# An Unexpected Reversal of Diastereoselectivity in the [4+3]-Cycloaddition Reaction of Nitrogen-Stabilized Oxyallyl Cations with Methyl 2-Furoate

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*Received 27 November 2007*

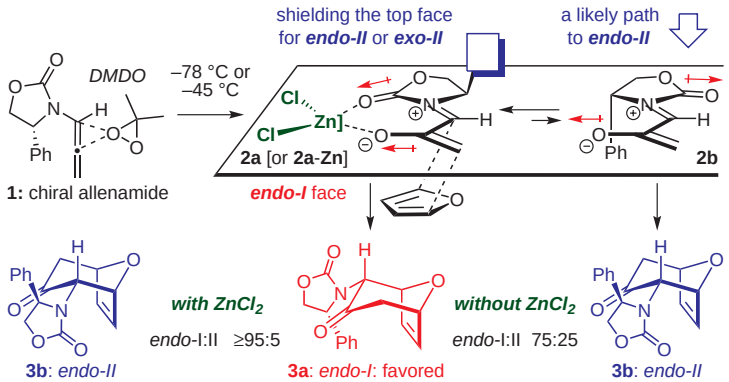
**Abstract:** An unexpected reversal of diastereoselectivity in the [4+3] cycloaddition of methyl 2-fuorate with nitrogen-stabilized oxyallyl cations derived from epoxidation of chiral allenamides is described here. This intriguing reversal in favor of the *endo-II* cycloaddition pathway is likely a result of minimizing the dipole interaction between the oxyallyl cation and ester carbonyl of methyl 2-fuorate.

**Key words:** stereoselective [4+3] cycloadditions, allenamides, nitrogen-stabilized oxyallyl cations, *endo-I* versus *endo-II* selectivity, dipole interaction

In the last twenty years, chemistry of heteroatom-substituted oxyallyl cations has played a significant role in the advancement of [4+3] cycloadditions[1–3] particularly in addressing the challenge of developing diastereoselective[4] and asymmetric[5,6] approaches. Our interest in the chemistry of allenamides[7–10] has led to a unique variant of nitrogen-substituted chiral oxyallyl cations.[11] We demonstrated that nitrogen-stabilized oxyallyl cation **2** derived from DMDO epoxidations[12] of allenamide **1** can undergo highly diastereoselective[13–16] [4+3] cycloadditions (Scheme 1).

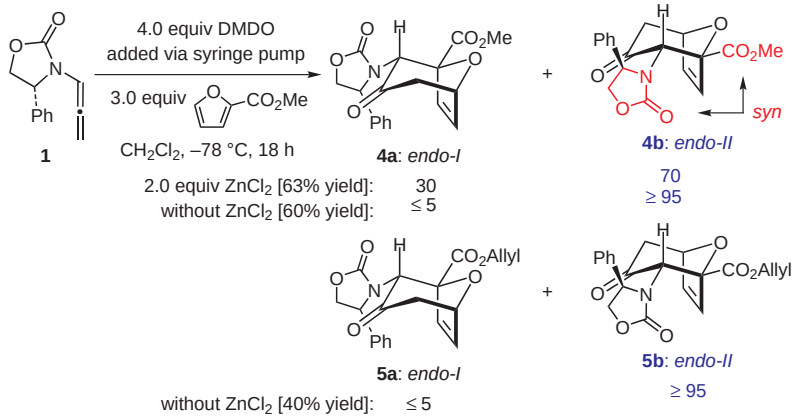
Mechanistically, we have consistently rationalized that the observed stereoselectivity is a result of furan approaching in a favorable *endo* manner[17] from the less-hindered bottom or *endo-I* face of the oxyallyl cation assuming the preferred conformation **2a**. This preference can be further enhanced with a bidentate metal cation such as Zn (**2a-Zn**) that can chelate to both the oxyallyl oxygen atom and the oxazolidinone carbonyl oxygen. On the other hand, while a metal chelation is not possible in conformation **2b**, it possesses a minimized dipole interaction relative to **2a** and is likely the source of minor *endo-II* cycloadducts. This model has been in accord with the observed *endo-I*:*endo-II* ratios in the presence and absence of $ZnCl_2$ (Scheme 1), and served as a foundation for our approach to asymmetric [4+3] cycloadditions employing achiral allenamides.[18] However, when investigating regioselectivity patterns in our [4+3] cycloaddition using methyl 2-furoate, we encountered an unexpected reversal of stereoselectivity favoring the *endo-II* pathway. We report herein this intriguing observation and its implications for our mechanistic model.

