Organometallics **1998,** *17,* 5713−5716

Oxovanadium(V)-Induced Oxidative Coupling of Organolithium and -magnesium Compounds

Takuji Ishikawa, Akiya Ogawa, and Toshikazu Hirao*

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Yamada-oka, Suita, Osaka 565-0871, Japan

Received July 16, 1998

The homocoupling of various organolithium and -magnesium compounds was effectively induced by oxidation with oxovanadium(V) compounds under mild conditions, affording the diynes and biaryls selectively. The oxidation capability of oxovanadium(V) compounds depends on their substituents, giving the reactivity order, $VO(OR)Cl_2$ > $VO(OR)_2Cl$ > $VO(OR)_3$. The reaction path was investigated by ^{51}V NMR.

Introduction

Transition-metal-induced oxidative coupling of metalated organic anions is of considerable interest, since it provides a convenient method for carbon−carbon bond formation.[1] These reactions are believed in most instances to involve organo transition metal intermediates formed via transmetalation, which are thermally unstable and dimerize under the conditions given. A variety of transition metals possessing one-electron redox properties such as copper have been used for this purpose.[2]

Oxovanadium(V) compounds, which act as Lewis acids with one-electron oxidation capability, can conveniently be utilized in synthetic redox reactions.[3] For example, selective transformations such as oxidative decarboxylation−deoxygenation of 3-hydroxycarboxylic acids,[4] oxidation of α,β-unsaturated carbonyl compounds,[5] oxidative desilylation of organosilicon compounds,[6] and stereocontrolled phenolic oxidative coupling[7] have been effected by use of these reagents.

Although a few aryl and alkyl oxovanadium(V) derivatives were prepared by the arylation and alkylation of $VO(OR)_xCl_{3-x}$ with RLi, R_2Zn, and R_2Hg,[8] the application to organic synthesis has been virtually unexplored. We report here that the homocoupling of various organolithium and -magnesium compounds is effectively induced by oxidation with $VO(OR)Cl_2$ [9] under mild conditions.

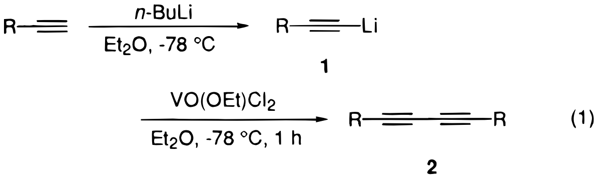
Table 1. Oxidative Coupling of 1-Alkynyllithiums[a]

entry	**1**	R	$VO(OEt)Cl_2$, equiv	**2**	yield,[b] %
1	**1a**	Ph	1	**2a**	42
2	**1a**	Ph	1[c]	**2a**	61
3	**1a**	Ph	2	**2a**	71
4	**1a**	Ph	3	**2a**	92 (86)
5	**1a**	Ph	4	**2a**	88
6	**1b**	Me_3Si	3	**2b**	98 (90)
7	**1c**	*t*-Bu	3	**2c**	98 (89)
8	**1d**	*n*-Hex	3	**2d**	89 (80)
9	**1e**	$PhCH_2OCH_2$	3	**2e**	84 (65)

[a] Reaction temperature, −78 °C; time, 1 h unless otherwise stated. [b] Yields were determined by ^1H NMR on the basis of 1-alkynes. Isolated yields are shown in parentheses. [c] Reaction time, 12 h.

Results and Discussion

Oxidative homocoupling of 1-alkynyllithiums **1** was performed by treatment with $VO(OEt)Cl_2$ in ether at −78 °C, affording the corresponding 1,3-butadiynes **2** (eq 1). A longer reaction time or use of 2 or 3 molar equiv of $VO(OEt)Cl_2$ raised the yield of **2** without polymerization (Table 1, entries 1−4). A variety of 1-alkynes were converted to the expected 1,3-diynes **2** in good yield under the conditions employed in entry 4 (3 molar equiv of $VO(OEt)Cl_2$, −78 °C). Trimethylsilyl and benzyloxy groups are tolerated to give the butadiynes **2b** and **2e**, respectively (entries 6 and 9). An attempted cross-



---

(1) (a) Lipshutz, B. H. In *Organometallics in Synthesis*; Schlosser, M., Eds.; John Wiley & Sons Ltd.: Chichester, U.K., 1994; pp 283−382. (b) Kauffmann, T. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 291.

