DOI: 10.1002/asia.201400110

## Enantiospecific Synthesis and Cytotoxicity Evaluation of Ligudentatol: A Programmed Aromatization Approach to the 2,3,4-Trisubstituted Phenolic Motif via Visible-Light-Mediated Group Transfer Radical Cyclization

# Gamal A. I. Moustafa, Hiroshi Suizu, Hiroshi Aoyama, Masayoshi Arai, Shuji Akai, and Takehiko Yoshimitsu\*<sup>[a]</sup>

Abstract: A facile enantiospecific approach to (+)-ligudentatol (1) and (-)-ligudentatol (ent-1) is reported. The approach features the construction of a trisubstituted phenolic motif fused to a chiral aliphatic ring by a sequence of visible-light-mediated radical seleno transfer cyclization, bromination, concomitant selenoxide elimination–dehydrobromination, and demethoxycarbonylation, namely, a programmed aromatization. Biological evaluation of the enantiomers of ligudentatol obtained by the present route revealed for the first time their cytotoxicity towards various cancer cell lines.

Natural phenols are a rich source of bioactive materials that exhibit antioxidant, cytotoxic, and antibacterial activities. (+)-Ligudentatol (1), a unique trisubstituted phenolic norsesquiterpene isolated from the rhizomes of the perennial herb *Ligularia dentata* Hara in 1990 by Naya and coworkers, is a member of 14-noreudesmanes (Figure 1).<sup>[1]</sup> In 1998, Jia and Gao reported that (+)-liguhodgsonal (2), a closely related phenol isolated from the roots of *Ligularia dentata* Cass., exhibited strong antiproliferative activities against human hepatoma (H-7402), human myelogenous leukemia (K562), and mouse melanin carcinoma (B16) cell



(+)-Ligudentatol (1) (-)-Ligudentatol (*ent*-1) (+)-Liguhodgsonal (2)

Figure 1. Ligudentatol (1) and liguhodgsonal (2).

[a] G. A. I. Moustafa, H. Suizu, Prof. Dr. H. Aoyama, Prof. Dr. M. Arai, Prof. Dr. S. Akai, Prof. Dr. T. Yoshimitsu Graduate School of Pharmaceutical Sciences, Osaka University 1-6 Yamadaoka, Suita, Osaka 565-0871 (Japan) Fax: (+81)6-6879-8214 E-mail: yoshimit@phs.osaka-u.ac.jp

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/asia.201400110.

lines.<sup>[2]</sup> In our unrelenting effort to develop natural products-based medicinal resources,<sup>[3,4]</sup> ligudentatol (1) caught our attention and prompted us to assess its potential biological activity. Herein, we report a facile approach to the enantiomers of ligudentatol, which features visible-light-mediated seleno transfer radical cyclization, followed by aromatization. Furthermore, the cytotoxicity of synthetic (+)-ligudentatol (1) and (-)-ligudentatol (*ent*-1) toward various cancer cell lines is demonstrated for the first time, paving the way for the development of new antiproliferative agents of natural origin.

An enantioselective synthesis of natural (+)-ligudentatol (1) was previously reported by Haddad and Salman, who devised a [2+2] photochemical access to the phenolic motif.<sup>[5]</sup> Our synthetic route to ligudentatol features the construction of a phenolic core by facile aromatization of highly functionalized decalin system **iii** that is accessible by seleno transfer radical cyclization of **iv** (Scheme 1).<sup>[6,7]</sup> Intermediate



Scheme 1. Retrosynthesis of (-)-ligudentatol (ent-1).

iv, the precursor of decalin scaffold iii, is readily obtainable from perillyl bromide (3) in an optically pure form. It has been well documented in the literature that, unlike reductive radical cyclizations that are commonly terminated by hydrogen abstractions, atom or group transfer approaches allow the cyclized material to bear functionalities suitable

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for further chemical transformations. This is the case for our approach to ligudentatol in which a phenylseleno functionality is transferred to the ring system and a bromide is installed thereafter to set the stage for dienone formation. Dienone **i**, obtainable by simple elimination reactions of the functionalities is converted into phenol **1** by thermodynamically favorable aromatization.

