

A Novel Catalytic Effect of Lead on the Reduction of a Zinc Carbenoid with Zinc Metal Leading to a Geminal Dizinc Compound. Acceleration of the Wittig-Type Olefination with the $\text{RCHX}_2\text{-TiCl}_4\text{-Zn}$ Systems by Addition of Lead

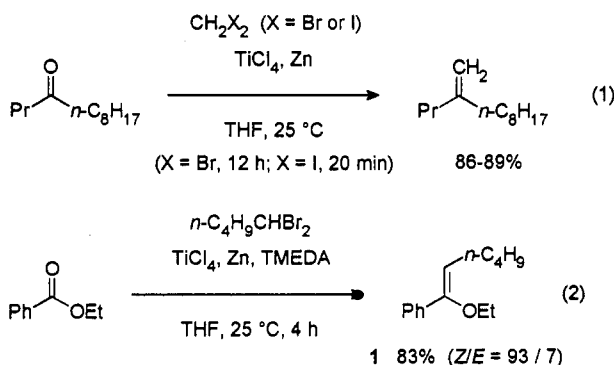
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Summary: A catalytic amount of lead promotes further reduction of zinc carbenoid (ICH_2ZnI) with zinc in THF to give a geminal dizinc compound ($\text{CH}_2(\text{ZnI})_2$), which is a key intermediate for the methylenation of carbonyl compounds with a CH_2I_2 , zinc, and TiCl_4 system.

Metals such as lithium, magnesium, and zinc are usually employed in organic synthesis without further purification. Thus, it is difficult to know the influence of trace impurities that are not eliminated completely by standard smelting methods.^{1,2} In 1978, we reported the methylenation of aldehydes and ketones with a $\text{CH}_2\text{Br}_2\text{-TiCl}_4\text{-Zn}$ system (eq 1).³ This reagent was modified for the alkylideneation



of carbonyl groups of carboxylic acid derivatives (eq 2).⁴ Recently, we were informed that the reported yields could not be reproduced by following the protocol given for the latter reaction.⁵ Because all of the relevant organic and inorganic materials except zinc powder⁶ are purified as part of the procedure,⁷ we suspected the zinc powder of causing the difference.⁸

Analysis of fluorescent X-rays of both samples of zinc powder revealed that the effective lots of zinc contained

0.04–0.07 mol % of lead on the basis of zinc and that the less effective sample was free of lead.⁹ Addition of a catalytic amount (0.5 mol %) of lead powder (or PbCl_2)¹⁰ to pure zinc powder showed the reproducible results originally reported.^{4,11} Moreover, addition of a catalytic amount of PbCl_2 revealed a remarkable acceleration of the methylenation of carbonyl groups, especially in the case of a $\text{CH}_2\text{I}_2\text{-TiCl}_4\text{-Zn}$ system (Figure 1).^{3c} Treatment of 4-phenyl-2-butanone with a mixture of CH_2I_2 , TiCl_4 , and zinc in THF at 0 °C for 90 min produced the methylenation product **2** in 5–8% yield. The reaction accelerated suddenly after the addition of PbCl_2 (1 mol % based on zinc) to the mixture, and the yield of **2** went up to 65%. When a catalytic amount of PbCl_2 was added to the zinc from the beginning, the methylenation proceeded smoothly at 0 °C to give **2** in 81% yield within 30 min.

Treatment of dodecanal in the presence of Me_3SiCl with the filtrate derived from CH_2I_2 , pure zinc powder, and a catalytic amount of PbCl_2 in THF furnished 1-tridecene in 72% yield,¹² while the same reaction without PbCl_2 did not produce 1-tridecene at all (eq 3).^{3a} This suggests that a catalytic amount of PbCl_2 (or lead), added to zinc, promotes further reduction of ICH_2ZnI ,^{14–16} forming a methylene dianion equivalent, $\text{CH}_2(\text{ZnI})_2$.^{17–20}

(7) Zinc powder was simply washed several times with 5% hydrochloric acid, washed in turn with water, methanol, and ether, and dried *in vacuo* according to the literature. Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. I, p 1276.

