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Nazarov Cyclizations of an Allenyl Vinyl Ketone with Interception of the Oxyallyl Cation Intermediate for the Formation of Carbon−Carbon Bonds

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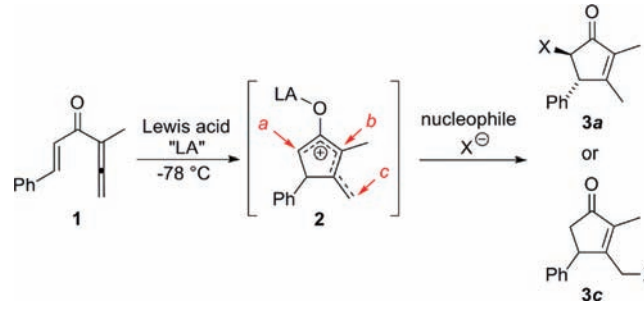
Abstract: Treatment of an allenyl vinyl ketone with $BF_3 \cdot Et_2O$ leads to a cyclic oxyallyl cation by a Nazarov reaction, and when this reaction is conducted in the presence of an acyclic diene, [4 + 3] and [3 + 2] products are obtained efficiently with high regio- and stereoselectivity. The proportion of [4 + 3] to [3 + 2] product depends on the substitution on the diene. Cyclic dienes react with the oxyallyl cation by forming only one carbon−carbon bond, but the site of bond formation can be affected by steric hindrance. Electron-rich alkenes intercept the allyl cation by forming one carbon−carbon bond, or two carbon−carbon bonds through [3 + 2] cyclization. In some instances, further treatment of the initial products with $BF_3 \cdot Et_2O$ leads to equilibrated products in good yield.

Introduction

Oxyallyl cations are key intermediates in the synthesis of seven-membered carbocycles via [4 + 3] cyclizations with 1,3-dienes.[1] The reaction is known to proceed efficiently with furan and cyclopentadiene, but the analogous reaction with acyclic dienes remains underexplored likely because this process can be complicated by alternative [4 + 2] and [3 + 2] cyclizations and by competing decomposition pathways.[2] Recently, oxyallyl cations generated by Nazarov cyclization[3,4] have been shown to be effective partners in [4 + 3] cyclizations with furan, cyclopentadiene, and a few acyclic dienes.[5] Furthermore, there are two reports of Nazarov cyclizations being followed by [3 + 2] cyclizations.[6−8] Recently, we described Nazarov cyclizations of allenyl vinyl ketones (AVK's) such as **1**,[9,10] where the only products isolated were those resulting from interception of the cationic intermediate **2** by heteroatom nucleophiles, giving ***3a*** by interception at position *a*, or ***3c*** by interception at position *c* (Scheme 1).

Scheme 1. Interrupted Nazarov Reaction of AVK **1**



There are at least four reasons why the cationic intermediate **2** presents an especially well suited coupling partner for cyclization reactions: (1) An AVK is a particularly reactive substrate for the Nazarov reaction,[11] cyclizing rapidly under acidic conditions to generate the oxyallyl cation. (2) The oxyallyl cation **2** is stabilized by extra conjugation and simple loss of a

(1) (a) Noyori, R. *Acc. Chem. Res.* **1979**, *12*, 61. (b) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 1. (c) Mann, J. *Tetrahedron* **1986**, *42*, 4611. (d) Rigby, J. H.; Pigge, F. C. *Org. React.* **1997**, *51*, 351. (e) Hosomi, A.; Tominagi, Y. in *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 593−615. (f) Harmata, M. *Acc. Chem. Res.* **2001**, *34*, 595. (g) Harmata, M.; Rashatasakhon, P. *Tetrahedron* **2003**, *59*, 2371, and references therein.

(2) (a) Chidgey, R.; Hoffmann, H. M. R. *Tetrahedron Lett.* **1977**, 2633. (b) Hoffmann, H. M. R.; Chidgey, R. *Tetrahedron Lett.* **1978**, 85. (c) Takaya, H.; Makino, S.; Hayakawa, H.; Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 1765. (d) Sasaki, T.; Ishibashi, Y.; Ohno, M. *Tetrahedron Lett.* **1982**, *23*, 1693. (e) Blackburn, C.; Childs, R. F.; Kennedy, R. A. *Can. J. Chem.* **1983**, *61*, 1981. (f) Föhlisch, B.; Korfant, H.; Meining, H.; Frey, W. *Eur. J. Org. Chem.* **2000**, 1335. (g) Fujita, M.; Oshima, M.; Okuno, S.; Sugimura, T.; Okuyama, T. *Org. Lett.* **2006**, *8*, 4113.

