JOC Article

Regioselectivity in Palladium−Indium Iodide-Mediated Allylation Reaction of Glyoxylic Oxime Ether and *N*-Sulfonylimine

Hideto Miyabe,[†] Yousuke Yamaoka,[†] Takeaki Naito,[‡] and Yoshiji Takemoto*,[†]

Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan, and Kobe Pharmaceutical University, Motoyamakita, Higashinada, Kobe 658-8558, Japan

takemoto@pharm.kyoto-u.ac.jp

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Allylation reaction of electron-deficient imines with allylic alcohol derivatives in the presence of a catalytic amount of palladium(0) complex and indium(I) iodide was studied. The reversibility of allylation was observed in the reaction of glyoxylic oxime ether having camphorsultam. As the important effect of water on regioselectivity, the γ-adducts were kinetically formed from monosubstituted allylic reagents in the presence of water. The selective formation of thermodynamically stable α-adducts was observed in anhydrous THF. In contrast, the allylation of *N*-sulfonylimine gave the γ-adducts with high regioselectivities even under anhydrous reaction conditions.

Introduction

The reaction of allylmetals with electrophiles has been developed as a fundamentally important carbon−carbon bond-forming method.[1] In general, the γ-adducts (branched products) were predominantly obtained in the allylation of aldehydes and imines using allylmetals. Thus, the selective synthesis of the α-adducts (linear products) has been a subject of current interest (Figure 1). Recently, some highly regioselective allylations giving α-adducts have been acheived.[2]

The indium-mediated allylation reactions have been of great importance from both economic and environmental points of view.[3] In general, allylindium reagents have been prepared from allylic bromides or iodides and indium.[3] Recently, the alternative method for preparation of allylindium reagents via transient organopalladium intermediates has been studied by Araki et al.,[4] and then several successful examples of allylation of aldehydes under new reaction conditions were reported by Grigg, Kang, and our groups.[5] In these reactions, allylindium reagents were generated via transmetalation of transient π-allylpalladium intermediates with indium(I) halides. However, the corresponding reaction of imine derivatives has not been widely studied;[6] therefore, the allylation of imine derivatives through the umpolung process of electrophilic palladium intermediates into nucleophilic indium reagents has been a subject of current interest. As a part of our program directed toward the development of indium-mediated reaction of imine derivatives,[7,8]

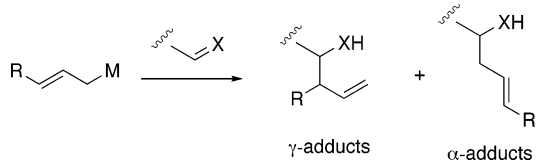

FIGURE 1. Regioselectivity in allylation.

[†] Kyoto University.

[‡] Kobe Pharmaceutical University.

(1) For reviews, see: (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207. (b) Bloch, R. *Chem. Rev.* **1998**, *98*, 1407. (c) Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163.

(2) For some examples, see: (a) Tan, K.-T.; Chng, S.-S.; Cheng, H.-S.; Loh, T.-P. *J. Am. Chem. Soc.* **2003**, *125*, 2958. (b) Loh, T.-P.; Tan, K.-T.; Hu, Q.-Y. *Tetrahedron Lett.* **2001**, *42*, 8705. (c) Ito, A.; Kishida, M.; Kurusu, Y.; Masuyama, Y. *J. Org. Chem.* **2000**, *65*, 494. (d) Yanagisawa, A.; Ogasawara, K.; Yasue, K.; Yamamoto, H. *J. Chem. Soc., Chem. Commun.* **1996**, 367. (e) Isaac, M. B.; Chan, T. H. *Tetrahedron Lett.* **1995**, *36*, 8957. (f) Yamamoto, Y.; Saito, Y.; Maruyama, K. *J. Org. Chem.* **1983**, *48*, 5408.

(3) For a recent review, see: Li, C. J.; Chan, T. H. *Tetrahedron* **1999**, *55*, 11149. For some examples of indium-mediated reactions, see: (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. (c) Paquette, L. A.; Rothhaar, R. R. *J. Org. Chem.* **1999**, *64*, 217. (d) Woo, S.; Sqires, N.; Fallis, A. G. *Org. Lett.* **1999**, *1*, 573. (e) Engstrom, G.; Morelli, M.; Palomo, C.; Mitzel, T. *Tetrahedron Lett.* **1999**, *40*, 5967. (f) Loh, T.-P.; Zhou, J. R. *Tetrahedron Lett.* **1999**, *40*, 9115.

(4) Araki, S.; Kamei, T.; Hirashita, T.; Yamamura, H.; Kawai, M. *Org. Lett.* **2000**, *2*, 847.

(5) (a) Anwar, U.; Grigg, R.; Rasparini, M.; Savic, V.; Sridharan, V. *Chem. Commun.* **2000**, 645. (b) Anwar, U.; Grigg, R.; Sridharan, V. *Chem. Commun.* **2000**, 933. (c) Kang, S.-K.; Lee, S.-W.; Jung, J.; Lim, Y. *J. Org. Chem.* **2002**, *67*, 4376. We reported InI−Pd(0)-promoted metalation and addition of chiral 2-vinylaziridines. See: (d) Takemoto, Y.; Anzai, M.; Yanada, R.; Fujii, N.; Ohno, H.; Ibuka, T. *Tetrahedron Lett.* **2001**, *42*, 1725. (e) Anzai, M.; Yanada, R.; Fujii, N.; Ohno, H.; Ibuka, T.; Takemoto, Y. *Tetrahedron* **2002**, *58*, 5231.

(6) Recently, the palladium−indium-mediated cascade allylation of *N*-sulfonylimines was reported. See: Cooper, I. R.; Grigg, R.; MacLachlan, W. S.; Thornton-Pett, M.; Sridharan, V. *Chem. Commun.* **2002**, 1372.

(7) (a) Miyabe, H.; Ueda, M.; Nishimura, A.; Naito, T. *Org. Lett.* **2002**, *4*, 131. (b) Miyabe, H.; Nishimura, A.; Ueda, M.; Naito, T. *Chem. Commun.* **2002**, 1454. (c) Yanada, R.; Kaieda, A.; Takemoto, Y. *J. Org. Chem.* **2001**, *66*, 7516.

(8) For examples of metallic indium-mediated allylation of imines, see: (a) Lu, W.; Chan, T. H. *J. Org. Chem.* **2001**, *66*, 3467. (b) Lu, W.; Chan, T. H. *J. Org. Chem.* **2000**, *65*, 8589. (c) Chan, T. H.; Lu, W. *Tetrahedron Lett.* **1998**, *39*, 8605. (d) Basile, T.; Bocoum, A.; Savoia, D.; Umani-Ronichi, A. *J. Org. Chem.* **1994**, *59*, 7766. (e) Beuchet, P.; Marrec, N. L.; Mosset, P. *Tetrahedron Lett.* **1992**, *33*, 5959. (f) Lee, J. G.; Choi, K. I.; Pae, A. N.; Koh, H. Y.; Kang, Y.; Cho, Y. S. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1314.

