# Indium-Mediated Organometallic Reactions in Aqueous Media. Stereoselectivity in the Crotylation of Sulfonimines Bearing a Proximal Chelating Group

Wenshuo Lu and Tak Hang Chan*

*Department of Chemistry, McGill University, Montreal, Quebec, H3A 2K6 Canada*

*thchan@chemistry.mcgill.ca*

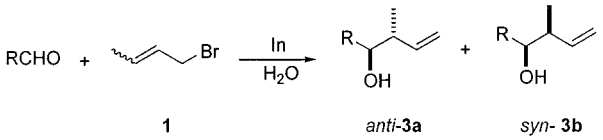
*Received December 30, 2000*

Reaction of sulfonimines having proximal chelating groups with crotyl bromide and indium in aqueous media gave α-crotylation products stereoselectively with *syn*-selectivity.

## Introduction

The recent discovery that the indium-mediated allylation of carbonyl compounds can be carried out in aqueous media[1] has led to considerable interest in the application of the reaction in organic synthesis.[2] In addition to being an environmentally benign solvent, water offers the advantage of compatibility with hydroxy and carboxylic functional groups without the requirement of protection protocols. This has rendered the reaction particularly useful in the synthesis of carbohydrates.[3] The reaction showed good regioselectivity and reasonable diastereoselectivity when an unsymmetrical allylic bromide was used. For example, when crotyl bromide (**1**) was coupled to an aldehyde by indium in aqueous media, the products were two α-regioisomers **3a** and **3b**. The diastereoselectivity was however low, with small to moderate preference for the *anti*-diastereomer **3a** over the *syn*-isomer **3b** (Scheme 1). The regio- and diastereoselectivity were explained[4] by the preferred Zimmerman type transition state **4** involving coordination between the presumed crotylindium[5] and the carbonyl compound. On the other hand, for carbonyl compounds bearing an α- or *β*-substituent such as a hydroxy or an amino group, good stereoselectivity was observed in the coupling with allyl bromide. This is illustrated by the example of the α-hydroxyaldehyde **5** in Scheme 2. The product **6a** was favored over **6b** by a ratio of nearly 10:1. This is explained by the preferred transition state **7** where there is chelation between the α-hydroxy group and the allylindium

**Scheme 1**




**1** *anti*-**3a** *syn*- **3b**

species.[6] Such stereoselectivity enhances considerably the synthetic usefulness of the indium-mediated reaction.[7]

In contrast to the richness of carbonyl chemistry, the corresponding indium-mediated allylation of imines in aqueous media has been rather limited.[8] This is ascribed to the lower electrophilicity of the C=N function and its ease of hydrolysis in aqueous media. The hydrolysis is especially facial under indium-mediated aqueous reaction conditions where acidic indium halide is generated. Recently, we reported that sulfonimines were successfully allylated with allyl bromides and indium in aqueous media to give the corresponding homoallylic sulfonamides in good yields.[9] Our preliminary results showed that in the crotylation of the benzaldehyde sulfonimine **8**, the reaction was regioselective in giving the α-products. The stereochemical outcome was found to be dependent on the solvents used. The ratio of the two diastereomers **9a** and **9b** varied from *anti*-selective in water (**9a/9b** = 39:61) to *syn*-selective in water−THF (1:1) mixture (**9a/9b** = 79:21). These results suggest that the stereochemistry in the crotylation of sulfonimines may be quite sensitive to various factors. We therefore examined the crotylation of a number of sulfonimines which possess proximal groups capable of chelation in order to probe the influence of the chelating group on the stereoselectivity. To simplify

* To whom correspondence should be addressed. Fax: (514) 398-3797.

(1) Li, C. J.; Chan, T. H. *Tetrahedron Lett.* **1991**, *32*, 7020.

(2) For the most recent review see: Li, C. J.; Chan, T. H. *Tetrahedron* **1999**, *55*, 11149. For some recent examples of indium-mediated reactions in aqueous media, see (a) Paquette, L. A.; Rothhaar, R. R.; Issac, M.; Rogers, L. M.; Rogers, R. D. *J. Org. Chem.* **1998**, *63*, 5463. (b) Melekhov, A.; Fallis, A. G. *Tetrahedron Lett.* **1999**, *40*, 7867. (c) Engstrom, G.; Morelli, M.; Palomo, C.; Mitzel, T. *Tetrahedron Lett.* **1999**, *40*, 5967. (d) Loh, T.-P.; Zhou, J. R. *Tetrahedron Lett.* **1999**, *40*, 9115.

(3) For some examples, see (a) Chan, T. H.; Lee, M. C. *J. Org. Chem.* **1995**, *60*, 4228. (b) Gordon, D. M.; Whitesides, G. M. *J. Org. Chem.* **1993**, *58*, 7939. (c) Chan, T. H.; Xin, Y.-C.; von Itzstein, M. *J. Org. Chem.* **1997**, *62*, 3500. (d) Choi, S. K.; Lee, S.; Whiteside, G. M. *J. Org. Chem.* **1996**, *61*, 8739. (e) Woo, S.; Sqires, N.; Fallis, A. G. *Org. Lett.* **1999**, *1*, 573.

(4) Issac, M. B.; Chan, T. H. *Tetrahedron Lett.* **1995**, *36*, 8957.

(5) (a) Yang, Y.; Chan, T. H. *J. Am. Chem. Soc.* **2000**, *122*, 402. (b) Chan, T. H.; Yang, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3228.

(6) (a) Paquette, L. A.; Mitzel, T. M. *J. Am Chem. Soc.* **1996**, *118*, 1931. (b) Paquette, L. A.; Bennett, G. D.; Chhatriwalla, A.; Isaac, M. B. *J. Org. Chem.* **1997**, *62*, 3370. (c) Bernardelli, P.; Paquette, L. A. *J. Org. Chem.* **1997**, *62*, 8284. (d) Paquette, L. A.; Lobben, P. C. *J. Org. Chem.* **1998**, *63*, 5604. (e) Paquette, L. A.; Bennett, G. D.; Isaac, M. B.; Chhatriwalla, A. *J. Org. Chem.* **1998**, *63*, 1836. (f) Maguire, B.; Mulzer, J.; Bats, J. W. *J. Org. Chem.* **1996**, *61*, 6936. (g) Paquette, L. A.; Rothhaar, R. R. *J. Org. Chem.* **1999**, *64*, 217 and references therein.

