Tetrahedron Letters 49 (2008) 5431–5435

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

A novel synthesis of spiro[2.6]nonadienones by the reaction of magnesium cyclopropylidenes with naphtholates and phenolates

Tsuyoshi Satoh *, Shinobu Nagamoto, Masanobu Yajima, Yukie Yamada, Yuki Ohata, Makoto Tadokoro

Department of Chemistry, Faculty of Science, Tokyo University of Science, Ichigaya-funagawara-machi 12, Shinjuku-ku, Tokyo 162-0826, Japan

ARTICLE INFO

Article history:
Received 30 June 2008
Revised 9 July 2008
Accepted 10 July 2008
Available online 12 July 2008

Keywords:
Magnesium carbenoid
Magnesium cyclopropylidene
Cyclopropylation
Ring-expansion
Spiro[2.6]nonadienone

ABSTRACT

The sulfoxide–magnesium exchange reaction of aryl 1-chlorocyclopropyl sulfoxides with *i*-PrMgCl in THF at low temperature gave magnesium cyclopropylidenes. Treatment of the magnesium cyclopropylidenes with lithium naphtholates or phenolates resulted in the formation of spiro[2.6]nonadienones in up to 82% yield. The structure of the spiro[2.6]nonadienones was found to be dependent on the structure of the naphtholates and phenolates.

1. Introduction

Cyclopropanes are one of the most important and fundamental compounds in organic and synthetic organic chemistry. Because of their highly strained nature, cyclopropanes have long been recognized to be highly versatile compounds in organic synthesis and innumerable studies on their chemistry, synthesis, and synthetic uses have been carried out;[1] however, new methods for the synthesis of cyclopropanes are still very much desired. Recently, we are interested in the use of magnesium cyclopropylidenes in organic synthesis,[2] and some new synthetic methods were reported. Those are as follows: generation and properties of magnesium cyclopropylidenes,[3] synthesis of alkylidenecyclopropanes,[4] *N*-cyclopropylation of arylamines,[5] and direct *ortho*-cyclopropylation of arylamines.[6]

In continuation of our investigation for the development of new synthetic method utilizing the magnesium cyclopropylidenes, we studied the reaction of the magnesium cyclopropylidenes with lithium naphtholates and phenolates, and very interesting results were obtained. Thus, the magnesium cyclopropylidenes **2**, derived from aryl 1-chlorocyclopropyl sulfoxides **1** with *i*-PrMgCl, were treated with lithium naphtholates or lithium phenolates **3** to afford unexpected spiro[2.6]nonadienones **4** or **5** in variable yields. This reaction offers a new method for a short synthesis of various kinds of spiro[2.6]nonadienones **4** or **5** from naphthols and phenols (Scheme 1).

2. Results and discussion

Recently, we reported that the reaction of magnesium cyclopropylidenes with *N*-lithio arylamines resulted in the formation of *ortho*-cyclopropylated arylamines.[6] In continuation of this chemistry, we investigated the reaction of magnesium cyclopropylidene **7**, which was generated from 1-chlorocyclopropyl phenyl sulfoxide **1** (R^1 = H, Ar = Ph) with *i*-PrMgCl at −78 °C, with lithium 1-naphtholate **6a**, and 2-cyclopropylated 1-naphthol **8a** was obtained in 37% yield (Scheme 2).

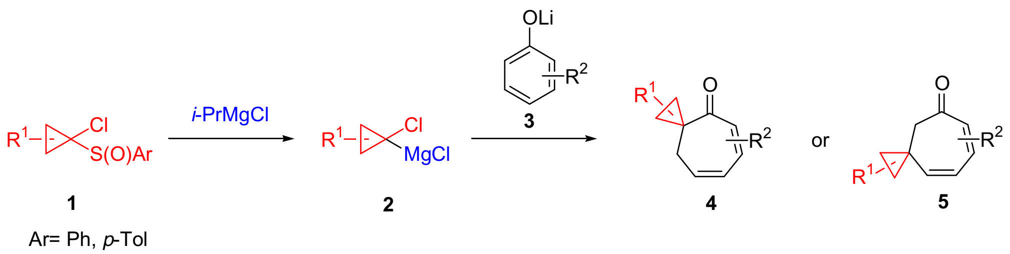
Next, the reaction was carried out with lithium 4-methoxy-1-naphtholate **6b**. Very interestingly, this reaction afforded 2-cyclopropylated compound **8b** (23%) and unexpected ring-expanded spiro[2.6]nona-5,7-dien-4-one derivative **9b** in 47% yield. Further, the reactions of **6a** and **6b** with magnesium cyclopropylidene having *gem*-dimethyl groups **10** were investigated. Interestingly, these reactions afforded ring-expanded spiro[2.6]nonadienones **11a** (70%)[7] and **11b** (82%), respectively, as a sole product without 2-cyclopropylated product.