(3) (a) Pellissier, H. *Tetrahedron* **2005**, *61*, 6479. (b) Frontier, A. J.; Collison, C. *Tetrahedron* **2005**, *61*, 7577. (c) Tius, M. A. *Eur. J. Org. Chem.* **2005**, 2193.

(4) Grant, T. N.; Rieder, C. J.; West, F. G. *Chem. Commun.* **2009**, 5676, and references therein.

(5) (a) Wang, Y.; Schill, B. D.; Arif, A. M.; West, F. G. *Org. Lett.* **2003**, *5*, 2747. Intramolecular [4 + 3] cyclization: (b) Wang, Y.; Arif, A. M.; West, F. G. *J. Am. Chem. Soc.* **1999**, *121*, 876. (c) Yungai, A.; West, F. G. *Tetrahedron Lett.* **2004**, *45*, 5445.

(6) Giese, S.; Kastrup, L.; Stiens, D.; West, F. G. *Angew. Chem., Int. Ed.* **2000**, *39*, 1970.

(7) Mahmoud, B.; West, F. W. *Tetrahedron Lett.* **2007**, *48*, 5091.

(8) Regarding [3 + 2] cyclizations: see refs 1f,g, 2g and (a) Hayakawa, Y.; Yokoyama, K.; Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 1799. (b) Lee, T. V.; Richardson, K. A.; Taylor, D. A. *Tetrahedron Lett.* **1986**, *27*, 5021. (c) Lee, T. V.; Boucher, R. J.; Porter, J. R.; Taylor, D. A. *Tetrahedron* **1988**, *44*, 4233. (d) Lee, T. V.; Porter, J. R.; Roden, F. S. *Tetrahedron* **1991**, *47*, 139. (e) Hardinger, S. A.; Bayne, C.; Kantorowski, E.; McClennan, R.; Larres, L.; Nuesse, M.-A. *J. Org. Chem.* **1995**, *60*, 1104. (f) Masuya, K.; Domon, K.; Tanino, K.; Kuwajima, I. *J. Am. Chem. Soc.* **1998**, *120*, 1724. (g) Mizuno, H.; Domon, K.; Masuya, K.; Tanino, K.; Kuwajima, K. *J. Org. Chem.* **1999**, *64*, 2648. (h) Nakamura, E.; Yamago, S. *Acc. Chem. Res.* **2002**, *35*, 867.

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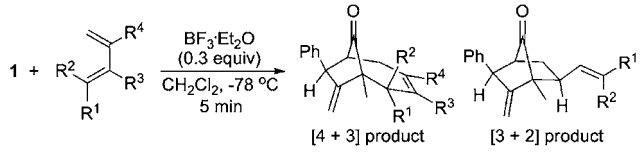
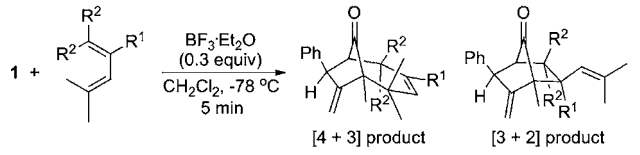
(10) Marx, V. M.; Cameron, T. S.; Burnell, D. J. *Tetrahedron Lett.* **2009**, *50*, 7213.

Table 1. Reactions of AVK **1** with Substituted Butadienes (2 equiv) Mediated by $BF_3 \cdot Et_2O$



entry	diene	[4 + 3]	[3 + 2]	yield (%) product ratio
1	R^1 = Me, R^2 = H, R^3 = H, R^4 = H	**4a**	**5**	51 **4a/5** 1:2.7
2	R^1 = H, R^2 = Me, R^3 = H, R^4 = H	–	**6**	54
3	R^1 = H, R^2 = H, R^3 = Me, R^4 = H	**7a,b**[a]	–	56 **7a/7b** 1:2.8
4	R^1 = H, R^2 = H, R^3 = Me, R^4 = Me	**8**	–	99



entry	diene	[4 + 3]	[3 + 2]	yield (%) product ratio
5	R^1 = H, R^2 = H	–	**9a**	85
6	R^1 = Me, R^2 = H	**10**	**11a,b**[b]	71 **10/11a,b** 1:2
7	R^1 = H, R^2 = Me	–	**12a,b**[c]	49

[a] **7a** R^3 = Me, R4 = H; **7b** R^3 = H, R4 = Me. [b] Intractable material. [c] **11a** R1 endo, **11b** R1 exo, ratio 1:1. [d] **12a** R1 endo, **12b** R1 exo, ratio 5:1, respectively.