(2) See, for example: (a) Ishiguro, K.; Ikeda, M.; Sawaki, Y. *J. Org. Chem.* **1992**, *57*, 3057. (b) Wang, F.; Sayre, L. M. *J. Am. Chem. Soc.* **1992**, *114*, 248. (c) Baesjou, P. J.; Driessen, W. L.; Challa, G.; Reedijk, J. *J. Am. Chem. Soc.* **1997**, *119*, 12590.

(3) Hirao, T. *Chem. Rev.* **1997**, *97*, 2707.

(4) Meier, I. K.; Schwartz, J. *J. Am. Chem. Soc.* **1989**, *111*, 3069.

(5) (a) Hirao, T.; Mori, M.; Ohshiro, Y. *J. Org. Chem.* **1990**, *55*, 358. (b) Hirao, T.; Mori, M.; Ohshiro, Y. *Tetrahedron Lett.* **1991**, *32*, 1741.

(6) (a) Fujii, T.; Hirao, T.; Ohshiro. Y. *Tetrahedron Lett.* **1992**, *33*, 5823. (b) Fujii, T.; Hirao, T.; Ohshiro. Y. *Tetrahedron Lett.* **1993**, *34*, 5601. (c) Hirao, T.; Fujii, T.; Ohshiro. Y. *Tetrahedron* **1994**, *50*, 10207. (d) Ryter, K.; Livinghouse, T. *J. Am. Chem. Soc.* **1998**, *120*, 2658.

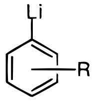
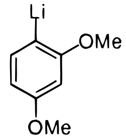
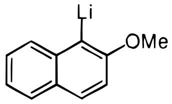
(7) (a) Gottlieb, L.; Meyers, A. I. *J. Org. Chem.* **1990**, *55*, 5659. (b) White, J. D.; Butlin, R. J.; Hahn, H.-G.; Johnson, A. T. *J. Am. Chem. Soc.* **1990**, *112*, 8595. (c) Comins, D. L.; Morgan, L. A. *Tetrahedron Lett.* **1991**, *32*, 5919. (d) Evans, D. A.; Dinsmore, C. J.; Evrard, D. A.; DeVries, K. M. *J. Am. Chem. Soc.* **1993**, *115*, 6426.

(8) (a) Reichle, W. T.; Carrick, W. L. *J. Organomet. Chem.* **1970**, *24*, 419. (b) Yagupsky, G.; Mowat, W.; Shortland, A.; Wilkinson, G. *J. Chem. Soc., Chem. Commun.* **1970**, 1369. (c) Lachowicz, A.; Thiele, K.-H. *Z. Anorg. Allg. Chem.* **1977**, *431*, 88. (d) Holliday, A. K.; Makin, P. H.; Puddephatt, R. J. *J. Chem. Soc., Dalton Trans.* **1979**, 228. (e) Choukroun, R.; Sabo, S. *J. Organomet. Chem.* **1979**, *182*, 221. (f) Preuss, F.; Ogger, L. *Z. Naturforsch.* **1982**, *37b*, 957. (g) Seidel, W.; Kreisel, G. *Z. Chem.* **1982**, *22*, 113. (h) Seidel, W.; Kreisel, G. *Z. Anorg. Allg. Chem.* **1988**, *559*, 118.

(9) (a) Funk, H.; Weiss, W.; Zeising, M. *Z. Anorg. Allg. Chem.* **1958**, *36*, 296. (b) Hirao, T.; Mori, M.; Ohshiro, Y. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2399.

