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Zinc-Catalyzed Nucleophilic Substitution Reaction of Chlorosilanes with Organomagnesium Reagents

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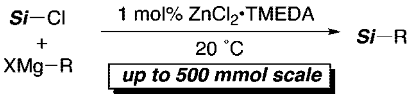
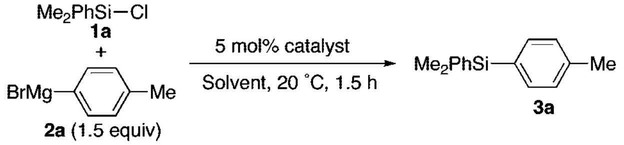


Zinc-catalyzed nucleophilic substitution reactions of chlorosilanes with organomagnesium reagents afford various tetraorganosilanes under mild reaction conditions. The reactions can be performed on large scale and allow efficient preparation of functionalized tetraorganosilanes.

The nucleophilic substitution reaction of chlorosilanes with organometallic reagents is a fundamental method to synthesize various tetraorganosilanes. The reactions of chlorosilanes with organolithium reagents generally proceed smoothly at very low temperature.[1] However, the reactions with the less reactive organomagnesium reagents often require prolonged reaction times and high temperature to complete the reaction. Addition of a catalytic amount of cyanide or thiocyanate is known to facilitate the transmetalation reaction of chlorosilanes with organomagnesium reagents.[2] However, the use of the toxic anions should be avoided.

During the course of our study on metal-catalyzed transmetalation of chlorosilanes,[3] we found zinc salts are efficient catalysts for transmetalation reactions between chlorosilanes and organomagnesium reagents. Zinc has many practical advantages as a catalyst due to its low cost, environmental friendliness, and low toxicity.[2] In addition, the present zinc-catalyzed reactions have proved to be more versatile than the previous silver-catalyzed ones.[3,4]

TABLE 1. Zinc-Catalyzed Reaction of Chlorodimethylphenylsilane with *p*-Tolylmagnesium Bromide



entry	catalyst	solvent	yield (%)[a]
1	none	THF	13
2	$ZnCl_2$	THF	67
3	$ZnBr_2$	THF	75
4	ZnI_2	THF	69
5	ZnF_2	THF	80
6	$Zn(OAc)_2$	THF	62
7	$ZnCl_2$•TMEDA	THF	77
8	$ZnCl_2$•TMEDA[b]	1,4-dioxane	84[c]
9	ZnF_2	1,4-dioxane	18

[a] The yields were determined by ^{1}H NMR spectroscopy. [b] The reaction was performed with 1 mol % of $ZnCl_2$•TMEDA for 1 h. [c] Isolated yield.

Treatment of chlorodimethylphenylsilane (**1a**) with *p*-tolylmagnesium bromide (**2a**) in the presence of a catalytic amount of zinc chloride in THF at 20 °C for 1.5 h provided the corresponding tetraorganosilane **3a** in 67% yield (Table 1, entry 2). In the absence of zinc chloride, **3a** was obtained in only 13% yield (Table 1, entry 1). Other zinc salts, such as zinc halides, acetate, and zinc chloride•*N*,*N*,*N*′,*N*′-tetramethylethylenediamine complex ($ZnCl_2$•TMEDA), accelerated the reaction (Table 1, entries 3−7). We chose $ZnCl_2$•TMEDA as the best catalyst because $ZnCl_2$•TMEDA is stable and easy to handle under air as well as being sufficiently active. Finally, the use of 1,4-dioxane improved the catalytic activity, and the reaction completed within 1 h with the aid of only 1 mol % of the catalyst to furnish **3a** in 84% yield (Table 1, entry 8). Zinc fluoride, which showed a competing catalytic activity in THF, was not effective in 1,4-dioxane (entry 5 vs entry 9).[5]