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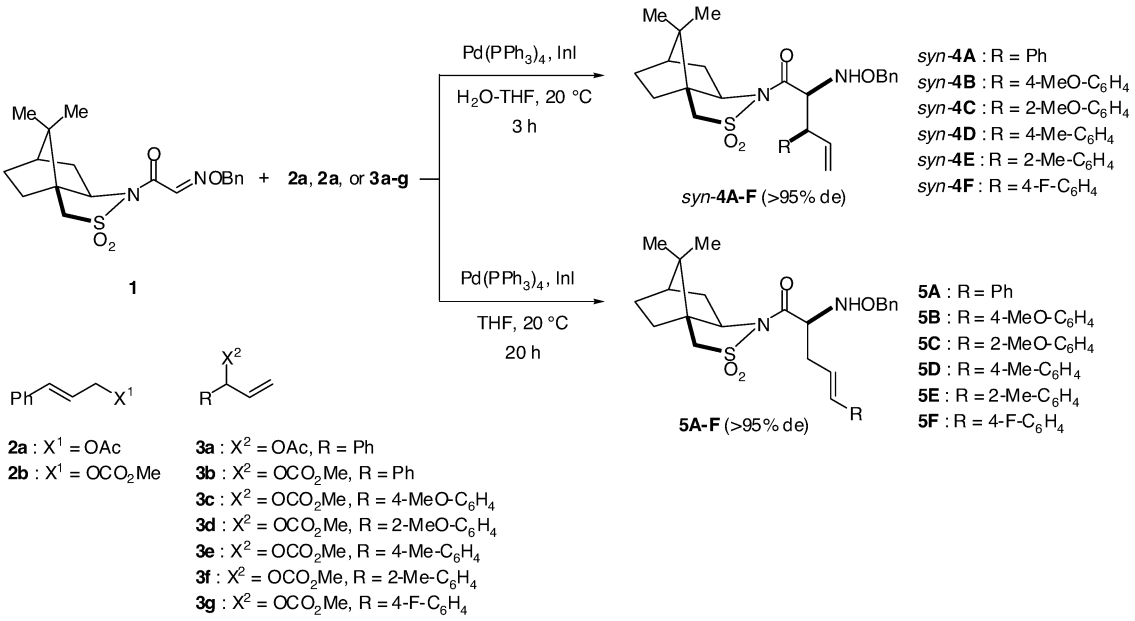
SCHEME 1



we now report the reactions of electron-deficient imine derivatives such as glyoxylic oxime ether[9,10] and *N*-tosylimine[11] with allylic acetates and carbomates in the presence of a catalytic amount of palladium(0) complex and indium(I) iodide. We also report that the palladium−indium iodide-mediated allylation of glyoxylic oxime ether afforded either γ-adducts or α-adducts by simple change of the reaction conditions, allowing the preparation of a variety of α-amino acids.

Results and Discussion

Reaction of Glyoxylic Oxime Ether. We first examined the reaction of Oppolzer's camphorsultam derivative of glyoxylic oxime ether **1**, which has shown excellent reactivity in our previous work on allylation and radical reactions using metallic indium.[7b] Thus, we expected that the direct comparison of metallic indium-mediated reactions with palladium−indium iodide-mediated reactions would lead to informative and instructive suggestions regarding the reactivity, regioselectivity, diastereoselectivity, and absolute stereochemical course in the present method.

The reactions of **1** with allylic acetate **3a** (2 equiv) were carried out in the presence of $Pd(PPh_3)_4$ (0.05 equiv) and indium(I) iodide (2 equiv) at 20 °C (Scheme 1). As expected, glyoxylic oxime ether **1** exhibits a good reactivity to give the desired allylated products *syn*-**4A** and **5A**, without formation of significant byproducts such as a reduced product. To our surprise, the selective formation of α-adduct **5A** was observed in anhydrous THF (Table 1). A 1:2 mixture of the γ-adduct *syn*-**4A** and the α-adduct **5A** was obtained in 74% combined yield after being stirred for 0.5 h, accompanied with 10% yield of the starting material **1** (entry 1). The formation of the α-adduct **5A** was shown to be dependent on the reaction time; thus, the prolonged reaction led to a selective formation of the α-adduct **5A** (entry 2). In our previous studies on metallic indium-mediated reaction of **1** in aqueous media, the γ-adducts were obtained as a single regioisomer.[7b] Therefore, we next investigated the effect of water on the palladium−indium iodide-mediated reaction. In the presence of water, the γ-adduct *syn*-**4A** was obtained in 90% yield as a single diastereomer without the formation of the α-adduct **5A**, after being stirred at 20 °C for 3 h (entry 3). Under the aqueous reaction

TABLE 1. Reaction of 1 with Allyl Alcohol Derivatives 2a,b and 3a−g[a]

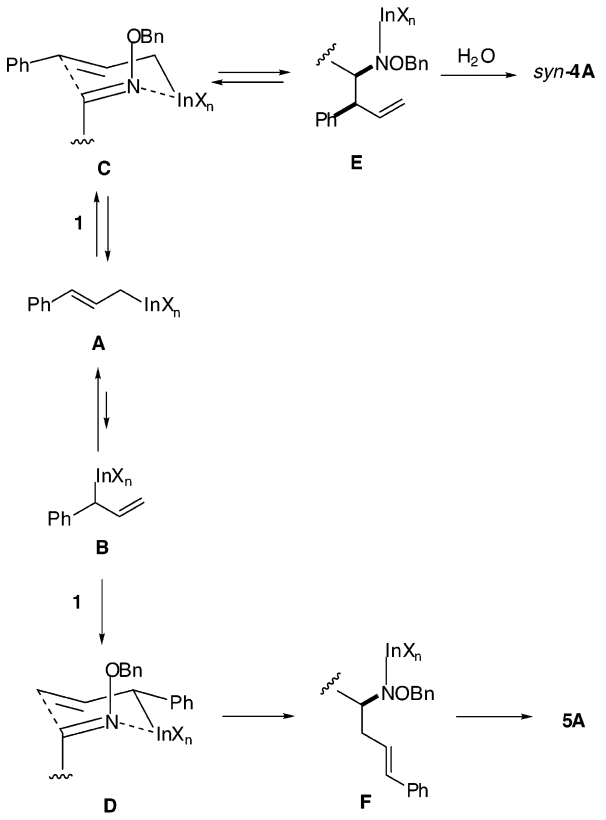
entry	reagent	solvent	time (h)	product	yield[b] (%)
1	**3a**	THF	0.5	*syn*-**4A**/**5A** (1:2)	74 (10)
2	**3a**	THF	20	**5A**	95
3	**3a**	H_2O−THF	3	*syn*-**4A**	90
4	**3a**	H_2O−THF	20	*syn*-**4A**	89
5	**3b**	H_2O−THF	3	*syn*-**4A**	94
6	**2a**	H_2O−THF	3	*syn*-**4A**	95
7	**2b**	H_2O−THF	3	*syn*-**4A**	94
8	**3b**	THF	20	**5A**	93
9	**2a**	THF	20	**5A**	85
10	**2b**	THF	20	**5A**	87
11	**3c**	H_2O−THF	3	*syn*-**4B**	90
12	**3d**	H_2O−THF	3	*syn*-**4C**	81
13	**3e**	H_2O−THF	3	*syn*-**4D**	71
14	**3f**	H_2O−THF	3	*syn*-**4E**	72
15	**3g**	H_2O−THF	3	*syn*-**4F**	66
16	**3c**	THF	20	**5B**	93
17	**3d**	THF	20	**5C**	95
18	**3e**	THF	20	**5D**	90
19	**3f**	THF	20	**5E**	93
20	**3g**	THF	20	**5F**	81