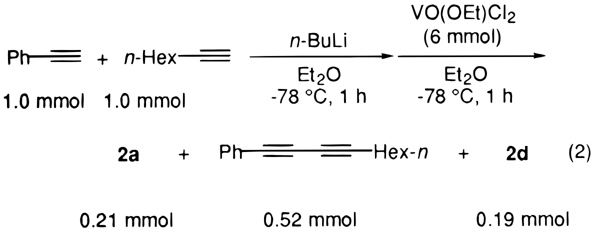
10.1021/om980607c CCC: $15.00

Table 2. Oxidative Coupling of Aryllithiums[a]

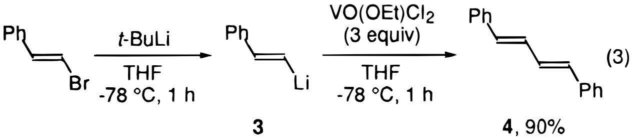
entry	7				8	yield,[b] %
1		R =	H	**7a**	**8a**	90
2			H	**7a**	**8a**	90[c]
3			*o*-OMe	**7b**	**8b**	90
4			*m*-OMe	**7c**	**8c**	91
5			*p*-OMe	**7d**	**8d**	91
6			*o*-Me	**7e**	**8e**	62
7			*o*-SMe	**7f**	**8f**	60
8			*o*-Ph	**7g**	**8g**	80
9			*o*-CN	**7h**	**8h**	45
10				**7i**	**8i**	62
11				**7j**	**8j**	89

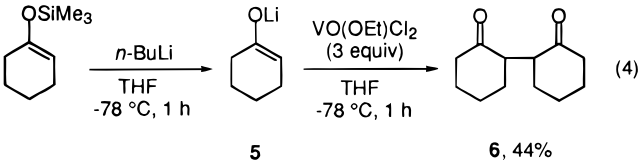
[a] Reaction temperature, room temperature; time, 1 h unless otherwise stated. $VO(OEt)Cl_2$, 3 equiv. [b] Isolated yields on the basis of aryl bromides. [c] Phenol was obtained in 4% yield. Reaction temperature, −78 °C.

coupling reaction resulted in statistical distribution of diynes along with the cross-coupled product (eq 2).



This method is applicable to the homocoupling of the 1-alkenyllithium **3** and lithium enolate **5** to the 1,3-diene **4** and 1,4-diketone **6**, respectively, as shown in eqs 3 and 4.





The oxidative coupling of aryllithiums **7** at room temperature afforded symmetrical biphenyls **8** bearing various substituents in good yield (eq 5, Table 2).

$$\mathrm{ArBr}\ \xrightarrow[\substack{\mathrm{Et_2O}\\ \text{rt, 15 min}}]{n\text{-BuLi}}\ \underset{\mathbf{7}}{\mathrm{ArLi}}\ \xrightarrow[\substack{\mathrm{Et_2O}\\ \text{rt, 1h}}]{\mathrm{VO(OEt)Cl_2}}\ \underset{\mathbf{8}}{\mathrm{Ar{-}Ar}} \qquad (5)$$

Table 3. Oxidative Coupling of (2-Methoxyphenyl)lithium[a]

entry	oxovanadium(V)	time, h	**8b** yield,[b] %
1	$VO(OEt)Cl_2$	1	86
2	$VO(OPr\text{-}i)Cl_2$	1	79
3	$VO(OPr\text{-}i)_2Cl$	1	66
4	$VO(OPr\text{-}i)_2Cl$	24	72
5	$VO(OPr\text{-}i)_3$	1	59

[a] Oxovanadium(V) compound, 1 equiv; reaction temperature, room temperature. [b] Yields were determined by ^1H NMR on the basis of 2-bromoanisole.

