at m/z 1411 and 1305 accounting for allylic cleavages at C-64/C-65 and C-56/C-57 were prominent in the spectra. These MS results coupled with NMR data lead to the whole structure of amphidinol. The stereochemistry of **1** remains unknown because its 27 chiral centers are remote and most of them reside on acyclic parts.

Amphidinol (**1**) is the first representative of a new class of polyketide metabolites and exhibits potent antifungal and hemolytic activities.

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Supplementary Material Available: All ^1H and ^{13}C NMR assignments of **1** and ^1H NMR spectrum, ^1H-^1H and ^{13}C-^1H COSY, ^1H-^1H and ^{13}C-^1H HOHAHA, ^{13}C NMR spectra for deuterium shifts, 2D J (resolution) spectrum, and 1D/2D NOE spectra of amphidinol (13 pages). Ordering information is given on any current masthead page.

Alkoxyvinyl Thionium Ions in Intramolecular 4 + 3 Cycloaddition Reactions

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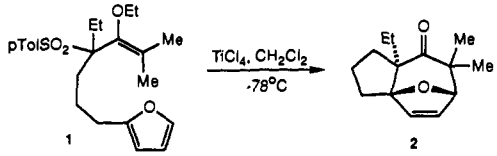
We recently reported new methodology for the intramolecular 4 + 3 cycloaddition reaction based on the paradigm defining the "chameleon" nature of the sulfone functional group.[1-3] Thus, treatment of a solution of sulfone **1** in CH_2Cl_2 with $TiCl_4$ gave cycloadduct **2** as a single isomer in good yield (eq 1).[1] Unfortunately, the generality of this process is limited by the reluctance of alkoxyallylic sulfones with less alkyl substitution to undergo the reaction.[4] It appeared that a means to circumvent this problem could be found using alkoxyallylic sulfones which possessed substituents capable of assisting the ionization process

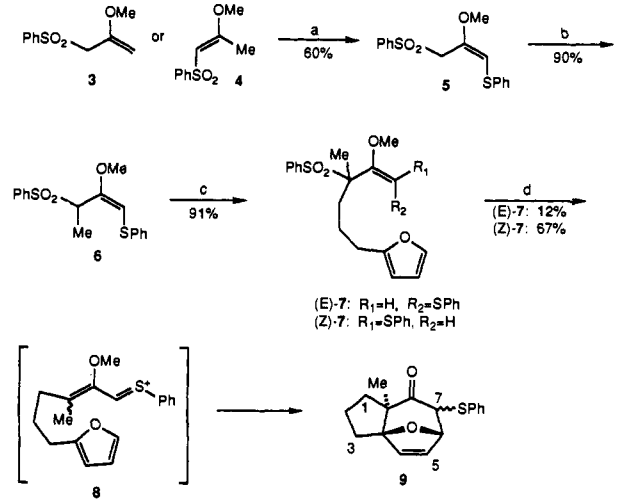


(1)

through resonance delocalization of the incipient positive charge.[5] Obvious choices included sulfur-, oxygen-, or nitrogen-containing functional groups as substituents. We chose to examine sulfur initially.

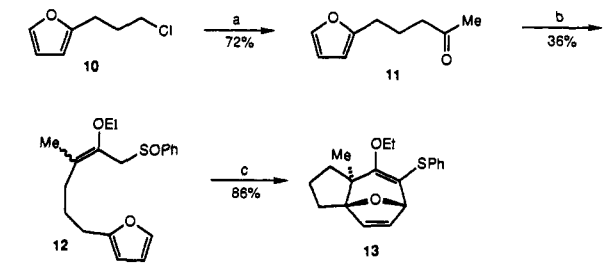
To that end, treatment of either 2-methoxy-3-(phenylsulfonyl)-1-propene (**3**) or its double-bond isomer **4** with phenylsulfenyl chloride followed by DBU gave **5** in 60% isolated yield after trituration with *tert*-butyl methyl ether.[6-8] Deprotonation with *n*-BuLi and alkylation with methyl iodide gave **6** in 90% yield with complete regiocontrol.[9] Subsequent deprotonation and alkylation with 2-(3-iodopropyl)furan gave (*E*)- and (*Z*)-**7** in 91% combined yield, along with recovered starting material[10] (Scheme I).