As shown in Scheme 2, DMDO epoxidation of allenamide **1** and subsequent cycloaddition with methyl 2-furoate led to the respective cycloadducts **4a** and **4b**[19,20] in good yields. While regiochemically, the methoxy carbonyl group and oxazolidinone ring could be readily assigned as being *syn*[2b,4e,f] {or on the same side of the [3.2.1]oxabicyclooctene} using proton NMR and COSY, the diastereomeric ratio provoked our suspicion because they are opposite from what we have been accustom to (see Scheme 1): A lower dr (70:30) was obtained in the presence of $ZnCl_2$ while a higher dr (≥95:5) was seen without using $ZnCl_2$. A closer inspection initially through NOSEY




**Scheme 1** *Endo-I* versus *endo-II* in the [4+3] cycloaddition

***SYNLETT*** 2008, No. 5, pp 0739–0744
Advanced online publication: 26.02.2008
DOI: 10.1055/s-2008-1042765; Art ID: Y01607ST




**Scheme 2** An *endo-II* selective [4+3] cycloaddition

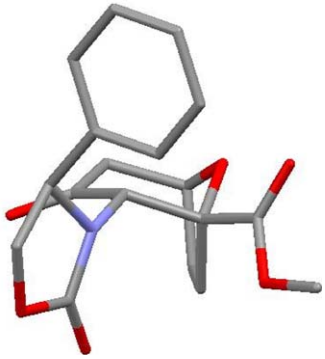


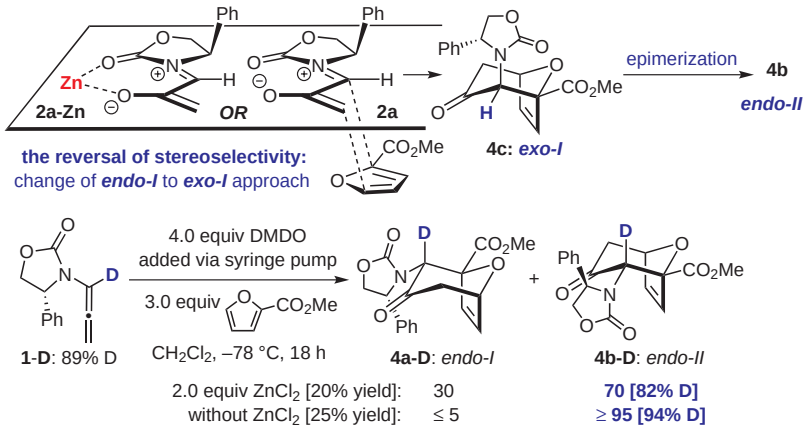
**Figure 1** X-ray crystal structure of *endo-II* cycloadduct **4b**

and ultimately via single-crystal X-ray structure (Figure 1) revealed that the major isomer **4b** is actually the *endo-II* product. When employing allyl 2-furoate without $ZnCl_2$, the same outcome was attained for the respective cycloadducts **5a** and **5b**.

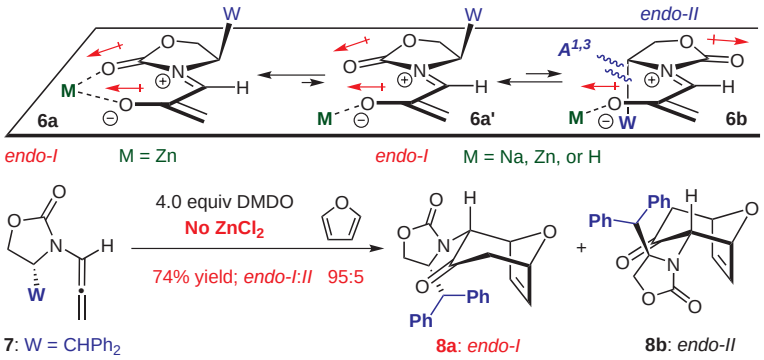
This reversal of stereoselectivity in favor of *endo-II* surprised us because based on our mechanistic model: With or without $ZnCl_2$, *endo-I* should dominate through the preferred conformation **2a** (or **2a**-**Zn**) with the chelating metal serving to further enhance the *endo-I* pathway. However, in this case, although $ZnCl_2$ does sway the selectivity toward *endo-I*, *endo-II* is favored with or without $ZnCl_2$.

To be consistent with conformation **2a** being preferred, we initially proposed that 2-fuorate esters might have switched from an *endo-I* approach to *exo-I* approach and that *endo-II* **4b** was derived from an epimerization from the initial *exo-I* cycloadduct **4c** (Scheme 3). However, this assertion is likely not correct based on our deuterium labeling study. With or without $ZnCl_2$, the cycloaddition using deuterated allenamide **1-D** led to **4a-D** and **4b-D** with the same respective *endo-I*/*endo-II* ratios with essentially no loss of deuterium content. If an epimerization had taken place to afford the *endo-II* cycloadduct, the deprotonation–protonation process should have led to a significant loss of deuterium labeling.