The scope of arylmagnesium reagents and chlorosilanes was studied, and the results are summarized in Table 2. The reactions with sterically hindered, electron-rich, and electron-deficient arylmagnesium reagents (Table 2, entries 1−3) proceeded as smoothly as that described in entry 8 in Table 1. A chlorosilane **1b** having a chloromethyl moiety (Table 2, entry 4) reacted without any observable side reactions. The reaction of bulkier chloromethyldiphenylsilane (**1c**) with *p*-tolylmagnesium bromide under zinc catalysis proceeded to completion after extended reaction time (Table 2, entry 5). However, the reaction of chlorotriethylsilane (**1d**) was slow and did not complete even at 40 °C for 12 h (Table 2, entry 6).[6] The reaction of more reactive triethylsilyl triflate (**1d′**) proceeded smoothly at 20 °C in 7 h and the yield was improved to 73% (Table 2, entry 7).

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(1) (a) *Science of Synthesis (Houben-Weyl)*; Fleming, I., Ed.; Georg Thieme Verlag: Stuttgart, Germany, 2002; Vol. 4, Chapter. 4.4. (b) Brook, M. A. *Silicon in Organic, Organometallic, and Polymer Chemistry*; Wiley: New York, 2000, Chapter 5. (c) Birkofer, L.; Stuhl, O. *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1989; Chapter 10.

(2) Lennon, P. J.; Mack, D. P.; Thompson, Q. E. *Organometallics* **1989**, *8*, 1121–1122.

(3) Murakami, K.; Hirano, K.; Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 5833–5835.

(4) Historically, alkylations of halosilane were demonstrated for the first time by using diorganozinc reagents under harsh reaction conditions: (a) Friedel, C.; Crafts, J. M. *Ann.* **1863**, *127*, 28–29. (b) Friedel, C.; Crafts, J. M. *Ann.* **1865**, *136*, 203–204.

(5) Treatment of **1a** with zinc fluoride in THF provided Me_2PhSiF, which is more reactive toward the nucleophilic substitution with **2a**. Thus, the mechanism of activating chlorosilane **1a** may be different from that of other zinc salts.

(6) The reaction of chlorotriethylsilane proceeded smoothly in the presence of a catalytic amount of silver nitrate, see ref 3.

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TABLE 2. Scope of Chlorosilanes and Arylmagnesium Reagents

$$\underset{\mathbf{1}}{\textit{Si}\text{–Cl}} + \underset{\mathbf{2}\text{ (1.5 equiv)}}{\text{BrMg–Ar}} \xrightarrow[\text{1,4–Dioxane, 20 °C}]{\text{1 mol\% ZnCl}_2\text{•TMEDA}} \underset{\mathbf{3}}{\textit{Si}\text{–Ar}}$$

entry	**1**, Si	**2**, Ar	*t* (h)	**3**	yield (%)[a]
1	**1a**, $PhMe_2Si$	**2b**, *o*-MeC_6H_4	5	**3b**	92
2	**1a**, $PhMe_2Si$	**2c**, *p*-$MeOC_6H_4$	1	**3c**	87
3	**1a**, $PhMe_2Si$	**2d**, *m*-$CF_3C_6H_4$	3	**3d**	99
4	**1b**, $(ClCH_2)Me_2Si$	**2e**, Ph	1	**3e**	74
5	**1c**, Ph_2MeSi	**2a**, *p*-MeC_6H_4	15	**3f**	89
6	**1d**, Et_3Si	**2a**, *p*-MeC_6H_4	12	**3g**	30[b]
7	**1d′**[c], Et_3Si	**2a**, *p*-MeC_6H_4	7	**3g**	73
8	**1e**, ${}^tBuMe_2Si$	**2a**, *p*-MeC_6H_4	24	**3h**	trace[d]

[a] Isolated yield. [b] The reaction was performed at 40 °C. [c] Et_3SiOTf (**1d′**) was used instead of Et_3SiCl (**1d**). [d] The reaction was performed at 100 °C.

