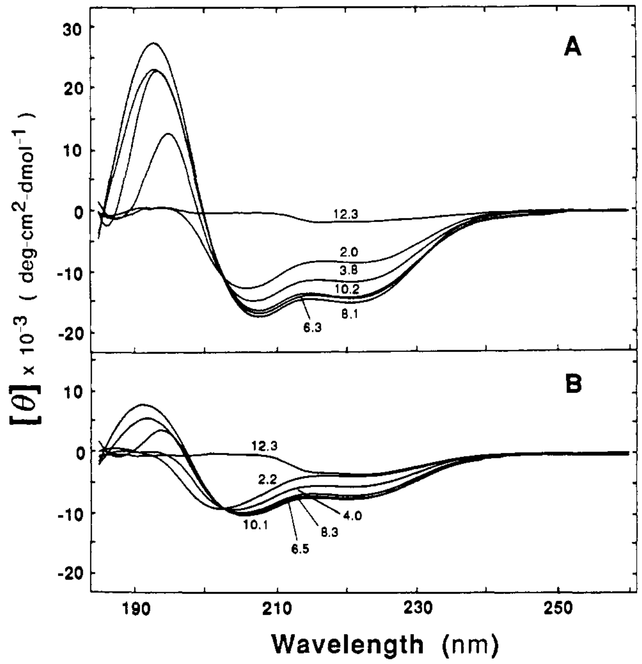

Figure 1. Circular dichroism spectra of peptides in 10 mM KF, 4 °C, at various pHs as indicated on the curves: (A) peptide I and (B) peptide II.

suggesting that ion pairing is a major component in stabilizing the helix in this molecule.

Peptide I was synthesized by the solid-phase method on an ABI 430A automatic synthesizer using *t*-Boc chemistry in the laboratory of P. S. Kim (Whitehead Institute, MIT, Cambridge, MA). Peptide II was made by F-moc solid-phase peptide synthesis on a Biosearch 9600 peptide synthesizer with dimethyl formamide as solvent and trifluoroacetic acid/dimethyl sulfide/dichloromethane (14:1:5) for deprotection. The C-terminal amide group in II was introduced by use of Biosearch PAL resin. Peptides I and II were succinylated and acetylated with succinic anhydride and acetic anhydride, respectively, in dimethyl formamide containing an equivalent of trimethylamine. The peptides were purified on a reversed-phase Deltapack 15 micron C_{18} HPLC column (Waters). Solvent A is 0.1% TFA in water, B is 0.1% TFA in 70% acetonitrile, with the detector set at 229 nm. The peaks corresponding to each peptide were rerun on HPLC, and FAB MS analysis (by Dr. Leonard Schronk, M-Scan, Inc.) of the products shows [M + H] = 2410 for I and 1718 for II, with additional ions corresponding to $[M + j\text{Na}]$, $j = 1, 2, ...$

Circular dichroism spectra were recorded on a modified Cary spectropolarimeter (Aviv DS60) in 10 mM KF solution titrated to appropriate pH values. Peptide concentrations were determined spectrophotometrically by a modification of the Lowry method.[11] The CD spectrum in the region of peptide bond absorption provides a test for helicity of a peptide; the characteristic spectrum of α helices exhibits a double minimum at 222 and 208 nm and a maximum at 190 nm.[12] The value of the mean residue ellipticity, $[\theta]_{222}$, for a perfect helix is about −35 000 at 222 nm, while that for a "coil" is estimated to be +3000.[12] The CD spectra of peptides I and II are shown in Figure 1, for several values of pH. Both indicate the presence of helix: we estimate that I contains up to about 35% α helix at 4 °C, while II has 16%. In both cases, an isodichroic point occurs at 203 nm in the spectra between pH 2 and 10, consistent with the presence of mixed helix and coil in these systems. Beyond pH 10, no isodichroic point occurs, and a different spectrum is seen. In both cases, the CD spectra are independent of concentration from 5–100 μM, consistent with intramolecular helical structure (see ref 8). Both peptides are highly soluble in water.