Having effectively ruled out the *exo-I* pathway, we re-evaluated *endo-I* and *endo-II* pathways. As shown in Scheme 4, if the *endo-II* cycloadduct originates from the oxyallyl cation assuming conformation **6b**, its advantage is a minimized dipole interaction, and its distinct disadvantage relative to conformer **6a** [locked in a bidentate manner] or **6a′** (monocoordinated) is the $A^{1,3}$-strain (in blue) for which the severity would be dependent upon the size of the W group. Support for this $A^{1,3}$-strain is seen with the high *endo-I*:*endo-II* ratio obtained from the cycloaddition of allenamide **7** substituted with Sibi's auxil-




**Scheme 3** Ruling out the *exo-I* approach with deuterium labeling



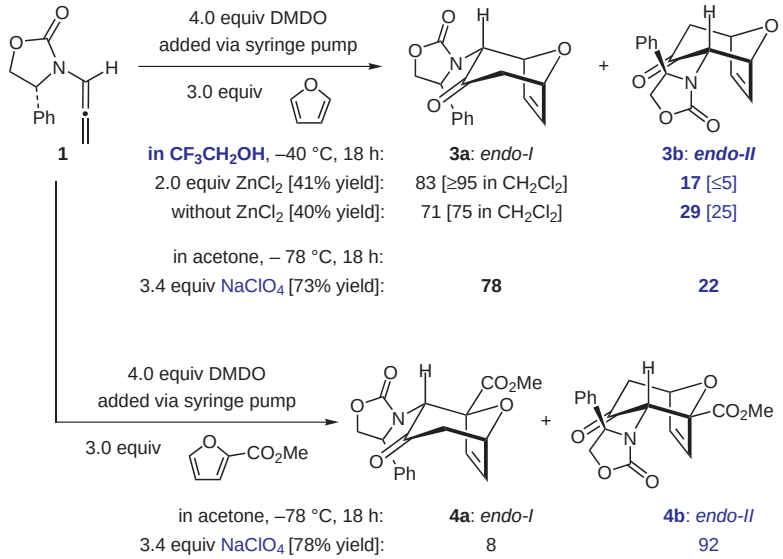

**Scheme 4** Reevaluations of *endo-I* and *endo-II* pathways

iary.[22] Even when $ZnCl_2$ was not employed, the utility of a more bulky diphenyl methyl group resulted in a greater $A^{1,3}$-strain in conformer **6b** and precluded any formation of the *endo-II* cycloadduct **8b**.

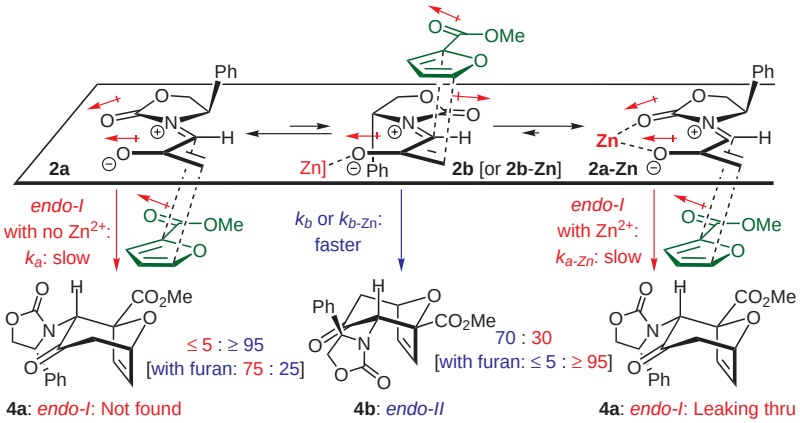
The question became if we had underestimated the presence of conformer **6b** in spite of the $A^{1,3}$-strain. Toward that goal, we probed conditions that could be in its favor. As shown in Scheme 5, we examined the cycloaddition of allenamide **1** with furan in $CF_3CH_2OH$ because Walters[11a] observed a similar stereoselectivity change toward *endo-II* (and even *exo*) cycloadducts when $CF_3CH_2OH$ was the reaction solvent for their [4+3] cycloadditions. However, we found that either in the presence or absence of $ZnCl_2$, the respective ratio shifted only slightly toward *endo-II*. In addition, when using monodentate Lewis acid $NaClO_4$, the ratio again remained essentially the same as not using $ZnCl_2$. It is noteworthy that the polarity of the reaction solvent does not exhibit any real impact on the *endo-I*:*II* ratio, and this was true in our previous study as well.[13] Overall, for furan, the *endo-I* pathway dominates under all conditions. In contrast, the reaction for methyl 2-furoate using $NaClO_4$ led to the *endo-II* cycloadduct **4b** as the distinct major diastereomer. Methyl 2-furoate appears to be unique in its preference to react through the *endo-II* pathway.