TABLE 3. Scope of Organomagnesium Reagents

$$\underset{\mathbf{1}}{\textit{Si}\text{–Cl}} + \underset{\mathbf{2}\text{ (1.5 equiv)}}{\text{R–MgX}} \xrightarrow[\text{THF, 20 °C}]{\text{1 mol\% ZnCl}_2\text{•TMEDA}} \underset{\mathbf{4}}{\textit{Si}\text{–R}}$$

entry	**1**, Si	**2**, RMgX	*t* (h)	**4**	yield (%)[a]
1	**1a**, $PhMe_2Si$	**2f**, $CH_2{=}CMeMgBr$	3	**4a**	84 (46)[b]
2	**1c**, Ph_2MeSi	**2g**, $CH_2{=}CHMgBr$	2	**4b**	71
3	**1e**, ${}^tBuMe_2Si$	**2h**, $PhCH_2MgCl$	7	**4c**	70
4	**1f**, ${}^iPr_3Si$	**2i**, $CH_2{=}CHCH_2MgCl$	12	**4d**	91 (trace)[b]
5	**1f**, ${}^iPr_3Si$	**2j**, BuMgBr	1	**4e**	trace

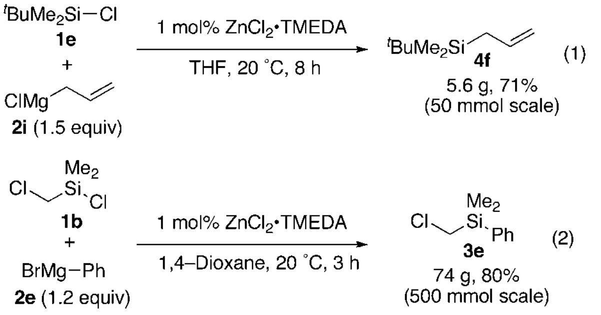
[a] Isolated yield. [b] $AgNO_3$ was used instead of $ZnCl_2$•TMEDA.

Sterically congested *t*-butylchlorodimethylsilane failed to react with arylmagnesium reagents (Table 2, entry 8).

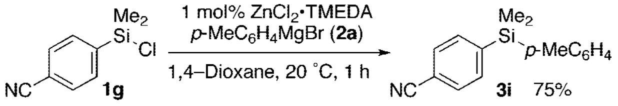
Generally, the thermal stability of organosilver reagents was poor.[7] Therefore, only aryl- and bulky 1-alkenylmagnesium reagents were applicable to the arylation and alkenylation of chlorosilanes under the silver catalysis.[3] On the other hand, zinc catalysis broadened the scope of the organomagnesium reagents. Treatment of chlorodimethylphenylsilane (**1a**) with isopropenylmagnesium bromide (**2f**) in the presence of a catalytic amount of $ZnCl_2$•TMEDA in THF[8] provided the corresponding tetraorganosilane **4a** in 84% yield (Table 3, entry 1). Silane **4a** was obtained in 46% yield in the presence of silver nitrate[3] instead of $ZnCl_2$•TMEDA. The reaction with vinylmagnesium bromide also proceeded smoothly (Table 3, entry 2). Not only vinylmagnesium reagents but also benzylmagnesium reagent was applicable (Table 3, entry 3). Sterically congested chlorotriisopropylsilane (**1f**) was treated with allylmagnesium chloride. The corresponding allylsilane **4d** was obtained in 91% yield (Table 3, entry 4). Under the silver catalysis **1f** was too congested to react. Treatment of chlorotriisopropylsilane with butylmagnesium bromide in the presence of zinc salts did not provide the corresponding butylsilane **4e** (Table 3 entry 5).[9]

The reaction can be performed on a large scale. *tert*-Butylchlorodimethylsilane (**1e**, 50 mmol) was treated with allylmagnesium chloride (**2i**) in the presence of 1 mol % of $ZnCl_2$•TMEDA for 8 h. After distillation, allyl(*tert*-butyl)dimethylsilane (**4f**) was obtained in 71% yield (Scheme 1, eq 1).[10] Treatment of 500 mmol of chloro(chloromethyl)dimethylsilane (**1b**) with 1.2 equiv of phenylmagnesium bromide for 3 h provided 74 g (80%) of (chloromethyl)dimethylphenylsilane (**3e**) (Scheme 1, eq 2).

