Intermolecular cycloaddition of ethyl glyoxylate O-tert- butyldimethylsilyloxime with alkenes

著者	Tamura Osamu, Morita Nobuyoshi, Takano Yuu, Fukui Kenji, Okamoto Iwao, Huang Xin, Tsutsumi Yoshiyuki, Ishibashi Hiroyuki
journal or publication title	Synlett
volume	4
page range	658-660
year	2007-03-01
URL	http://hdl.handle.net/2297/7022

doi: 10.1055/s-2007-967939

Intermolecular Cycloaddition of Ethyl Glyoxylate *O*-*tert*-Butyldimethylsilyloxime with Alkenes

Osamu Tamura,*[a] Nobuyoshi Morita,[a] Yuu Takano,[a] Kenji Fukui,[a] Iwao Okamoto,[a] Xin Huang,[b] Yoshiyuki Tsutsumi,[b] Hiroyuki Ishibashi *[b]

[a] Showa Pharmaceutical University, Higashi-tamagawagakuen, Machida, Tokyo 194-8543, Japan

Fax +81(42)721-1579; E-mail: tamura@ac.shoyaku.ac.jp

[b] Division of Pharmaceutical Sciences, Graduate School of National Science and Technology, Kanazawa University, Kanazawa 920-1192, Japan

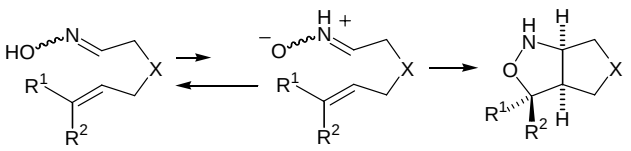
Fax +81(76)234-4476; E-mail: isibasi@p.kanazawa-u.ac.jp

Received: *The date will be inserted once the manuscript is accepted*

Abstract: Ethyl glyoxylate *O*-*tert*-butyldimethylsilyloxime (**12**), on treatment with various alkenes **7** in the presence of 2.2 equiv. of BF_3•OEt_2, generated *C*-ethoxycarbonyl *N*-boranonitrone (**13**), which underwent intermolecular cycloaddition to afford 3-(ethoxycarbonyl)isoxazolidines **14** in moderate to high yields.

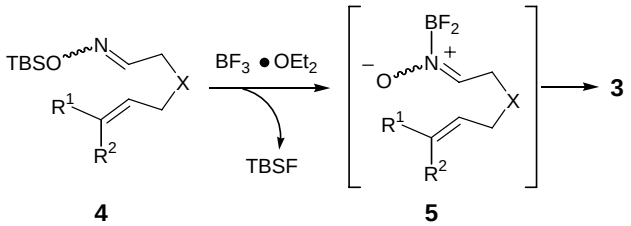
Key words: cycloaddition, boron trifluoride, *N*-boranonitrone, alkenes, cycloadducts

Intramolecular oxime-olefin cycloaddition, so called IOOC, appears to be one of the operationally simplest cycloadditions. Thus, heating oximes **1** bearing an olefin moiety in the molecule give *N*-nonsubstituted isoxazolidines **3** via tautomerization from **1** to NH-nitrone **2**.[1,2] However, the cycloaddition often require very high temperature conditions because of the thermodynamically unfavorable tautomerization (Scheme 1).[3] In addition, intermolecular oxime-olefin cycloaddition is known to be restricted to reactions of only a few oximes with *N*-methyl or *N*-phenylmareimides.[4,5]