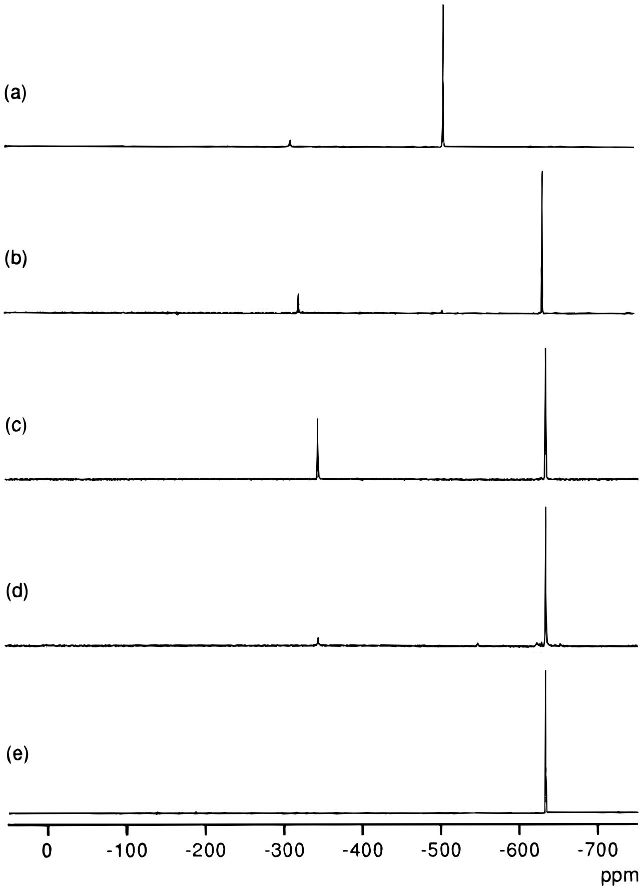
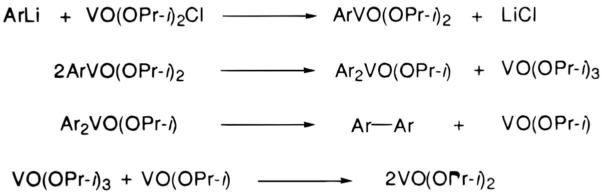


Figure 1. ^{51}V NMR spectra in ether at room temperature ($VOCl_3$, 0 ppm). (a) $VO(OPr\text{-}i)_2Cl$. (b) $VO(OPr\text{-}i)_2Cl$ was added to PhLi at −78 °C (the molar ratio, 1:1). (c) $VO(OPr\text{-}i)_2Cl$ was added to 2-methoxyphenyllithium at −78 °C (the molar ratio, 1:1). (d) The mixture obtained by (c) was kept at room temperature for 24 h. (e) $VO(OPr\text{-}i)_3$.

Oxidation of PhLi with $VO(OEt)Cl_2$ even at −78 °C led to biphenyl (90%) together with a small amount of phenol (4%, entry 2). This finding implies the intermediacy of the aryl oxovanadium(V) species since these products are known to be formed through the similar intermediate derived from $VOCl_3$ and Ph_2Hg.[8a] The presence of the cyano group as an electron-withdrawing group lowered the yield (entry 9), suggesting that the coupling reaction depends on the electronic nature of the aryl group. The result is consistent with the reaction path in which the degradation of V(V) to V(IV) with the formation of biaryl is likely to be facilitated by the high electron density of the aromatic ring.

The oxidation reaction also was effected by the substituents of organovanadium(V) compounds. Their oxidation capability decreases with the increasing number of alkoxy groups that they contain. Accordingly, the yield of the biaryl was lowered in the order of $VO(OPr\text{-}i)Cl_2 > VO(OPr\text{-}i)_2Cl > VO(OPr\text{-}i)_3$ (Table 3). These results are related to the above-mentioned reaction

Scheme 1

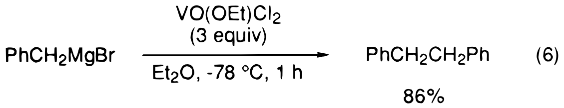


$$ArLi + VO(OPr\text{-}i)_2Cl \longrightarrow ArVO(OPr\text{-}i)_2 + LiCl$$
$$2ArVO(OPr\text{-}i)_2 \longrightarrow Ar_2VO(OPr\text{-}i) + VO(OPr\text{-}i)_3$$
$$Ar_2VO(OPr\text{-}i) \longrightarrow Ar{-}Ar + VO(OPr\text{-}i)$$
$$VO(OPr\text{-}i)_3 + VO(OPr\text{-}i) \longrightarrow 2VO(OPr\text{-}i)_2$$

path. A longer reaction time increased the yield of **8b** (entries 3 and 4).