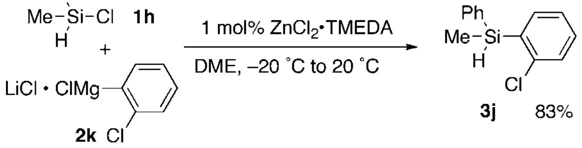
SCHEME 1. Large-Scale Reactions



SCHEME 2. Reaction of Functionalized Chlorosilane



SCHEME 3. Reaction with *o*-Chlorophenylmagnesium Chloride•LiCl Complex



Because this reaction can proceed under mild reaction conditions, functionalized chlorosilanes such as chloro(*p*-cyanophenyl)dimethylsilane (**1g**) were also available for this method (Scheme 2). Treatment of chloromethylphenylsilane (**1h**) with *o*-chlorophenylmagnesium chloride•LiCl complex, which was prepared by halogen–magnesium exchange,[11] provided the corresponding organosilane **3j** in 83% yield (Scheme 3). The reaction was clean, and only a trace amount of disiloxane $(PhMeHSi)_2O$ was detected.

To gain information about the active species of this reaction, the reaction of **1a** with stoichiometric zinc reagents was examined with varying amounts of *p*-MeC_6H_4MgBr. Treatment of **1a** (0.5 mmol) with a zinc complex, prepared from $ZnCl_2$•TMEDA (0.75 mmol) and *p*-MeC_6H_4MgBr (0.75 mmol), did not provide **3a** at all. A diarylzinc reagent, generated from $ZnCl_2$•TMEDA (0.75 mmol) and *p*-MeC_6H_4MgBr (1.5 mmol), also failed to react with **1a**. A reagent prepared from $ZnCl_2$•TMEDA (0.75 mmol) and *p*-MeC_6H_4MgBr (2.25 mmol) dramatically changed the outcome. The desired arylsilane **3a**

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[7] Schmidbaur, H.; Bayler, A. *The chemistry of organic derivatives of gold and silver*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1999; Chapter 7.

[8] THF was the best solvent in the reactions with vinyl-, benzyl-, and allylmagnesium reagents. 1,4-Dioxane retarded the reactions.

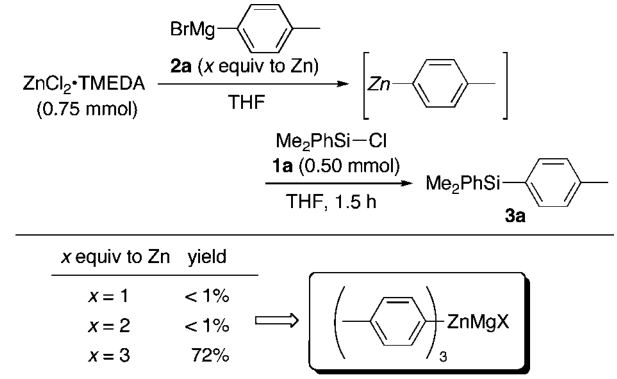
[9] Treatment of chloromethyldiphenylsilane with 4-pentenylmagnesium bromide for 3 h provided the desired product in 32% yield in the absence of any zinc salts. However, no acceleration of the reaction was observed even when zinc salts were added.

[10] Ultrasound irradiation was required for the synthesis of allylsilane **4f**, see: Hagen, G.; Mayr, H. *J. Am. Chem. Soc.* **1991**, *113*, 4954–4961.

[11] Krasovskiy, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 3333–3336.