A plausible mechanism of this reaction is as follows (Scheme 3). Addition reaction of magnesium carbenoid **10** is expected to take place with naphtholate **6b** at the most electron-rich double bond to afford the highly strained spiro[2.2]pentane intermediate **A**. Carbon–carbon bond-cleavage of the cyclopropanolate moiety, depicted in **A**, would take place easily because of the ring-strain

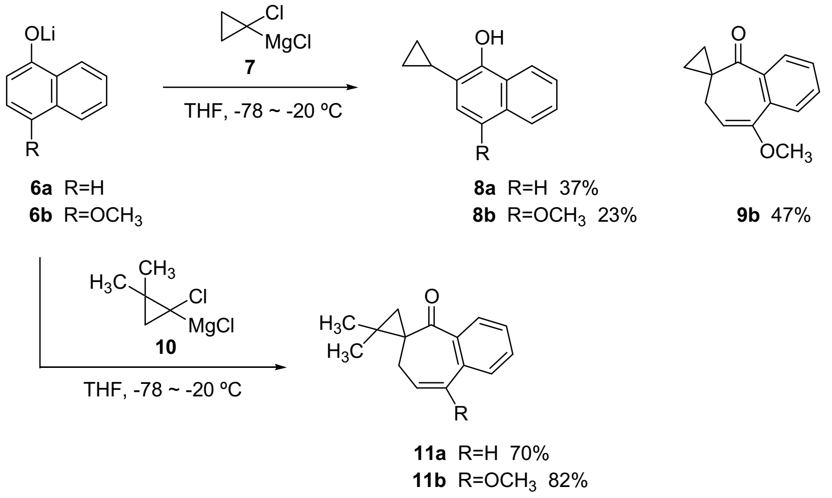
---

* Corresponding author. Tel.: +81 3 5228 8272; fax: +81 3 5261 4631.
E-mail address: tsatoh@rs.kagu.tus.ac.jp (T. Satoh).

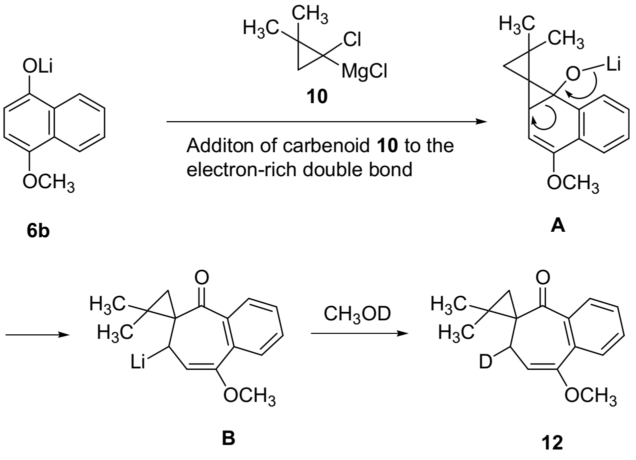
0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.07.066



Scheme 1.



Scheme 2.

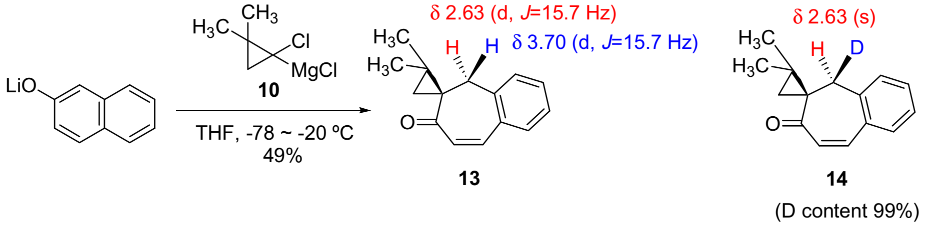


Scheme 3.

to afford the final ring-expanded intermediate **B**. Protonolysis of **B** will give the product **11b**. In order to confirm the final intermediate of this reaction to be **B**, deuteriolysis of this reaction with CH_3OD was carried out and indeed deuterated product **12** was obtained with perfect deuterium incorporation.