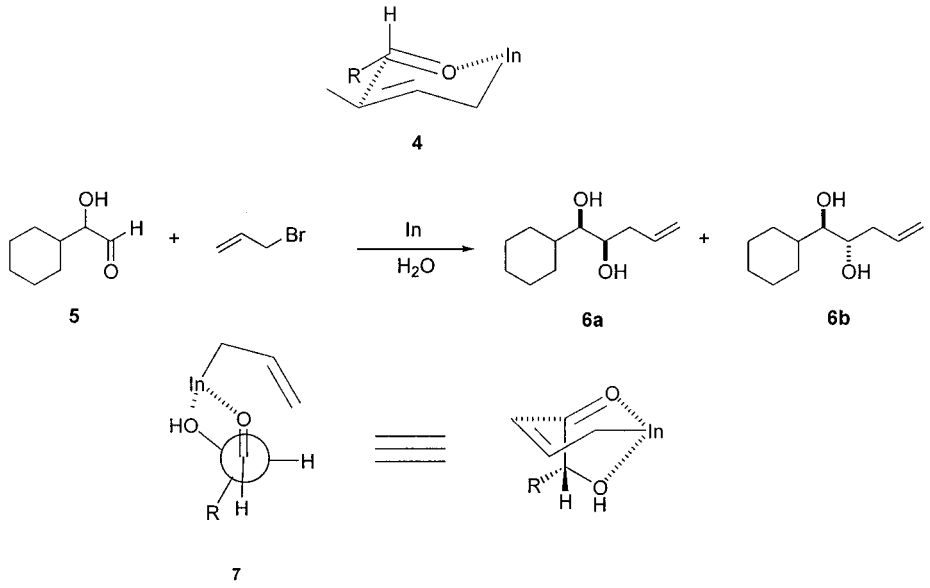
(7) (a) Marshall, J. A. *Chemtracts−Org. Chem.* **1997**, 481. (b) Paquette, L. A. In *Green Chemical Syntheses and Processes*; Anastas, P. T., Heine, L. G., Williamson, T. C., Eds.; Oxford: New York, 2000.

(8) For the allylation of imines with indium in organic solvents, see (a) Beuchet, P.; Marrec, M. L.; Mosset, P. *Tetrahedron Lett.* **1992**, *33*, 5959. (b) Basile, T.; Bocoum, A.; Savoie, D.; Umani-Ronchi, *J. Org. Chem.* **1994**, *59*, 7766.

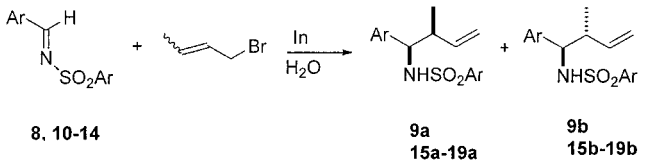
(9) (a) Chan, T. H.; Lu, W. *Tetrahedron Lett.* **1998**, *39*, 8605. (b) Lu, W.; Chan, T. H. *J. Org. Chem.* **2000**, *65*, 8589.

10.1021/jo0018038 CCC: $20.00 © 2001 American Chemical Society
Published on Web 04/20/2001

**Scheme 2**




**Scheme 3**




the stereochemical determination, we concentrate at this time on substrates that will give only two contiguous stereocenters in the final products.

## Results and Discussions

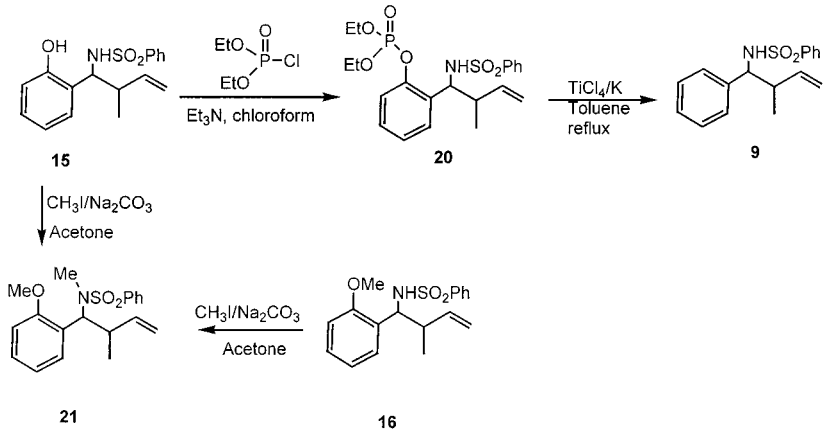
**(1) Substituted Benzaldehyde Sulfonimines.** A number of 2-, 3-, and 4-OH and OMe substituted benzaldehyde sulfonimines (**10**−**14**) were prepared from the precursor aldehydes.[10] They were then reacted with crotyl bromide and indium in water and in water/THF (1:1) to give the substituted sulfonamides **15**−**19** (Scheme 3). In all cases, two diastereomers were formed. Their stereochemistries were correlated to the unsubstituted **9a/9b** in the following manner. Compound **15** (as a mixture of two diastereomers) was converted to the phosphate **20**. The phosphate group in **20** was then reduced to give the known compound **9**. From the $^1$H NMR of **9**, the ratio of the two diastereomers can be determined. This was then related to the ratio of the two diasteromers in the original mixture in **15**. There was no loss of stereochemical integrity in the transformations in Scheme 4 since different ratios in the starting **15** correlated to the resulting ratios in **9**. The stereochemistry of compound **16** was related to compound **15** through the dimethyl derivative **21** according to Scheme 4. For compounds **17**−**19**, the ratios of the diastereomers were determined using $^1$H NMR, with the assumption that the coupling constants for the benzylic protons of the *syn*-isomers are larger than that of the *anti*-isomers in accordance with the pattern observed for **9**.