[a] Reactions were carried out with **1** and allyl alcohol derivatives **2a**,**b** and **3a**−**g** at 20 °C. [b] Isolated yields. Yield in parentheses is that for the recovered starting material.

(9) We recently reported the radical addition to glyoxylic oxime ether, see: Miyabe, H.; Ushiro, C.; Ueda, M.; Yamakawa, K.; Naito, T. *J. Org. Chem.* **2000**, *65*, 176.

(10) The zinc-mediated allylation reaction of glyoxylic oxime ether reported by Hanessian's group. See (a) Hanessian, S.; Yang, R.-Y. *Tetrahedron Lett.* **1996**, *37*, 5273. (b) Hanessian, S.; Bernstein, N.; Yang, R.-Y.; Maguire, R. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1437. (c) Hanessian, S.; Lu, P.-P.; Sanceau, J.-Y.; Chemla, P.; Gohda, K.; Fonne-Pfister, R.; Prade, L.; Cowan-Jacob, S. W. *Angew. Chem., Int. Ed.* **1999**, *38*, 3160.

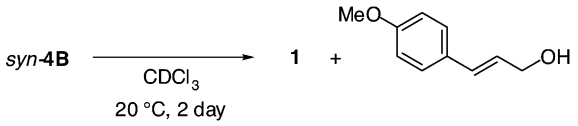
SCHEME 2



conditions, the formation of the α-adduct **5A** was not observed after being stirred even for 20 h (entry 4).

Although the precise reason for the effect of water was unclear, these observations can be explained by the reversibility of allylation reaction (Scheme 2). The reversibility in allylation reaction of imines using other allylmetals has been observed.[2d,12] Under the anhydrous reaction conditions, the prolonged reaction would allow the reversibility between the γ-adduct **E** and the linear indium reagent **A**, giving the branched indium reagent **B** via the allylic rearrangement of indium atom.[13] Finally, the kinetically formed adduct **E** isomerized to the thermodynamically stable α-adduct **F**. Recently, a new mechanism based on [3,3]-sigmatropic rearrangement was reported.[5a,b] Thus, an alternative mechanistic hypothesis involving [3,3]-sigmatropic rearrangement would not be rigorously excluded. In contrast, water suppress the reversibility between adduct **E** and the indium reagent **A**, as a result of the quick trapping reaction of the branched adduct **E** with H_2O. As an effect of water, an alternative mechanism involving an open transition state in the presence of water would not be excluded. The absolute configuration of major product **4A** was determined to be *S* and syn by comparison with authentic spectral data.[7b,10b] The absolute configuration of major product **5A** was assigned to be *S* since its ^{1}H NMR data showed similarity with that of the major isomer of allylated compound of **1** obtained by our previous studies.[7b] To study the reversibility in this reaction, the γ-adduct *syn*-**4A** was treated with $Pd(PPh_3)_4$ and indium(I) iodide in anhydrous THF. However, the formation of α-adduct **5A** was not observed. Additionally, treatment of *syn*-**4A** with *n*-BuLi did not lead to the formation of α-adduct **5A**.

SCHEME 3



To learn about the effect of allylic reagents, we next examined the reactions of **1** with other allylic reagents. The branched and linear reagents **3b** and **2a**,**b** would give the same transient organopalladium intermediate, providing same allylic indium reagent was used. The reactions with **3b** and **2a**,**b** proceeded smoothly in H_2O−THF (1:10, v/v) to give the γ-adduct *syn*-**4A** without formation of the α-adduct **5A** (entries 5−7). Allylic reagents **3b** and **2a**,**b** also worked well in anhydrous THF to give the α-adduct **5A** (entries 8−10). The advantage of the reaction using branched allylic acetates such as **3a** is that a wide range of branched allylic acetates can be prepared by the reaction of corresponding aldehydes with vinylmagnesium bromide followed by acetylation. We next investigated the reaction of **1** with the aromatic allylic acetates **3c**−**g**. As expected, the γ-adducts *syn*-**4B**−**F** were obtained in H_2O−THF (1:10, v/v) and the α-adducts **5B**−**F** were obtained in anhydrous THF (entries 11−20). The absolute configuration of **4B**−**F** and **5B**−**F** was assigned since these ^{1}H NMR data showed similarity with those of **4A** and **5A**. The hydrolysis of γ-adducts *syn*-**4B**−**F** into oxime ether **1** and the corresponding allyl alcohols was frequently observed, as exemplified in the conversion of γ-adduct *syn*-**4B** into oxime ether **1** and the corresponding alcohol, which was confirmed by the authentic compound,[14] in $CDCl_3$ (Scheme 3). These results also support the reversibility in the present reaction.