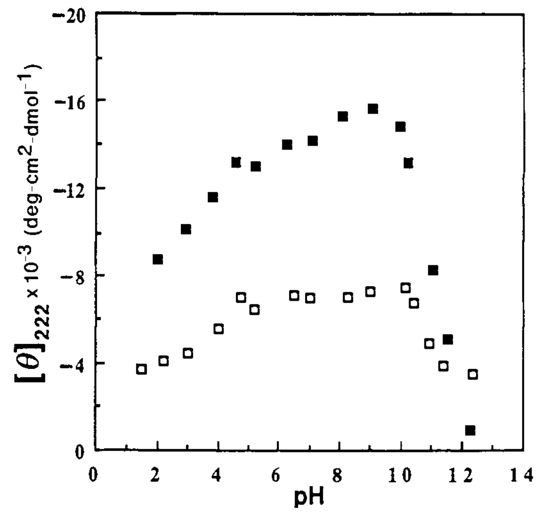

Figure 2. The pH dependence of the mean residue ellipticity at 222 nm, 4 °C, and 10 mM KF for peptide I (■) and peptide II (□).

The dependence of $[\theta]_{222}$ on pH for these peptides is shown in Figure 2. As the pH approaches that of the pK_a for lysine side chains, the apparent helix content of both peptides diminishes, as has been seen for other helix forming synthetic and natural peptides.[6-8] Loss of helix in the case of I is nearly complete, much greater than that in II. Comparison of these data with those of Marqusee and Baldwin[8] suggests that there may be a roughly linear relation between loss of helix on titrating lysines near pH 11 and the number of potential bridges. Thus the alkaline titration of these two peptides provides suggestive evidence that ion pairing is in fact a major component in stabilizing them, since the charge distribution on titrating either the lysines or glutamates side chains still favors helix according to the results of Shoemaker et al.[7]

These models should make it possible directly to assess the thermodynamic effect of ion pairs on helix relative to the presence of alanine side chains or other specific helix stabilizing interactions.

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Observation of Gas-Phase Anionic Bismuth Zintl Ions

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We report in this communication the first observation of gas-phase anionic Zintl ions of bismuth. Laser-ionization time-of-flight mass spectra of mixed bismuth/alkali clusters produced by a gas aggregation source were investigated in our laboratory and found to exhibit maxima for clusters corresponding to reported Zintl ions. Bonding in homoatomic clusters is a topic of fundamental as well as practical importance. The electronic and geometric structure of metal clusters in particular is currently the subject of intense investigation among a great number of researchers. "Magic numbers" corresponding to particularly abundant gas-phase cluster ions are observed to depend on the identity of the metal or alloy and on the ionization conditions. Reasons for the exceptional stabilities of such "magic numbers" have been ascribed to preferred electronic and structural configurations for either the neutral or ionic species.

Figure 1 displays a typical distribution obtained for intermetallic clusters of bismuth and sodium. Each group of peaks represents clusters possessing a specific number of bismuth, and various

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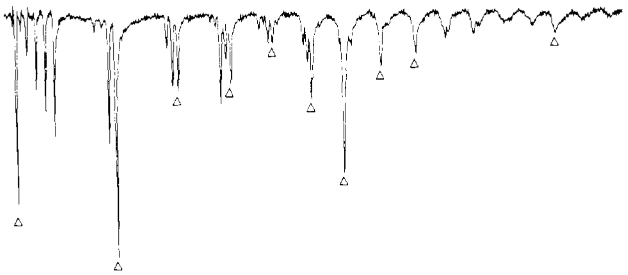

Figure 1. $Bi_xNa_y^+$ cluster distribution. Marked peaks correspond to (x,y) = (1,0), (2,3), (3,4), (4,5), (5,5), (6,5), (7,4), (8,5), (9,6), and (14,7). Ionization via 248 nm, 5.5 mJ/cm^2.

Table I. Anionic Zintl Ions of Bismuth

Zintl ion	ion observed
Bi_3^{3-}	$Bi_3Na_4^+$
Bi_4^{2-}	$Bi_4Na_3^+$
Bi_5^{3-}	$Bi_5Na_4^+$
Bi_7^{3-}	$Bi_7Na_4^+$

numbers of sodium atoms. Cationic clusters $Bi_xNa_{y+1}^+$, corresponding to Bi_x^{y-}, appear as magic numbers in the distribution for every reported anionic Zintl ion of bismuth,[1] with the exception of Bi_2^{4-}. Instead $Bi_2Na^{3+} \doteq Bi_2^{2-}$ is observed, suggesting the electronic octet rule determines the stability of this small cluster. $Bi_7Na_4^+$, which is isoelectronic with Bi_7^{3-}, is particularly prominent, and though the trivalent anion of antimony heptamer has been isolated,[2] the existence of the analogous bismuth species previously has not been unambiguously established. Additionally, clusters corresponding to Bi_4^{4-}, Bi_6^{4-}, Bi_8^{4-}, Bi_9^{5-}, and Bi_{14}^{6-} are exceptionally abundant, and it is expected some of these may exist in solution. In general, "magic numbers" correspond to the largest cluster within a group; the ion possessing an additional alkali atom is only weakly, if at all, observed.

