with the above results strongly supports formation of silylene complexes in reactions 1 and 3a.

The above results provide compelling evidence for formation of stable Fe–silene and Fe–silylene cationic complexes in the gas phase. These isomers do not interconvert, even upon formation of the ethene collision complex (ca. 40 kcal/mol excess energy).[29] High-level ab initio theory has revealed that $SiCH_4$ isomers (silene and silylene) have nearly identical stability (less than 10 kcal/mol difference).[30] Furthermore, there is a significant barrier (ca. 40 kcal/mol) for interconversion of these $SiCH_4$ isomers.[31,32] There is clearly a prohibitive barrier for this interconversion mediated by Fe^+. The ability to generate stable iron–silene and –silylene cations in the gas phase allows for studies concerning their role in important chemical transformations of silicon compounds.

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Biosynthesis of the Brevianamides: Quest for a Biosynthetic Diels–Alder Cyclization†

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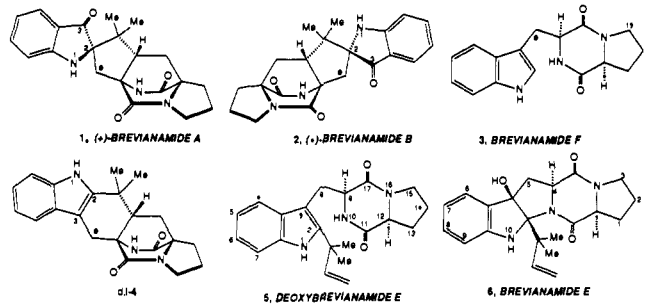
The brevianamides A (**1**) and B (**2**) are the simplest representatives of a curious class of mycotoxins[2] which also includes the paraherquamides[3] and the marcfortines.[4] While **1** has been shown to possess antifeedant and insecticidal effects,[5] several members of the structurally related paraherquamide family have potent antiparasitic properties.[3] In 1974, Birch and collaborators found that [15-^{3}H,8-^{14}C]brevianamide F (**3**) is biosynthetically incorporated into **1**[2e] and postulated[2b,c,e] a biosynthetic pathway, subsequently modified by us[6] to accommodate the observed absolute stereochemistries of **1** and **2**. The proposed biogenesis involved the formation of hexacyclic indole **4**, via a key [4 + 2] cycloaddition.[7]



In order to validate the proposed biosynthetic pathway, we synthesized *d,l*-[8-^{13}C]-**4** by using our synthesis,[8] only starting with *d,l*-proline and >90% ^{13}C-labeled gramine.[9,10] When fermentation extracts of *Penicillium brevicompactum* were screened for the production of **4**, this substance could not be found. Furthermore, the biosynthetic feeding of *d,l*-[8-^{13}C]-**4** gave cultures in which **1** showed no significant enhancement of C-8 in its ^{13}C NMR spectrum, indicating no incorporation.

We then synthesized [8-^{3}H]deoxybrevianamide E ([8-^{3}H]-**5**)[11] and [8-^{3}H]brevianamide E ([5-^{3}H]-**6**), following Kametani's synthesis.[12] Feeding experiments performed with [8-^{3}H]-**5** (16.5 mg with an activity of 1.605 μCi, and specific activity of 37.3 μCi/mmol) led to significant incorporation of the radioactivity into both **1** (7.8% specific incorporation, 0.125 μCi, 6.12 μCi/mmol) and **2** (0.93% specific incorporation, 0.015 μCi, 10.8 μCi/mmol). The specific activities of both **1** and **2** are comparable, thus confirming their common biosynthetic origin. As expected, **6** also showed significant incorporation (24.9% specific incorporation, 0.40 μCi, 32.0 μCi/mmol). The high values for the specific incorporations indicate that **5** is a biosynthetic precursor of **1**, **2**, and **6**. To check the possible intermediacy of **6** we obtained [5-^{3}H]-**6** from [8-^{3}H]-**5** as previously described.[12] In this case, however, the feeding experiment with [5-^{3}H]-**6** (17 mg; 1.60 μCi, 37.3 μCi/mmol) gave **1** and **2** with no significant incorporation. It thus seems that **6** does not lead to **1** or **2**.