It can be seen from Table 1 that similar yields were obtained in the reactions regardless of the substituents on the benzene ring. Interestingly, the *p*-OH substituent showed no effect on the stereoselectivity of the reaction. In water alone, both **8** and **14** gave the *anti*-isomers preferentially to nearly the same extent, and the stereoselectivity is reversed to give the *syn*-isomers mainly in water/THF (1:1), also to nearly the same extent. This suggests that electronic effect of the substituent does not play a significant role in the stereoselectivity of the reaction. On the other hand, the *o*-OH-substituted compound **10** gave preferentially the *syn*-isomer irrespective of the solvent systems used (Table 1, entry 2). Since electronic effect is not involved, the difference in stereoselectivity between compounds **8** and **10** in water may be ascribed to either the steric or the chelation effect of the *o*-OH on the reaction. By comparing the *o*-OH compound **10** with the *o*-OMe compound **11** (Table 1, entry 3), it seems that the change in stereoselectivity cannot be due to steric effect since compound **11** gave nearly the same stereochemical results as compound **8**. The change is consistent with the chelation effect of the *o*-OH group which exists in pure water as well as in water/THF (1:1) and is diminished on becoming OMe. Compounds **12** with OH at the *meta* position of the benzene ring showed a small change toward *syn*-selectivity relative to the parent compound **8** but less so than compound **10**. The observation is consistent with the expectation that chelation of the *m*-OH with the crotylindium intermediate would be weak due to the strain imposed by the *trans*-cycloheptene-like requirement. With compound **13**, where the *m*-OH was replaced by *m*-OMe, the stereoselectivity was the same as either compound **8** or **14**.

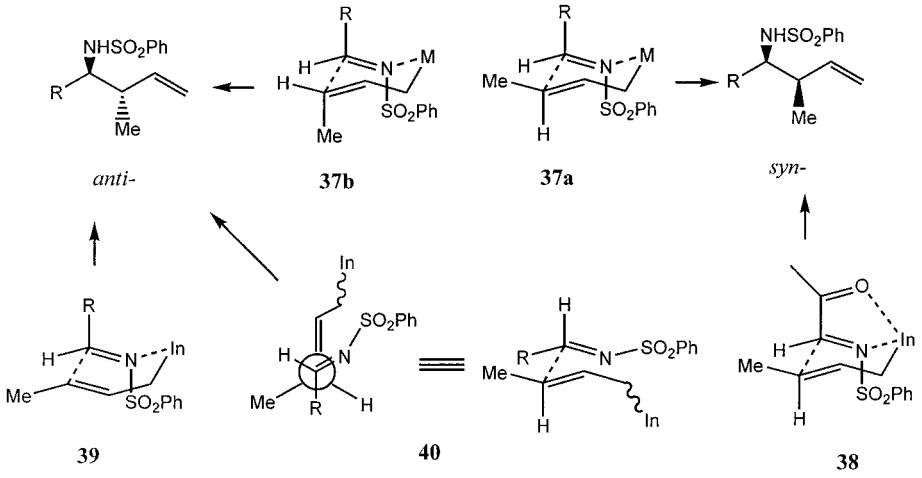
**(2) Heteroarylaldehyde Sulfonimines.** Encouraged by what appeared to be a chelation effect in the aqueous crotylation of *o*-hydroxybenzaldehyde sulfonimine **10**, we extended the study to a series of heteroarylaldedyde sulfonimines. The results are summarized in Table 2. In the case of compound **24** (Table 2, entry 3), the major isomer of the product **32** was obtained as colorless

(10) (a) Davis, F. A.; Lamendola, J.; Nadir, U.; Kluger, E. W.; Sedergran, T. C.; Panunto, T. W.; Billmers, R.; Jenkins, R., Jr.; Turchi, I. J.; Watson, W. H.; Chen, J. S.; Kimura, M. J. *J. Org. Chem.* **1980**, *45*, 2000. (b) Boger, D. L.; Corbett, W. L.; Curran, T. T.; Kasper, A. M. *J. Am. Chem. Soc.* **1991**, *113*, 1713. (c) Trost, B. M.; Marrs, C. *J. Org. Chem.* **1991**, *56*, 6468.

**Scheme 4**




**Scheme 5**




crystals, and its stereochemistry was determined by X-ray crystallography to be the *syn*-isomer.[11] Using this compound as the reference, $^1$H NMR was used to determine the relative ratios of *syn*- and *anti*-isomers for the other compounds in Table 2 (entries 1−5). In all cases, *syn*- selectivity was observed, and the selectivity was enhanced as the solvent changed from water alone to a THF:water (1:1) mixed solvent. A selectivity of *syn:anti* = 93:7 could be obtained for the furan compound **22** as well as the pyrrole compound **25**. A higher proportion of THF beyond the 1:1 ratio in the solvent did not seem to improve the selectivity further. In the thiophene case (compound **26**), the stereoselectivity was slightly less, though still *syn*-selective. Finally, in the case of the pyridine compound **27** (entry *6*), crotylation was not successful, because the sulfonimine was hydrolyzed to the aldehyde prior to crotylation.

**(3) Crotylation of α-Sulfonimino Esters.** Allylic α-amino acids are quite useful building blocks in organic synthesis because the *γ*,*δ*-double bond can easily be transformed into other functionalities.[12] Reactions of various allylic metals with α-imino esters in organic solvents have been used extensively to prepare these allylic α-amino acids.[13] Relatively few reactions were carried out in aqueous media and none with indium.[14] We therefore examined the crotylation of the α-sulfonimino esters **28** and **29**. Crotylation was not successful in 100% aqueous media but gave moderate yields of the crotylation products in a 50:50 $H_2O$/THF solvent mixture. (Table 2, entries 7 and 8). The stereoselectivity was however high, giving a ratio of *syn*:*anti* as high as 19:1 in the case of **29**. By comparison, a *syn:anti* ratio of 6−10:1 was obtained in the crotylation of similar α-sulfonylimino esters with *trans*-2-butenyl-tri-*n*-butylstannane in organic solvents.[13d]

**(4) Discussion.** The diastereoselectivity in the reaction of crotylmetals with carbonyl compounds has been well studied.[15] In general, it is accepted that for crotyl organometals incorporating boron, aluminum, pentavalent silicon, and tin (thermal and neutral reaction conditions), they react with aldehydes via chairlike transition states (similar to **4**). The stereochemical outcome of the product from C−C bond formation is controlled by the double bond geometry of the starting crotyl organo-

(11) We thank Dr. Francine Bélanger Gariépy of Université de Montréal for the X-ray crystallographic determination of **32**. The X-ray data has been deposited in the Cambridge Data Centre.

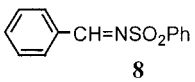
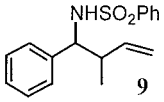
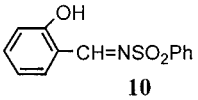
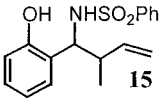
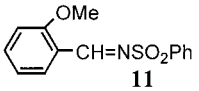
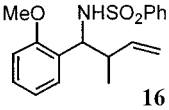
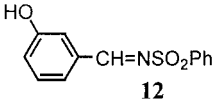
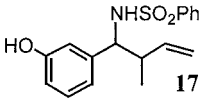
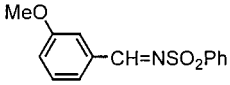
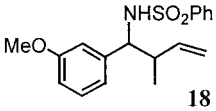
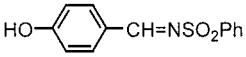
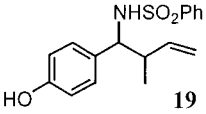
(12) See, for examples, (a) Bolton, G. L.; Hodges, J. C.; Rubin, J. R. *Tetrahedron* **1997**, *53*, 6611. (b) Miller, S. J.; Blackwell, H. E.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 9606.

