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Revision of the Stereostructure of Mirabazole C

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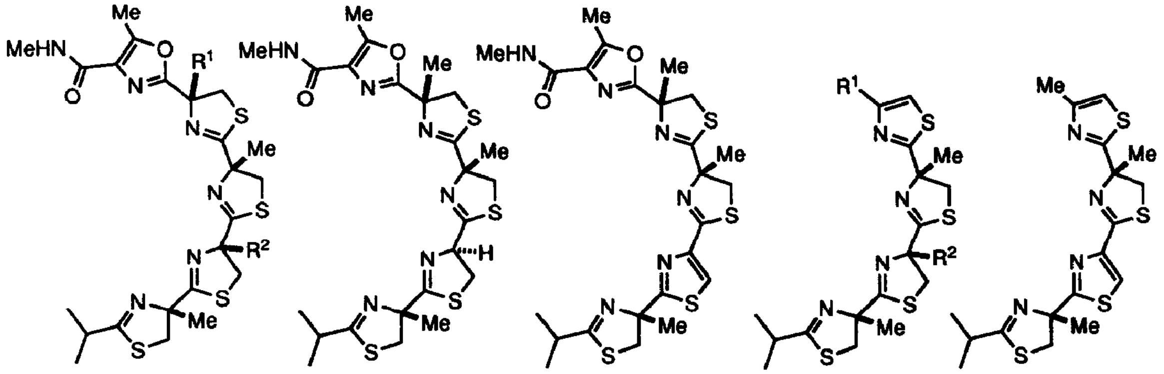
Abstract: The stereostructure of mirabazole C is revised to **11** on the basis of total synthesis.

The tantazoles and mirabazoles are a series of polythiazoline natural products isolated by Moore and coworkers from blue-green algae.[1,2] Their structures were originally assigned as **1-5** (tantazoles) and **6-9** (mirabazoles).



1: R^1 = H, R^2 = Me
2: R^1 = R^2 = Me
3: R^1 = Me, R^2 = H

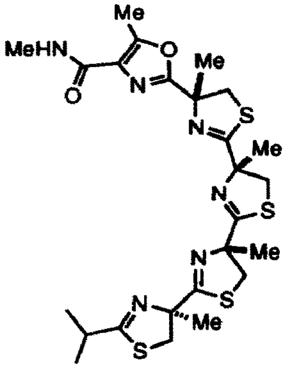
4

5

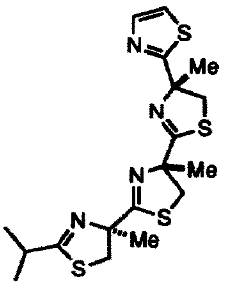
6: R^1 = R^2 = Me
7: R^1 = Me, R^2 = H
8: R^1 = H, R^2 = Me

9

Recent synthetic work by Fukuyama and Xu has shown that the structure of tantazole B must be revised to **10**, in which the ring-A stereocenter has the *R*, rather than the *S*-configuration.[3] Subsequently, Moore and his coworkers carried out Marfey analysis of the acid hydrolyzates of tantazoles A and B and confirmed that both have the *R* configuration at the stereocenter in ring A, confirming the Fukuyama-Xu structural revision.[4] Furthermore, it was found that the acid hydrolyzates of the mirabazoles also show one equivalent of (*S*)-2-methylcysteine, showing that these structures also need revision. We have reported the total synthesis of **8**, which we concluded to be identical with natural mirabazole C.[5] This conclusion was reached because: (1) the synthetic material displayed the same $[\alpha]_D$ as was reported for the natural product (however, see later comments on this measurement); (2) the ^{1}H NMR spectrum of the synthetic material was very similar to that reported for the natural product. We did not carry out a direct comparison of our synthetic material with the natural product, which was only isolated in minute amounts (300 μg) and was not available to us.