(8) We sent a sample of our zinc powder purchased from Wako to R. K. Boeckman, Jr. Reaction with zinc dust from Wako produced **1** in 85% yield, while that with zinc from Aldrich gave **1** in 39% yield. It was suggested that Wako zinc powder includes some unknown impurities which promote the reaction.

(9) The difference of the purity has proved to stem from the smelting method. Zinc powder (distilled zinc) derived by pyrometallurgy contained 0.04–0.07 mol % of lead based on zinc. In contrast, zinc (electrolytic zinc) produced by hydrometallurgy was pure (>99.998%) and it did not contain lead.

(10) Lead powder (99.999% purity) and PbCl_2 (99.999% purity) were purchased from Rare Metallic Co., Japan.

(11) Yields and stereoselectivities of **1** with such potential catalysts (0.5 mol % of zinc) in THF at 25 °C for 4.5 h are as follows: FeCl_2 , 14% (Z/E = 95/5); CoCl_2 , 22% (96/4); NiCl_2 , 0%; CuCl , 22% (95/5); AgCl , 28% (95/5); PtCl_2 , 14% (92/8); AuCl_3 , 26% (93/7); SnCl_2 , 10% (96/4); BiCl_3 , 13% (91/9); none, 10–15% (Z/E = 92/8–95/5).

(12) Geminal dimetallic compounds having weak nucleophilicity require Lewis acids such as Me_3Al ,^{3a} Me_3SiCl , $\text{Ti}(\text{O}-i\text{-Pr})_4$,^{3c} and $\text{BF}_3\text{-OEt}_2$ ^{13c} to promote methylenation or alkylideneation. The Lewis acid-assisted reagents have different reactivity (e.g., aldehyde-selective methylenation) from the present TiCl_4 -containing reagent systems. The methylenation in the presence of PbCl_2 produced 1-tridecene in only 10% yield without Me_3SiCl .

(13) For some representative examples of geminal dimetallic reagents, see: (a) Al: Zweifel, G.; Steele, R. B. *Tetrahedron Lett.* 1966, 6021–6025. (b) Cr: Okazoe, T.; Takai, K.; Utimoto, K. *J. Am. Chem. Soc.* 1987, 109, 951–953. (c) Zn and Mg: Knochel, P.; Normant, J. F. *Tetrahedron Lett.* 1986, 27, 1039–1042.

(14) (a) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React.* 1973, 20, 1–131. (b) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* 1966, 28, 3353–3354. (c) Sidduri, A.-R.; Rozema, M. J.; Knochel, P. *J. Org. Chem.* 1993, 58, 2694–2713.

(15) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* 1992, 114, 2592–2602 and references cited therein.

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(1) A small amount of sodium in commercially available lithium is advantageous for the case of organolithium preparations. See: Beel, J. A.; Koch, W. G.; Tomasi, G. E.; Hermansen, D. E.; Fleetwood, P. *J. Org. Chem.* 1959, 24, 2036–2038. Kamienski, C. W.; Esmay, D. L. *J. Org. Chem.* 1960, 25, 1807–1808 and references cited therein.

(2) A catalytic amount of impurity in chromium(II) salt played an important role in the following reaction. (a) Takai, K.; Tagashira, M.; Kuroda, T.; Oshima, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* 1986, 108, 6048–6050. (b) Jin, H.; Uenishi, J.; Christ, W. J.; Kishi, Y. *J. Am. Chem. Soc.* 1986, 108, 5644–5646.

(3) (a) Takai, K.; Hotta, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* 1978, 2417–2420. (b) Takai, K.; Hotta, Y.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* 1980, 53, 1698–1702. (c) Hibino, J.; Okazoe, T.; Takai, K.; Nozaki, H. *Tetrahedron Lett.* 1985, 26, 5579–5580, 5581–5584. (d) Lombardo, L. *Org. Synth.* 1987, 65, 81–89.