(13) See, for examples, (a) Allylzinc: Yamamoto, Y.; Ito, W. *Tetrahedron* **1988**, *44*, 5415. (b) Allylboron: Yamamoto, Y.; Itoh, W.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1985**, 1131. (c) Allyltin: Hamon, D. P. G.; Massey-Westropp, R. A.; Razzino, P. *J. Chem. Soc., Chem. Commun.* **1991**, 722. (d) Allylsilicon: Fang, X.; Johannsen, M.; Yao, S.; Gathergood, N.; Hazell, R. G.; Jorgensen, K. A. *J. Org. Chem.* **1999**, *64*, 4844.

(14) Hanessian, S.; Yang, R.-Y. *Tetrahedron Lett.* **1996**, *37*, 5273.

(15) For reviews, see (a) Klienmann, E. F.; Volkmann, R. A. In *Comprehensive Organic Synthesis*; Heathcock, C. H., Ed.; Pergamon: Oxford, 1990; vol. 2, p 975. (b) Roush, W. R. In *Comprehensive Organic Synthesis*; Heathcock, C. H., Ed.; Pergamon: Oxford, 1990; vol. 2, p 1.

**Table 1. Crotylation of Substituted Benzenesulfonimines**

| Entry | Sulfonimines | THF:$H_2O$ | Product | Yield%[a] | *Syn* : *Anti*[b] |
|---|---|---|---|---|---|
| 1 |  **8** | 0:100 |  **9** | 98[c] | 39:61 |
| | | 50:50 | | 95 | 79:21 |
| 2 |  **10** | 0:100 |  **15** | 74[c] | 76:24 |
| | | 50:50 | | 88 | 77:23 |
| 3 |  **11** | 0:100 |  **16** | 75 | 35:65 |
| | | 50:50 | | 90 | 62:38 |
| 4 |  **12** | 0:100 |  **17** | 71[c] | 57:43 |
| | | 50:50 | | 80 | 74:26 |
| 5 |  **13** | 0:100 |  **18** | 95 | 37:63 |
| | | 50:50 | | 98[c] | 81:19 |
| 6 |  **14** | 0:100 |  **19** | 80 | 37:63 |
| | | 50:50 | | 83[c] | 78:22 |

[a] All the reactions are conducted in 0.5 mmol scale. All the yields are isolated yields unless specified. [b] The ratio of *syn*:*anti* is determined by $^1$H NMR spectra of the crude product. [c] The yield was determined by $^1$H NMR.

metal.[16] For crotylmetals incorporating lithium, magnesium, or zinc where metallotropic rearrangement of the crotylmetals can occur with isomerization of the double bond geometry, then the stereochemical information of the reagent cannot be transmitted to the product. Crotyl indium is likely to belong to this latter class of crotylmetallic reagents since it has been established that the double bond geometry of the starting bromide has no bearing on the stereochemical outcome of the final product.[4] The reactions of crotylmetals with imines are more complicated, because the imine nitrogen possesses an additional group and the imines often have *E*-geometry. If there is coordination between the imino nitrogen with the metal in a chairlike transition state, the groups on the C═N double bond will assume the axial geometry. Depending on the double bond geometry of the crotylmetal, there will be two diastereomeric transition states (**37a** and **37b**). The *syn*-diastereomer will be formed via the C (*E*,*E*) transition state **37a** (chair with *E*-crotyl and *E*-imine) whereas the *anti*-diastereomer will arise from the energetically less favorable C (*Z*,*E*) transition state **37b** (chair with *Z*-crotyl and *E*-imine). This is presumably what happened in cases where the imine had a proximal chelating group (as in compounds **10**, **22**, **24**, **25**, **26**, **28**, and **29**). The C (*E*,*E*) transition state structure is reinforced by the additional chelating stabilization as illustrated in **38** giving rise to the *syn*-product preferentially irrespective of the solvents used. It is, however, more difficult to explain the *anti*-selectivity in the nonchelating case (as in compounds **8**, **11**, **13**, and **14**) because the C (*Z*,*E*) transition state **37b** is clearly energetically not favorable. In the reactions between crotylboronates and imines, a B (*E*,*E*) transition state **39** (boat with *E*-crotyl and *E*-imine) has been invoked to account for the selective formation of the *anti*-diastereomer.[17] It is argued that the unfavorable 1,3-diaxial interactions in **37b** are relieved in **39**. It is not clear whether this is the appropriate explanation for the reaction of crotylindium with benzaldehyde sulfonimine **8** (and related compounds with no additional chelation). It would seem that the change from *anti*- to *syn*-selectivity as the solvent is changed from water to THF:water mixture cannot be explained on the basis of structure **39**. A more plausible explanation is to argue that, in water as solvent, there is no coordination between the indium metal and the imine nitrogen. The crotylindium and imine simply approach each other in the synclinal transition state **40** which minimizes the gauche interactions at the incipient C−C bond. The resulting product would lead to the *anti*-isomer. As the solvent changes from water to a less polar medium with THF, coordination between the indium metal and the imine nitrogen becomes important, and the C (*E*,*E*) transition state **37a** dominates, leading to more *syn*-stereoisomer.