The reaction of magnesium cyclopropylidene **10** with lithium 2-naphtholate gave spiro[2.6]nona-5,7-dien-4-one **13** in 49% yield (Scheme 4).[8] The structure of **13** was confirmed by X-ray analysis (Fig. 1).[9] The structure of **13** and **11** (see Scheme 2) are quite similar; however, the position of the carbonyl group is different. The same reaction mechanism shown in Scheme 3 can be applied to this reaction. Quenching of the reaction mixture with CH_3OD again gave mono deuterated compound **14**. The deuterium incorporation was found to be highly stereoselective; only the hydrogen appearing at δ 3.70 in the ^1H NMR was perfectly replaced by deuterium.

Further reactions of the magnesium cyclopropylidenes with phenolates and naphtholates were carried out and the results are summarized in Table 1. The reaction of magnesium cyclopropylidene **7** with lithium phenolate gave only *ortho*-cyclopropylated



Scheme 4.

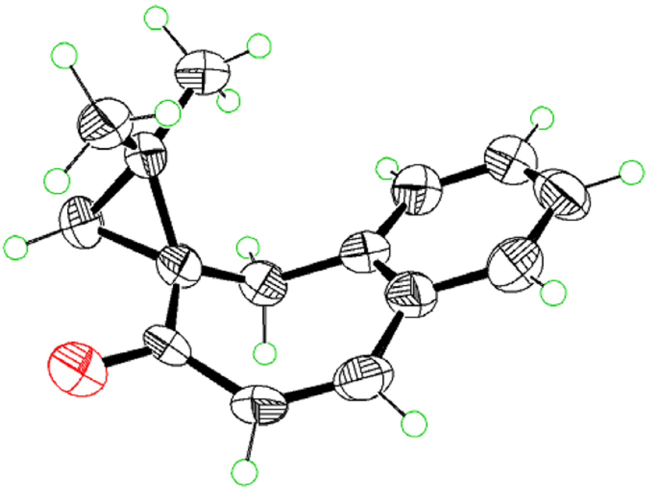


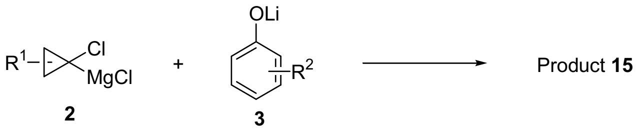
Figure 1. Crystal structure of spiro[2.6]nonadienone **13**.

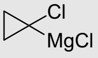
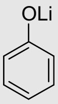
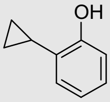
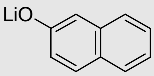
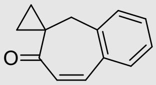
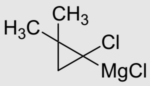
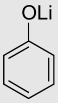
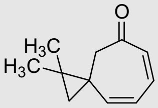
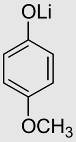
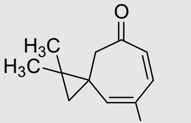
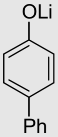
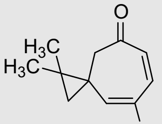
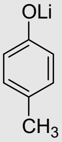
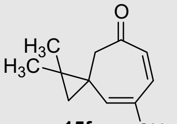
phenol **15a** in low yield without any ring-expanded product (entry 1). The reaction of magnesium cyclopropylidene **7** with lithium 2-naphtholate gave ring-expanded product **15b** in 37% yield without 1-cyclopropylated 2-naphthol (entry 2).