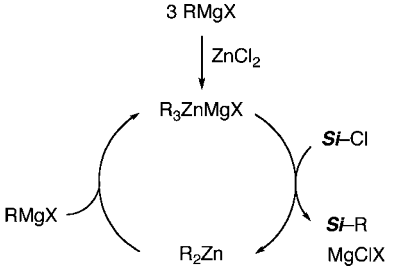
[12] For recent examples of zincate chemistry see: (a) Hatano, M.; Suzuki, S.; Ishihara, K. *J. Am. Chem. Soc.* **2006**, *128*, 9998–9999. (b) Studte, C.; Breit, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 5451–5455. (c) Mulvey, R. E.; Mongin, F.; Uchiyama, M.; Kondo, K. *Angew. Chem., Int. Ed.* **2007**, *47*, 3802–3824. (d) Nakamura, S.; Uchiyama, M.; Ohwada, T. *J. Am. Chem. Soc.* **2004**, *126*, 11146–11147. (e) Uchiyama, M.; Nakamura, S.; Ohwada, T.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 10897–10903. (f) Uchiyama, M.; Kameda, M.; Mishima, O.; Yokoyama, N.; Koike, M.; Kondo, Y.; Sakamoto, T. *J. Am. Chem. Soc.* **1998**, *120*, 4934–4946. (g) Uchiyama, M.; Furumoto, S.; Saito, M.; Kondo, Y.; Sakamoto, T. *J. Am. Chem. Soc.* **1997**, *119*, 11425–11433.

SCHEME 4. Reactions of 1a with Arylzinc Reagents



x equiv to Zn	yield
x = 1	< 1%
x = 2	< 1%
x = 3	72%

SCHEME 5. A Plausible Mechanism



was obtained in 72% yield (Scheme 4). Hence, the active species of this reaction would be a zincate, (p-$MeC_6H_4)_3ZnMgX$ (X = Cl or Br).[12]

Scheme 5 illustrates a plausible reaction mechanism. Triorganozincate is initially generated from zinc chloride and 3 equiv of a Grignard reagent. The zincate effects smooth organic group transfer to afford the corresponding silane with concomitant formation of diorganozinc. The initial triorganozincate is regenerated by the reaction of diorganozinc with the remaining Grignard reagent. The exact role of TMEDA is not clear at this stage.

In summary, we report the zinc-catalyzed nucleophilic substitution reaction of chlorosilanes with organomagnesium reagents. The reaction described here provides a mild and efficient method for the preparation of tetraorganosilanes.

Experimental Section

Typical Procedure for Zinc-Catalyzed Reactions. The reaction of **1a** with *p*-methylphenylmagnesium bromide (Table 1, entry 8) is representative. $ZnCl_2 \cdot TMEDA$ (1.3 mg, 0.005 mmol) was placed in a 20-mL reaction flask under argon. Chlorodimethylphenylsilane (85 mg, 0.50 mmol) in 1,4-dioxane (1 mL) was added to the flask. Then, *p*-methylphenylmagnesium bromide (1.0 M THF solution, 0.75 mL, 0.75 mmol) was added. The mixture was stirred at 20 °C for 1 h. A saturated aqueous solution of NH_4Cl (2 mL) was added. The organic compounds were extracted with ethyl acetate three times. The combined organic part was dried over Na_2SO_4 and concentrated in vacuo. Chromatographic purification on silica gel by using hexane as an eluent afforded dimethyl(*p*-methylphenyl)phenylsilane (**3a**, 95.2 mg, 0.42 mmol) in 84% yield.

Procedure for Large-Scale Reaction (Scheme 1, Eq 2). $ZnCl_2 \cdot TMEDA$ (1.26 g, 5 mmol) was placed in a 2-L reaction flask under argon. Chloro(chloromethyl)dimethylsilane (71.5 g, 500 mmol) in 1,4-dioxane (500 mL) was added to the flask. The flask was cooled to 0 °C. Phenylmagnesium bromide (1.2 M THF solution, 500 mL, 600 mmol) was subsequently added over 20 min. After the completion of the addition, the mixture was warmed to 20 °C and stirred at the same temperature for 3 h. The reaction mixture was quenched with an ice-cold saturated aqueous solution of NH_4Cl (300 mL). The organic compounds were extracted with ethyl acetate three times (3 × 100 mL). The combined organic part was washed with brine (100 mL). Then the organic part was dried over Na_2SO_4 and concentrated in vacuo. After evaporation, the residue was distilled to give (chloromethyl)dimethylphenylsilane (**3e**, 74.0 g, 400 mmol, bp 105 °C at 19 mmHg) in 80% yield.