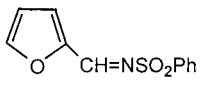
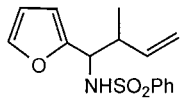
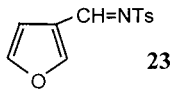
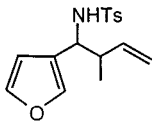
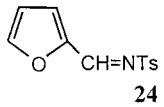
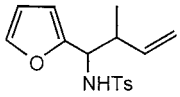
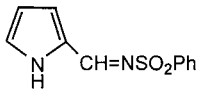
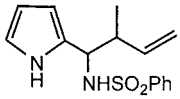
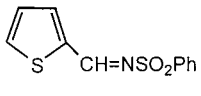
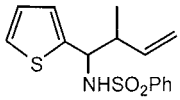
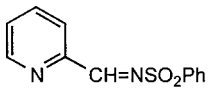
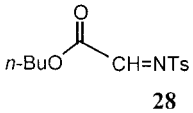
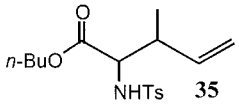
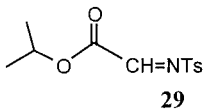
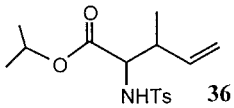
## Experimental Section

Analytical thin-layer chromatography (TLC) was performed on silica gel 60 $F_{254}$ plastic-backed plates and was visualized by dipping into a solution of ammonium molybdate (2.5 g) and ceric sulfate (1 g) in concentrated $H_2SO_4/H_2O$ (10 mL/90 mL) and heating with a heat gun. Solvents were reagent grade unless otherwise specified. Indium powder and crotyl bromide were freshly commercial samples and used directly without any further purification. Sulfonimines were prepared following the methods reported in the literature.[10]

(16) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.

(17) (a) Hoffmann, R. W.; Eichler, G.; Endesfelder, A. *Liebigs Ann. Chem.* **1983**, 2000. (b) Hoffmann, R. W.; Endesfelder, A. *Liebigs Ann. Chem.* **1986**, 1823. (c) Hoffmann, R. W.; Endesfelder, A. *Liebigs Ann. Chem.* **1987**, 215. (d) Reference 15, p 2234.

**Table 2. Aqueous Allylindation Reaction of Sulfonimines Bearing α-Chelating Groups**

| Entry | Sulfonimine | Product | Solvent THF:$H_2O$ | Yield%[a] | syn:anti[b] |
|---|---|---|---|---|---|
| 1 |  **22** |  **30** | 0:100<br>50:50<br>10:1 | 90[c]<br>94<br>99[c] | 76:34<br>93:7<br>93:7 |
| 2 |  **23** |  **31** | 0:100<br>50:50 | 85[c]<br>91 | 59:41<br>86:14 |
| 3 |  **24** |  **32** | 0:100<br>50:50<br>5:1 | 90[c]<br>95<br>99[c] | 76:34<br>93:7[d]<br>93:7 |
| 4 |  **25** |  **33** | 0:100<br>50:50 | 72<br>80 | 68:32<br>94:6 |
| 5 |  **26** |  **34** | 0:100<br>50:50 | 83<br>92 | 57:43<br>85:15 |
| 6 |  **27** | only hydrolyzed products were observed | 0:100<br>50:50 | 0<br>0 | ---<br>--- |
| 7 |  **28** |  **35** | 50:50<br>100:0<br>0:100 | 45<br>56<br>0 | 93:7[e]<br>87:13<br>---- |
| 8 |  **29** |  **36** | 50:50<br>0:100 | 40<br>0 | 95:5[e]<br>---- |

[a] Isolated yields. [b] The ratio of *syn*:*anti* was determined by $^1$H NMR of the crude product. [c] Yields determined by $^1$H NMR of the crude product. [d] The relative configuration was determined by single crystal X-ray crystallography. [e] The relative configuration was determined by comparison of the reported compounds data in ref 13d.

**Typical Procedure of Crotylation of Sulfonimines.** To a rigorously stirred mixture of crotyl bromide (1.5 mmol, 3 equiv) and sulfonimine (0.5 mmol, 1 equiv) in 4 mL solvent was added indium powder (1 mmol, 2 equiv) in one portion. The reaction was lasted for 6 h and quenched by adding 2 mL of 1 N HCl. The aqueous layer was extracted by diethyl ether (3 × 20 mL). The combined organic phase was washed with saturated sodium bicarbonate and brine, respectively, and dried over sodium sulfate. Pure allylation product was obtained by silica gel flash column chromatography, eluent 10% ethyl acetate in hexane.

***N*-[1-(2-Hydroxyphenyl)-2-methylbut-3-enyl]benzenesulfonamide (15)**: white solid, mp 98−100 °C; major *syn* isomer: $^1$H NMR (200 MHz, $CDCl_3$): ppm 7.70−7.58 (m, 2H), 7.40−7.25 (m, 3H), 6.95−6.85 (m, 1H), 6.72−6.50 (m, 3H), 6.20 (br., 1H), 5.89 (d, 1H, $J$ = 9.6 Hz), 5.51−5.37 (m, 1H), 4.91−4.80 (m, 2H), 4.20−4.11 (m, 1H), 2.81−2.61 (m, 1H), 1.13 (d, 3H, $J$ = 6.7 Hz); $^{13}$C NMR (50 MHz, $CDCl_3$): ppm 152.89, 140.21, 139.97, 132.52, 130.09, 128.84, 127.10, 125.06, 120.30, 116.53, 116.25, 62.73, 43.82, 18.49; *anti* isomer: $^1$H NMR (200 MHz, $CDCl_3$): ppm 7.70−7.58 (m, 2H), 7.40−7.25 (m, 3H), 6.95−6.85 (m, 1H), 6.72−6.50 (m, 3H), 6.20 (br., 1H), 5.60 (d, 1H, $J$ = 9.0 Hz), 5.80−5.67 (m, 1H), 5.17−5.09 (m, 2H), 4.19−4.11 (m, 1H), 2.81−2.61 (m, 1H), 0.81 (d, 3H, $J$ = 6.8 Hz); $^{13}$C NMR (50 MHz, $CDCl_3$): 153.18, 140.66, 139.84, 132.80, 129.92, 128.69, 127.21, 125.01, 120.52, 116.74, 115.79, 62.19, 43.64, 19.12; IR (neat on NaCl, cm$^{-1}$): 3421.7, 3314.2, 1609.3, 1457.0, 1311.8, 1157.8; MS (FAB) 318 (M + 1, 31.7), 154 (100); HRMS (FAB), calcd for $C_{17}H_{19}NO_3S + H^+$ 318.11626, found 318.11639. Anal. Calcd for $C_{17}H_{19}NO_3S$: C, 64.33; H, 6.03; N, 4.41; found C, 64.36; H, 6.39; N, 4.34.