(-)-Perillyl bromide (3),<sup>[8]</sup> which was obtained from (S)perillaldehyde in two steps, was reacted with a dienolate generated from methyl acetoacetate (4) using two equivalents of LDA at -78 °C to furnish ester 5 in 78% yield (Scheme 2). Ester 5 was then treated with methyl iodide in



Scheme 2. Total synthesis of (-)-ligudentatol (*ent*-1). Reagents and conditions: a) LDA (2 equiv), THF, -78 °C; b) K<sub>2</sub>CO<sub>3</sub>, MeI, acetone, 60 °C; c) PhSeCl, NaH, THF, -40 °C; d) cat. (PhSe)<sub>2</sub>,  $h\nu$  (visible light), CH<sub>2</sub>Cl<sub>2</sub>, 0 to 5 °C; e) LDA, NBS, THF, -78 °C; f) H<sub>2</sub>O<sub>2</sub>, THF, pyridine, rt, then Me<sub>2</sub>S, DBU, rt, 50 % over 2 steps; g)  $\mu$ W, NaCl, aq. DMSO, 200 °C

the presence of  $K_2CO_3$  in acetone at 60°C to afford compound **6** in 87% yield. Selenylated compound **7** (d.r.=1:1) was prepared by installing a phenylseleno functionality into the  $\alpha$ -position of  $\beta$ -keto ester **6** by treatment with NaH followed by phenylselenyl chloride at -40°C in THF.

With this selenide **7**, the key group transfer radical cyclization was examined. Pioneering studies on the addition of carbon–selenium (C–SePh) bonds to carbon–carbon multiple bonds were recorded by Byers,<sup>[9]</sup> Curran,<sup>[10]</sup> Back,<sup>[11]</sup> and Renaud,<sup>[12]</sup> who disclosed the utility of the seleno transfer processes under radical conditions.<sup>[13]</sup> Yang and co-workers also reported highly stereoselective seleno transfer cyclizations of alkenylated  $\alpha$ -phenylseleno- $\beta$ -keto and  $\alpha$ -phenylseleno- $\beta$ -hydroxyesters.<sup>[14]</sup>

We opted to adopt visible-light irradiation to promote the seleno transfer processes. Substrate 7 was irradiated by a tungsten lamp (150 W) in the presence of 0.2 equivalent of

Table 1. Visible-light-mediated seleno transfer radical cyclization of 7.

8			5		
Entry	Additive	<i>T</i> [°C]	t	Yield [%]	8a:8b
1	no	0–5	3 h	30	3:1
2	0.2 equiv (PhSe) <sub>2</sub>	0–5	3 h	88	3:1
3	$0.2 \text{ equiv } (PhSe)_2$	reflux	70 min	90	2:1

diphenyldiselenide in CH<sub>2</sub>Cl<sub>2</sub> at 0 to 5°C to produce cyclized products **8a** and **8b** in a diastereomeric ratio of 3:1 (the reaction time necessary for the consumption of **7** was 3 h; Table 1, entry 2). Diphenyldiselenide was essential for efficient transformation: its omission led to poor conversion (~30% yield after 3 h; Table 1, entry 1). It should be noted that at higher temperature (i.e., in refluxing CH<sub>2</sub>Cl<sub>2</sub>), the reaction was accelerated to provide the cyclized compounds in 90% yield, albeit with lower diastereoselectivity (**8a:8b**= 2:1; Table 1, entry 3). Although the stereochemistry of major product **8a** could not be elucidated at this stage, minor cyclized material **8b** fortunately gave a crystalline material suitable for X-ray analysis. The analysis showed that compound **8b** has a *trans*-decalin architecture with a  $\beta$ configurational methyl substituent (Figure 2).<sup>[15]</sup> On the



Figure 2. X-ray crystallographic structure of minor isomer **8b** with thermal ellipsoids at 50% probability levels.

other hand, after several trials to determine the stereochemistry of major product 8a, we were delighted to find that, by visible-light irradiation in the presence of diphenyldiselenide in refluxing dichloroethane, compound 8a (a diastereomerically enriched material with a ratio 8a:8b=7.5:1) underwent epimerization at the selenylated carbon to afford compound 10 (Figure 3). The stereochemistry of the ring juncture of compound 10 was unambiguously confirmed again by X-ray crystallography and to our surprise, it was *trans*.<sup>[16]</sup> The epimerization likely took place via radical scission of the carbon-selenium (C-SePh) bond by  $S_H2$  reaction with a phenylselenyl radical generated by photolysis of diphenyldiselenide, followed by capture of the resultant carbon radical with diphenyldiselenide to give the thermodynamically more stable trans-decalin 10. As only the carbon-selenium bond is cleavable under the irradiation conditions, the trans configuration of compound 10 suggested that major isomer

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Figure 3. Production of *trans*-decalin **10** from **8a** via epimerization of the selenylated carbon and its X-ray structure with thermal ellipsoids at 50% probability levels.