Being intrigued with this phenomenon, we propose here a kinetic model shown in Scheme 6 that accounts for the significance of the dipole interaction in the oxyallyl cation conformers. Given the $A^{1,3}$-strain present in conformer **2b**, conformer **2a** would remain as the preferred conformer in the oxyallyl cation equilibrium especially when coordinated in a bidentate fashion as shown in **2a-Zn**. However, conformer **2b** (or **2b-Zn**) is the more reactive conformer when using methyl 2-furoate with $k_b > k_a$ (or $k_{b\text{-}Zn} > k_{a\text{-}Zn}$) because the transition state involving **2b** (or **2b-Zn**) consists of the least number of aligned dipoles (see red arrows) when accounting for the ester carbonyl dipole of methyl 2-furoate.

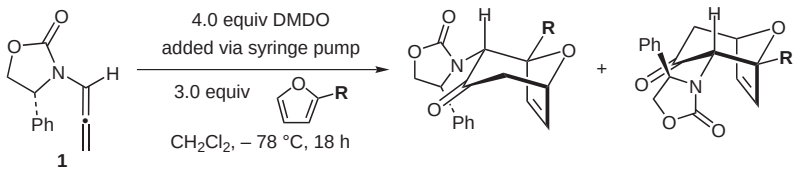
The observed ratios could begin to make intuitive sense on the basis of this proposed model. In the absence of $ZnCl_2$, if the cycloaddition of methyl 2-furoate would proceed through conformer **2b** at a faster rate than **2a** [$k_b > k_a$], one could envision the *endo-II* cycloadduct **4b** prevailing. In addition, the *endo-I*:*endo-II* ratio of 75:25 from the cycloaddition of furan (in brackets) implies the presence of a substantial amount of conformer **2b**, assuming furan reacts at a comparable rate through **2a** and **2b**. Al-




**Scheme 5** Preference for 2-furoate to proceed via the *endo-II* pathway




**Scheme 6** A dipole-minimized *endo-II* cycloaddition pathway




| | | |
|---|---|---|
| For R = CN: | **9a**: *endo-I* | **9b**: *endo-II* |
| 2.0 equiv $ZnCl_2$ [47% yield]: | 17 | 83 |
| For R = Me: | **10a**: ***endo-I*** | **10b**: *endo-II* |
| 2.0 equiv $ZnCl_2$ [47% yield]: | ≥ 95 | ≤ 5 |
| without $ZnCl_2$ [54% yield]: | 75 | 25 |

**Scheme 7** Support for the dipole-minimized *endo-II* pathway

though the equilibrium ratio of **2a**:**2b** may not be critical in a kinetic model, with the presence of conformer **2b** possibly being substantial, one could then predict a complete domination of the *endo-II* pathway when using methyl 2-furoate based on the premise of $k_b$ being greater than $k_a$. This is what we observed.

On the other hand, in the presence of $ZnCl_2$, for the cycloaddition of methyl 2-furoate to proceed through conformer **2b-Zn** in a kinetically favored manner, it will have to siphon slowly away from the predominant conformer **2a-Zn** in the equilibrium. This would serve to disfavor the *endo-II* pathway and allow the cycloaddition to proceed via (or leaking through) **2a-Zn**, leading to a ratio with decreased preference for the *endo-II* cycloadduct **4b** than the reaction without $ZnCl_2$. It is noteworthy that with the equilibrium being heavily in favor of conformer **2a-Zn**, the final *endo-I*:*endo-II* ratio of 30:70 suggests that the assessment of $k_{b\text{-}Zn}$ being greater than $k_{a\text{-}Zn}$ for the cycloaddition of methyl 2-furoate is appropriate.

To support this model, we pursued the following experiments. First, when we ran the reaction of methyl 2-furoate in the presence of 7.0 equivalents of $ZnCl_2$, the reaction did not provide any cycloadducts but led to decompositions. This implies that methyl 2-furoate reacts extremely slowly through conformer **2a-Zn**, and its reaction could be essentially shut down when the equilibrium is shifted almost exclusively toward **2a-Zn** with excess $ZnCl_2$.

Secondly, we carried out the reaction of 2-cyanofuran with chiral allenamide **1** in the presence of $ZnCl_2$ (Scheme 7).[23] The observed *endo-I*:*endo-II* ratio suggests that given the strong CN dipole, the cycloaddition again prefers the transition state that presents the least amount of dipole interaction, leading to the *endo-II* product **9b** as the major diastereomer. Moreover, since there is only one conformation for the CN group relative to the furan ring, the dipole model proposed in Scheme 6 for methyl 2-furoate is applicable for a range of conformations that the ester carbonyl group can assume during the cycloaddition and not specific to the one shown.