1 **2** **3**

Scheme 1



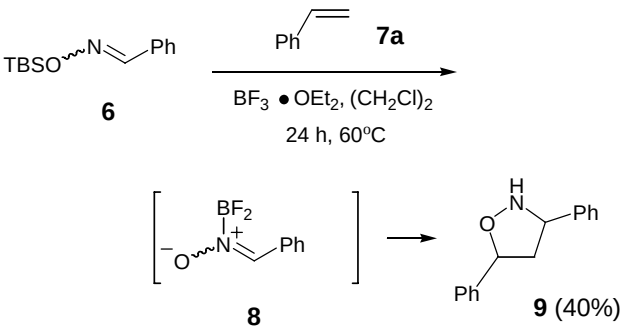
4 **5**

Scheme 2

Recently, we reported BF_3-mediated cycloaddition of *O*-*tert*-butyldimethylsilyloximes (*O*-TBS oximes) as an alternative method for the efficient synthesis of isoxazolidines **3**. Treatment of oximes **4** with BF_3•OEt_2 generates *N*-boranonitrones **5**, which undergo intramolecular cycloaddition affording the products **3** after extractive workup (Scheme 2).[6] This procedure is highly useful for synthesis of isoxazolidine derivatives because the reaction proceeds smoothly at room temperature using the strong N-B and Si-F affinity and is applicable to various substrates giving the corresponding products in good to high yields.

We envisioned the extension of this procedure to the intermolecular counter part, and have now found that exposure of ethyl glyoxylate *O*-TBS oxime **12** to BF_3•OEt_2 in the presence of various alkenes **7** underwent intermolecular cycloaddition to afford cycloadducts **14** in moderate to good yields.[7,8]

Our investigation began with the simplest extension of the intramolecular cycloaddition to intermolecular version (Scheme 3). When benzaldehyde *O*-TBS oxime **6** was treated with styrene (**7a**) (10 eq.) in the presence of 2.2 eq. of BF_3•OEt_2 in $(CH_2Cl)_2$ at 60 °C for 24 h, intermolecular cycloaddition proceeded, however, to give only 40% yield of cycloadduct **9**.[9]

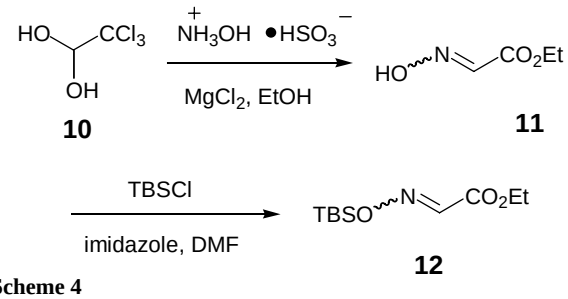


6 **7a** **8** **9** (40%)

Scheme 3

From the viewpoint of the electrophilic nature of *N*-boranonitrone, replacement of the phenyl group in

nitrone **8** by an ester group was examined to activate the intermediary *N*-boranonitrone.[10] The requisite *O*-TBS oxime **12** was readily prepared from chloral hydrate (**10**) which react with hydroxyammonium sulfate in the presence of $MgCl_2$ in ethanol solution to furnish glyoxylate oxime (**11**)[11] (Scheme 4). Silylation of ethyl glyoxylate oxime **11** afforded ethyl glyoxylate *O*-TBS oxime **12** in 86% yield.[12]



Scheme 4

The intermolecular cycloadditions of the starting *O*-TBS oxime **12** with various alkenes **7** were carried out in the presence of 2.2 eq. of BF_3•OEt_2 in $(CH_2Cl)_2$ under argon at 60 °C. (Scheme 5, Table 1). In contrast to the reaction of benzaldehyde oxime **6**, reaction of oxime **12** with styrene (**7a**) smoothly proceeded to give the corresponding cycloadduct **14a** in 71% yield, probably via nitrone **13** as active intermediate (entry 1).[13] Reaction of aliphatic terminal alkene **7b** and **7c** also afforded the cycloadduct **14b** and **14c** in 78% and 61% yields as 77:1 (**14b**) and 7:1 (**14c**) mixture of diastereomer respectively (entries 2 and 3). As expected, 1,1-disubstituted alkenes **7d** reacted with nitrone **13**, giving rise to 5,5-disubstituted isoxazolidine **14d** in low yield (entry 4). This low yield may be due to porimerization of alkene **7d** during the reaction. Reactions of 1-methyl cyclopentene (**7e**) afforded bicyclic products **14e** in 79% yields as 3.4:1 mixture of diastereomer (entry 5).