Scheme 3. Plausible mechanism for the production of selenides **8a** and **8b**.

**8a** originally produced by the radical cyclization possessed the *cis*-decalin structure.

The preferential formation of *cis*-configurational decalin **8a** over *trans*-congener **8b** suggested that the visible-lightmediated reaction favored kinetic control (Scheme 3). As evidenced by the fact that the seleno transfer cyclization took place in the absence of diphenyldiselenide, albeit in poor yield (see above), the carbon–selenium bond of substrate **7** was indeed cleavable by photolysis, generating carbon radicals (**v**/**vii**) stabilized by the two carbonyls. The orientation of the two carbonyl groups of resultant radical (**v**/**vii**) was likely due to the alleviation of their dipolar interaction. The carbon radical further underwent *6-endo* mode cyclization on the double bond to provide a tertiary radical that captured a phenylselenyl group from another substrate **7**, thereby creating a radical chain pathway. In the presence of catalytic diphenyldiselenide, however, the cyclization was accelerated by facilitating the radical chain propagation through efficient capture of the tertiary radical intermediates (vi/viii) with diphenyldiselenide.[17] It is also likely that the visible-light irradiation of diphenyldiselenide generated phenylselenyl radical<sup>[18]</sup> that efficiently produces radical intermediates (v/vii) via  $S_H2$  reaction with 7 to promote the cyclization. Although seemingly the less stable cis-isomer 8a was predominantly produced, this could be rationalized by considering the steric interaction between the methoxycarbonyl substituent and the allylic hydrogen atom as exemplified in vii, which underwent flipping to v that eventually produced cis-selenide 8a rather than trans-isomer 8b. Furthermore, the 1,3-diaxial interaction between the methoxycarbonyl group and the phenylselenyl donors (7 or diphenyldiselenide) in transient intermediate viii could retard radical trapping and facilitate ring opening to give v via vii, thus leading to the preferential production of 8a.

The next task was to aromatize cyclized products 8a and **8b** to furnish the phenol motif by oxidative functionalization of the B ring of the decalins. Firstly, a mixture of the two decalins 8a/8b (d.r.=3:1) was subjected to bromination with LDA/NBS in THF at -78 °C to furnish  $\alpha$ -brominated compounds as a diastereomeric mixture. Then, hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>)/pyridine were added to the crude mixture followed by DBU (DBU=1,8-diazabicyclo[5.4.0]undec-7ene) to produce desired dienone 9 (d.r.  $\approx 3.6:1$ ) in 50% vield over two steps via concomitant selenoxide-hydrogen bromide eliminations. To ensure the complete conversion of all the diastereomeric bromides, DBU was employed to enhance the dehydrobromination. As expected, the cis-configuration of the decalin architecture of major isomer 8a allowed the preferential formation of internal tetrasubstituted olefin ix over other regioisomeric olefins via syn-elimination mechanisms (Scheme 4): bromination of diastereomerically enriched selenide 8a (8a:8b=7.5:1) with NBS followed by oxidation with H<sub>2</sub>O<sub>2</sub>/pyridine/DBU afforded exclusively dienone 9a (56%), whereas minor isomer 8b under the same conditions gave dienone 9b (36%) along with regioisomeric olefin 12 (22%). Careful examination of dienone formation from 8b revealed that 9b was formed via x, which underwent dehydrobromination via deprotonation at the  $\delta$ -position. Nevertheless, it is worthy to note that both 8a and 8b in those transformations could be converted into dienones 9a and 9b, respectively.