The biosynthetic pathways leading to **1** and **2** proposed thus far[2b,c,e,6] do not explain the appearance of **6**, the presence of which in *P. brevicompactum* appears to be significant. It has been speculated that **6** may just be an artifact, because autoxidation of **5** leads to the production of **6**.[13] However, **5** was quite stable under the culture conditions in our feeding experiments. Moreover, **5** has been isolated from cultures of *Aspergillus ustus*,[11] while **6**, however, was not found in those cultures. In our opinion, this points to the conclusion that **6** is not an artifact. The results of our feeding experiments, together with these facts, lead us to

† This manuscript is dedicated to Professor A. I. Meyers on the occasion of his 60th birthday.
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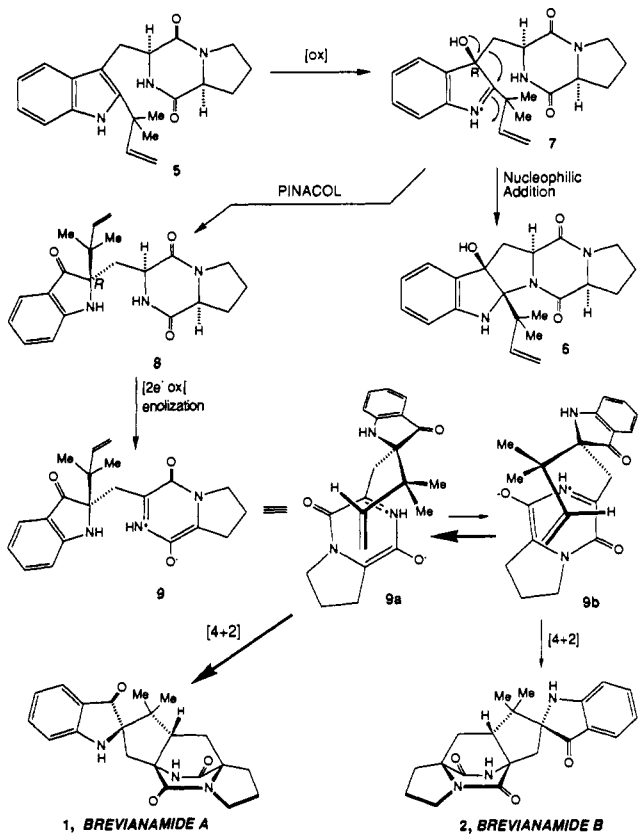
Scheme I



suggest an alternate biosynthetic pathway that is detailed in Scheme I. We presume that, following the conversion of **3** into **5**, an *R*-selective hydroxylation reaction occurs at the 3-position of **5** furnishing **7**. Nucleophilic addition to the C=N bond of **7** leads to **6**. On the other hand, catalyzed pinacol-type rearrangement of **7**[14] sets the *R*-absolute stereochemistry at C-2, to give **8**. This rearrangement justifies the *R*-stereochemistry of the indoxyl, since the 3-hydroxyindolenine **7** is the sterically favored product of oxidation, as shown in the autoxidation of **5**.[12] This is a much more difficult stereochemical issue to rectify via **4** since, experimentally, oxidation of **4** with a peracid proceeds from the least hindered face giving solely **2**.[8] Oxidation of **8** followed by enolization forms the aza diene **9**.[15] An *intramolecular Diels–Alder cyclization* from a major rotamer (**9a**) directly leads to **1**, and a minor rotamer (**9b**) cyclizes to **2**. Molecular mechanics calculations on the rotamers **9a** and **9b** hint that rotamer **9a** is ca. 1 kcal/mol more stable than rotamer **9b**. This is due to a favorable H-bond between the indoxyl ketone and the proximal amide NH of the piperazinedione in **9a**. This proposal accommodates the existence of the two enantiomorphic bicyclo[2.2.2] ring systems, and it also accounts for the preponderance of **1** over **2**.

In conclusion, the intermediacy of **4** in the biosynthesis of **1**/**2** seems unlikely at present. On the other hand, our feeding experiments show that while **5** is a biosynthetic intermediate of both **1** and **2**, **6** is a shunt metabolite which does not lead to these compounds. Studies on the synthesis and possible intermediacy of **8** and **9** are currently in progress in our laboratories.

Acknowledgment. This work was supported by the National Institutes of Health (Grant CA 43969) and the Colorado State University Agricultural Experiment Station as part of USDA SAES Western Project W-122. R.M.W. also acknowledges additional support from Hoffman-La Roche, Inc.; Merck, Sharp & Dohme Research Laboratories; and Symphony Pharmaceutical Co., Inc. J.F.S.-C. thanks the DGICYT of Spain for a fellowship. Technical assistance from Renee Gallegos and James K. Stille is also gratefully acknowledged.

Supplementary Material Available: Details of the biosynthetic feeding and incorporation experiments (1 page). Ordering information is given on any current masthead page.

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(11) Compound **5** has been isolated from *A. ustus* and serves as the biosynthetic precursor to a product of alternative ring-closure, austamide: Steyn, P. S. *Tetrahedron Lett.* **1971**, 3331. Steyn, P. S. *Tetrahedron* **1973**, *29*, 107.

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Structural Characterization of Organocopper Reagents by EXAFS Spectroscopy

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Organocopper compounds are among the most versatile organometallic reagents for forming new carbon–carbon bonds.[2,3] Although the synthetic utility of these reagents is well established, their reaction mechanisms and their structures remain controversial.[4-7] NMR investigations of their solution structures have revealed the presence of complex equilibria.[5,8] Recently, several

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