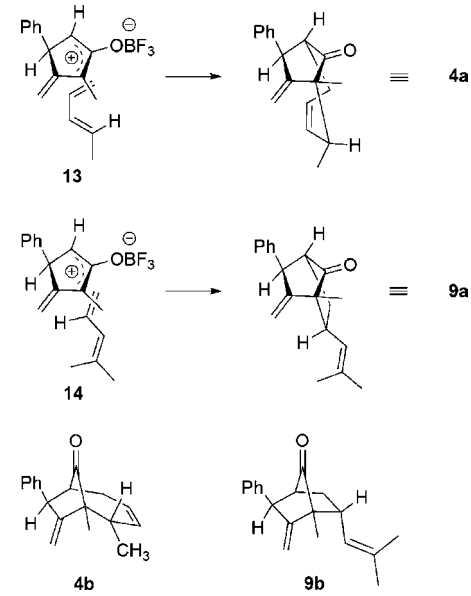
proton from **2** to generate a double bond might be unfavorable as the product would be a fulvene. Thus, the oxyallyl cation would be more likely to be trapped. (3) The products resulting from either [4 + 3] or [3 + 2] cyclizations would contain an exocyclic methylene unit, providing a good synthetic handle for further transformations. (4) The oxyallyl cation **2** has two unencumbered positions, *a* and *c*, to which a nucleophile might add readily, which would allow for the production of diverse cyclopentenone-containing ring systems.

We present here the first survey of Nazarov reactions of an AVK accompanied by tandem carbon−carbon bond formation that leads to a diversity of product types with high regio- and stereoselectivity and often in good to excellent yield. The product types depend on the nature of the carbon nucleophile, and the range of examples will now allow generalizations to be made regarding the outcomes of the reactions.

Results and Discussion

$BF_3 \cdot Et_2O$ was chosen as the acid for most reactions because no nucleophilic species, which might compete with a carbon-

Scheme 2. Geometries of Cycloadditions that would Lead to [4 + 3] and [3 + 2] Products



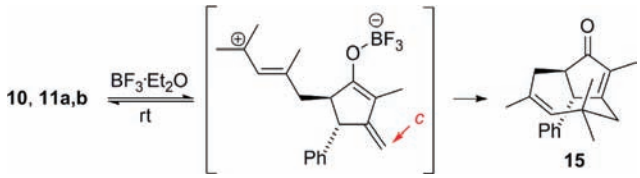
nucleophile to trap the oxyallyl cation derived from **1**, had been seen to be generated from this Lewis acid.[9] AVK **1** was treated with $BF_3 \cdot Et_2O$ in the presence of various methyl-substituted butadienes (Table 1). Reactions were rapid (5 min at −78 °C) and yielded products of [4 + 3] and [3 + 2] cyclizations onto positions *a* and *b* in **2**. Whereas $BF_3 \cdot Et_2O$ elicited the quantitative formation of **8**[12] (entry 4) in 5 min, $InCl_3$ and $Cu(OTf)_2$ gave **8** more slowly (2 h) and in yields of only 59 and 68%, respectively. $InCl_3$ is known to give the product of trapping **2** with chloride at position *c*,[10] but the reaction of the diene with **2** must be much faster because chlorinated products were not observed when the diene was added. This was true of other experiments involving alkenes with $InCl_3$ (*vide infra*). It is interesting to note that the much more electron-rich trans-1-methoxy-3-trimethylsilyloxy-1,3-butadiene did not yield any Nazarov product with **1**.