To gain insight into the mechanism, the reaction was followed by ^{51}V NMR spectroscopy (Figure 1). When phenyllithium (**7a**) and (2-methoxyphenyl)lithium (**7b**) in ether were treated with an equimolar amount of $VO(OPr\text{-}i)_2Cl$ (−505 ppm; $VOCl_3$, 0 ppm; Figure 1a) at −78 °C, two peaks were observed at −322, −633 ppm and −345, −633 ppm, respectively, as shown in Figure 1b,c. The peak at −633 ppm is assigned to $VO(OPr\text{-}i)_3$ by comparison of the authentic sample. The peak at −345 ppm was found to decrease when the reaction mixture was kept at room temperature for 24 h (Figure 1d). The peaks at −322 and −345 ppm (Figure 1b,c), which were about 200 ppm downfield from $VO(OPr\text{-}i)_2Cl$, are probably assigned to $ArVO(OPr\text{-}i)_2$ (Ar = Ph, $o\text{-}MeOC_6H_4$).[10] These observations suggest that $ArVO(OPr\text{-}i)_2$ decomposes to the biaryl via disproportionation to $Ar_2VO(OPr\text{-}i)$ (Scheme 1). The thus-generated V(III) and V(V) species are assumed ultimately to be converted to a V(IV) species. A similar reaction path has been proposed by Reichle.[8a] These findings are consistent with the result described above.

Grignard reagents similarly underwent the present coupling reaction, as exemplified by the homocoupling of benzylmagnesium bromide bearing a sp^3-carbon (eq 6).



$$PhCH_2MgBr \xrightarrow[Et_2O,\ -78\ °C,\ 1\ h]{VO(OEt)Cl_2\ (3\ equiv)} \underset{86\%}{PhCH_2CH_2Ph} \qquad (6)$$

Conclusions

$VO(OR)Cl_2$ was found to be an efficient oxidant to induce the homocoupling of organolithium and -magnesium compounds, in which organo oxovanadium intermediates are considered to be formed. The conversion depends on the oxidation capability of oxovanadium(V) compounds. From the synthetic viewpoint, the present transformation is a versatile method for oxidative dimerization.

Experimental Section

All solvents were dried and distilled. 3-Benzyloxy-2-propyne (**1e**) was prepared according to the standard procedure.[11] $VO(OEt)Cl_2$, $VO(OPr\text{-}i)Cl_2$, and $VO(OPr\text{-}i)_2Cl$ were easily obtained from $VOCl_3$ and the corresponding alcohol and distilled.[9] $VO(OPr\text{-}i)_3$ was supplied by Nichia Chemical Industries, Ltd.

General Procedure for Oxidative Coupling of 1-Alkynyllithium. To a stirred solution of 1-alkyne (1.0 mmol) in dry ether (or tetrahydrofuran (THF), 4 mL) at −78 °C under argon was added *n*-BuLi (1.0 mmol, 0.63 mL, 1.6 M in hexane) to generate the 1-alkynyllithium **1**. After stirring at −78 °C for 1 h, $VO(OEt)Cl_2$ (549 mg, 3.0 mmol) was added dropwise to the resulting solution over 10 min at −78 °C. The mixture was stirred at −78 °C for 1 h, and then ether (15 mL) and 1.5 M aqueous HCl (1 mL) were added to the reaction mixture. After extraction with ether (3 × 10 mL), the combined ethereal solution was washed with saturated NH_4Cl, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$ and concentrated. Purification by chromatography on silica gel column gave the 1,3-diyne **2** as shown in Table 1. Yields were determined on the basis of 1-alkynes. The products were identified by comparison of spectral data with those of commercially available or authentic samples.[12]

2e. Compound $R_f = 0.55$ (hexane−chloroform, 1:1 (v/v)). ^1H NMR (300 MHz, $CDCl_3$): δ 7.40−7.30 (m, 10H), 4.63 (s, 4H), 4.27(s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.9, 128.3, 128.0, 127.9, 75.3, 71.4, 70.6, 57.2. Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.42; H, 6.31.