In contrast to monosubstituted allylic reagents **2a**,**b** and **3a**−**g**, the reaction with disubstituted allylic reagents **2c**,**d** and **3h**−**j** gave exclusively γ-adducts **4G** and **4H** as a single diastereomer even in anhydrous THF (Scheme 4). The absolute configuration of **4G** was determined to be *S* by comparison with authentic spectral data.[7b,10b] These observations indicate that the allylic rearrangement of indium atom from the linear indium reagent **H** to the branched indium reagent **I** would be suppressed due to steric effects; thus, α-adducts were not obtained from **I** via the chelated six-membered ring transition state (Scheme 5). The chemical efficiency giving γ-adduct **4G** was shown to be dependent on the structure in allyl reagents (Table 2). In the case of linear γ,γ-dimethylallyl acetate **2c**, a similar reaction procedure did not give a good result (entry 1). The reaction of **1** with linear allyl carbonate **2d** proceeded slowly to give the desired product

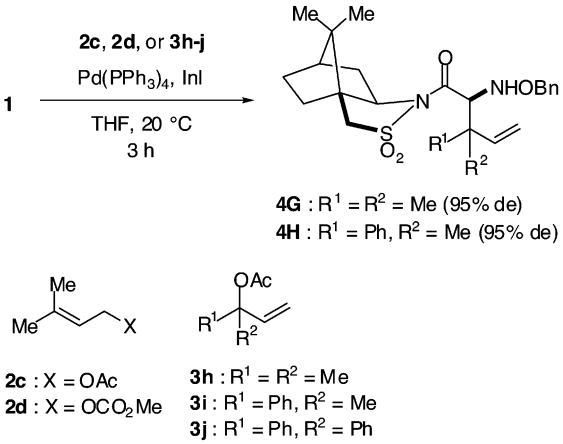
(11) We recently reported that *N*-sulfonylimines have shown the excellent reactivity toward nucleophilic carbon radical. See: (c) Miyabe, H.; Ueda, M.; Naito, T. *Chem. Commun.* **2000**, 2059.

(12) (a) Miginiac, L.; Mauzé, B. *Bull. Soc. Chim. Fr.* **1968**, 4674. (b) Mauzé, B.; Miginiac, L. *Bull. Soc. Chim. Fr.* **1973**, 1832. (c) Mauzé, B.; Miginiac, L. *Bull. Soc. Chim. Fr.* **1973**, 1838. (b) Mauzé, B.; Miginiac, L. *Bull. Soc. Chim. Fr.* **1973**, 1082.

(13) Isomerization of indium reagents via the allylic rearrangement of indium atom was reported. See: Hirashita, T.; Hayahi, Y. Mitsui, K.; Araki, S. *J. Org. Chem.* **2003**, *68*, 1309.

(14) Engler, T. A.; LaTessa, K. O.; Iyengar, R.; Chai, W.; Agrios, K. *Bioorg. Med. Chem.* **1996**, *4*, 1755.

SCHEME 4



SCHEME 5

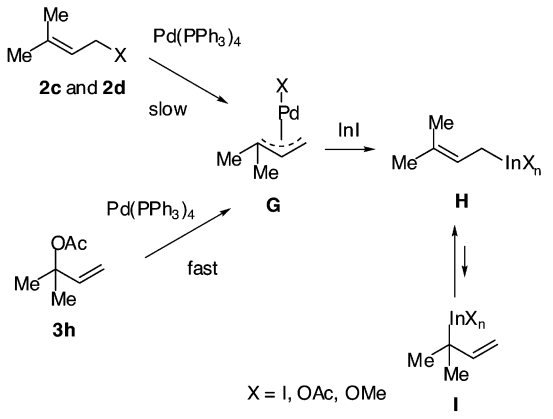


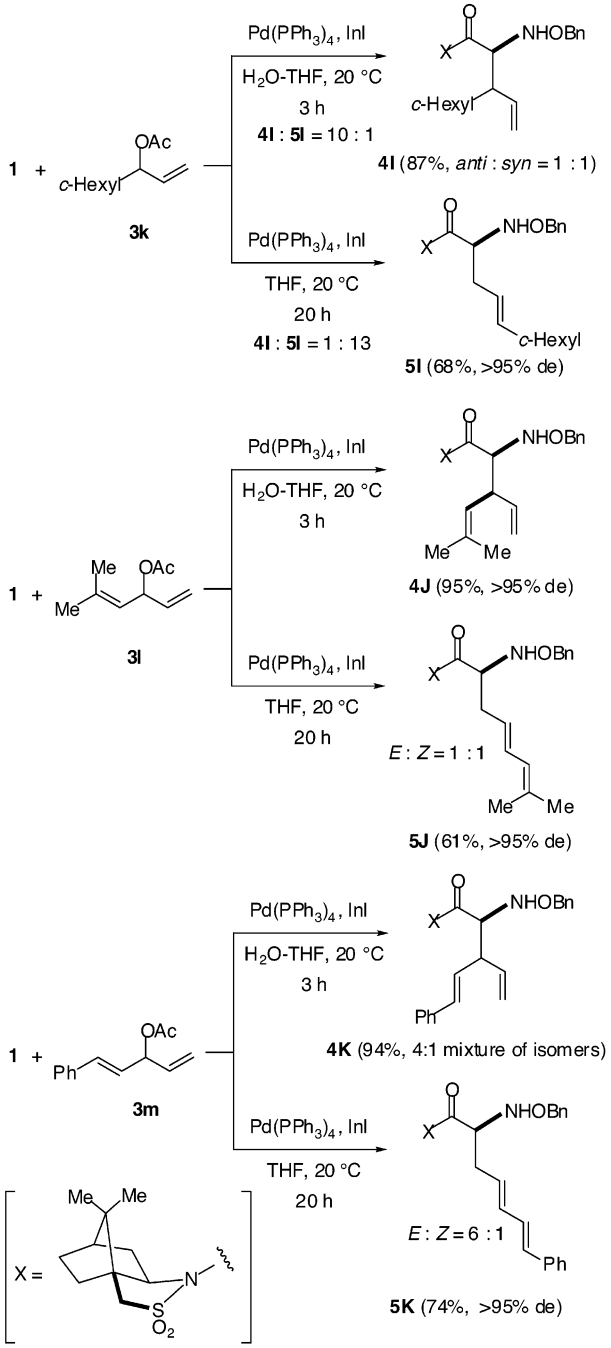
TABLE 2. Reaction of 1 with Allyl Alcohol Derivatives 2c,d and 3h−j[a]

entry	reagent	solvent	time (h)	product	yield[b] (%)
1	**2c**	THF	20	**4G**	trace
2[c]	**2c**	THF	20	**4G**	trace
3	**2d**	THF	20	**4G**	27 (61)
4	**3h**	THF	20	**4G**	87
5	**3h**	H_2O−THF	3	**4G**	85
6	**3i**	H_2O−THF	20		no reaction
7	**3i**	THF	10	**4H**	12 (80)
8	**3j**	THF	30		no reaction

[a] Reactions were carried out with **1** and allyl alcohol derivatives **2c**,**d** and **3h**−**j**. [b] Isolated yields. Yields in parentheses are that for the recovered starting material. [c] Reaction was carried out with **1** and **2c** at 70 °C.