The regioselectivity of all cyclizations,[13] with the exception of entry 3, was high, and this could be rationalized as arising from the most reactive cationic site in **2** being *a* and significant amounts of charge in the diene moieties at the transition states. NOE measurements showed that every product had the phenyl group in an exo position, indicating a high degree of facial selectivity in the additions to **2**. The only [4 + 3] product using trans-piperylene was **4a** (entry 1), but calculations[14] showed that its epimer **4b** is 3.0 kJ.mol^{-1} lower in energy. These findings would be consistent with a concerted, but asynchronous, cycloaddition mechanism via an extended geometry similar to **13** in Scheme 2 for the formation of the [4 + 3] products. This was consistent with a computational study involving the reaction of butadiene with a metal-bound acyclic oxyallyl species, which had suggested a concerted pathway to be lower in energy than a stepwise one for adducts resulting from extended transition states.[15]

(11) (a) Tius, M. A.; Kwok, C.-K.; Gu, X.; Zhao, C. *Synth. Commun.* **1994**, *24*, 871. (b) Hashmi, A. S. K.; Bats, J. W.; Choi, J.-H.; Schwarz, L. *Tetrahedron Lett.* **1998**, *39*, 7491. (c) Tius, M. A. *Acc. Chem. Res.* **2003**, *36*, 284–290, and references therein. (d) Dhoro, F.; Tius, M. A. *J. Am. Chem. Soc.* **2005**, *127*, 12472. (e) delos Santos, D. B.; Banaag, A. R.; Tius, M. A. *Org. Lett.* **2006**, *8*, 2579. (f) Banaag, A. R.; Tius, M. A. *J. Am. Chem. Soc.* **2007**, *129*, 5328. (g) Basak, A. K.; Tius, M. A. *Org. Lett.* **2008**, *10*, 4073. (h) Banaag, A. R.; Tius, M. A. *J. Org. Chem.* **2008**, *73*, 8133. (i) Cao, P.; Sun, X.-L.; Zhu, B.-H.; Shen, Q.; Xie, Z.; Tang, Y. *Org. Lett.* **2009**, *11*, 3048.

(12) The structure of **8** was confirmed by X-ray crystallography.
(13) The regiochemistry of the reactions was determined by analysis of 2D NMR spectra (COSY, HSQC, and HMBC) of the products.
(14) HF/6-31G//HF/6-311G(d, p) using Gaussian 03, Revision C.02.
(15) (a) Cramer, C. J.; Barrows, S. E. *J. Phys. Org. Chem.* **2000**, *13*, 176. See also the earlier paper: (b) Cramer, C. J.; Barrows, S. E. *J. Org. Chem.* **1998**, *63*, 5523.

Scheme 3. Conversion of **10** and **11a,b** into **13**

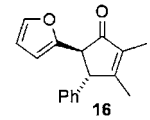
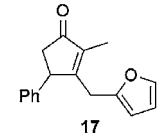
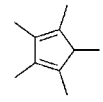
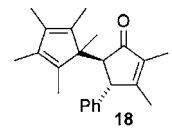
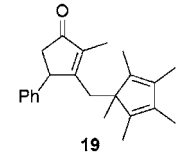
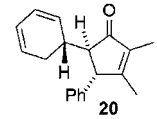


A concerted reaction would require the diene to assume an *s*-cis conformation. *s*-Cis conformations would be disfavored for the dienes in entries 2, 5, and 7, and these dienes gave no [4 + 3] products, but provided [3 + 2] products, only, in moderate to good yield. In contrast, the dienes in entries 1, 3, 4, and 6 have more accessible *s*-cis conformers, and these dienes did afford [4 + 3] products. It was significant that **5**, **6**, and **9a** were the only [3 + 2] products in entries 1, 2, and 5, indicating a high degree of stereoselectivity in this cyclization, also. This might be expected for a cycloaddition via a geometry similar to **14** (Scheme 2) or a very rapid stepwise reaction.[16] The product **9a** in entry 5 was compared with its (undetected) epimer **9b** computationally,[14] and it was **9b** that was lower in energy by 2.2 kJ.mol^{-1}, suggesting that **9a** forms as the result of a concerted reaction.

All products were stable with $BF_3 \cdot Et_2O$ at −78 °C, but with $BF_3 \cdot Et_2O$ at room temperature over a period of hours some compounds equilibrated. One may presume that this much slower process involved ring cleavage to give the enolate and the delocalized cation, which then recyclized. The [3 + 2] product **5** equilibrated to a 2.2:1 mixture of the [4 + 3] compound **4a** and the epimer **4b**. On the other hand, compound **6** remained unchanged in the presence of $BF_3 \cdot Et_2O$. Resubjecting the mixture of **10** and **11a**,**b** to $BF_3 \cdot Et_2O$ provided **15** in 75% yield. This remarkable outcome indicates that each compound underwent ring-opening, and then reclosure of the enolate onto position *c* (Scheme 3). Compound **15** represents the product of a formal [5 + 4] cyclization of **2** with the diene. In every instance in Table 1 where the reaction products were mixtures of different ring-systems, addition of more $BF_3 \cdot Et_2O$ to the mixture resulted in confluence to a single ring-system.