The end game in the total synthesis of (-)-ligudentatol (*ent-***1**) involved a facile aromatization-driven demethoxycarbonylation of dienone **9**. Dienone **9** (d.r.=3.6:1) was heated in wet DMSO in the presence of NaCl under microwave irradiation (200 °C) to efficiently furnish (-)-ligudentatol (*ent-***1**) in 82 % yield ( $[\alpha]_D^{25} = -80.8$  (c=0.325, CHCl<sub>3</sub>); the reported value for (+)-**1** is  $[\alpha]_D^{22} = +82.4$  (c=0.80, CHCl<sub>3</sub>)).<sup>[1]</sup> The same synthetic protocol using an enantiomer of ketoester **7** available from (*R*)-perillyl bromide (*ent-***3**) provided access to natural (+)-ligudentatol (**1**) ( $[\alpha]_D^{24} = +83.0$  (c=0.125, CHCl<sub>3</sub>); Scheme 5).

With these enantiomerically pure (+)- and (-)-ligudentatol (1) in hand, their antiproliferative activities were evaluat-

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Scheme 4. Sequential dienone formation from diastereomeric selenides **8a** and **8b**. Reagents and conditions: a) LDA, NBS, THF, -78 °C; b) H<sub>2</sub>O<sub>2</sub>, pyridine, THF, rt; c) DBU, rt.



Scheme 5. Total synthesis of (+)-ligudentatol (1).

Table 2.  $IC_{50}$  values ( $\mu$ M) of (+)-ligudentatol (1) and (-)-ligudentatol (*ent*-1) against cancer cell lines.

Compound	Cytotoxicity (IC <sub>50</sub> , µм)				
-	S180	PANC-1	HeLa	DU145	
(+)-ligudentatol (1)	27.5	34.7	42.5	40.3	
(-)-ligudentatol (ent-1)	26.6	32.7	27.9	36.0	

ed against several cancer cell lines, including mouse sarcoma (S180), human pancreatic carcinoma (PANC-1), human cervical cancer (HeLa), and human prostate cancer (DU145) (Table 2). The evaluation revealed that both compounds exerted similar, moderate antiproliferative activities against all the tested cancer cells, with  $IC_{50}$  values ranging from 26.6 to 42.5  $\mu$ M, suggesting their potential application in medicinal research.

In conclusion, we have established a new expeditious access to the enantiomers of the norsesquiterpene ligudentatol, which involved a sequential seleno transfer reaction and aromatization protocol. The present chemical synthesis has also allowed us to uncover the antiproliferative activities of both natural and unnatural ligudentatol, adding a new dimension to the development of phenolic medicinal resources.

#### **Experimental Section**

The synthetic procedures and the characterization of the compounds studied herein can be found in the Supporting Information.

#### Acknowledgements

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan (MEXT). G.A.I.M. acknowledges a scholarship awarded by the Egyptian Ministry of Higher Education for his graduate study.