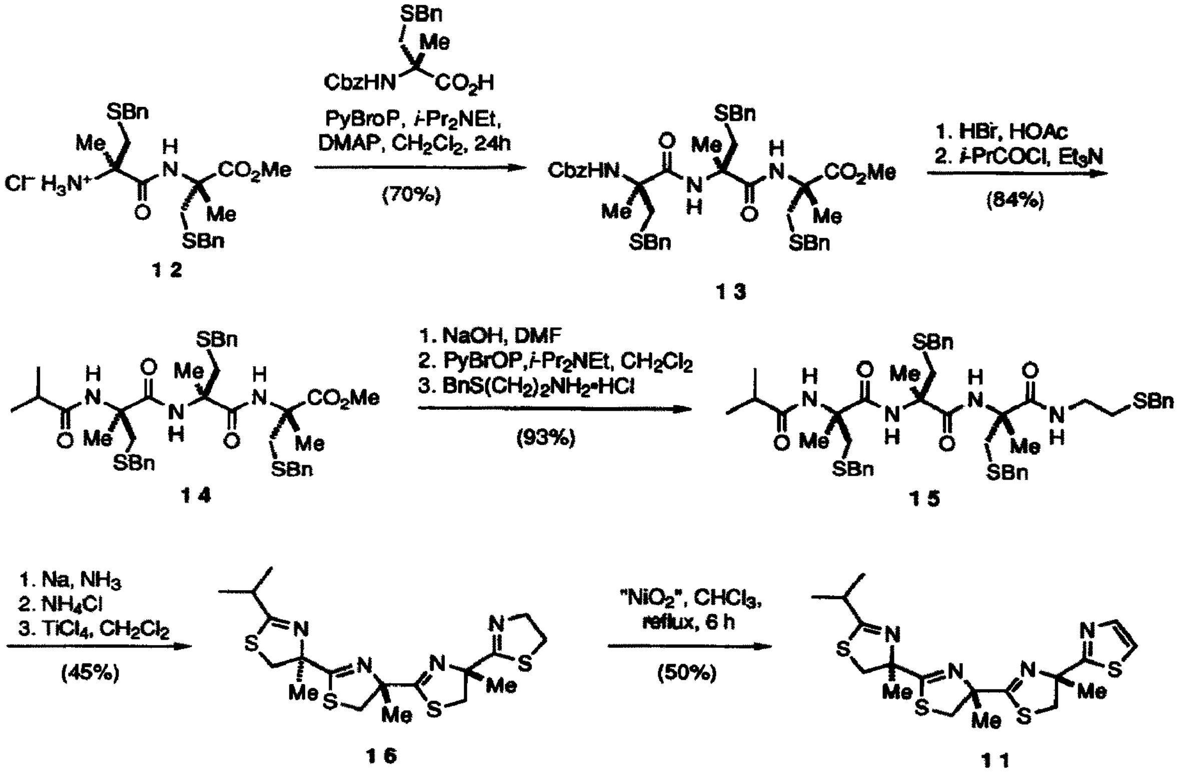
10



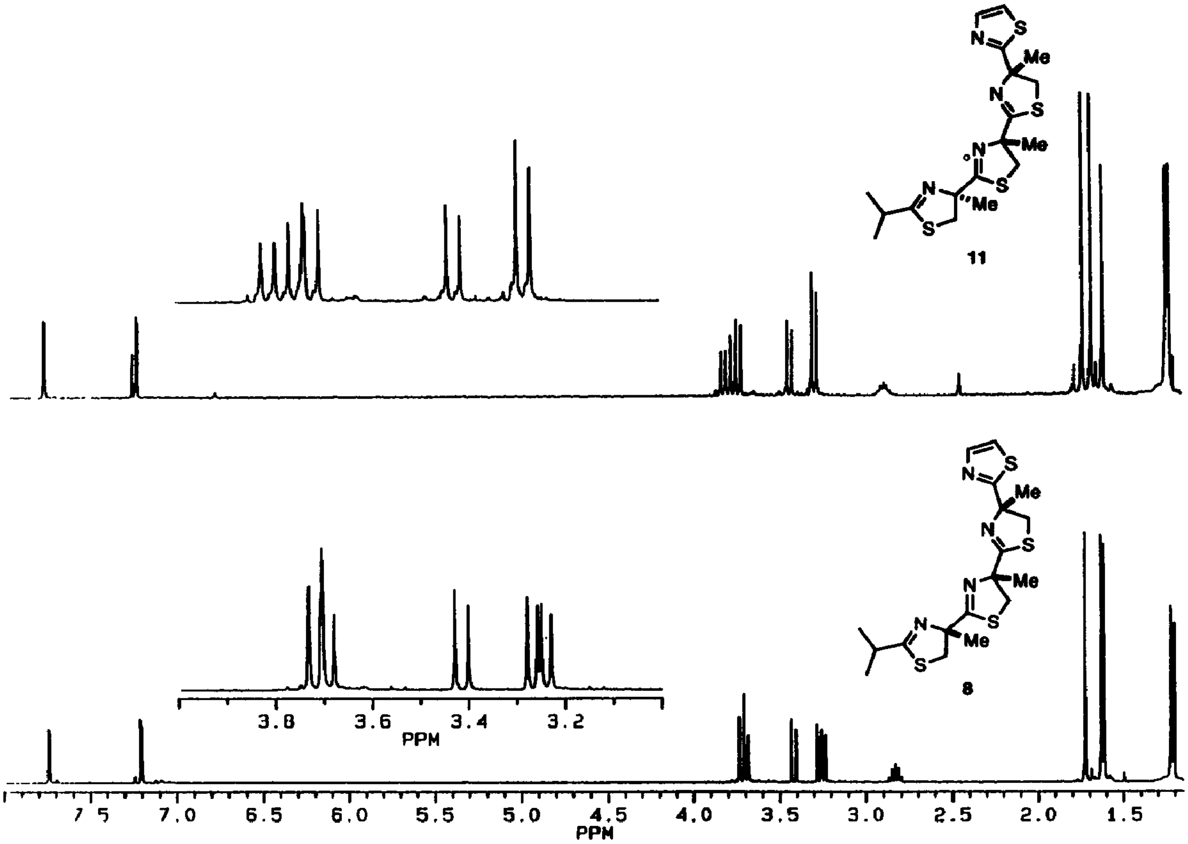
11

In this Letter we report a synthesis of **11**, the isomer having the *R*-configuration in ring-A. The synthesis of **11** was carried out essentially as previously described for isomer **8**,[5] as shown in the following Scheme.

Scheme



Both synthetic materials, **8** and **11**, have been compared with natural mirabazole C in Professor Moore's laboratory. Compound **11** was found to be identical with the natural product by ^{1}H NMR spectroscopy and HPLC mobility.[6] The ^{1}H NMR spectra of synthetic compounds **8** and **11** are reproduced below:



The observed specific rotations for compounds **8** and **11** were $[\alpha]_D$ −500 (c = 0.033, $CHCl_3$) and $[\alpha]_D$ −104 (c = 0.049, $CHCl_3$), respectively. The reported specific rotation for natural mirabazole C is $[\alpha]_D$ −110 (c = 0.03, $CHCl_3$).[2] Compound **8** was previously reported to have $[\alpha]_D$ −113 (c = 0.024, $CHCl_3$).[5] However, this value was clearly in error, as the actual sample prepared by the previous coworker has recently been remeasured and found to have $[\alpha]_D$ −500 (c = 0.036, $CHCl_3$). The error probably resulted from the uncritical use of an antique polarimeter of doubtful stability.

Acknowledgement

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6. We thank Dr. Seunguk Paik for making these comparisons.

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