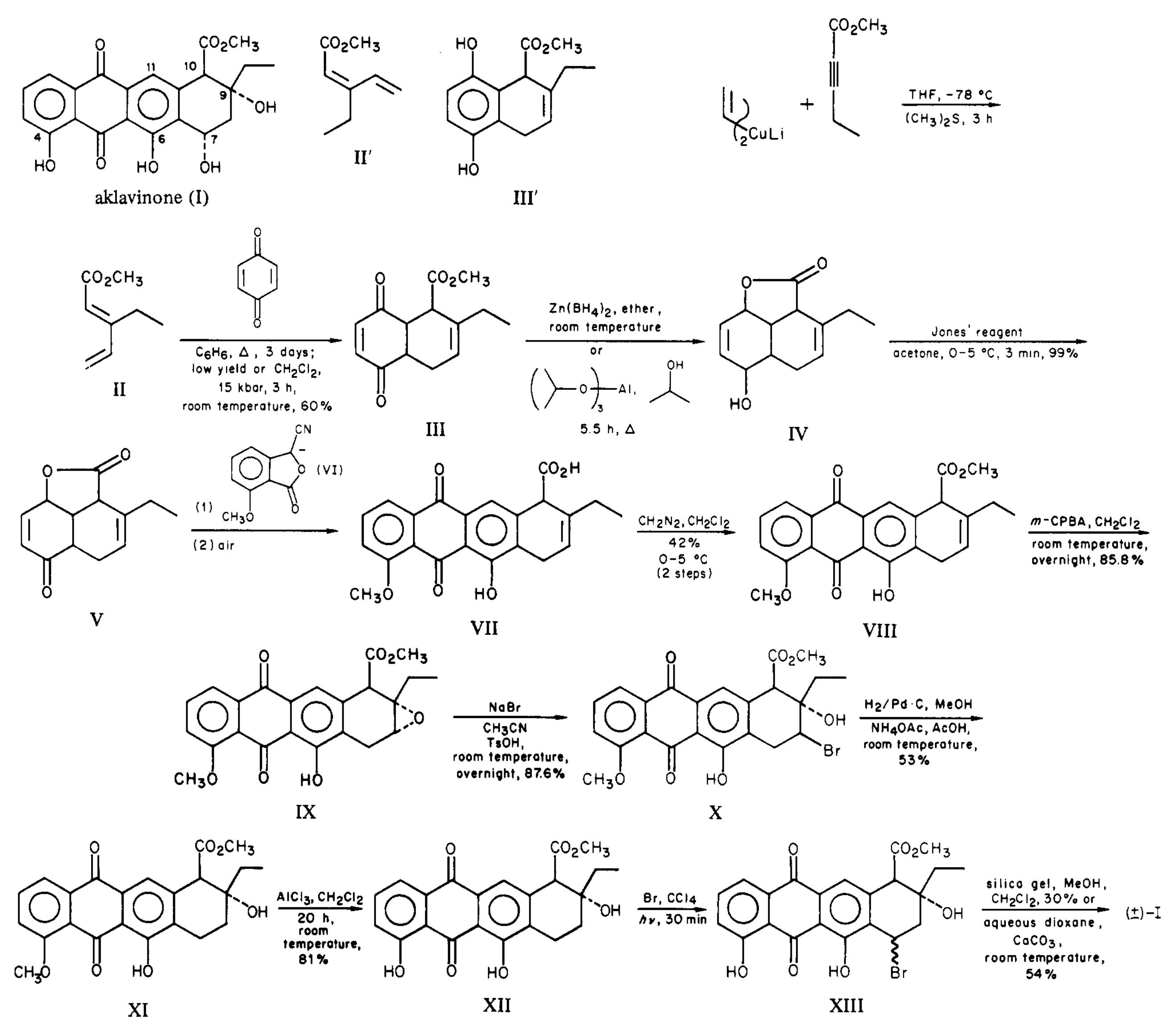
Scheme I



attention of many research laboratories.[6] We now report the successful application of our strategy to the total synthesis of this anthracyclinone in the racemic form.