**Keywords:** cytotoxicity • natural products • radical reactions • seleno transfer • total synthesis

- [1] K. Naya, T. Okayama, M. Fujiwara, M. Nakata, T. Ohtsuka, S. Kurio, Bull. Chem. Soc. Jpn. 1990, 63, 2239.
- [2] K. Gao, Z.-J. Jia, Phytochemistry 1998, 49, 167.
- [3] Z. Li, D. Shigeoka, T. R. Caulfield, T. Kawachi, Y. Qiu, T. Kamon, M. Arai, H. W. Tun, T. Yoshimitsu, *Med. Chem. Commun.* 2013, 4, 1093.
- [4] G. A. I. Moustafa, S. Nojima, Y. Yamano, A. Aono, M. Arai, S. Mitarai, T. Tanaka, T. Yoshimitsu, *Med. Chem. Commun.* 2013, 4, 720.
- [5] N. Haddad, H. Salman, Tetrahedron Lett. 1997, 38, 6087.
- [6] For selected reviews on atom/group transfer radical chemistry, see: a) D. P. Curran, Synthesis 1988, 489; b) D. P. Curran in Comprehensive Organic Synthesis, Vol. 4 (Eds.: B. M. Trost, I. Flemming), Pergamon, Oxford, 1991, Chap. 4.2; c) C. P. Jasperse, D. P. Curran, T. L. Fevig, Chem. Rev. 1991, 91, 1237; d) S. Z. Zard, Angew. Chem. Int. Ed. Engl. 1997, 36, 672; Angew. Chem. 1997, 109, 724; e) J. Byers in Radicals in Organic Synthesis, Vol. 1 (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, 2001, Chap. 1.5; f) S. Z. Zard in Radicals in Organic Synthesis, Vol. 1 (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, 2001, Chap. 1.6; g) S. Z. Zard, Radical Reactions in Organic Synthesis, Oxford University Press, New York, 2003, Chap. 6; h) A. J. Clark, Chem. Soc. Rev. 2002, 31, 1-11; i) B. Quiclet-Sire, S. Z. Zard, Top. Curr. Chem. 2006, 264, 201; j) G. J. Rowlands, Tetrahedron 2010, 66, 1593; k) B. Quiclet-Sire, S. Z. Zard, Chem. Eur. J. 2006, 12, 6002; 1) C. Li in Encyclopedia of Radicals in Chemistry, Biology and Materials, Vol. 2 (Eds.: C. Chatgilialoglu, A. Studer), Wiley, Chichester, 2012, Chap. 32; m) T. Pintauer, K. Matyjaszewiski in Encyclopedia of Radicals in Chemistry, Biology and Materials, Vol. 4 (Eds.: C. Chatgilialoglu, A. Studer), Wiley-VCH, Weinheim, 2012, Chap. 62; n) B. Quiclet-Sire, S. Z. Zard, Beilstein J. Org. Chem. 2013, 9, 557; o) R. A. Gossage, L. A. van de Kuil, G. van Koten, Acc. Chem. Res. 1998, 31, 423; p) J. Iqbal, B. Bhatia, N.K. Nayyar, Chem. Rev. 1994, 94, 519; q) D. Bellus, Pure Appl. Chem. 1985, 57, 1827; r) F. Minisci, Acc. Chem. Res. 1975, 8, 165; s) S. Francois, A. Demonceau, A. F. Noels in Recent Research Developments in Organic Chemistry, Vol. 3 (Pt. 2), Transworld Research Network, 1999, p. 455; t) K. Severin, Chimia 2012, 66, 386.
- [7] For selected papers on atom/group transfer reactions in organic synthesis, see: a) R. S. Grainger, P. Innocenti, Angew. Chem. Int. Ed. 2004, 43, 3445; Angew. Chem. 2004, 116, 3527; b) C.-J. Wallentin, J. D. Nguyen, P. Finkbeiner, C. R. J. Stephenson, J. Am. Chem. Soc. 2012, 134, 8875; c) H. Yorimitsu, T. Nakamura, H. Shinokubo, K.

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Oshima, K. Omoto, H. Fujimoto, J. Am. Chem. Soc. 2000, 122, 11041; d) L. Chabaud, Y. Landais, P. Renaud, Org. Lett. 2005, 7, 2587; e) P. Renaud, C. Ollivier, P. Panchaud, Angew. Chem. Int. Ed. 2002, 41, 3460; Angew. Chem. 2002, 114, 3610; f) C. D. Edlin, J. Faulkner, M. Helliwell, C. K. Knight, J. Parker, P. Quayle, J. Raftery, Tetrahedron 2006, 62, 3004; g) S. Sumino, A. Fusano, I. Ryu, Org. Lett. 2013, 15, 2826.