Scheme I[a]



[a](a) (1) PhSCl, −78 °C (10 min) to 25 °C (1 h), CH_2Cl_2. (2) DBU, −78 °C (5 min), then 25 °C (30 min). (b) (1) *n*-BuLi, THF, −78 °C. (2) MeI. (c) (1) *n*-BuLi, THF, −78 °C. (2) 2-(3-Iodopropyl)furan, −78 to 25 °C, slowly. (d) $TiCl_4$, CH_2Cl_2, −78 °C, inverse addition.

Scheme II[a]



[a](a) (1) Mg, ether. (2) Add to excess Ac_2O, ether, −78 °C. (b) (1) (Ethoxyvinyl)lithium THF, −78 °C. (2) *n*-BuLi, then PhSCl, THF, −78 °C. (c) Tf_2O (1 equiv), 2,6-lutidine (2 equiv), CH_2Cl_2, 25 °C.

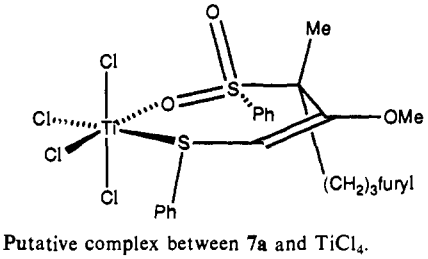


Figure 1. Putative complex between **7a** and $TiCl_4$.

Interestingly, treatment of (*E*)-**7** with $TiCl_4$ (0.02 M, CH_2Cl_2, −78 °C, inverse addition) resulted in only a 12% yield (based on recovered starting material) of cycloadduct **9** as a mixture of two

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(8) The nature of the rearrangement in the conversion of **4** to **5** has not been investigated.
(9) The stereochemistry of the double bond of **6** was established by X-ray crystallography: Enraf-Nonius CAD4 diffractometer, Mo Kα radiation, $C_{17}H_{18}O_3S_2$, space group $P\bar{1}$, a = 10.007 (4) Å, b = 10.922 (6) Å, c = 8.353 (5) Å, V = 830.2 (7) Å^3, Z = 2, d_{calcd} = 1.338. The structure was solved (2348 reflections, $I > 2.5\sigma(I)$) by direct methods and refined to R = 0.037 (R_w = 0.056). See supplementary material for more details.
(10) Recovered starting material was not stereochemically homogeneous.

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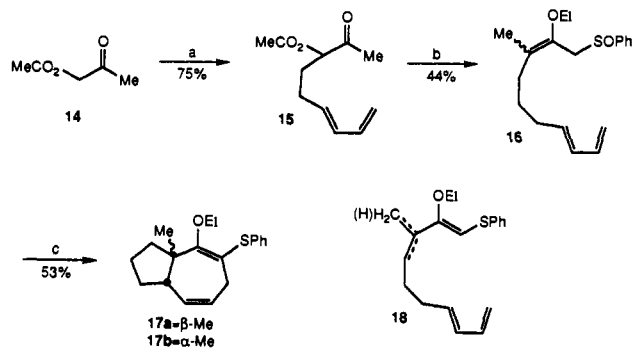
Scheme III[a]



[a] (a) (1) NaH, THF. (2) (*E*)-6-Iodo-1,3-hexadiene, reflux. (b) (1) LiCl, DMF/H_2O, heat. (2) (Ethoxyvinyl)lithium, THF. (3) *n*-BuLi, then PhSCl, THF, −78 °C. (c) Tf_2O (1 equiv), 2,6-di-*tert*-butylpyridine (2 equiv), CH_2Cl_2, 25 °C.