***N*-[1-(2-Methoxyphenyl)-2-methylbut-3-enyl]benzenesulfonamide (16)**: colorless solid, mp 93−95 °C; *syn* isomer: $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ (ppm) 7.55−7.47 (m, 2H), 7.34−7.26 (m, 1H), 7.21−7.10 (m, 2H), 7.01−6.95 (m, 1H), 6.70−6.52 (m, 3H), 5.57 (d, 1H, $J$ = 10.4 Hz), 5.48−5.31 (m, 1H), 4.85−4.75 (m, 2H), 4.27−4.18 (m, 1H), 3.69 (s, 3H), 2.80−2.51 (m, 1H), 1.10 (d, 3H, $J$ = 6.8 Hz); $^{13}$C NMR (50 MHz, $CDCl_3$): 156.13, 140.31, 132.07, 130.08, 128.70, 128.63, 128.54, 127.06, 126.90, 120.55, 115.51, 110.98, 62.40, 56.23, 43.98, 18.59; *anti* isomer: $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ (ppm) 7.21−7.10 (m, 2H), 7.01−6.95 (m, 1H), 6.70−6.52 (m, 3H), 5.83−5.90 (m, 1H), 5.39 (d, 1H, $J$ = 10.2 Hz), 5.08−4.98 (m, 2H), 4.27−4.18 (m, 1H), 3.69 (s, 3H), 2.80−2.51 (m, 1H), 0.79 (d, 3H, $J$ = 6.8 Hz); $^{13}$C NMR (50 MHz, $CDCl_3$): 140.64, 140.56, 132.07, 129.78, 128.76, 128.63, 128.54, 127.06, 126.90, 120.66, 116.22, 110.98, 61.68, 56.23, 43.65, 19.04; IR (neat on NaCl, cm$^{-1}$): 3288.2, 2965.8, 1601.6, 1447.3, 1324.7, 1163.5; MS (FAB), 332 (M + 1, 45), 175 (100); HRMS (FAB), calcd for $C_{18}H_{21}NO_3S + H^+$

332.13204, found 332.13216. Anal. Calcd for $C_{18}H_{21}NO_3S$: C, 65.23; H, 6.39; N, 4.23. Found: C, 65.14; H, 6.77; N, 4.18.

***N*-[1-(3-Hydroxyphenyl)-2-methylbut-3-enyl]benzenesulfonamide (17)**: white solid; mp 94−98 °C major *syn* isomer: $^1$H NMR (400 MHz, $CDCl_3$): 7.65−7.57 (m, 2H), 7.47−7.37 (m, 1H), 7.35−7.24 (m, 2H), 7.03−6.91 (m, 1H), 6.61−6.44 (m, 3H), 5.44−5.35 (m, 1H), 5.04−4.95 (m, 2H), 5.23 (br. 1H), 4.22 (dd, 1H, $J$ = 8.4, 5.8 Hz), 2.58−2.40 (m, 1H), 0.91 (d, 3H, $J$ = 7 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): 155.59, 141.2, 140.24, 138.86, 132.59, 129.42, 128.85, 127.22, 120.07, 117.18, 114.55, 114.53, 61.72, 43.90, 16.34; *anti* isomer: $^1$H NMR (400 MHz, $CDCl_3$): 7.65−7.57 (m, 2H), 7.47−7.37 (m, 1H), 7.35−7.24 (m, 2H), 7.03−6.91 (m, 1H), 6.61−6.44 (m, 3H), 5.56−5.46 (m, 1H), 5.14−5.08 (m, 2H), 5.19 (br. 1H), 4.02 (dd, 1H, $J$ = 8, 6.1 Hz), 2.42−2.29 (m, 1H), 0.81 (d, 3H, $J$ = 7 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): 155.59, 141.55, 139.46, 132.56, 129.59, 128.78, 127.30, 120.07, 117.81, 114.71, 114.41, 62.15, 44.63, 17.20; IR (neat on NaCl, cm$^{-1}$): 2821.1, 1457.1, 1318.3, 1155.7; MS (FAB): 356 (M + K$^+$, 12), 307 (100); HRMS (FAB), calcd for $C_{17}H_{19}NO_3S$ + K$^+$ 356.0723, found. 356.0724. Anal. Calcd for $C_{17}H_{19}NO_3S$: C, 64.33; H, 6.03; N, 4.41. Found: C, 64.61; H, 6.47; N, 4.40.

***N*-[1-(3-Methoxyphenyl)-2-methylbut-3-enyl]benzenesulfonamide (18)**: white solid, mp 88−90 °C; *Syn* isomer: $^1$H NMR (300 MHz, $CDCl_3$): ppm 7.62−7.54 (m, 2H), 7.43−7.38 (m, 1H), 7.30−7.26 (m, 2H), 7.08−7.01 (m, 1H), 6.67−6.63 (m, 2H), 6.55−6.50 (m, 1H), 5.50−5.40 (m, 1H), 5.07−5.02 (m, 1H), 4.91 (d, 1H, $J$ = 8.4 Hz), 4.30−4.26 (dd, 1H, $J$ = 7.8, 6.3 Hz), 3.67 (s, 1H), 2.58−2.49 (m, 1H), 0.93 (d, 3H, 6.6 Hz); $^{13}$C NMR (50 MHz, $CDCl_3$): 159.91, 139.52, 132.31, 129.39, 128.83, 128.72, 127.37, 127.29, 120.36, 118.07, 113.42, 113.24, 63.16, 56.25, 45.80, 18.66; *anti* isomer: $^1$H NMR (200 MHz, $CDCl_3$): 7.62−7.54 (m, 2H), 7.43−7.38 (m, 1H), 7.30−7.26 (m, 2H), 7.08−7.01 (m, 1H), 6.67−6.63 (m, 2H), 6.55−6.50 (m, 1H), 5.66−5.53 (m, 1H), 5.18−5.12 (m, 1H), 4.86 (d, 1H, $J$ = 8.2 Hz), 4.10−4.05 (dd, 1H, $J$ = 8.1, 5.4 Hz), 3.67 (s, 1H), 2.44−2.37 (m, 1H), 0.84 (d, 3H, $J$ = 6.6 Hz); $^{13}$C NMR (50 MHz, $CDCl_3$): 159.91, 140.86, 138.85, 129.25, 128.83, 128.72, 128.38, 127.29, 120.28, 117.38, 113.67, 113.09, 62.72, 56.25, 45.04, 17.88; IR (neat on NaCl, cm$^{-1}$): 3285.7, 2966.6, 1601.8, 1448.4, 1321.3, 1161.0; MS (CI) 332 (M + 1, 1.8), 276 (100); HRMS (FAB), calcd for $C_{18}H_{21}NO_3S$ + H$^+$ 332.13204, found. 332.13193. Anal. Calcd for $C_{18}H_{21}NO_3S$: C, 65.23; H, 6.39; N, 4.23. Found: C, 65.23; H, 6.61; N, 4.21.