- [8] a) R. Buchecker, U. Marti, C. H. Eugster, *Helv. Chim. Acta* 1982, 65, 896; b) G. Pelletier, S. Lie, J. J. Mousseau, A. B. Charette, *Org. Lett.* 2012, 14, 5464.
- [9] a) J. H. Byers, G. C. Lane, *Tetrahedron Lett.* 1990, *31*, 5697; b) J. H.
   Byers, T. G. Gleason, K. S. Knight, *J. Chem. Soc. Chem. Commun.* 1991, 354.
- [10] a) D. P. Curran, M. H. Chen, E. Spletzer, C. M. Seong, C. T. Chang, J. Am. Chem. Soc. 1989, 111, 8872; b) D. P. Curran, C. M. Seong, J. Am. Chem. Soc. 1990, 112, 9401; c) D. P. Curran, J. Tamine, J. Org. Chem. 1991, 56, 2746; d) D. P. Curran, E. Eichenberger, M. Collis, M. G. Roepel, G. Thoma, J. Am. Chem. Soc. 1994, 116, 4279.
- [11] T. G. Back, P. L. Gladstone, Synlett 1993, 699.
- [12] a) S. Abazi, L. P. Rapado, K. Schenk, P. Renaud, Eur. J. Org. Chem. 1999, 477; b) P. Renaud, S. Abazi, Synthesis 1996, 253.
- [13] For pertinent reviews on synthetic radical chemistry using organose-leniums, see: a) T. G. Back, Organoselenium Chemistry, (Ed.: T. G. Back), 1999, p. 173; b) P. Renaud in Topics in Current Chemistry: Organoselenium Chemistry, Vol. 208 (Ed.: T. Wirth), Springer, Berlin, 2000, p. 81; c) A. Ogawa in Main Group Metals in Organic Synthesis, Vol. 2 (Eds.: H. Yamamoto, K. Oshima), Wiley-VCH, Weinheim, 2004, Chap. 15.4; d) B. Cardinal-David, J.-F. Brazeau, I. A. Katsoulis, Y. Guindon, Curr. Org. Chem. 2006, 10, 1939; e) D. M. Freudendahl, S. A. Shahzad, T. Wirth, Eur. J. Org. Chem. 2009, 1649; f) W. R. Bowman in Organoselenium Chemistry: Synthesis and Reactions (Ed.: T. Wirth), Wiley-VCH, Weinheim, 2011, Chap. 3, p. 111; g) T. G. Back, D. J. Press in Chemistry of Organic Selenium and Tellurium Compounds, 3 (Pt. 1) (Eds.: S. Patai, Z. Rap-

poport), **2012**, p. 357; h) A. Nomoto, A. Ogawa in *Chemistry of Or*ganic Selenium and Tellurium Compounds, 3 (Pt. 1) (Eds.: S. Patai, Z. Rappoport), **2012**, p. 623.

- [14] a) D. Yang, Q. Gao, O.-Y. Lee, Org. Lett. 2002, 4, 1239; b) D. Yang,
  Q. Gao, B.-F. Zheng, N.-Y. Zhu, J. Org. Chem. 2004, 69, 8821; c) D.
  Yang, B.-F. Zheng, Q. Gao, S. Gu, N.-Y. Zhu, Angew. Chem. Int. Ed.
  2006, 45, 255; Angew. Chem. 2006, 118, 261; d) D. Yang, G.-Y. Lian,
  H.-F. Yang, J.-D. Yu, D.-W. Zhang, X. Gao, J. Org. Chem. 2009, 74, 8610; e) J.-D. Yu, W. Ding, G.-Y. Lian, K.-S. Song, D.-W. Zhang, X. Gao, D. Yang, J. Org. Chem. 2010, 75, 3232.
- [15] CCDC 981449 (8b) contains the supplementary X-ray crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data\_request/cif.
- [16] CCDC 980715 (10) contains the supplementary X-ray crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data\_request/cif. The poor chemical yield of isomerized material 10 from compound 8a (a diastereomerically enriched material with 8a:8b ratio=7.5:1) is attributed to the concomitant formation of a tetra-substituted alkene (24%), which was likely produced by elimination of the phenylseleno group during the isomerization process. The unreacted 8b was also recovered.
- [17] A. Ogawa, H. Yokayama, K. Yokayama, T. Masawaki, N. Kambe, N. Sonoda, J. Org. Chem. 1991, 56, 5721.
- [18] a) U. Schmidt, A. Müller, K. Markau, Chem. Ber. 1964, 97, 405;
  b) R. Franzi, M. Geoffroy, J. Organomet. Chem. 1981, 218, 321.
  Also, see: c) A. Ogawa, M. Doi, I. Ogawa, T. Hirao, Angew. Chem. Int. Ed. 1999, 38, 2027; Angew. Chem. 1999, 111, 2066; d) A. Ogawa,
  I. Ogawa, R. Obayashi, K. Umezu, M. Doi, T. Hirao, J. Org. Chem.
  1999, 64, 86; e) T. G. Back, M. V. Krishna, J. Org. Chem. 1988, 53, 2533.

Received: January 23, 2014 Published online: April 2, 2014