Addition of vinyl cuprate to methyl 2-pentynoate gave mainly the *E* form of methyl 3-ethylpenta-2,4-dienoate (II)[7] [bp 62.5–64 °C (32 mm)], which could be isolated from the ~10% *Z* isomer (II′) [bp 64 °C (27 mm)] by spinning band distillation (Scheme I). When a benzene solution of the diene II and *p*-benzoquinone was heated to reflux for 3 days, the Diels–Alder adduct enedione III was obtained in conjunction with the crystalline hydroquinone (III′) (mp 154–155 °C) as a major side product. The enedione III thus obtained could not be purified[8] but was directly reduced with zinc borohydride or aluminum isopropoxide to give the lactone IV,[22a] isolable as crystals (mp 149–150 °C). The overall yield from diene II was 20%. Under 15-kbar pressure,[9] the diene II reacted with *p*-benzoquinone in a methylene chloride solution at room temperature in 3 h, giving the enedione III in 60% yield in the form of crystals (mp 54–54.5 °C) without significant contamination by the hydroquinone side product. Meerwein–Ponndorf–Verley reduction of the enedione III[10] produced the lactone IV in 40% yield. Jones' reagent[11] converted the allylic alcohol moiety of lactone IV to the enone V[23a] (mp 132–132.5 °C) in 99% yield, setting the stage for the connective annelation experiment.[1,12]

The anion of cyanophthalide V[13] was formed at −78 °C with lithium diisopropylamide in tetrahydrofuran in the presence of hexamethylphosphoramide. Subsequent addition of enone V was

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(6) While this manuscript was in the hands of the referee, we were notified that three independent total syntheses of this "second generation" anthracycline antibiotic had been accepted for publication in this journal. These reports have now appeared in print. [Kende, A. S.; Rizzi, J. P., *J. Am. Chem. Soc.* **1981**, *103*, 4247. Pearlman, B. A.; McNamara, J. M.; Hasan, I.; Hatakeyama, S.; Sekizaki, H.; Kishi, Y. *Ibid.* **1981**, *103*, 4248. Confalone, P. N.; Pizzolato, G. *Ibid.* **1981**, *103*, 4251.]

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(8) Brief treatment of a solution of a purified sample of enedione III with silica gel, Florisil, or alumina at room temperature caused complete aromatization, and the hydroquinone III′ was the only isolable product.

(9) This experiment was carried out in Professor W. Dauben's laboratories by Dr. W. Baker and will be the subject of a separate publication. Dauben, W. G.; Krabbenhoft, H. O. *J. Org. Chem.* **1977**, *42*, 282.

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(13) The phthalide VI was prepared from *N,N*-diethyl-6-formylanisamide, which was prepared in one step from *N,N*-diethyl-*o*-anisamide according to the method of Snieckus [de Silva, S.; Reed, J.; Snieckus, V. *Tetrahedron Lett.* **1978**, 5099]. Treatment of the formylanisamide with sodium cyanide in the presence of an equivalent amount of *p*-toluenesulfonic acid in aqueous tetrahydrofuran at 0 °C to room temperature gave the crystalline cyanophthalide in 95% yield, mp 120–127 °C.

followed by stirring at room temperature for 2 h. The workup procedure included the bubbling of a stream of air through an acidic aqueous suspension of the reaction mixture, giving the crystalline tetracyclic acid VII, which was converted into the methyl ester VIII[23a] (mp 197.5–198.5 °C) in 42% yield for the two steps. Epoxidation of ester VIII with *m*-chloroperbenzoic acid gave epoxide IX (mp 233–234.5 °C), isolated in 85.8% yield.[14,23a] When a solution of the epoxide IX in acetonitrile was treated with sodium bromide and *p*-toluenesulfonic acid at room temperature, a single bromohydrin (X) (mp 192–194 °C) was obtained (87.6%). Examination of a Dreiding model reveals that trans-diaxial displacement on the epoxide ring[15] is favored from the C-8 direction. Removal of the bromide was accomplished by hydrogenolysis over palladium on charcoal in methanol in the presence of ammonium acetate and acetic acid,[16] giving the alcohol (XI)[23b] (mp 234–235 °C) in 53% yield. Demethylation of the 4-methoxy group proceeded smoothly with aluminum chloride in methylene chloride[17] at room temperature, and racemic 7-deoxyaklavinone[18] (XII) (mp 214–216 °C) was obtained in 81% yield. Radical initiated bromination gave the 7-bromo derivative[19] XIII, which was solvolyzed on a preparative silica gel thick layer chromatography plate during purification, giving racemic aklavinone (I)[20] (mp 207–209 °C) in 30% yield. When the solvolysis reaction was carried out in aqueous dioxane in the presence of calcium carbonate, the overall yield was improved to 54%.[21] The synthetic material was identical with a sample of the natural product[22] in terms of chromatographic properties and mass, infrared, ultraviolet, and nuclear magnetic resonance spectra.