The reaction of magnesium cyclopropylidene bearing *gem*-dimethyl groups **10** with lithium phenolate gave ring-expanded product, 1,1-dimethylspiro[2.6]nona-6,8-dien-5-one **15c**,[10] in 22% yield (entry 3). Quite interestingly, the structure of the product **15c** was somewhat different compared with that of the product from 1-naphthol (**11a**). The cyclopropane and the carbonyl carbon adjoin in the structure of **11a**; however, a methylene carbon is present between them in the structure of **15c**. All the products from the reactions of magnesium cyclopropylidene **10** with phenolates have the same structure as shown in entries 3–6 in Table 1.

The structure of the products (**15c**–**f**) of the reaction with phenolates cannot be explained by the mechanism shown in Scheme 3. Another reaction mechanism shown in Scheme 5 is proposed for the products. We still find it difficult to propose the reason why

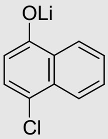
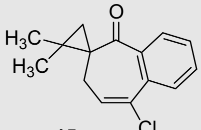
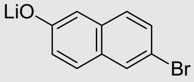
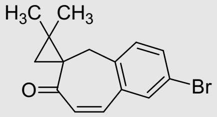
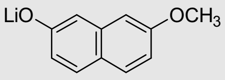
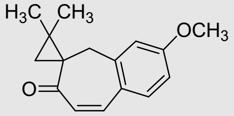
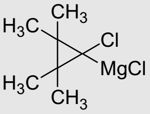
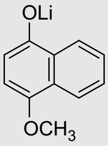
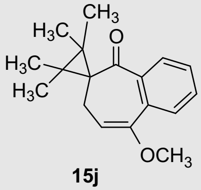
Table 1
The reaction of magnesium cyclopropylidenes with lithium phenolates or naphtholates



Entry	Magnesium cyclopropylidene	Naphtholate or phenolate	Product **15**	Yield (%)
1	 **7**		 **15a**	21
2	**7**		 **15b**	37
3	 **10**		 **15c**	22
4	**10**		 **15d**	26
5	**10**		 **15e**	20
6	**10**		 **15f**	32

(continued on next page)

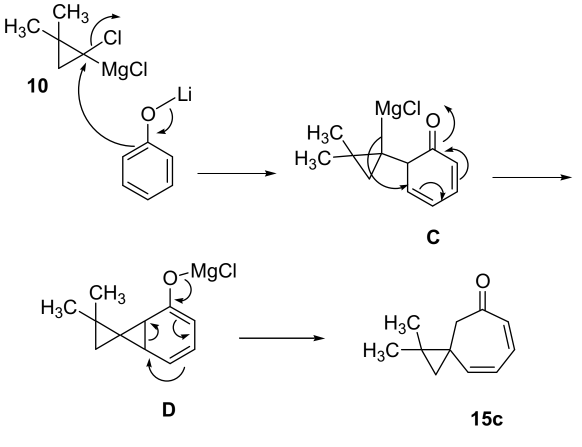
Table 1 (*continued*)

Entry	Magnesium cyclopropylidene	Naphtholate or phenolate	Product **15**	Yield (%)
7	**10**		 **15g**	33
8	**10**		 **15h**	36
9	**10**		 **15i**	64
10	 **16**[a]		 **15j**	26

[a] 1-Chloro-2,2,3,3-tetramethylcyclopropyl phenyl sulfoxide was used as the starting material.

the mechanism is different between the reactions with naphtholates and phenolates at present.

The reaction of magnesium cyclopropylidene **10** with lithium 4-chloro-1-naphtholate gave the expected product **15g**; however, the yield was found to be lower than that of **11a** and **11b**. This result implied that an electron-withdrawing group may retard the carbenoid reaction presented herein. The reactions shown in entries 8 and 9 gave the desired 1,1-dimethylspiro[2.6]nona-5,7-dien-4-ones **15h** and **15i** in variable yields. Finally, fully substituted magnesium cyclopropylidene **16** was treated with lithium 4-methoxynaphtholate. This reaction gave the desired product **15j**; however, the yield was not satisfactory (entry 10). Many unknown by-products, each as a small amount, were obtained when the yields of the spiro[2.6]nonadienones were low.



Scheme 5.

In conclusion, we report for the first time, a novel reaction of magnesium cyclopropylidenes with lithium naphtholates and phenolates to give ring-expanded spiro[2.6]nonadienones. There are only a few reports on the reactions of lithium cyclopropylidenes;[11] however, no report has appeared for the reaction with naphtholates and phenolates. The results described in this Letter are the first example of the reaction of cyclopropylidenes with naphtholates and phenolates giving ring-expanded spiro[2.6]nonadienones.