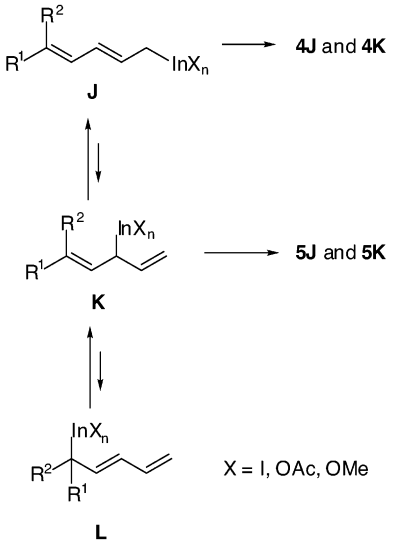
4G in 27% yield, accompanied with 70% yield of starting compound **1** (entry 3). In contrast, the reaction with branched α,α-dimethylallyl acetate **3h** gave the γ-adduct **4G** in 87% yield as a single diastereomer after being stirred at 20 °C for 20 h (entry 4). These results indicate that the branched allyl acetate **3h** shows excellent reactivity toward Pd(0) in the formation process of transient organopalladium intermediates **G** (Scheme 5). In the presence of water, the reaction with **3h** also proceeded smoothly to give **4G** (entry 5). In the case of bulky acetate **3i**, the reaction proceeded slowly in anhydrous THF to give the γ-adduct **4H** in 12% yield, accompanied with 80% yield of starting compound **1**, although the reaction did not occur in H_2O−THF (entries 6 and 7). However, the branched α,α-diphenylallyl acetate **3j** did not worked (entry 8).

SCHEME 6

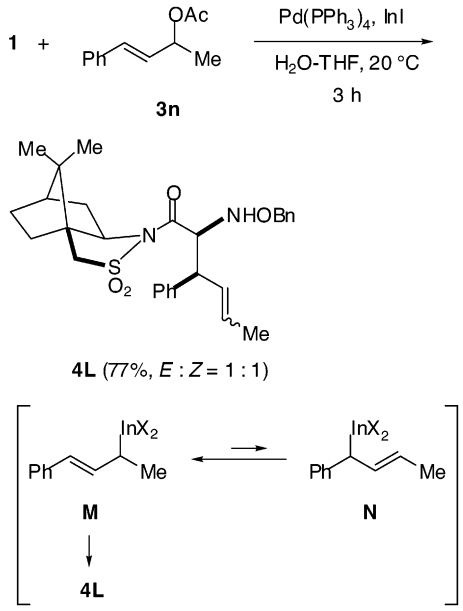


To survey the scope and limitations of the present reaction, the reaction of **1** with allylic acetates **3k**−**m** was studied (Scheme 6). The reaction with aliphatic allylic acetate **3k** in H_2O−THF gave the syn/anti mixture of γ-adduct **4I**, accompanied with a small amount of α-adduct **5I**. The similar trend in syn/anti selectivity was observed in the zinc-mediated reaction of **1** with aliphatic allylic bromide.[10b] In contrast, the reaction with **3k** in anhydrous THF gave selectively the α-adduct **5I**. The acetates having additional olefin moiety **3l** and **3m** worked. The γ-adducts *syn*-**4J** and *syn*-**4K** were obtained from the indium reagent **J** as a single isomer in H_2O−

SCHEME 7



SCHEME 8



THF (Scheme 7).[15] In contrast, the reactions in anhydrous THF gave the α-adducts **5J** and **5K** via the indium reagent **K**.[16] Thus, the γ-adducts and α-adducts could be obtained by change of the reaction conditions.

The reaction with α,γ-disubstituted acetate **3n** in H_2O−THF gave selectively the product *syn*-**4L** in 77% yield as a single diastereomer, as a result of the reaction with the stable indium reagent **M**, although the reaction with **3n** in anhydrous THF gave a complex mixture (Scheme 8).

Reaction of *N*-Sulfonylimine. In comparison with the reaction of glyoxylic oxime ether **1**, we next investigated the allylation of *N*-sulfonylimine **6** under the similar reaction conditions (Scheme 9).[6,17] Although the reaction of **6** proceeded smoothly, the formation of α-adducts was not observed. In all case, the γ-adducts were obtained even in anhydrous THF. These observations indicate that the allylation of *N*-sulfonylimine **6** was not a reversible process due to the extra stabilization of indium-bonding adduct **P** by the electron-withdrawing *N*-sulfonyl group. The reaction of **6** with allyl acetate **8** proceeded smoothly in THF at 20 °C to give 86% yield of the product **7A** (Table 3, entry 1). In contrast to glyoxylic oxime ether **1**, the reactions of **6** with substituted allylic acetates and carbonates **2a**,**b** and **3a**−**c** proceeded smoothly to give the γ-adducts *syn*-**7B** and *syn*-**7C**,

SCHEME 9

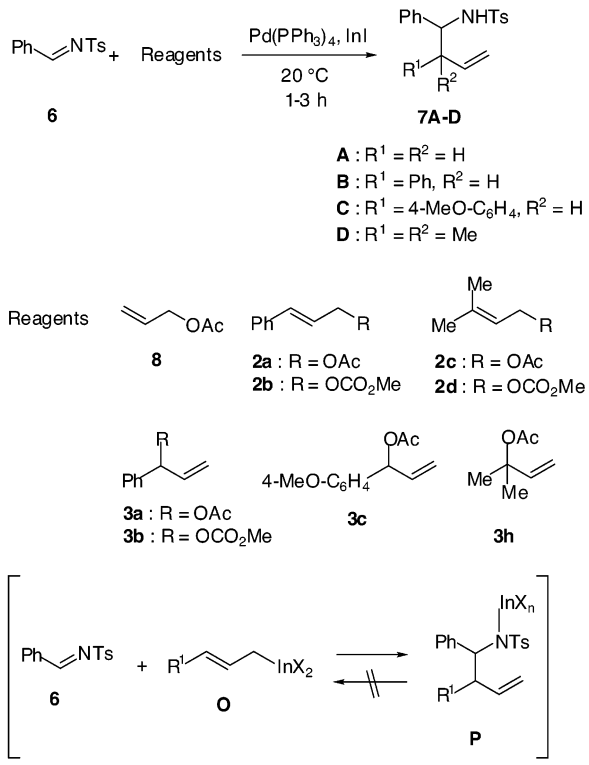


TABLE 3. Reaction of 6 with Allyl Alcohol Derivatives[a]

entry	reagent	solvent	product	yield[b] (%)
1	**8**	THF	**7A**	86
2	**2a**	THF	*syn*-**7B**[c]	66
3	**2b**	THF	*syn*-**7B**[c]	77
4	**3a**	THF	*syn*-**7B**[c]	65
5	**3b**	THF	*syn*-**7B**[c]	68
6	**3c**	THF	*syn*-**7C**[c]	85
7	**2c**	THF	**7D**	trace
8	**2d**	THF	**7D**	21
9	**3h**	THF	**7D**	36
10	**3a**	H_2O−THF	*syn*-**7B**[c]	58
11	**3c**	H_2O−THF	*syn*-**7C**[c]	65
12	**3a**	H_2O−EtOH	*syn*-**7B**[c]	31
13	**3h**	H_2O−THF	**7D**	16

[a] Reactions were carried out with **6** and allyl alcohol derivatives at 20 °C. [b] Isolated yields. [c] Only syn isomers were obtained (>95% de).