We have achieved a regio- and stereospecific total synthesis of racemic aklavinone in 12 steps, in 1.7% yield, from readily available starting materials.

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Supplementary Material Available: Spectroscopic data (NMR, IR, MS, UV) and elemental analysis for compounds V and VIII–XII (3 pages). Ordering information is given on any current masthead page.

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[15] See, for example: Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. "Conformational Analysis"; Wiley: New York, 1965; p 296. [The NMR spectrum of the bromohydrin X has a one-proton peak at δ 4.49 for C_8-H which appears as a d x d coupled to C_7-H_2 with J = 6, 9 Hz.]

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[21] Shanghai Institute of Organic Chemistry: *Hua Hsueh Hsueh Pao* **1978**, *36* (2), 155; *Chem. Abstr.* **1978**, *89*, 214953z.

[22] We are grateful to Dr. T. Oki and Dr. T. Takita of Tokyo Microbial Institute for a generous gift of an authentic sample of this natural product.

[23] (a) Spectroscopic data (NMR, IR, MS, UV) and elemental analysis for this compound are in accordance with the assigned structure. (b) Spectroscopic data (NMR, IR, MS, UV) and high-resolution MS for this compound are in accordance with the assigned structure. Melting points are measured in a Fisher–Jones hot plate and are uncorrected.

Unusual Sesterterpenoids from the Secretion of *Ceroplastes floridensis* (Coccidae), an Orchard Pest. Application of the Allylic Benzoate Method for Determination of Absolute Configuration

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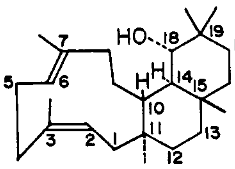
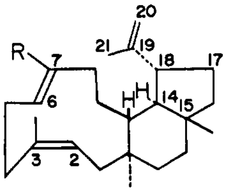
We report the structures of floridenol (**1**), 5α-hydroxyfloridenol (**2**), flocerol (**3**), and floceric acid (**4**), which represent two new skeletal classes of sesterterpenes, and the first actual application of a nonempirical method for determination of absolute configurations.

In recent years we have isolated numerous terpenoids and waxes including 12 new 14-membered-ring sesterterpenes from the secretion of the scale insect *Ceroplastes ceriferus* Anderson.[1-4] The present series **1–4** was isolated from *C. floridensis* (*japonicus*) Comstock (collected in Osaka Prefecture, March, 1979), a pest insect which infests persimmon, tangerine, and other orchards. The planar structure and relative configurations were determined by X-ray crystallographic studies of floridenone **5** (derived from floridenol **1**), NMR studies, and chemical correlations, whereas the absolute configuration rests on application of the recently developed allylic and homoallylic benzoate chirality method[5] to **2**. The compounds **1–4** were isolated by chloroform extraction of the insects, filtration of insect debris, concentration, addition of acetone,[2,4] and successive silica gel chromatography of the acetone-soluble fraction.



1 floridenol
2 5α-OH-floridenol(see 2a)
5 floridenone, 18-one



3 flocerol, R:CH_2OH
4 floceric acid, R:COOH
6 flocerene, R: Me

Floridenol (**1**), $C_{25}H_{42}O$ (EI–MS, m/z 358.322, calcd 358.323, M^+), mp 62–63 °C (from AcOH), $[\alpha]^{27}{}_D$ −81.2° (c 1.0, $CHCl_3$), has an IR (neat) band assignable to an OH at 3550 cm^{-1} which resisted acetylation. The ^1H NMR spectrum[6] of **1** showed the

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