Lastly, because we were unsuccessful in attempting the reaction of 2-methoxyfuran due to competing epoxidation and/or decompostions under the Lewis acidic conditions,[20] we examined reactions of 2-methylfuran. The stereochemical outcome in cycloadducts **10a**,**b** returned to normal in favor of the *endo-I* isomer both in the presence and absence of $ZnCl_2$. These results firmly rule out any steric factors that could play a role in the stereoselectivity reversal, and suggest that alleviating the aligned dipole interaction in the transition state for the reaction of methyl 2-furoate took place at the expense of *endo-I* cycloaddition pathway.

We have described here an unexpected reversal of stereoselectivity in the [4+3] cycloadditions of methyl 2-fuorate with nitrogen-stabilized oxyallyl cations derived from epoxidation of chiral allenamides. Although further studies

are needed to fully support our model, this intriguing reversal in favor of the *endo-II* cycloaddition pathway appears to be related to minimizing the dipole interaction between the oxyallyl cation and the ester carbonyl in the transition state of cycloaddition.

## Acknowledgment

Authors thank NIH-NIGMS [GM066055] and UW-Madison for financial support.

## References and Notes

(1) For excellent reviews on heteroatom-substituted oxyallyl cations, see: (a) Harmata, M. *Adv. Synth. Catal.* **2006**, *348*, 2297. (b) Harmata, M. *Recent Res. Dev. Org. Chem.* **1997**, *1*, 523.

(2) For general reviews, see: (a) Hartung, I. V.; Hoffmann, H. M. R. *Angew. Chem. Int. Ed.* **2004**, *43*, 1934. (b) Harmata, M.; Rashatasakhon, P. *Tetrahedron* **2003**, *59*, 2371. (c) Harmata, M. *Acc. Chem. Res.* **2001**, *34*, 595. Also see: (d) Davies, H. M. L. In *Advances in Cycloaddition*, Vol. 5; Harmata, M., Ed.; JAI: Greenwich, **1998**, 119. (e) West, F. G. In *Advances in Cycloaddition*, Vol. 4; Lautens, M., Ed.; JAI: Greenwich, **1997**, 1. (f) Rigby, J. H.; Pigge, F. C. *Org. React.* **1997**, *51*, 351. (g) Harmata, M. *Tetrahedron* **1997**, *53*, 6235.

(3) For some examples of other heteroatom-substituted oxyallyl cations, see: (a) Harmata, M.; Wacharasindhu, S. *Org. Lett.* **2005**, *7*, 2563. (b) Sáez, J. A.; Arnó, M.; Domingo, L. R. *Tetrahedron* **2005**, *61*, 7538. (c) Harmata, M.; Kahraman, M.; Adenu, G.; Barnes, C. L. *Heterocycles* **2004**, *62*, 583. (d) Sáez, J. A.; Arnó, M.; Domingo, L. R. *Org. Lett.* **2003**, *5*, 4117. (e) Funk, R. L.; Aungst, R. A. *Org. Lett.* **2001**, *3*, 3553. (f) Harmata, M.; Sharma, U. *Org. Lett.* **2000**, *2*, 2703. (g) Lee, K.; Cha, J. K. *Org. Lett.* **1999**, *1*, 523. (h) Masuya, K.; Domon, K.; Tanino, K.; Kuwajima, I. *J. Am. Chem. Soc.* **1998**, *120*, 1724. (i) Harmata, M.; Elomari, S.; Barnes, C. J. *J. Am. Chem. Soc.* **1996**, *118*, 2860; and references cited within.

(4) For recent stereoselective attempts, see: (a) Davies, H. M. L.; Dai, X. *J. Am. Chem. Soc.* **2004**, *126*, 2693. (b) Prié, G.; Prévost, N.; Twin, H.; Fernandes, S. A.; Hayes, J. F.; Shipman, M. *Angew. Chem. Int. Ed.* **2004**, *43*, 6517. (c) Grainger, R. S.; Owoare, R. B.; Tisselli, P.; Steed, J. W. *J. Org. Chem.* **2003**, *68*, 7899. (d) Montanã A. M., Grima P. M.; *Tetrahedron;* **2002**, *58*: 4769. (e) Beck, H.; Stark, C. B. W.; Hoffman, H. M. R. *Org. Lett.* **2000**, *2*, 883; and reference 11 cited within. (f) Harmata, M.; Rashatasakhon, P. *Synlett* **2000**, 1419. (g) Cho, S. Y.; Lee, J. C.; Cha, J. K. *J. Org. Chem.* **1999**, *64*, 3394. (h) Harmata, M.; Jones, D. E.; Kahraman, M.; Sharma, U.; Barnes, C. L. *Tetrahedron Lett.* **1999**, *40*, 1831. (i) Kende, A. S.; Huang, H. *Tetrahedron Lett.* **1997**, *38*, 3353. (j) Harmata, M.; Jones, D. E. *J. Org. Chem.* **1997**, *62*, 4885.