(15) At present, the rigorous stereochemical assignment of the mixture of diastereomers **4K** was not achieved. However, a high degree of stereocontrol regarding the stereocenter on α-carbon was generally observed by using camphorsultam derivative of glyoxylic oxime ether **1**. See refs 7b, 9, and 10.

(16) The diastereoselectivities of products **5J** and **5K** were determined after hydrogenolysis of the olefin moiety, which gave the single diastereoisomer, respectively.

(17) Chan's group reported the metallic indium-mediated allylation of *N*-sulfonylimines in aqueous media through an allylindium(I) intermediate. See ref 8a−c.

accompanied by a trace amount of anti isomer, without the formation of the α-adducts (entries 2−6). The bulky γ,γ-dimethylallyl acetate **2c** and carbonate **2d** were less effective for the allylation reaction of *N*-sulfonylimine **6** (entries 7 and 8). The reaction of **6** with α, α-dimethylallyl acetate **3h** gave the γ-adduct **7D** in 36% yield (entry 9). The reaction of *N*-sulfonylimine **6** also proceeded in aqueous media (entries 10−13).

Conclusions

We have demonstrated that the palladium−indium iodide-mediated reaction of glyoxylic oxime ether afforded either the γ-adducts or the α-adducts by change of the reaction conditions. In contrast, the reactions of *N*-sulfonylimine proceeded regioselectively to provide the γ-adducts. In addition to the radical reaction of glyoxylic oxime ether,[7,9] the present reaction disclosed a broader aspect of the utility of glyoxylic oxime ether for the asymmetric synthesis of various types of α-amino acid derivatives.

Experimental Section

General Procedure for Allylation of Oxime Ether 1 in THF. A mixture of **1** (47.1 mg, 0.125 mmol), allylic reagents (0.25 mmol), $Pd(PPh_3)_4$ (7.3 mg, 0.0063 mmol), and indium iodide (60 mg, 0.25 mmol) in THF (1.0 mL) was stirred under argon atmosphere at 20 °C for 20 h. The reaction mixture was diluted with saturated aqueous potassium sodium (+)-tartrate and then extracted with AcOEt. The organic phase was dried over $MgSO_4$ and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane/AcOEt = 4:1, 2-fold development) afforded the α-adducts.

General Procedure for Allylation of Oxime Ether 1 in H_2O−THF (1:10, v/v). A mixture of **1** (47.1 mg, 0.125 mmol), allylic reagents (0.25 mmol), $Pd(PPh_3)_4$ (7.3 mg, 0.0063 mmol), and indium iodide (60 mg, 0.25 mmol) in H_2O−THF (1:10, v/v, 1.1 mL) was stirred under argon atmosphere at 20 °C for 3 h. The reaction mixture was diluted with saturated aqueous potassium sodium (+)-tartrate and then extracted with AcOEt. The organic phase was dried over $MgSO_4$ and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane/AcOEt = 4:1, 2-fold development) afforded the γ-adducts.

The diastereoselectivities of products were determined by ^{1}H NMR analysis of diastereomeric mixture obtained after rough purification of chromatography (hexame/AcOEt = 2:1).