epimers. Normal addition either destroyed (*E*)-**7** or resulted in the recovery of starting material. Fortunately, (*Z*)-**7** reacted smoothly under the same reaction conditions to give a 67% yield of **9** as a mixture of isomers. On the basis of these results, we speculate that (*E*)-**7** can serve as a bidentate ligand for $TiCl_4$ to produce a chelate which is unreactive with respect to ionization to alkoxyvinyl thionium ion **8** and subsequent cycloaddition (Figure 1).[11,12] The stereochemistry of the cycloadduct **9** with respect to the angular positions was assigned in accordance with stereochemical assignments made on related cycloadducts.[1] It was clear from the NMR spectrum of **9** that the isomers arose from epimerization at carbon 7 (azulenone numbering).

In order to address the difficulties associated with the cyclization of (*E*)-**7**, we considered other means of generating **8** and concluded that the Pummerer rearrangement of alkoxyallylic sulfoxides offered one of the best options.[12,13] The substrate needed to examine this idea was prepared as shown in Scheme II. Treatment of 2-(3-chloropropyl)furan[14] with magnesium and quenching the resulting Grigand reagent with excess acetic anhydride gave ketone **11** in 72% yield.[15] Condensation of **11** with (ethoxyvinyl)lithium[16] and treatment with phenylsulfenyl chloride gave sulfoxide **12** as a 1:1 *E*/*Z* mixture.[17]

After some experimentation we found that the best conditions for 4 + 3 cycloaddition consisted of treatment of a 0.017 M CH_2Cl_2 solution of **12** with Tf_2O and 2 equiv of 2,6-lutidine at room temperature. This gave enol ether **13** in exceptionally high yield. The stereochemical assignment was made on the basis of aforementioned considerations.[1]

A substrate containing a free diene was tested as well (Scheme III). Alkylation of the sodium enolate[18] of **14** with 6-iodo-1,3-hexadiene[19] gave keto ester **15** in good yield. Krapcho decarboxylation[20] and straightforward manipulations gave **16** as a 1:1 mixture of isomers. Considerable difficulties were associated with attempts to induce cycloaddition using protocols successful with **12**. Elimination to form **18** as a mixture of regioisomers competed effectively with cycloaddition over a wide range of conditions. Eventually we found that treatment of a 0.015 M CH_2Cl_2 solution of **16** with Tf_2O in the presence of 2 equiv of 2,6-di-*tert*-butylpyridine at room temperature gave cycloadduct **17** as a 1:1 mixture of isomers in 53% isolated yield. Apparently, a combination of the decreased nucleophilicity and conformational mobility of the diene in **16** relative to the furan in **12** is detrimental to the cycloaddition process.[21]

In summary, we have invented two convenient means of generating alkoxyvinyl thionium ions for use in the intramolecular 4 + 3 cycloaddition reaction to form functionalized, fused 5,7 carbocyclic systems. Work continues on improving the stereoselectivity of these reactions, applying the methodology to synthetic targets, and expanding the reaction profile of these unique intermediates.

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Supplementary Material Available: Experimental procedures and spectral data for compounds **5–7**, **11–13**, and **15–17** and tables of bond lengths, bond angles, and dihedral angles for **6** and **17a** (21 pages). Ordering information is given on any current masthead page.

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Intrinsic Barriers to Atom Transfer (Abstraction) Processes. Self-Exchange Rates for $Cp(CO)_3M^{\bullet}$ Radical/$Cp(CO)_3M$–X Halogen Couples

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The significant role played by radical pathways is now widely recognized[1,2] for organometallic reagents once believed to undergo even-electron changes exclusively. These pathways are evident in reactions as diverse as olefin hydrogenation by metal hydrides[3] and radical-chain substitution[4] of metal halide complexes. The reactivities of both metal hydrides[3,5] and halides[4,6] with respect to atom transfer (abstraction) are now being systematically addressed. However, the self-exchange process itself has not received attention. Here we apply "isotopically labeled" materials and a

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