(5) Harmata, M.; Ghosh, S. K.; Hong, X.; Wacharasindu, S.; Kirchhoefer, P. *J. Am. Chem. Soc.* **2003**, *125*, 2058.

(6) For a recent account that constitutes an enantioselective formal [4+3] cycloaddition, see: Dai, X.; Davies, H. M. L. *Adv. Synth. Catal.* **2006**, *348*, 2449.

(7) For a compendium on the chemistry of allenes, see: Krause, N.; Hashmi, A. S. K. *Modern Allene Chemistry*, Vol. 1 and 2; Wiley-VCH: Weinheim, **2004**.

(8) For reviews on the chemistry and synthesis of allenamides, see: (a) Hsung, R. P.; Wei, L.-L.; Xiong, H. *Acc. Chem. Res.* **2003**, *36*, 773. (b) Tracey, M. R.; Hsung, R. P.; Antoline, J.; Kurtz, K. C. M.; Shen, L.; Slafer, B. W.; Zhang, Y. In *Science of Synthesis, Houben–Weyl Methods of Molecular Transformations*; Weinreb, S. M., Ed.; Thieme: Stuttgart, **2005**, Chap. 21.4.

(9) For recent reports on the allenamide chemistry, see: (a) Watanabe, T.; Oishi, S.; Fuji, N.; Ohno, H. *Org. Lett.* **2007**, 9 in press. (b) Hyland, C. J. T.; Hegedus, L. S. *J. Org. Chem.* **2006**, *71*, 8658. (c) Parthasarathy, K.; Jeganmohan, M.; Cheng, C.-H. *Org. Lett.* **2006**, *8*, 621. (d) Fenández, I.; Monterde, M. I.; Plumet, J. *Tetrahedron Lett.* **2005**, *46*, 6029. (e) de los Rios, C.; Hegedus, L. S. *J. Org. Chem.* **2005**, *70*, 6541. (f) Alouane, N.; Bernaud, F.; Marrot, J.; Vrancken, E.; Mangeney, P. *Org. Lett.* **2005**, *7*, 5797. (g) Hyland, C. J. T.; Hegedus, L. S. *J. Org. Chem.* **2005**, *70*, 8628.

(10) For our recent efforts, see: (a) Song, Z.; Hsung, R. P.; Lu, T.; Lohse, A. G. *J. Org. Chem.* **2007**, *72*, in press. (b) Song, Z.; Hsung, R. P. *Org. Lett.* **2007**, *9*, 2199. (c) Huang, J.; Ianni, J. C.; Antoline, J. E.; Hsung, R. P.; Kozlowski, M. C. *Org. Lett.* **2006**, *8*, 1565. (d) Berry, C. R.; Hsung, R. P.; Antoline, J. E.; Petersen, M. E.; Rameshkumar, C.; Nielson, J. A. *J. Org. Chem.* **2005**, *70*, 4038. (e) Shen, L.; Hsung, R. P.; Zhang, Y.; Antoline, J. E.; Zhang, X. *Org. Lett.* **2005**, *7*, 3081.

(11) For leading examples of nitrogen-stabilized oxyallyl cations in [4+3] cycloadditions, see: (a) MaGee, D. I.; Godineau, E.; Thornton, P. D.; Walters, M. A.; Sponholtz, D. J. *Eur. J. Org. Chem.* **2006**, 3667. (b) Myers, A. G.; Barbay, J. K. *Org. Lett.* **2001**, *3*, 425. (c) Sung, M. J.; Lee, H. I.; Chong, Y.; Cha, J. K. *Org. Lett.* **1999**, *1*, 2017. (d) Walters, M. A.; Arcand, H. R. *J. Org. Chem.* **1996**, *61*, 1478. (e) Walters, M. A.; Arcand, H. R.; Lawrie, D. J. *Tetrahedron Lett.* **1995**, *36*, 23. (f) Dennis, N.; Ibrahim, B.; Katritzky, A. R. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2307.

(12) Rameshkumar, C.; Xiong, H.; Tracey, M. R.; Berry, C. R.; Yao, L. J.; Hsung, R. P. *J. Org. Chem.* **2002**, *67*, 1339.

(13) For our asymmetric [4+3] cycloaddition, see: Xiong, H.; Hsung, R. P.; Berry, C. R.; Rameshkumar, C. *J. Am. Chem. Soc.* **2001**, *123*, 7174.

(14) Antoline, J. E.; Hsung, R. P.; Huang, J.; Song, Z.; Li, G. *Org. Lett.* **2007**, *9*, 1275.

(15) Xiong, H.; Huang, J.; Ghosh, S. K.; Hsung, R. P. *J. Am. Chem. Soc.* **2003**, *125*, 12694.