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-1-oxo-5-phenyl-2-[(phenylmethoxy)amino]-4-pentenyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (5A): colorless oil; $[\alpha]^{33}_D$ −59.4 (*c* 0.94, $CHCl_3$); IR ($CHCl_3$) 3270, 1692, 1601 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.39−7.15 (10H, m), 6.38 (1H, d, *J* = 15.6 Hz), 6.13 (1H, dt, *J* = 15.6, 7.0 Hz), 4.73, 4.68 (2H, AB q, *J* = 11.6 Hz), 4.54 (1H, br s), 3.96 (1H, br t, *J* = 6.1 Hz), 3.48, 3.45 (2H, AB q, *J* = 13.8 Hz), 2.51−2.45 (2H, m), 2.10−1.74 (5H, m), 1.46−1.26 (2H, m), 0.93, 0.90 (each 3H, s); ^{13}C NMR ($CDCl_3$) δ 173.1, 137.8, 137.0, 133.1, 128.6, 128.4, 128.1, 127.6, 127.3, 126.3, 124.3, 75.9, 65.1, 62.8, 53.0, 48.5, 47.6, 44.5, 38.2, 34.3, 32.8, 26.3, 20.6, 19.8; MS (FAB) *m*/*z* 495 (M + H$^+$, 90), 91 (100); HRMS calcd for $C_{28}H_{35}N_2O_4S$ (M + H$^+$) 495.2318, found 495.2327.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-5-(4-methoxyphenyl)-1-oxo-2-[(phenylmethoxy)amino]-4-pentenyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (5B): colorless oil; $[\alpha]^{34}_D$ −130 (*c* 2.17, $CHCl_3$); IR ($CHCl_3$) 3270, 1692, 1606 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.47−7.20 (7H, m), 6.81 (2H, d, *J* = 8.5 Hz), 6.32 (1H, d, *J* = 15.9 Hz), 5.97 (1H, m), 4.74, 4.69 (2H, AB q, *J* = 11.9 Hz), 4.53 (1H, br s), 3.96 (1H, br m), 3.80 (3H, s), 3.48, 3.45 (2H, AB q, *J* = 14.1 Hz), 2.47 (2H, br m), 2.10−1.78 (5H, m), 1.46−1.23 (2H, m), 0.94, 0.91 (each 3H, s); ^{13}C NMR ($CDCl_3$) δ 173.2, 159.0, 137.8, 132.6, 129.9, 128.6, 128.2, 127.6, 127.4, 121.9, 113.8, 75.9, 65.1, 62.9, 55.3, 53.1, 48.5, 47.7, 44.6, 38.3, 34.3, 32.8, 26.4, 20.7, 19.9; MS (FAB) *m*/*z* 525 (M + H$^+$, 35), 154 (100); HRMS calcd for $C_{29}H_{37}N_2O_5S$ (M + H$^+$) 525.2423, found 525.2409.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-5-(2-methoxyphenyl)-1-oxo-2-[(phenylmethoxy)amino]-4-pentenyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (5C): colorless crystal; mp 133−136 °C (AcOEt/hexane); $[\alpha]^{25}_D$ −85.0 (c 1.05, $CHCl_3$); IR ($CHCl_3$) 3032, 1693 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.43−7.22 (6H, m), 7.18 (1H, t, *J* = 6.4 Hz) 6.88 (1H, t, *J* = 6.4 Hz) 6.82 (1H, d, *J* = 8.2 Hz), 6.71 (1H, d, *J* = 15.9 Hz) 6.20 (1H, d, *J* = 11.0 Hz) 6.10 (1H, m), 4.74, 4.68 (2H, AB q, *J* = 10.6 Hz), 4.60−4.48 (1H, m), 4.01−3.92 (1H, m), 3.79 (3H, s), 3.53−3.40 (2H, m), 2.59−2.48 (2H, m), 2.05−2.03 (2H, br m), 1.94−1.79 (2H, m), 1.79−1.72 (1H, s), 1.43−1.26 (2H, m) 0.95, 0.90 (each 3H, s); ^{13}C NMR ($CDCl_3$) δ 173.2, 156.4, 137.9, 128.6, 128.1, 127.6, 126.9, 126.1, 124.7, 120.5, 110.6, 75.8, 65.0, 62.8, 55.3, 53.0, 48.4, 47.6, 44.5, 38.1, 34.7, 32.7, 26.3, 20.5, 19.7; MS (FAB) *m*/*z* 525 (M + H$^+$, 100); HRMS calcd for $C_{29}H_{37}N_2O_5S$ (M$^+$) 525.2423, found 525.2438. Anal. Calcd for $C_{29}H_{36}N_2O_5S$: C, 66.39; H 6.92; N 5.34; S, 6.11. Found: C, 66.24; H 6.88; N 5.06; S, 6.16. Some peaks of ^{13}C NMR were missing due to overlap.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-5-(4-methylphenyl)-1-oxo-2-[(phenylmethoxy)amino]-4-pentenyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (5D): colorless crystal; mp 157−161 °C (AcOEt/hexane); $[\alpha]^{25}_D$ −67.0 (c 0.93, $CHCl_3$); IR ($CHCl_3$) 1693 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.43−7.22 (5H, m), 7.18 (2H, d, *J* = 7.4 Hz), 7.08 (2H, d, *J* = 7.4 Hz), 6.34 (1H, d, *J* = 15.3 Hz), 6.19 (1H, br d, *J* = 10.7 Hz), 6.06 (1H, m), 4.73, 4.68 (2H, AB q, *J* = 11.6 Hz), 4.52 (1H, br m), 3.96 (1H, br m), 3.48, 3.46 (2H, AB q, *J* = 14.4 Hz), 2.47 (2H, br m), 2.32 (3H, s), 2.07−1.75 (5H, m), 1.47−1.25 (2H, m), 0.95, 0.91 (each 3H, s); ^{13}C NMR ($CDCl_3$) δ 173.2, 137.8, 137.0, 134.2, 133.0, 129.0, 128.7, 128.1, 127.6, 126.2, 123.1, 75.9, 65.1, 62.8, 53.1, 48.5, 47.7, 44.5, 38.3, 34.3, 32.8, 26.4, 21.2, 20.7, 19.8; MS (FAB) *m*/*z* 509 (M + H$^+$, 100); HRMS calcd for $C_{29}H_{37}N_2O_4S$ (M + H$^+$) 509.2474, found 509.2482. Anal. Calcd for $C_{29}H_{36}N_2O_4S$: C, 68.47; H, 7.13; N, 5.51; S, 6.30. Found: C, 68.20; H, 7.07; N, 5.25; S, 6.37.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-5-(2-methylphenyl)-1-oxo-2-[(phenylmethoxy)amino]-4-pentenyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (5E): colorless crystal; mp 129−132 °C (AcOEt/hexane); $[\alpha]^{25}_D$ −75.8 (c 0.87, $CHCl_3$); IR ($CHCl_3$) 3032, 1693 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.37−7.24 (6H, m), 7.13−7.10 (3H, m), 6.69 (1H, d, *J* = 15.6 Hz), 6.20 (1H, m), 6.00 (1H, m), 4.74, 4.67 (2H, AB q, *J* = 11.9 Hz), 4.54 (1H, m), 3.97 (1H, br t), 3.48 (2H, m) 2.55 (2H, m), 2.26 (3H, s), 2.05 (2H, m), 2.19−1.79 (3H, m), 1.42−1.30 (2H, m) 1.26, 1.15 (each 3H, s); ^{13}C NMR ($CDCl_3$) δ 173.0, 137.8, 136.0, 135.0, 131.1, 131.0, 128.6, 128.1, 127.6, 127.2, 125.9, 125.7, 125.5, 75.9, 65.0, 62.9, 62.7, 53.0, 48.5, 47.7, 44.5, 38.2, 34.5, 32.7, 26.2, 20.6, 19.7; MS (FAB) *m*/*z* 509 (M + H$^+$, 100); HRMS calcd for $C_{29}H_{37}N_2O_4S$ (M + H$^+$) 509.2474, found 509.2479. Anal. Calcd for $C_{29}H_{36}N_2O_4S$: C, 68.47; H 7.13; N 5.51; S, 6.30. Found: C, 68.25; H 7.06; N 5.27; S, 6.42.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-5-(4-fluorophenyl)-1-oxo-2-[(phenylmethoxy)amino]-4-pentenyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (5F): colorless crystal; mp 157−161 °C (AcOEt/hexane); $[\alpha]^{25}_D$ −67.0 (*c* 0.93, $CHCl_3$); IR ($CHCl_3$) 1693 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.43−7.22 (5H, m), 7.18 (2H, d, *J* = 7.4 Hz), 7.08 (2H, d, *J* = 7.4 Hz), 6.34 (1H, d, *J* = 15.3 Hz), 6.19 (1H, br d, *J* = 10.7 Hz), 6.06 (1H, m), 4.73, 4.68 (2H, AB q, *J* = 11.6 Hz), 4.52 (1H, br m), 3.96 (1H, br m), 3.48, 3.46 (2H, AB q, *J* = 14.4 Hz), 2.47 (2H, br m), 2.32 (3H, s), 2.07−1.75 (5H, m), 1.47−1.25 (2H, m), 0.95, 0.91 (each 3H, s); ^{13}C