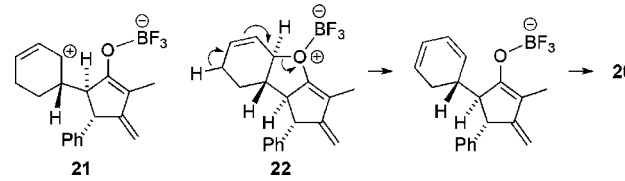
The number of examples of [4 + 3] cyclizations employing cyclic dienes is large.[1] Also, the cyclic cations of Nazarov reactions have been reported to be trapped with cyclic dienes.[5] When some cyclic dienes were mixed with AVK **1** and $BF_3 \cdot Et_2O$, the Nazarov reactions were interrupted readily by the cyclic dienes, but it was surprising that no products of [4 + 3] cyclization were detected. Only one carbon−carbon bond formed (Table 2). Furan, which has been used in a number of [4 + 3] cyclizations with oxyallyl cations,[1g,5] trapped **2** only at position *a* to provide **16** when the reaction was mediated by $BF_3 \cdot Et_2O$ or $Cu(OTf)_2$ (entry 1). $InCl_3$ elicited the formation of a minor amount of **17** via capture at position *c* (entry 2). Intractable material was obtained when cyclopentadiene or 6,6-dimethylfulvene were added, but addition of 1,2,3,4,5-pentamethylcyclopentadiene led to the formation of a minor product **18**, by interception of **2** at position *a*, and a major product **19**, by capture of **2** at the less sterically hindered position *c*. Using 1,3-cyclohexadiene to trap the oxyallyl cation provided only

Table 2. Reactions of AVK **1** with Cyclic Dienes in CH_2Cl_2 at −78 °C

entry	diene Lewis acid	products		yield (%) product ratio
1	 $BF_3 \cdot Et_2O$[a]	 **16**	–	50[b]
2	 $InCl_3$[c]	**16**	 **17**	69 **16**/**17** 3.5:1
3	 $BF_3 \cdot Et_2O$[d]	 **18**	 **19**	72[e] **18**/**19** 1:5.5
4	 $BF_3 \cdot Et_2O$[d]	 **20**	–	70

[a] Five equivalents of furan, 5 equiv of $BF_3 \cdot Et_2O$, 5 min. [b] In addition, there was 22% of a product where one furan added to two of **2** at position *a*. [c] Five equivalents of furan, 5 equiv of $InCl_3$, 2 h. [d] Two equivalents of diene, 1.1 equiv of $BF_3 \cdot Et_2O$, 5 min. [e] In addition, there was 8% of the product of the Diels−Alder reaction of the diene with the allene of **1**.

Scheme 4. Formation of **20**



20, as a single diastereomer. The relative stereochemistry of **20** was established by a *J*-based configuration analysis method.[18] The position of the diene moiety in **20** is intriguing because loss of a proton from a putative intermediate **21** should be expected to lead to a more substituted diene. However, a [3 + 2] cyclization involving the enol oxygen would give **22** as an intermediate,[19] and conjugate elimination/ring-opening during workup would result in the preferential formation of **20** (Scheme 4). It has been suggested by the calculations of Cramer and Barrows[15] that a dipolar [3 + 2] cycloaddition can be comparable, or even lower, in energy to all-carbon [3 +2] and [4 + 3] cycloadditions, depending on the nature of the oxyallyl cation and the diene involved. In the case of AVK **1** with the cyclic dienes, it is plausible that the direct formation of [4 + 3] and [3 + 2] products would suffer from considerable steric hindrance in transition state geometries similar to **13** and **14**, disfavoring these pathways relative to a dipolar [3 + 2] cycloaddition generating **22**.

