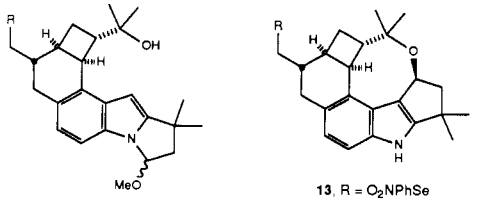

12a, R = HO
12b, R = O_2NPhSe

13, R = O_2NPhSe

Figure 4.

A–E–F ring system, whose successful establishment would validate our basic strategy for the penitrems. Notably, aniline **4** was the most complex substrate to which we had applied our indole protocol.[5b,c] With this proviso in mind, **4** was silylated in situ (*n*-BuLi, TMSCl, Et_2O, −78 °C → room temperature) and then exposed to *s*-BuLi (2 equiv, room temperature, 0.75 h) to generate the presumed dianion.[17] Addition of dimethylbutyrolactone[18] at −78 °C resulted in a 20–30% yield of the desired indole (**11**),[9] in addition to 40–50% of recovered aniline **4**; attempts to improve upon this conversion were unsuccessful. Fortunately, indole **11** could be obtained in high yield from **4** by acylation with dimethylbutyrolactone (2.5 equiv of LDA, THF, −78 °C → room temperature, 88%) and subsequent subjection to the modified Madelung conditions of Fuhrer and Gschwend (4 equiv of *n*-BuLi, THF, 0 °C → room temperature, 80%).[19]

Turning next to oxocane formation,[20] the primary hydroxyl group of **11** was oxidized to the corresponding aldehyde under Moffatt conditions;[21] camphorsulfonic acid in methanol then served to deprotect the remaining hydroxyl groups to afford anomeric mixture **12a**,[9a] which was selenated ($O_2NPhSeCN$, Bu_3P, THF, room temperature)[22] to give **12b**[9a] (46% from **11**). At this juncture, we intended to exploit the previously developed Mannich cyclization for construction of the F ring;[7] oxocane formation would then follow via gramine fragmentation and carbocation capture.[6] *To our delight, however, simple exposure of* ***12b*** *to camphorsulfonic acid (benzene, room temperature) resulted in direct tandem cyclization to oxocane* ***13***[9] *in 58–64% yield*! That the relative configuration at the new stereocenter in **13** had been correctly established was deduced initially from NOE experiments and then confirmed by single-crystal X-ray diffraction.[12] Oxidative elimination of the seleno group (*m*-CPBA, collidine, CH_2Cl_2)[23] completed construction of **10**.[9] The colorless crystalline solid (mp 187 °C dec, 69%) so obtained was fully characterized. Importantly, the derived spectroscopic data (MS, UV, ^1H and ^{13}C NMR) were found to correlate well in all pertinent respects with the data obtained by Steyn for penitrem D,[1c] thereby providing additional support for the structures assigned to the penitrems.

In summary, we have completed an economic (i.e., short) synthesis of an advanced tricyclic aniline that embodies the B–C–D rings of penitrem D. In addition, we demonstrated the viability of two strategic transformations by successfully completing construction of an A–B–C–D–E–F hexacyclic analogue of the natural product. These achievements affirm the potential of the proposed penitrem synthetic strategy. Further progress in this area will be reported in due course.

Acknowledgment. Support of this research was provided by the National Institutes of Health (Institute of Neurology, Communicative Disorders and Stroke) through Grant 18254 and by the American Cancer Society through a fellowship to M.V. We also thank Drs. G. Furst, J. Dykins, and P. Carroll, Directors of the University of Pennsylvania Spectroscopic Facilities, for aid in obtaining respectively the high-field NMR, high-resolution mass spectral, and X-ray crystallographic data.

Supplementary Material Available: Full spectral and analytical data for compounds **7a**, **8**, **9**, **4**, **11**, and **10** (3 pages). Ordering information is given on any current masthead page.

(17) The use of *sec*-butyllithium in ether at ambient temperature for the formation of such dianions represents an improvement in the previously reported method,[5b,c] wherein a solution of an *N*-TMS-*o*-toluidine in hexane was treated with *n*-butyllithium (2 equiv) and then heated at reflux for 6 h under an inert atmosphere.

(18) Baas, J. L.; Davies-Fidder, A.; Huisman, H. O. *Tetrahedron* **1966**, *22*, 285–291.

(19) Fuhrer, W.; Gschwend, H. W. *J. Org. Chem.* **1979**, *44*, 1133–1136. See also: Houlihan, W. J.; Parrino, V. A.; Uike, Y. *J. Org. Chem.* **1981**, *46*, 4511–4515.

(20) For examples of cationic formation of medium-ring cyclic ethers, see: Overman, L. E.; Blumenkopf, T. A.; Castaneda, A.; Thompson, A. S. *J. Am. Chem. Soc.* **1986**, *108*, 3516–3517 and references cited therein.

(21) Pfitzner, K. E.; Moffatt, J. G. *J. Am. Chem. Soc.* **1965**, *87*, 5661–5678.

(22) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485–1486.

(23) Sharpless, K. B.; Young, M. W. *J. Org. Chem.* **1975**, *40*, 947–949.

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Additions and Corrections

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Peter M. Gannett,* Donald L. Nagel, Pam J. Reilly, Terence Lawson, Jody Sharpe, and Bela Toth. The Capsaicinoids: Their Separation, Synthesis, and Mutagenicity.

Page 1064. The following reference was inadvertently omitted: Suzuki, T.; Iwai, K. In *The Alkaloids*; Brossi, A., Ed.; Academic Press; New York, 1984; Vol. 23, pp 227–229. We thank Drs. J. Jurenitsch and H. Viernstein for bringing this to our attention.

Jurenitsch and co-workers (Jurenitsch, J.; David, M.; Heresch, F.; Kubelka, W. *Plant Med.* **1979**, *36*, 61) have concluded from degradation studies of homocapsaicin (**2c**) that the double bond is in the 6-position of the side chain and not the 7-position as we claimed.

Page 1065, column 1, line 13. Replace "norcapsaicin (**2a**)" with "norcapsaicin (**1a**)".

Page 1067, Table III. Footnotes *c*, *d*, and *f* should read as follows: [c] ***1b*/2b** control 18 ± 1, 2-aminoanthracene (AA) 2498 ± 147, red pepper extract (RPE) 32 ± 2, AA 1989 + 105. [d] ***1b*/2b** control 32 ± 3, AA 2656 ± 69, RPE 18 ± 2, AA 2566 ± 149. [f] ***1b*/2b** control 19 ± 2, AA 252 ± 39, RPE 14 ± 2, AA 224 ± 39.

Page 1067, column 2, line 49. Replace "**2a** (t_R 10.2 min), **1a** (t_R 14.8 min)" with "**1a** t_R 10.2 min), **2a** (t_R 14.8 min)".

Page 1070, column 2, line 53. Replace "procedures.[24]" with "procedures.[6,24]"

Page 1070, column 2, line 55. Replace "Bhide.[6]" with "Bhide.[7]"

The page number for ref 20a should be 3463.