Acknowledgments

This work was supported by a Grant-in-Aid for Scientific Research No. 19590018 from the Ministry of Education, Culture, Sports, Science and Technology, Japan, which is gratefully acknowledged.

References and notes

1. Some recent reviews concerning chemistry, synthesis, and synthetic uses of cyclopropanes: (a) Wong, H. N. C.; Hon, M.-Y.; Tse, C.-W.; Yip, Y.-C.; Tanko, J.; Hudlick, T. *Chem. Rev.* **1989**, *89*, 165; (b) Salaun, J. *Chem. Rev.* **1989**, *89*, 1247; (c) Sonawane, H. R.; Bellur, N. S.; Kulkarni, D.; Ahuja, J. R. *Synlett* **1993**, 875; (d) Doyle, M. P.; Protopopova, M. N. *Tetrahedron* **1998**, *54*, 7919; (e) Donaldson, W. A. *Tetrahedron* **2001**, *57*, 8589; (f) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977; (g) Pietruszka, J. *Chem. Rev.* **2003**, *103*, 1051; (h) Reissig, H.-U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151; (i) Kulinkovich, O. G. *Chem. Rev.* **2003**, *103*, 2597; (j) Halton, B.; Harvey, J. *Synlett* **2006**, 1975.
2. Satoh, T. *Chem. Soc. Rev.* **2007**, *36*, 1561.
3. Satoh, T.; Kurihara, T.; Fujita, K. *Tetrahedron* **2001**, *57*, 5369.
4. Satoh, T.; Saito, S. *Tetrahedron Lett.* **2004**, *45*, 347.
5. Satoh, T.; Miura, M.; Sakai, K.; Yokoyama, Y. *Tetrahedron* **2006**, *62*, 4253.
6. Yamada, Y.; Miura, M.; Satoh, T. *Tetrahedron Lett.* **2008**, *49*, 169.
7. Compound **11a**: Colorless oil; IR (neat) 1651 (CO), 1594 (C=C) cm^{-1}; ^{1}H NMR δ 0.75 (1H, d, J = 4.1 Hz), 1.03 (3H, s), 1.35 (3H, s), 1.67 (1H, d, J = 4.1 Hz), 2.15 (1H, dd, J = 15.9, 7.9 Hz), 2.87 (1H, ddd, J = 15.9, 5.3, 1.8 Hz), 6.33 (1H, ddd, J = 10.8, 7.9, 5.3 Hz), 6.52 (1H, dd, J = 10.8, 1.7 Hz), 7.18 (1H, d, J = 7.6 Hz), 7.30 (1H, t, J = 7.6 Hz), 7.45 (1H, t, J = 7.6 Hz), 7.99 (1H, d, J = 7.6 Hz). MS m/z (%) 212 (M$^+$,

100), 197 (48), 157 (79), 128 (78). Calcd for $C_{15}H_{16}O$: *M*, 212.1201. Found: *m/z* 212.1202.