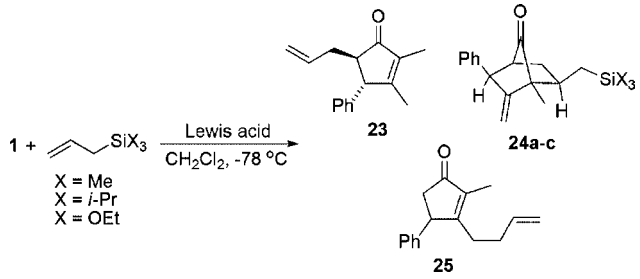
(16) The stepwise formation of [3 + 2] products might be considered a 5-(enolendo)-exo-trig closure, a disfavored process: Baldwin, J. E.; Lusch, M. J. *Tetrahedron* **1982**, *38*, 2939.

(17) Similar observation with furan: Rieder, C. J.; Fradette, R. J.; West, F. G. *Chem. Commun.* **2008**, 1572.

(18) (a) Matsumori, N.; Kaneno, D.; Murata, M.; Nakamura, H.; Tachibana, K. *J. Org. Chem.* **1999**, *64*, 866. Reviews: (b) Bifulco, G.; Dambruoso, P.; Gomez-Paloma, L.; Riccio, R. *Chem. Rev.* **2007**, *107*, 3744. (c) Kwan, E. E.; Huang, S. G. *Eur. J. Org. Chem.* **2008**, 2671. NOE measurements were in accord with the stereochemical assignment.

(19) A product of intramolecular cyclization involving an enol oxygen during Nazarov cyclization has been reported: Bender, J. A.; Blize, A. E.; Browder, C. C.; Giese, S.; West, F. G. *J. Org. Chem.* **1998**, *63*, 2430.

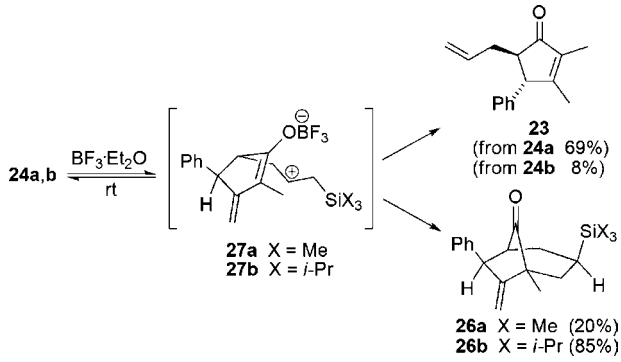
Table 3. Reactions of AVK **1** with Allylsilanes Mediated by Various Lewis Acids



entry	X	Lewis acid	time	yields (%) 23	24a–c	25
1	Me	$BF_3 \cdot Et_2O$[a]	5 min	27	54 (**24a–c**)	–
2	Me	$Cu(OTf)_2$[b]	1.5 h	20	10 (**24a**)	42
3	Me	$InCl_3$[b]	2 h	22	–	56
4	*i*-Pr	$BF_3 \cdot Et_2O$[a]	5 min	19	57 (**24b**)	–
5	*i*-Pr	$InCl_3O$[b]	2 h	27	28 (**24b**)	13
6	OEt	$BF_3 \cdot Et_2O$[a]	5 min	–	15 (**24c**)	–

[a] Two equivalents of allylsilane, 1.1 equiv of $BF_3 \cdot Et_2O$. [b] Five equivalents of allylsilane, 5 equiv of Lewis acid.

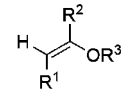
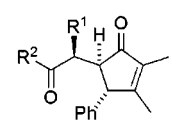
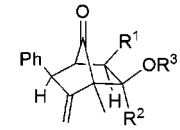
Scheme 5. Treatment of the [3 + 2] Products **24a,b** with $BF_3 \cdot Et_2O$ at Room Temperature



When $BF_3 \cdot Et_2O$ was added to **1** and allyltrimethylsilane, two Nazarov products formed very rapidly. One (**23**) was the product of addition to position *a* in **2**, but the major product was the [3 + 2] product **24a** (Table 3).[13] The relative stereochemistry was determined by measurement of NOE's. The effect of different Lewis acids and different silanes was briefly examined. When $Cu(OTf)_2$ was employed as the Lewis acid, the reaction was slower and three products were obtained: **23**, **24a**, and **25**, of which **25** was the result of capture of **2** at position *c*. With $InCl_3$, the reaction had approximately the same rate as with $Cu(OTf)_2$, **25** was the major product, and there was none of the [3 + 2] product. Utilization of a more robust silane, allyltriisopropylsilane, resulted in an increased proportion of the [3 + 2] product **24b** in the presence of either $BF_3 \cdot Et_2O$ or $InCl_3$. Allyltriethoxysilane with $BF_3 \cdot Et_2O$ gave a poor yield of the [3 + 2] product **25c**, but no other Nazarov product was detected.