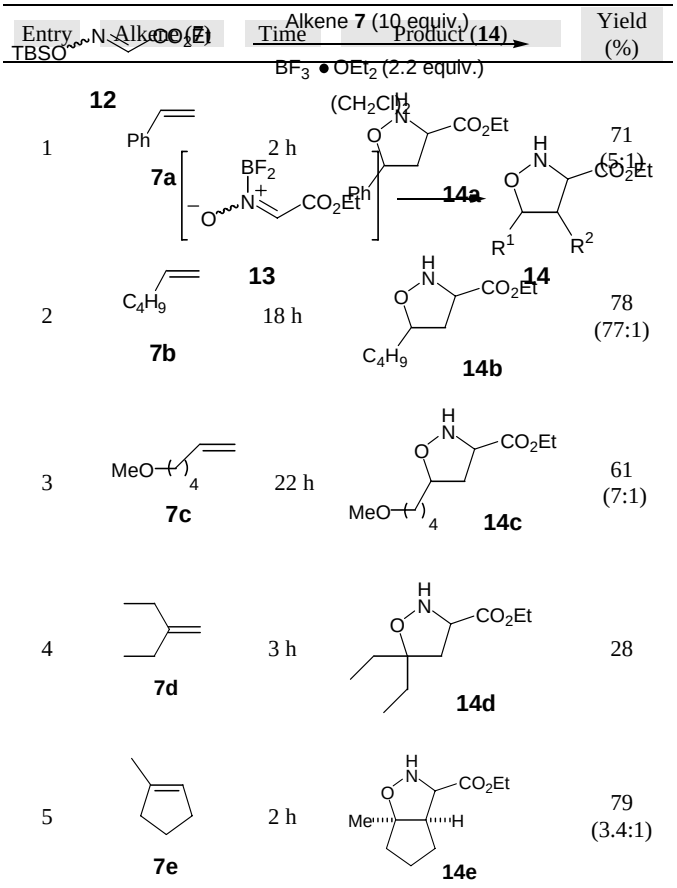
The *N*-boranonitrone **13** was found to react with 2-substituted acrylate (Scheme 6). When oxime **12** was treated with ethyl acrylate (**7g**) in the presence of BF_3•OEt_2 in $(CH_2Cl)_2$ at 60 °C for 15 h, cycloadduct **14g** was obtained in 53% yield as a 7:1 mixture of diastereomers. This reaction would be applicable for syntheses of naturally occurring 4-hydroxy-4-substituted glutamic acids.[14]

Scheme 6

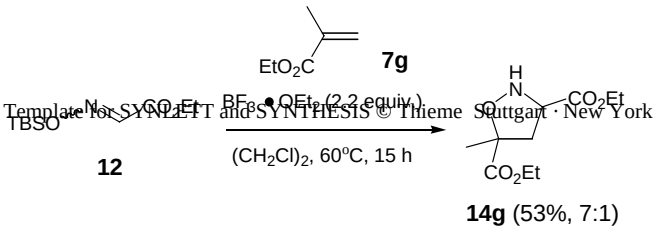
In conclusion, we have developed a novel intermolecular cycloaddition of *O*-TBS oxime **12** with various alkenes **7** via *N*-boranonitrone **13** as active intermediate, giving the corresponding isoxazolidines **14**. To the best of our knowledge, the present reaction is the first example of intermolecular cycloaddition of oxime derivatives that can react with various alkenes. Further work will be devoted to the extension of the procedure to the other functionalized oximes and alkenes, as well as to the application of the procedure in natural product synthesis.

Scheme 5

Table 1. Intermolecular Cycloaddition of *O*-TBS oxime **12** with Alkenes **7a-e** in the presence of BF_3•OEt_2[a]



[a] All reactions were carried out with 2.2 equiv of BF_3•OEt_2 in $(CH_2Cl)_2$ at 60 °C.



Acknowledgment

Financial support of this study by a Grant-in-Aid for Scientific Research on Priority Area “Creation of Biologically Functional Molecules” from the Ministry of Education, Culture, Sports, Science, and Technology of Japan is gratefully acknowledged.

References

(1) For pioneering works, see: (a) Oppolzer, W.; Keller, K. *Tetrahedron Lett.* **1970**, *11*, 1117. (b) Wildman, W. C.; Slabaugh, M. R. *J. Org. Chem.* **1971**, *36*, 3202.