8. To a solution of 2-naphthol (0.9 mmol) in 0.8 mL of dry THF in a flame-dried flask at −78 °C under argon atmosphere was added *n*-BuLi (0.9 mmol) dropwise with stirring. A solution of 1-chloro-2,2-dimethylcyclopropyl *p*-tolyl sulfoxide (72.8 mg; 0.3 mmol) in 0.7 mL of dry THF was added to the reaction mixture dropwise with stirring. Finally, *i*-PrMgCl (2.0 mol/L in THF; 0.75 mmol) was added to the reaction mixture and the temperature of the reaction mixture was slowly allowed to warm to −20 °C for 1.5 h. The reaction mixture was quenched with satd aq NH_4Cl and the whole was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$. After removal of the solvent, the product was purified by silica gel column chromatography followed by preparative thin layer chromatography (hexane–1,4-dioxane = 30:1) to give **13** (31.3 mg, 49%) as colorless crystals; mp 39.5–40.5 °C (hexane); IR (KBr) 2951, 2346, 1643 (CO), 1408, 1361, 1314, 1281, 1202, 1099, 831, 801, 748 cm^{-1}; ^1H NMR δ 0.68 (1H, d, $J = 4.0$ Hz), 0.89 (3H, s), 1.08 (3H, s), 1.65 (1H, d, $J = 4.0$ Hz), 2.63 (1H, d, $J = 15.7$ Hz), 3.70 (1H, d, $J = 15.7$ Hz), 6.25 (1H, d, $J = 12.6$ Hz), 7.07 (1H, d, $J = 12.6$ Hz), 7.18–7.20 (1H, m), 7.27–7.30 (2H, m), 7.33–7.36 (1H, m). MS *m/z* (%) 212 (M^+, 76), 197 (20), 157 (100), 141 (33), 128 (67), 115 (38). Calcd for $C_{15}H_{16}O$: *M*, 212.1200. Found: *m/z* 212.1197.
9. Crystal data for spiro[2.6]nonadienone **13**: $C_{15}H_{16}O$, $M = 212.12$, *monoclinic*, space group $P2_1/c$ (#14), $a = 21.26(3)$ Å, $b = 6.075(8)$ Å, $c = 18.92(2)$ Å, $\beta = 104.06(2)^\circ$, $V = 2370(5)$ Å^3, $Z = 4$, $F(000) = 1824$, $D_{calc} = 1.190$ g cm^{-3}, μ(Mo Kα) = 0.73 cm^{-1}, $T = 173$ K, radiation = 0.71073 Å, $R_1 = 0.1406$ for $I > 2.0\sigma(I)$, $wR_2 = 0.3986$ for all data (5321 reflections), GOF = 0.981 (294 parameters), crystal dimensions $0.63 \times 0.09 \times 0.02$ mm^3. The single crystal of **13**, coated with Fluorinert FC-70 (3M), was mounted using loop method at 173 K. Diffraction data were measured on a Bruker APEX CCD-Detector X-ray diffractometer with monochromated Mo Kα radiation from a rotating anode source apparatus. The data reduction, structure solution and refinement, and all the necessary computational data processes were performed using APEX, SAINT, and SHELXTL programs. The small platelet crystal of **13** was recrystallized from hexane. The low resolution from the data collection is the reason for a fragile and very small thin crystal. Therefore, we have restricted the discussion to only molecular formationand did not discuss the bond lengths and angles of **13**. Crystallographic data excluding structures have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 683165 for **13**. A copy of the data can be obtained free of charge from CCDC, 12 Union road, Cambridge CB2 1EZ. UK [DIRECT LINE: +44 1223 762910, Fax: +44 (0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk.
10. Structure of the product **15c** was unambiguously determined from its spectral data. Colorless oil; IR (neat) 1659 (CO), 1626 (C=C) cm^{-1}; ^1H NMR δ 0.77 (2H, s), 1.06 (3H, s), 1.19 (3H, s), 2.35 (1H, dt, $J = 15.5$, 1.3 Hz), 3.04 (1H, d, $J = 15.5$ Hz), 6.04–6.13 (3H, m), 6.64 (1H, ddd, $J = 12.2$, 7.0, 1.0 Hz). MS *m/z* (%) 162 (M^+, 39), 147 (83), 119 (32), 107 (100), 91 (76). Calcd for $C_{11}H_{14}O$: *M*, 162.1044. Found: *m/z* 162.1046.
11. Some recent papers for the chemistry of lithium cyclopropyl carbenoids: (a) Oku, A.; Harada, T. *J. Synth. Org. Chem. Jpn.* **1986**, *44*, 736; (b) Harada, T.; Yamaura, Y.; Oku, A. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 1715; (c) Oku, A. *J. Synth. Org. Chem. Jpn.* **1990**, *48*, 710; (d) Creary, X.; Jiang, Z.; Butchko, M.; McLean, K. *Tetrahedron Lett.* **1996**, *37*, 579; (e) Tverezovsky, V. V.; Baird, M. S.; Bolesor, I. G. *Tetrahedron* **1997**, *53*, 14773; (f) Azizoglu, A.; Ozen, R.; Hokelek, T.; Balci, M. *J. Org. Chem.* **2004**, *69*, 1202; (g) Thomas, E.; Kasatkin, A. N.; Whitby, R. J. *Tetrahedron Lett.* **2006**, *47*, 9181.