***N*-[1-(4-Hydroxyphenyl)-2-methylbut-3-enyl]benzenesulfonamide (19)**: white solid; mp 100−104 °C major *syn* isomer: $^1$H NMR (400 MHz, $CDCl_3$): 7.62−7.52 (m, 2H), 7.46−7.38 (m, 1H), 7.36−7.26 (m, 2H), 6.88 (d, 2H, $J$ = 8.4 Hz) 6.55 (d, 2H, $J$ = 8.4 Hz), 5.52−5.34 (m, 1H), 4.99−4.86 (m, 2H), 4.96 (br., 1H), 4.23 (dd, 1H, $J$ = 8, 5.2 Hz), 2.54−2.44 (m, 1H), 0.90 (d, 3H, $J$ = 7 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): 154.90, 138.85, 133.08, 128.94, 128.86, 127.21, 126.67, 117.33, 114.99, 61.30, 44.09, 16.59; *anti* isomer: $^1$H NMR (400 MHz, $CDCl_3$): 7.62−7.52 (m, 2H), 7.46−7.38 (m, 1H), 7.36−7.26 (m, 2H), 6.88 (d, 2H, $J$ = 8.4 Hz) 6.55 (d, 2H, $J$ = 8.4 Hz), 5.66−5.56 (m, 1H), 5.18−5.08 (m, 2H), 4.87 (br., 1H), 4.00 (dd, 1H, $J$ = 8, 4.6 Hz), 2.44−2.28 (m, 1H), 0.79 (d, 3H, $J$ = 7 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): 154.90, 140.69, 132.37, 130.57, 129.42, 128.74, 127.32, 126.67, 117.33, 115.17, 61.80, 45.03, 17.27; IR (neat on NaCl, cm$^{-1}$): 2850.4, 1515.7, 1447.1, 1310.9, 1156.7; MS (FAB): 356 (M + K$^+$, 13), 161 (100); HRMS (FAB), calcd for $C_{17}H_{19}NO_3S$ + K$^+$ 356.0723, found. 356.0724. Anal. Calcd for $C_{17}H_{19}NO_3S$ C, 64.33; H, 6.03; N, 4.41. Found: C, 64.12, H, 6.45; N, 4.36.

***N*-(1-Furan-2-yl-2-methylbut-3-enyl)benzenesulfonamide (30)**: white solid, mp 105−106 °C; *syn* isomer: $^1$H NMR (300 MHz, $CDCl_3$): ppm 7.69−7.64 (m, 2H), 7.48−7.41 (m, 1H), 7.38−7.31 (m, 2H), 7.01−7.06 (m, 1H), 6.05−6.02 (m, 1H), 5.83 (d, 1H, $J$ = 3 Hz), 5.60−5.46 (ddd, 1H, $J$ = 16.8, 10.2, 8.7 Hz), 5.12−5.04 (m, 2H), 5.05 (br., 1H), 4.35 (dd, 1H, $J$ = 9.6, 5.7 Hz), 2.70−2.52 (m, 1H), 0.97 (d, 3H, $J$ = 6.9 Hz); $^{13}$C NMR (50 MHz, $CDCl_3$): ppm 151.17, 141.90, 140.70, 138.69, 132.43, 128.97, 127.24, 127.16, 117.53, 110.35, 108.58, 56.71, 44.38, 18.34; IR (neat on NaCl, cm$^{-1}$), 3251.6, 1449.0, 1321.8, 1163.8, 910.3, 731.7; MS (FAB) 292 (M + 1, 25.4), 236 (73.2), 135 (100); HRMS calcd for $C_{15}H_{17}NO_3S$ + H$^+$ 292.10074, found 292.10064. Anal. Calcd for $C_{15}H_{17}NO_3S$: C, 61.83; H, 5.88; N, 4.81. Found: C, 62.23;H, 6.10; N, 4.82.

***N*-(1-Furan-3-yl-2-methylbut-3-enyl)-4-methylbenzenesulfonamide (31)**: white solid; mp 91−94 °C syn isomer: $^1$H NMR (400 MHz, $CDCl_3$): ppm 7.61 (d, 2H, $J$ = 8.8 Hz), 7.17 (d, 2H, $J$ = 8.8 Hz), 7.16 (m, 1H), 7.00 (d, 1H, $J$ = 0.8 Hz), 6.04 (d, 1H, $J$ = 1.6 Hz), 5.57−5.48 (m, 1H), 5.15 (d, 1H, $J$ = 8.8 Hz), 5.05−5.01 (m, 2H), 4.25 (dd, 1H, $J$ = 8.8, 5.6 Hz), 2.51−2.42 (m, 1H), 2.37 (s, 3H), 0.94 (d, 3H, $J$ = 6.4 Hz), $^{13}$C NMR (100 MHz, $CDCl_3$): ppm 143.38, 143.08, 140.23, 138.91, 137.93, 129.54, 127.34, 123.31, 117.29, 109.4154.19, 43.32, 21.72, 16.57; IR (neat on NaCl, cm$^{-1}$): 2965.4, 1499.6, 1329.0, 1162.4, 1025.9; MS (EI), 306 (M + 1, 0.4), 250 (100). Anal. Calcd for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.59; found C, 63.01; H, 6.64; N, 4.62.

***N*-(1-Furan-2-yl-2-methylbut-3-enyl)-4-methylbenzenesulfonamide (32)**: colorless crystal; mp 94−95 °C *syn* isomer: $^1$H NMR (400 MHz, $CDCl_3$): ppm 7.55 (d, 2H, $J$ = 8 Hz), 7.15 (d, 2H $J$ = 8 Hz), 7.11 (m, 1H), 6.08−6.07 (m, 1H), 5.85 (d, 1H, $J$ = 3.2 Hz), 5.48−5.49 (m, 1H), 5.07−5.02 (m, 2H), 4.87 (d, 1H, $J$ = 9.6 Hz), 2.62−2.54 (m, 1H), 2.36 (s, 3H), 0.97 (d, 3H, $J$ = 6.8 Hz); $^{13}$C NMR (50 MHz, $CDCl_3$): ppm 151.50, 143.18, 141.97, 138.77, 137.78, 129.52, 127.12, 117.39, 110.04, 108.26, 55.66, 43.31, 21.71, 16.98; IR (neat on NaCl, cm$^{-1}$): 1422.4, 1320.1, 1159.9, 1009.3; MS (FAB): 344 (M + K$^+$, 14), 135 (100); HRMS (FAB), calcd for $C_{16}H_{19}NO_3S$ + K$^+$ 344.0723, found. 344.0722. Anal. Calcd for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.59. Found: C, 62.99; H, 6.30; N, 4.59.