Procedure for the Synthesis of *o*-Chlorophenylphenylmethylsilane. *o*-Chloroiodobenzene (179 mg, 0.75 mmol) was placed in a 20-mL reaction flask under argon and dissolved in DME (1 mL). The flask was cooled to −20 °C. $^{i}PrMgCl \cdot LiCl$ (1.0 M THF solution, 0.80 mL, 0.80 mmol) was introduced dropwise to the flask. The reaction mixture was stirred for 1 h at −20 °C. $ZnCl_2 \cdot TMEDA$ (1.3 mg, 0.005 mmol) and chloromethylphenylsilane (**1h**, 78.3 mg, 0.50 mmol) were sequentially added at the same temperature. The mixture was stirred for 8 h at −20 °C. The mixture was allowed to warm slowly to 20 °C and stirred for 12 h at the same temperature. A saturated aqueous solution of NH_4Cl (2 mL) was then added. The organic compounds were extracted with ethyl acetate three times. The combined organic part was dried over Na_2SO_4 and concentrated in vacuo. Purification by silica gel column chromatography with hexane as an eluent afforded *o*-chlorophenylmethylphenylsilane (**3j**, 97.4 mg, 0.42 mmol) in 83% yield.

Characterization Data of Products. Products **3a**−**g**,[3] **4a**,[13] **4c**,[14] and **4d**[15] are known compounds and showed the identical spectra according to the literature.

(*p*-Cyanophenyl)dimethyl(*p*-methylphenyl)silane (3i): oil; IR (neat) 2959, 2230, 1599, 1385, 1109, 818 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.56 (s, 6H), 2.36 (s, 3H), 7.18−7.21 (m, 2H), 7.37−7.40 (m, 2H), 7.59 (s, 4H); ^{13}C NMR ($CDCl_3$) δ −2.52, 21.66, 112.73, 119.18, 129.07, 131.15, 132.91, 134.30, 134.74, 139.81, 145.85; HRMS found 251.1127 ($\Delta = -1.4$ ppm), calcd for $C_{16}H_{17}NSi$ 251.1130.

***o*-Chlorophenylmethylphenylsilane (3j):** oil; IR (neat) 3052, 2139, 1581, 1428, 1252 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.70 (d, J = 3.9 Hz, 3H), 5.05 (q, J = 3.9 Hz, 1H), 7.19−7.42 (m, 7H), 7.57−7.60 (m, 2H); ^{13}C NMR ($CDCl_3$) δ −4.95, 126.30, 128.15, 129.26, 129.81, 131.49, 134.54, 135.14, 135.27, 137.41, 141.48. Anal. Calcd for $C_{13}H_{13}ClSi$: C, 67.08; H, 5.63. Found: C, 67.09; H, 5.77.

Methyldiphenylvinylsilane (4b): oil; IR (neat) 3069, 1593, 1428, 1251, 1113 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.63 (s, 3H), 5.78 (dd, J = 3.9, 20.1 Hz, 1H), 6.19 (dd, J = 3.9, 14.4 Hz, 1H), 6.47 (dd, J = 14.4, 20.1 Hz, 1H), 7.36−7.37 (m, 6H), 7.50−7.54 (m, 4H); ^{13}C NMR ($CDCl_3$) δ −3.96, 128.02, 129.49, 135.01, 135.11, 135.99, 136.41. Anal. Calcd for $C_{15}H_{16}Si$: C, 80.30; H, 7.19. Found: C, 80.54; H, 7.20.

Allyl(*tert*-butyl)dimethylsilane (4f): oil; IR (neat) 2929, 1632, 1472, 1252, 893 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.05 (s, 6H), 0.89 (s, 9H), 1.53 (d, J = 8.1 Hz, 2H), 4.79−4.88 (m, 2H), 5.73−5.87 (m, 1H); ^{13}C NMR ($CDCl_3$) δ −6.44, 16.95, 20.85, 26.74, 112.85, 135.90. Anal. Calcd for $C_9H_{20}Si$: C, 69.14; H, 12.89. Found: C, 69.05; H, 13.06.

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Supporting Information Available: . Characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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