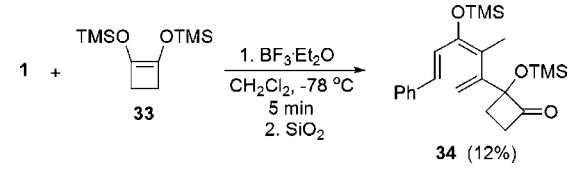
The trimethylsilyl [2.2.1]-compound **24a** could be converted in 5 h to **23** in moderate yield in the presence of $BF_3 \cdot Et_2O$ at room temperature, but a minor product was the trimethylsilyl [3.2.1]-compound **26a** (Scheme 5). This minor compound would have been the result of cyclization of intermediate **27a** in concert with a shift of the silyl group. This sort of process had been anticipated, but not observed, by West[6] in their study of interception of Nazarov reactions with allylsilanes. When the triisopropylsilyl [2.2.1]-compound **24b** was stirred with $BF_3 \cdot Et_2O$ at room temperature, not only was the analogous recyclization of **27b** evident, but it led to the triisopropylsilyl [3.2.1]-compound **26b** in very good yield.

Table 4. Reactions of AVK **1** with Electron-Rich Alkenes (2 equiv) Mediated by $BF_3 \cdot Et_2O$ (1.1 equiv) in CH_2Cl_2 at −78 °C for 5 min

entry	alkene	products and yields	
			
1	R^1 = H, R^2 = H, R^3 = TMS	**28** (35%)	–
2	R^1 = H, R^2 = H, R^3 = Ac	–	**29** (18%)
3	R^1 = H, R^2 = H, R^3 = *n*Pr	**28** (59%)	**30** (41%)[a]
4	R^1 = Me, R^2 = H, R^3 = Et	**31** (86%)[b]	–
5	R^1 = H, R^2 = Me, R^3 = Me	**32** (60%)[c]	–

[a] Ether group exo/endo 5:1. [b] Ca. 90% the isomer shown. [c] Included an inseparable byproduct from subsequent reaction of **32**.

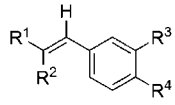
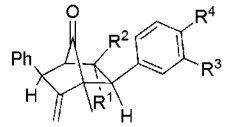
Scheme 6. Attempted Interrupted Nazarov Reaction of AVK **1** with **33**



Oxygen-substituted alkenes intercepted **2** with high facial selectivity by nucleophilic attack at position *a* or by the formation of [3 + 2] products (Table 4). The silyl enol ether and the enol acetate (entries 1 and 2) trapped the oxyallyl cation inefficiently to give low yields of **28** and **29**, respectively. The enol ether, *n*-propoxyethene, gave two types of products, **28** and **30**, in high overall yield (entry 3). However, the [3 + 2] product **30**, in contrast with **24a,b**, simply decomposed when treated with $BF_3 \cdot Et_2O$ at room temperature. Further substitution of the double bond as in entries 4 and 5 led to products of trapping **2** at position *a*, and **31** and **32** were not accompanied by [3 + 2] products. The [3 + 2] product **30** was obtained as an epimeric mixture, but it is important to note that the formation of **31** was stereoselective. The stereochemistry was determined by an NMR method.[18] This stereochemistry might have been the consequence of the formation of a transient intermediate, analogous to **22**, produced by a [3 + 2] process involving the enol oxygen.

In light of entries 1 and 4 in Table 4, it was somewhat surprising that introduction of neither the *tert*-butyldimethylsilyl enol ether derived from cyclopentanone nor a cyclic enol ether, dihydropyran, gave any trapped Nazarov product. Also, the enamine derived from cyclopentanone and pyrollidine and *N*-vinylpyrollidone failed to trap **2** to any significant degree, and intractable material was obtained. It is probable that if the alkene or diene is too electron-rich, it will add via a Michael reaction to the central allenic carbon of the AVK before the AVK has undergone the Nazarov reaction. Evidence for this comes from an attempted interception of **2** with an excess of the electron-rich cyclobutene derivative **33** (Scheme 6). The ^1H NMR spectrum of the initial product mixture showed signals mainly for the Michael product **34** and residual **33**. Although the isolated yield of **34** following flash chromatography was low, it was subsequently established that **34** decomposed rapidly on silica gel.