(2) For recent examples, see: (a) Abiko, A.; Liu, J.-F.; Wang, G.; Masamune, S. *Tetrahedron Lett.* **1997**, *38*, 3261. (b) Baskaran, S.; Aurich, H. G. *Synlett* **1998**, 277. (c) Sharma, G. V. M.; Srinivas, R. I.; Goverdhan, R. V.; Rama, R. A. V. *Tetrahedron: Asymmetry* **1999**, *10*, 229. (d) Falb, E.; Bechor, Y.; Nudelman, A.; Hassner, A.; Albeck, A.; Gottlieb, H. E. *J. Org. Chem.* **1999**, *64*, 498. (e) Dransfield, P. J.; Moutel, S.; Shipman, M.; Sik, V. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3349. (f) Noguchi, M.; Okada, H.; Tanaka, M.; Matsumoto, S.; Kakehi, A.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 917. (g)

Cheng, Q.; Zhang, W.; Tagami, Y.; Oritani, T. *J. Chem. Soc., Perkin Trans. 1* **2001**, 452. (h) Singh, S.; Ishar, M. P. S.; Singh, G.; Singh, R. *Canadian J. Chem.* **2005**, *83*, 260.

(3) For a theoretical study on oxime-nitrone isomerization, see: Long, J. A.; Harris, N. J.; Lammertsma, K. *J. Org. Chem.* **2001**, *66*, 6762.

(4) (a) Grigg, R.; Thianpantagul, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 653. (b) Shirai, M.; Kuwabara, H.; Matsumoto, S.; Yamamoto, H.; Kakehi A.; Noguchi, M. *Tetrahedron* **2003**, *59*, 4113.

(5) For related palladium-catalyzed cycloaddition of oximes, see: Frederickson, M.; Grigg, R.; Thornton-Pett, M.; Redpath, J. *Tetrahedron Lett.* **1997**, *38*, 7777.

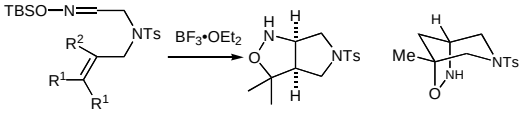
(6) (a) Tamura, O.; Mitsuya, T.; Ishibashi, H. *Chem. Commun.* **2002**, 1128. (b) Tamura, O; Mitsuya, T.; Huang, X.; Tsutsumi, Y.; Hattori, S.; Ishibashi, H. *J. Org. Chem.* **2005**, *70*, 10720.

(7) For a review on related *N*-metallo-azomethine ylides, see: Husineca, S.; Savic, V. *Tetrahedron: Asymmetry* **2005**, *16*, 2047.

(8) For related cycloaddition of acylhydrazones, see: (a) Wilson, R. M.; Rekers, J. W. *J. Am. Chem. Soc.* **1979**, *101*, 4005. (b) Kobayashi, S.; Shimizu, H.; Yamashita, Y.; Ishitani, H.; Kobayashi, J. *J. Am. Chem. Soc.* **2002**, *124*, 13678. (c) Kobayashi, S.; Hirabayashi, R.; Shimizu, H.; Ishitani, H.; Yamashita, Y. *Tetrahedron Lett.* **2003**, *44*, 3351. (d) Yamashita, Y.; Kobayashi, S. *J. Am. Chem. Soc.* **2004**, *126*, 11279. (e) Shirakawa, S.; Lombardi, P. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 9974.

(9) For completion of the cycloaddition, two equiv. of BF_3•OEt_2 are essential. See ref 6.

(10) During study on the intramolecular cycloaddition of *N*-boranonitrone, we observed the tendency that electron-rich carbon atom in the olefin attacks the nitrone-carbon. For example, reaction of oxime **15a** with BF_3•OEt_2 afforded cycloadduct **16** bearing bicyclo[3.3.0] system whereas a similar reaction of oxime **15b** afforded cycloadduct **17** having bicyclo[3.2.1] system. See ref 6b.



15a: R^1 = Me,R^2 = H **16** **17**
15b: R^1 = H, R^2 = Me

(11) Adachi, I.; Yamamori, T.; Hiramatsu, Y. JP 1977-50939.