NMR ($CDCl_3$) δ 173.2, 137.8, 137.0, 134.2, 133.0, 129.0, 128.7, 128.1, 127.6, 126.2, 123.1, 75.9, 65.1, 62.8, 53.1, 48.5, 47.7, 44.5, 38.3, 34.3, 32.8, 26.4, 21.2, 20.7, 19.8; MS (FAB) *m*/*z* 509 (M + H^+, 100); HRMS calcd for $C_{29}H_{37}N_2O_4S$ (M + H^+) 509.2474, found 509.2482. Anal. Calcd for $C_{29}H_{36}N_2O_4S$: C, 68.47; H, 7.13; N, 5.51; S, 6.30. Found: C, 68.20; H, 7.07; N, 5.25; S, 6.37.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-5-cyclohexyl-1-oxo-2-[(phenylmethoxy)amino]-4-pentenyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (5I): colorless crystal; mp 96−98 °C (AcOEt/hexane); $[\alpha]^{27}_D$ −74.5 (c 1.08, $CHCl_3$); IR ($CHCl_3$) 3280, 1694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40−7.22 (5H, m), 6.13 (1H, br d, *J* = 7.9 Hz), 5.39 (1H, dd, *J* = 15.3, 6.4 Hz), 5.25 (1H, m), 4.71, 4.66 (2H, AB q, *J* = 11.9 Hz), 4.41 (1H, br s), 3.96 (1H, br m), 3.49, 3.46 (2H, AB q, *J* = 13.7 Hz), 2.34, 2.26 (each 1H, m), 2.10−2.00 (2H, m), 1.95−1.78 (4H, m), 1.69−1.55 (5H, m), 1.48−0.90 (7H, m), 1.14, 0.97 (each 3H, s); ^{13}C NMR ($CDCl_3$) δ 173.0, 140.5, 137.9, 128.6, 128.1, 127.6, 121.1, 75.8, 64.9, 62.9, 53.0, 48.5, 47.7, 44.5, 40.5, 38.3, 33.7, 32.8, 32.6, 26.3, 26.0, 25.9, 20.8, 19.8; MS (FAB) *m*/*z* 91 (100), 501 (M + H^+, 98); HRMS calcd for $C_{28}H_{41}N_2O_4S$ (M + H^+) 501.2787, found 501.2782. Anal. Calcd for $C_{28}H_{40}N_2O_4S$: C, 67.17; H, 8.05; N, 5.59; S, 6.40. Found: C, 67.39; H, 7.89; N, 5.57; S, 6.69.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-5-methyl-1-oxo-2-[(phenylmethoxy)amino]-4-hexenyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (5J): colorless oil as a 1:1 *E*/*Z* mixture; $[\alpha]^{24}_D$ −94.0 (*c* 1.31, $CHCl_3$); IR ($CHCl_3$) 3280, 1693 cm^{-1};^1H NMR ($CDCl_3$) δ 7.43−7.23 (5H, m), 6.23 (1H, m), 6.14 (1H, m), 5.97 ($^1/_2$H, d, *J* = 11.6 Hz), 5.72 ($^1/_2$H, d, *J* = 11.0 Hz), 5.42 ($^1/_2$H, m), 5.26 ($^1/_2$H, m), 4.73, 4.67 ($^1/_2$ × 2H, AB q, *J* = 11.9 Hz), 4.72, 4.66 ($^1/_2$ × 2H, AB q, *J* = 11.9 Hz), 4.47 (1H, br s), 3.96 (1H, br m), 3.50, 3.46 (2H, AB q, *J* = 13.7 Hz), 2.58 ($^1/_2$H, m), 2.39 (1H, m), 2.35 ($^1/_2$H, m), 2.13−1.78 (5H, m), 1.77, 1.74, 1.71, 1.69 (each $^1/_2$ × 3H, s), 1.46−1.25 (2H, m), 1.13, 1.11 (each $^1/_2$ × 3H, s), 0.96 (3H, s); ^{13}C NMR ($CDCl_3$) δ 173.3, 173.2, 137.8, 136.6, 134.4, 130.3, 128.7, 128.2, 127.7, 127.6, 124.7, 124.3, 122.0, 120.0, 75.8, 65.0 (× 2), 62.8, 62.7, 53.0, 48.5 (× 2), 47.7 (× 2), 44.6, 38.2, 38.1, 34.1, 32.8, 28.6, 26.4, 26.3, 26.2, 25.8, 20.7, 19.8, 18.1 (× 2); MS (FAB) *m*/*z* 473 (M + H^+, 100); HRMS calcd for $C_{26}H_{37}N_2O_4S$ (M + H^+) 473.2474, found 473.2478. Some peaks of ^{13}C NMR were missing due to overlap.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-1-oxo-7-phenyl-2-[(phenylmethoxy)amino]-4,6-heptadienyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (5K): amorphous substance as a 6:1 *E*/*Z* mixture; $[\alpha]^{26}_D$ −54.1 (*c* 1.37, $CHCl_3$); IR ($CHCl_3$) 3280, 1730, 1693, 1601 cm^{-1};^1H NMR ($CDCl_3$) δ 7.42−7.17 (10H, m), 6.97 ($^1/_7$H, dd, *J* = 14.9, 11.6 Hz), 6.67 ($^6/_7$H, dd, *J* = 15.5, 10.7 Hz), 6.53 ($^1/_7$H, d, *J* = 15.8 Hz), 6.43 ($^6/_7$H, d, *J* = 15.8 Hz), 6.25−6.12 (2H, m), 5.72 ($^6/_7$H, m), 5.47 ($^1/_7$H, m), 4.73, 4.67 (2H, AB q, *J* = 11.6 Hz), 4.51 (1H, br s), 3.96 (1H, br m), 3.50, 3.47 (2H, AB q, *J* = 13.7 Hz), 2.72 ($^1/_7$H, m), 2.47 ($^6/_7$H, m), 2.43 (1H, m), 2.15−1.76 (5H, m), 1.48−1.20 (2H, m), 1.11, 0.94 (each 3H, s); ^{13}C NMR ($CDCl_3$) δ 173.1, 137.8, 137.3, 133.8, 131.5, 128.7, 128.6, 128.4, 128.2, 127.6, 127.4, 126.5, 126.3, 75.9, 65.0, 62.7, 53.0, 48.5, 47.7, 44.5, 38.2, 34.0, 32.7, 26.3, 20.7. 19.8; MS (FAB) *m*/*z* 521 (M + H^+, 100); HRMS calcd for $C_{30}H_{37}N_2O_4S$ (M + H^+) 521.2474, found 521.2470. ^{13}C NMR values are for the major *E*-isomer.

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Supporting Information Available: General experimental procedure for reaction of *N*-sulfonylimine **6** and characterization data for γ-adducts **4A**−**L** and **7A**−**D** and ^1H and ^{13}C NMR spectra of all obtained compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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