(16) (a) Rameshkumar, C.; Hsung, R. P. *Angew. Chem. Int. Ed.* **2004**, *43*, 615. For a very recent account on intramolecular [4+3] cycloadditions of allenyl dienes employing $PtCl_2$ as a catalyst, see: (b) Trillo, B.; López, F.; Gulías, M.; Castedo, L.; Mascareñas, J. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 951.

(17) For a review, see: (a) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 819; *Angew. Chem.* **1973**, *85*, 877. (b) Also see: Hoffmann, H. M. R.; Joy, D. R. *J. Chem. Soc. B* **1968**, 1182.

(18) Huang, J.; Hsung, R. P. *J. Am. Chem. Soc.* **2005**, *127*, 50.

(19) **General Procedure for the [4+3] Cycloaddition**
To a solution of the allenamide in $CH_2Cl_2$ [0.10 M] was added the appropriate furan (3.0–6.0 equiv) and 4 Å pulverized MS (0.50 g). The reaction solution was cooled to –78 °C, and $ZnCl_2$ (2.0 equiv, 1.0 M in $Et_2O$) was added. Then, DMDO in acetone (4.0–6.0 equiv) was added as a chilled solution (at –78 °C) via syringe pump over 3–4 h. The syringe pump was cooled by dry ice the entire addition time. After the addition the reaction mixture was stirred for another 14 h. The reaction was then quenched with sat. aq $NaHCO_3$, filtered through Celite®, concentrated in vacuo,

partitioned with $CH_2Cl_2$, extracted [4 × 20 mL], dried over $Na_2SO_4$, and concentrated in vacuo. The crude residue was purified via silica gel column chromatography (gradient eluent: 10–75% EtOAc in hexane).

(20) In our intermolecular nitrogen stabilized oxyallyl cation [4+3] cycloadditions, for electron-rich furans, while some of the low-yielding reactions are due to decomposition of the epoxidized starting allenamide, most are due to noticeable competing epoxidation of the respective electron-rich furan. This issue can be circumvented using 6–10 equiv of furan, leading to higher yields (see references 13 and 18). For electron-deficient furans, the competing furan-epoxidation is not a problem, and thus, we can employ a much lower loading. However, we have found that reactions with electron-deficient furans such as those shown in this study are overall slower and more sluggish. This is consistent with the fact that oxyallyl cation based [4+3] cycloadditions proceed in an electrophilic manner.

(21) **Analytical Data**

Compound **4b**: $R_f$ = 0.10 (50% EtOAc in hexane); $[\alpha]_D^{23}$ –86.2 (*c* 0.10, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$): δ = 2.53 (d, 1 H, *J* = 16.2 Hz), 2.83 (dd, 1 H, *J* = 5.4, 16.0 Hz), 3.67 (s, 3 H), 3.96 (s, 1 H), 4.18 (t, 1 H, *J* = 8.1 Hz), 4.66 (t, 1 H, *J* = 8.0 Hz), 4.82 (t, 1 H, *J* = 9.2 Hz), 5.06 (dd, 1 H, *J* = 5.2, 1.6 Hz), 6.28 (dd, 1 H, *J* = 6.0, 2.0 Hz), 7.15 (d, 1 H, *J* = 6.4 Hz), 7.28–7.46 (m, 5 H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 14.5, 21.3, 45.4, 53.1, 64.4, 68.6, 70.6, 79.1, 89.3, 128.4, 129.5, 129.4, 140.2, 167.4, 171.4, 199.4 cm$^{-1}$. IR (thin film): 3280 (w), 2911 (w), 1766 (s) cm$^{-1}$. MS (APCI): *m/e* (%) = 344.1 (90) $[M + H]^+$.

Compound **4b-D**: $R_f$ = 0.10 (50% EtOAc in hexane); $[\alpha]_D^{23}$ –132.6 (*c* 0.30, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$): δ = 2.52 (d, 1 H, *J* = 16.8 Hz), 2.84 (dd, 1 H, *J* = 5.2, 16.4 Hz), 3.65 (s, 3 H), 3.96 (s, 0.35 H), 4.20 (dd, 1 H, *J* = 8.8, 6.8 Hz), 4.74 (t, 1 H, *J* = 8.4 Hz), 4.96 (t, 1 H, *J* = 7.6 Hz), 5.05 (m, 1 H) 6.28 (dd, 1 H, *J* = 1.6, 5.6 Hz), 7.11 (d, 1 H, *J* = 6.0 Hz), 7.23–7.44 (m, 5 H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 29.5, 45.4, 53.0, 64.3, 70.5, 79.1, 89.2, 128.4, 129.5, 129.9, 132.6, 133.6, 136.4, 158.3, 167.3, 199.4. IR (thin film): 3300 (w), 2910 (w), 1748 (s) cm$^{-1}$. MS (APCI): *m/e* (%) = 345.1 (60) $[M + H]^+$.