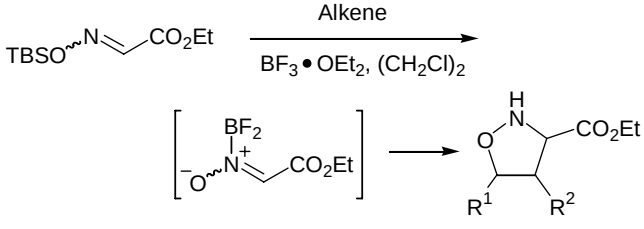
(12) Preparation of ethyl 2-[*tert*-butyldimethylsilyloxy-imino]acetate (**12**): The mixture of ethyl 2-hydroxyiminoacetate (**11**) [11] (0.91 g, 7.8 mmol), *tert*-butylchlorodimethylsilane (1.77 g, 11.8 mmol), and imidazole (1.60 g, 23.5 mmol) in DMF (12 ml) was stirred at room temperature for 46 h. The reaction mixture was poured into water and extracted with Et_2O. The combined organic phases were washed with brine and dried with $MgSO_4$. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography on silica gel with hexane-OEt_2 (20:1) to afford **12** (1.77 g, 98%) as a colorless oil. IR 2934, 1749, 1728 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (1H, s), 4.30 (2H, *J* = 7.1 Hz), 1.33 (3H, t, *J* = 7.1 Hz), 0.95 (9H, s), 0.23 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 146.1, 61.3, 25.7, 18.0, 14.0, -5.4; LRMS 231.14; HRMS (EI): calcd for $C_{10}H_{21}NO_3Si$ 231.1291, found 231.1270.

(13) Typical procedure for the cycloaddition: To a solution of **12** (300 mg, 1.3 mmol) in $(CH_2Cl)_2$ (10 mL) was added **7e** (1.1 mL, 13 mmol) and BF_3•OEt_2 (310 μL, 2.9 mmol) at room temperature, and then the mixture was heated at 60 °C for 2 h (The reaction was monitored by thin layer chromatography). After cooling, the reaction mixture was poured into saturated $NaHCO_3$ solution and was extracted with $CHCl_3$. The combined organic layer were washed with brine and dried with $MgSO_4$. The residue was concentrated under reduced pressure. The crude product was purified by chromatography on silica gel with hexane-AcOEt (3:2) to give two diastereomers, **14e** (160 mg, 61%) and **14e'** (47 mg, 18%) as light brown oil. IR (neat) 1733 cm^{-1}; **14e**: ^1H NMR (300 MHz, $CDCl_3$) δ 5.90 (1H, br s), 4.23 (1H, q, *J* = 7.1 Hz), 4.12 (1H, d, *J* = 7.5 Hz), 2.73 (1H, dd, *J* = 14.5, 7.0 Hz), 1.77 (4H, m), 1.50 (2H, m), 1.40 (3H, s), 1.29 (1H, t, *J* = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 95.5, 66.0, 61.1, 55.7, 39.5, 28.2, 26.4, 24.8, 14.2; LRMS 199.10; found HRMS (EI) calcd for $C_{10}H_{17}NO_3$ 199.1208, found 221.1187; **14e'**: ^1H NMR (300 MHz, $CDCl_3$) δ 5.93 (1H, br s), 4.23 (1H, q, *J* = 7.1 Hz), 3.56 (1H, d, *J* = 6.6 Hz), 2.49 (1H, s), 1.60 (6H, m), 1.37 (3H, m), 1.29 (3H, d, *J* = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 96.1, 70.2, 61.4, 59.5, 38.5, 32.2, 24.4, 23.5, 14.1;

(14) (a) Baldwin, S. W.; Long, A. *Org. Lett.* **2004**, *6*, 1653. (b) Tamura, O.; Shiro, T.; Ogasawara, M.; Toyao, A.; Ishibashi, H. *J. Org. Chem.* **2005**, *70*, 4569.

Graphic Abstract

Intermolecular Cycloaddition of Ethyl Glyoxylate *O-tert*-Butyldimethyl-silyloxime with Alkenes



Osamu Tamura* Nobuyoshi Morita, Yuu Takano, Kenji Fukui, Iwao Okamoto, Xin Huang, Yoshiyuki Tsutsumi, Hiroyuki Ishibashi*