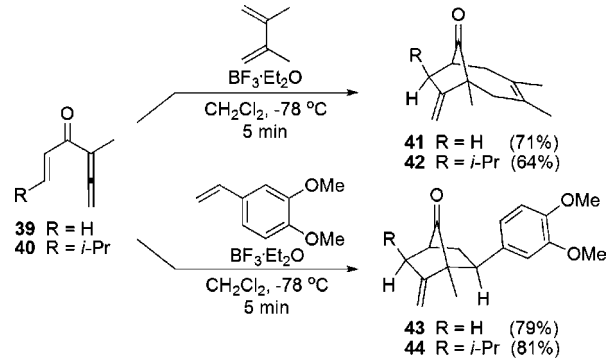
Table 5. Reactions of AVK **1** with Styrenes (2 equiv) Mediated by $BF_3 \cdot Et_2O$ (1.1 equiv) in CH_2Cl_2 at −78 °C for 5 min

entry	styrene	product and yield
		
1	R^1, R^2, R^3, R^4 = H	**35** (15%)
2	R^1, R^2, R^3 = H; R^4 = CF_3	–
3	R^1, R^2, R^3 = H; R^4 = OMe	**36** (52%)
4	R^1, R^2 = H; R^3, R^4 = OMe	**37** (76%)
5	R^1 = Me; R^2, R^3 = H; R^4 = OMe	**38** (59%)
6	R^1, R^3 = H; R^2 = Me; R^4 = OMe	–

Styrenes afforded only [3 + 2] products as single diastereomers, for which the relative stereochemistry was confirmed by NOE measurements (Table 5).[13] Styrene itself (entry 1) gave a poor yield of **35**, and an electron-poor derivative (entry 2) did not trap the oxyallyl cation at all. On the other hand, electron-donation was clearly advantageous (entries 3−5). Reaction of **1** with the trans-isomer provided **38** in a yield that was slightly higher (entry 5) than the yield from the less substituted styrene (entry 3), but the corresponding cis-isomer failed to trap **2** (entry 6). This curious result may reflect reduced electron-donation by the methoxyphenyl group into the alkene moiety in the cis isomer,[20] and it is also consistent with the hypothesis that the kinetic route to the [3 + 2] products must be concerted, or at least very rapid, at − 78 °C because bond rotation in an intermediate carbocation could have given **38** from the cis isomer.

Finally, two reactions previously observed with AVK **1** were reassessed with an unsubstituted AVK **39** and the isopropyl-substituted AVK **40** (Scheme 7).[13] Once again, in Nazarov reactions mediated by $BF_3 \cdot Et_2O$, 2,3-dimethylbutadiene intercepted the intermediate oxyallyl cations to provide the [4 + 3] products **41** and **42**, exclusively. Also, addition of 3,4-dimethoxystyrene led rapidly to the formation of only the [3 + 2] products **43** and **44**. In every instance, only one diastereomer was produced.

Scheme 7. Reactions of AVK's **39** and **40** Giving [4 + 3] and [3 + 2] Products



Conclusions

In summary, it has been shown that an AVK is a versatile source of cyclic molecules via a cascade reaction sequence beginning with Lewis acid-mediated Narazov cyclization and then interception of the intermediate, the oxyallyl cation **2**, by various acyclic dienes, cyclic dienes, electron-rich alkenes, or styrenes by the formation of an additional ring by a [4 + 3] and/or [3 + 2] cyclization or by the formation of one additional carbon−carbon bond. The bicyclic compounds generated in this way are densely substituted, and would be difficult to access as succinctly in other ways. The products of these interrupted Nazarov reactions generally reflect excellent regio- and stereoselectivity in the trapping reaction. In some instances, equilibrating conditions were shown to enhance the proportion of one product at the expense of another or to provide a different carbon skeleton. Preliminary studies show that this process is not only limited to aromatic derivatives, but is also amenable to unsubstituted or alkyl-substituted allenyl vinyl ketones. These results invite exploitation of AVK's for the synthesis of more complex carbocyclic compounds.

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Supporting Information Available: Experimental details and characterization data for all new compounds, including the X-ray crystal structure of **8** and *J*-HMBC data for compounds **20** and **31**. This material is available free of charge via the Internet at http://pubs.acs.org.

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