Compound **5b**: $R_f$ = 0.23 (50% EtOAc in hexane); $[\alpha]_D^{23}$ –72.8 (*c* 6.4, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$): δ = 2.51 (d, 1 H, *J* = 16.0 Hz), 2.84 (dd, 1 H, *J* = 16.4, 6.0 Hz), 4.00 (s, 1 H), 4.17 (t, 1 H, *J* = 8.8 Hz), 4.39 (ddt, 1 H, *J* = 13.2, 5.6, 1.3 Hz), 4.66 (t, 1 H *J* = 8.4 Hz), 4.69 (m, 1 H), 4.83 (t, 1 H, *J* = 8.4 Hz), 5.07 (dd, 1 H, *J* = 5.6, 1.9 Hz), 5.27 (ddd, 1 H, *J* = 10.4, 2.5, 1.3 Hz) 5.34 (ddd, 1 H, *J* = 17.2, 3.0, 1.4 Hz) 5.84 (ddt, 1 H, *J* = 6.0, 11.6, 16.4), 6.28 (dd, 1 H, *J* = 6.0, 2.0 Hz), 6.72 (d, 1 H, 6.0 Hz), 7.28–7.41 (m, 5 H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 45.4, 64.4, 66.7, 68.6, 70.6, 79.1, 89.3, 119.6, 128.5, 129.5, 129.9, 131.3, 132.8, 133.7, 136.5, 158.2, 166.8, 199.5. IR (thin film): 3629 (w), 3445 (w), 3065 (w), 1764 (s), 1726 (s) cm$^{-1}$. MS (APCI): *m/e* (%) = 370.1 (100) $[M + H]^+$.

Compound **9b**: $R_f$ = 0.13 (50% EtOAc in hexane); $[\alpha]_D^{23}$ –78.5 (*c* 2.0, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$): δ = 2.52 (d, 1 H, *J* = 16.5 Hz), 2.79 (dd, 1 H, *J* = 17.0, 5.5 Hz), 3.84 (s, 1 H), 4.26 (dd, 1 H, *J* = 9.0, 7.0 Hz), 4.77 (t, 1 H, *J* = 8.5 Hz), 5.08 (d, 1 H, *J* = 4.0 Hz), 5.16 (t, 1 H, *J* = 8.0 Hz) 6.34 (br d, 1 H, *J* = 4.5 Hz), 6.37 (dd, 0.5 H, *J* = 6.0, 2.0 Hz), 6.61 (d, 0.5 H, *J* = 6.0 Hz), 7.41–7.48 (m, 5 H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 29.6, 44.8, 45.3, 65.1, 71.4, 79.3, 79.7, 128.2, 128.8, 129.9, 130.2, 130.6, 132.8, 135.7, 197.2. IR (thin film): 3509 (w), 3110 (w), 2897 (w), 1755 (s), 1729 (s) cm$^{-1}$. MS (APCI): *m/e* (%) = 311.1 (10) $[M + H]^+$.

Compounds **10a**,**b**: $R_f$ = 0.31 (50% EtOAc in hexane). $^1$H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 3 H), 1.43 (s, 3 H), 2.43 (d, 1 H, *J* = 16.5 Hz), 2.49 (d, 1 H, *J* = 15.5 Hz), 2.65 (d, 1 H, *J* = 15.5 Hz), 2.75–2.82 (br, 1 H), 4.08 (dd, 1 H, *J* = 8.0, 4.4 Hz), 4.19 (dd, 1 H, *J* = 8.4, 8.4 Hz), 4.74 (t, 2 H, *J* = 8.8 Hz), 4.82 (dd, 1 H, *J* = 9.2, 4.4 Hz), 4.87 (dd, 2 H, *J* = 8.4, 4.8 Hz), 4.92 (d, 2 H, *J* = 4.4 Hz), 4.99 (dd, 1 H, *J* = 5.6, 0.8 Hz), 5.92 (d, 1 H, *J* = 6.0 Hz), 6.06 (br, 1.8 H), 6.13 (dd, 0.50 H, *J* = 6.4, 2.0 Hz), 6.45 (d, 0.20 H, *J* = 5.6 Hz), 6.48 (dd, 0.50 H, *J* = 4.4, 1.0 Hz), 7.27–7.44 (m, 10 H). IR (thin film): 3425 (w), 2927 (m), 1751 (s), 1719 (s) cm$^{-1}$. MS (APCI): *m/e* (%) = 300.1 (100) $[M + H]^+$.

(22) Sibi, M. P.; Porter, N. A. *Acc. Chem. Res.* **1999**, *32*, 163.

(23) When the reaction was carried out in the absence of $ZnCl_2$, it was very sluggish and inconclusive.