Oxidative Coupling of β-Stylyllithium. To a stirred solution of *t*-BuLi (1.25 mL, 1.6 M in hexane) in dry THF (4 mL) at −78 °C under argon was added (*E*)-β-bromostyrene (183 mg, 1.0 mmol) to generate the alkenyllithium **3**. After stirring at −78 °C for 1 h, $VO(OEt)Cl_2$ (549 mg, 3.0 mmol) was added dropwise to the resulting solution over 10 min at −78 °C. The mixture was stirred at −78 °C for 1 h, and then ether (15 mL) and 1.5 M aqueous HCl (1 mL) were added to the reaction mixture. After extraction with ether (3 × 10 mL), the combined ethereal solution was washed with saturated NH_4Cl, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$ and concentrated. Purification by chromatography on silica gel column eluting with hexane−chloroform (10:1 (v/v)) gave *E*,*E*-1,4-diphenyl-1,3-butadiene, (**4**, 186 mg, 90%).

Oxidative Coupling of Lithium 1-Cyclohexenolate. To a stirred solution of *n*-BuLi (0.63 mL, 1.6 M in hexane) in dry THF (4 mL) at −78 °C under argon was added 1-(trimethylsilyloxy)-1-cyclohexene (170 mg, 1.0 mmol) to generate the lithium enolate **5**. After stirring at −78 °C for 1 h, $VO(OEt)Cl_2$ (549 mg, 3.0 mmol) was added dropwise to the resulting solution over 10 min at −78 °C. The mixture was stirred at −78 °C for 1 h, and then ether (15 mL) and 1.5 M aqueous HCl (1 mL) were added to the reaction mixture. After extraction with ether (3 × 10 mL), the combined ethereal solution was washed with saturated NH_4Cl, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$ and concentrated. Purification by chromatography on silica gel column eluting with hexanes−ethyl acetate (5:1 (v/v)) gave 2,2′-dioxodicyclohexyl, (**6**, 43 mg, 44%).

General Procedure for Oxidative Coupling of Aryllithium. To a stirred solution of aryl bromide (1.0 mmol) in dry ether (4 mL) at 0 °C under argon was added *n*-BuLi (1.0 mmol, 0.63 mL, 1.6 M in hexane) to generate the aryllithium **7**. After stirring at room temperature for 15 min, $VO(OEt)Cl_2$ (549 mg, 3.0 mmol) was added dropwise to the resulting solution over 10 min at room temperature. The mixture was stirred at room temperature for 1 h, and then ether (15 mL) and 1.5 M aqueous HCl (1 mL) were added to the reaction mixture. After extraction with ether (3 × 10 mL), the combined ethereal solution was washed with saturated NH_4Cl, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$ and concentrated. Purification by chromatography on silica gel column gave the biaryl **8**, as shown in Table 2. Yields were determined on the basis of aryl bromides. The products were identified by comparison of spectral data with those of commercially available or authentic samples.[13]

Oxidative Coupling of Benzylmagnesium. To a stirred solution of $PhCH_2MgCl$ (2.0 mL, 1.0 M in hexane) in dry ether

---

(10) The example of ^{51}V NMR for alkyl transfer from aluminum to vanadium: Feher, F.; Blanski, R. L. *J. Am. Chem. Soc.* **1992**, *114*, 5886.

(11) Onaka, M.; Kawai, M.; Izumi, Y. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1761.

(12) **2b**, [4526-07-2]; **2c**, [78655-42-2]; **2d**, [18277-20-8].

(13) **8b**, [4877-93-4]; **8c**, [6161-50-8]; **8d**, [2132-39-0]; **8e**, [605−39−0]; **8f**, [7343-32-0]; **8g**, [641-96-3]; **8h**, [4341-02-0]; **8i**, [3153-72-8]; **8j**, [2960-93-2].

(4 mL) was added dropwise $VO(OEt)Cl_2$ (549 mg, 3.0 mmol) over 10 min at −78 °C under argon. The mixture was stirred at −78 °C for 1 h, and then ether (15 mL) and 1.5 M aqueous HCl (1 mL) were added to the reaction mixture. After extraction with ether (3 × 10 mL), the combined ethereal solution was washed with saturated NH_4Cl, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$ and concentrated. Purification by chromatography on silica gel column eluting with hexane−chloroform (10:1 (v/v)) gave bibenzyl (157 mg, 86%).

Acknowledgment. The use of the facilities of the Analytical Center, Faculty of Engineering, Osaka University, is acknowledged. This work was partly supported by a Grant-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Science, and Culture, Japan.

OM980607C