***N*-[2-Methyl-1-(1*H*-pyrrol-2-yl)but-3-enyl]benzenesulfonamide (33)**: yellow solid; decompose at 103−105 °C; major *syn* isomer: $^1$H NMR (200 MHz, $CDCl_3$): 8.35 (br. 1H), 7.76 (d, 2H), 7.55 (t, 1H), 7.45 (t, 2H), 6.60 (m, 1H), 6.02 (m, 1H), 5.87 (s, 1H), 5.52 (ddd, 1H, $J$ = 10.50, 10.00, 7.00 Hz), 5.04−4.96 (m, 2H), 4.81 (d, 1H, $J$ = 7.00 Hz), 4.34 (dd, 1H, $J$ = 8.5, 5.5 Hz), 2.64−2.60 (m, 1H), 0.96 (d, 3H, $J$ = 7.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): 140.24, 139.32, 132.87, 129.17, 127.35, 117.89, 116.95, 108.34, 107.13, 55.91, 42.07, 16.00; IR (neat on NaCl, cm$^{-1}$): 2950, 1447.8, 1310, 1158.7; MS(FAB) 291 (M + 1, 10), 235 (100); HRMS (FAB), calcd for $C_{15}H_{18}N_2O_2S$ + H$^+$ 291.1167, found. 291.1168.

***N*-(2-Methyl-1-thiophen-2-ylbut-3-enyl)benzenesulfonamide (34)**: clear oil, major *syn* isomer: $^1$H NMR (200 MHz, $CDCl_3$): 7.65−7.60 (m, 2H), 7.45−7.20 (m, 3H), 7.04 (dd, 1H, $J$ = 5.0, 1.4 Hz), 6.72 (dd, 1H, $J$ = 5.2, 3.6 Hz), 6.61−6.58 (m, 1H), 5.61 (ddd, 1H, $J$ = 10.2, 9.8, 8.0 Hz), 5.13−5.04 (m, 2H), 4.95 (d, 1H, $J$ = 8.6 Hz), 4.62 (dd, 1H, $J$ = 8.8, 6.0 Hz), 2.59 (m, 1H), 0.99 (d, 3H, $J$ = 7.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): 141.70, 140.37, 138.07, 132.10, 128.50, 126.78, 126.08, 125.74, 124.52, 117.37, 57.56, 44.03, 16.35; IR (neat on NaCl, cm$^{-1}$): 2935.8, 1448.8, 1320.8, 1160.9; MS(FAB) 346 (M + K$^+$, 10), 151(100); HRMS (FAB), calcd for $C_{15}H_{17}NO_2S_2$ + K$^+$ 346.0338, found. 346.0337. Anal. Calcd for $C_{15}H_{17}NO_2S_2$: C, 58.60; H, 5.57; N, 4.56. Found: C, 58.71; H, 5.63; N, 4.55.

**3-Methyl-2-(toluene-4-sulfonylamino)hex-5-enoic acid butyl ester (35)**: white solid mp 52−53 °C; major *syn* isomer: $^1$H NMR (200 MHz, $CDCl_3$): 7.69 (d, 2H, $J$ = 8.34 Hz), 7.26 (d, 2H, $J$ = 8.34 Hz), 5.73−5.55 (m, 1H), 5.13−5.01 (m, 2H), 5.07 (br, 1H), 3.84−3.75 (m, 1H), 3.86−3.76 (m, 2H), 2.60−2.40 (m, 1H), 2.40 (s, 3H), 1.49−1.32 (m, 2H), 1.33−1.15 (m, 2H), 1.03 (d, 3H, $J$ = 6.96 Hz), 0.88 (t, 3H, $J$ = 7.26 Hz); $^{13}$C NMR (50 MHz, $CDCl_3$): 170.47, 143.66, 138.20, 136.98, 129.82, 127.65, 117.16, 66.29, 61.03, 43.04, 31.78, 23.07, 20.56, 17.48, 15.23; IR (neat on NaCl, cm$^{-1}$): 3277.4, 2962.6, 1737.2, 1598.6, 1343.9, 1163.7; MS(FAB) 340 (M + 1, 2.5), 283 (100), 154 (100); HRMS (FAB), calcd for $C_{17}H_{25}NO_4S$ + H$^+$ 340.15825, found. 340.15823. Anal. Calcd for $C_{17}H_{25}NO_4S$: C, 60.15; H, 7.42; N, 4.13; found C, 60.49; H, 7.77; N, 4.18.

**3-Methyl-2-(toluene-4-sulfonylamino)hex-5-enoic acid isopropyl ester (36)**: white solid; mp 92−95 °C; major *syn* isomer: $^1$H NMR (200 MHz, $CDCl_3$): 7.69 (d, 2H, $J$ = 8.16 Hz), 7.25 (d, 2H, $J$ = 8.10 Hz), 6.65 (ddd, 1H, $J$ = 10.14, 10.10, 8.10 Hz), 5.19 (d, 1H, $J$ = 10.26 Hz), 5.09−5.01 (m, 2H), 4.69 (dt, 1H, $J$ = 12.58, 6.22 Hz), 3.76 (dd, 1H, $J$ = 10.14, 5.70 Hz),

2.48 (d, 1H, $J = 6.88$ Hz), 2.39 (s, 3H), 1.13−0.94 (m, 9H); $^{13}$C NMR (50 MHz, $CDCl_3$): 169.90, 143.68, 138.29, 137.01m 129.85, 127.65, 117.08, 70.44, 60.96, 43.12, 23.09, 22.99, 17.49; IR (neat on NaCl, $cm^{-1}$): 1720.9, 1334.2, 1163.5, 1087.7; MS-(CI), 326 (M + 1, 100), 238 (96); HRMS (FAB), calcd for $C_{16}H_{23}NO_4S + H^+$ 326.142605, found. 326.142630. Anal. Calcd for $C_{16}H_{23}NO_4S$: C, 59.05; H, 7.12; N, 4.30. Found: C, 59.16; H, 7.29; N, 4.32.

**Acknowledgment.** We thank NSERC for financial support of this research.

**Supporting Information Available:** X-ray crystallography data of compound **32**. This information is available free of charge at http://pubs.acs.org.

JO0018038