Asymmetric tailing of the alkali-saturated peaks to longer arrival times is seen in the figure and is evidence that fragmentation of larger cluster ions represents a significant contribution to the observed intensities of these species. It is concluded that larger clusters sequentially evaporate excess alkali atoms until the stable Zintl ionic configuration is obtained. This is the most likely fragmentation channel is bismuth-bismuth bond energies[3] are typically twice that of sodium-sodium bonds.[4]

These mass spectra should thus be interpreted as indicative of cluster ion stabilities, and not the actual neutral cluster distribution. The absence of such "tailing" for clusters possessing fewer alkali atoms than the Zintl structure suggests these species contain negligible contributions from fragmentation of larger cluster ions and are apparently stable under these ionization conditions. Magic numbers observed in the bismuth/alkali clusters distribution correspond to reported Zintl ions possessing the same number of bismuth atoms. It is concluded that the alkali atoms cover the surface of the anionic bismuth Zintl ion, which determines the structures and stabilities of these ions and to which the alkali atoms merely donate electron density. Further chemical evidence supporting this assertion is based on studies of a number of reactions of these mixed clusters which show that the sodium can be reacted away and the remaining distribution is similar to that typically obtained for the pure bismuth system; details will be presented in future communications.

Due to the relatively small number of loosely held electrons versus the large number of nearest neighbors in metal clusters, analogies to the delocalized electron-deficient multicenter bonding characteristic of boron compounds have been proposed to account for "magic numbers" observed for a number of metallic systems.[5] For example, the observed stability of $Pb_2Sb_3^+$ may be interpreted as resulting from its $2n + 2$ valence electrons characteristic of "closo" boranes. Correspondence with the known Zintl ion Pb_5^{2-} has also been invoked to explain the prominence of this ion in the mass spectrum.[6] In contrast to bismuth/sodium clusters, where sodium ions surround the homoatomic bismuth Zintl ion core, the antimony atoms participate in the geometrical structure of the heteroatomic lead/antimony Zintl ions.

While cesium-lead and cesium-tin clusters have previously been reported[7] and found to exhibit maxima for stoichiometries corresponding to known Zintl ions of these divalent post-transition metals, these clusters are all accountable using Wades rules. Since bismuth and antimony are typically trivalent, anionic clusters of these elements very quickly exceed the maximum $2n + 8$ electrons accountable under Wades rules for "hypo" compounds. In particular, the previously mentioned Bi_7^{3-} possesses $2n + 10$ valence electrons, and Bi_{14}^{6-} has $2n + 20$! Hence, anionic Zintl ions of these species are particularly intriguing due to the inability of current theories to account for them and lack of other corresponding metallic compounds with which they may be compared.

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Total Synthesis of (+)-Ophiobolin C

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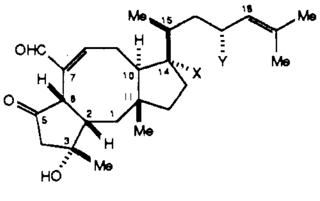
The ophiobolins (**1**) were characterized in the mid-1960s as the first naturally occurring sesterterpenes.[1] Since that time they have received much synthetic attention because of their complex molecular architecture and interesting biological activity.[2] Several approaches to these natural products have appeared in the literature,[3] focusing primarily on construction of the 5-8-5 ring system. To our knowledge, however, no total synthesis of ophiobolins has been reported thus far, probably due to the difficulties associated with the ring system, in particular the eight-membered ring, and also in the control of stereochemistry both on and outside the rings. We recently published an approach to this fused ring system[4] and now present a total synthesis of (+)-ophiobolin C (**1c**).



ophiobolin A	**1a**	X = Y = O
ophiobolin B	**1b**	X = OH, Y = H
ophiobolin C	**1c**	X = Y = H

We started with the previously prepared alcohol **2**.[4] The exocyclic olefin was ozonolyzed, and, after the primary alcohol

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