(4) (a) Okazoe, T.; Takai, K.; Oshima, K.; Utimoto, K. *J. Org. Chem.* 1987, 52, 4410–4412. (b) Takai, K.; Kataoka, Y.; Okazoe, T.; Utimoto, K. *Tetrahedron Lett.* 1988, 29, 1065–1068. (c) Takai, K.; Fujimura, O.; Kataoka, Y.; Utimoto, K. *Tetrahedron Lett.* 1989, 30, 211–214.

(5) The protocol was examined by Professors R. Noyori and R. K. Boeckman, Jr., who check *Organic Synthesis*.

(6) Zinc dust (purity 99.87 wt % (>90% on label), pyrometallurgy) was purchased from Wako Pure Chemical Industries Ltd., Japan.

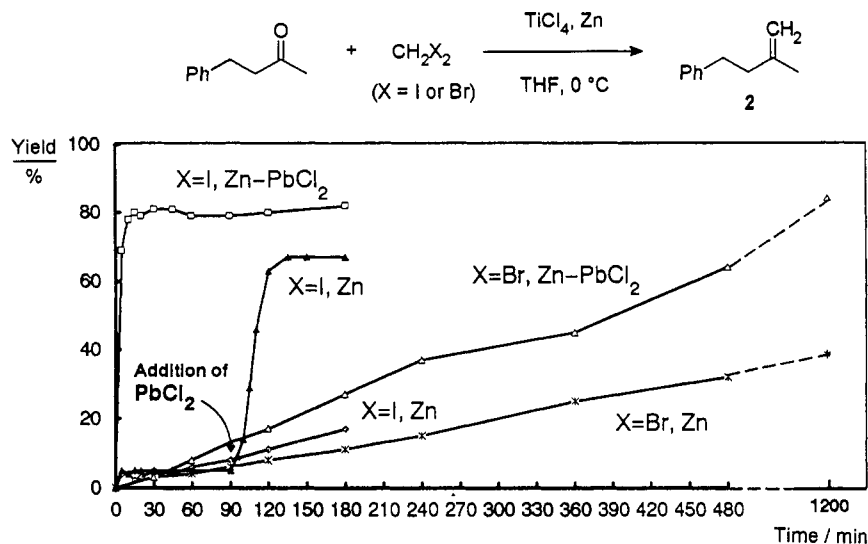
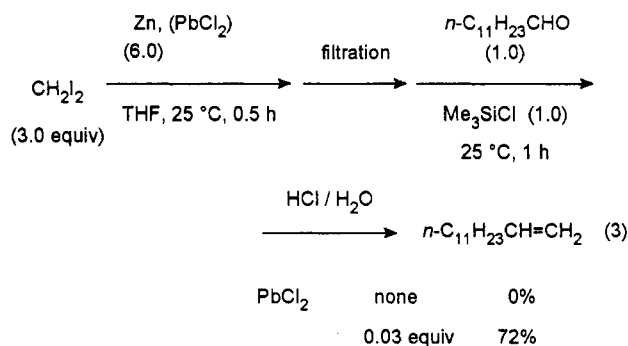


Figure 1. Yields of 2 by means of the CH_2X_2 - TiCl_4 -Zn systems.



The ^1H NMR spectrum of the supernatant solution of CH_2I_2 and zinc (3 equiv) in $\text{THF-}d_8$ showed a characteristic singlet at 1.40 ppm that was assigned to ICH_2ZnI (or $\text{Zn}(\text{CH}_2\text{I})_2$), according to Denmark's results.¹⁵ Several small peaks corresponding to CH_2I_2 , CH_3I , and THF were also observed. When a catalytic amount of lead and 2 equiv of zinc were added to the solution of ICH_2ZnI , the peak at 1.40 ppm disappeared and a new peak appeared at -0.78 ppm. The same signal was observed as the major peak with the supernatant solution derived by reaction of CH_2I_2 with zinc (3 equiv) in the presence of lead (5 mol % based on zinc) in $\text{THF-}d_8$ at 25 °C for 1 h. The peak at -0.78 ppm disappeared upon addition of a drop of water to the

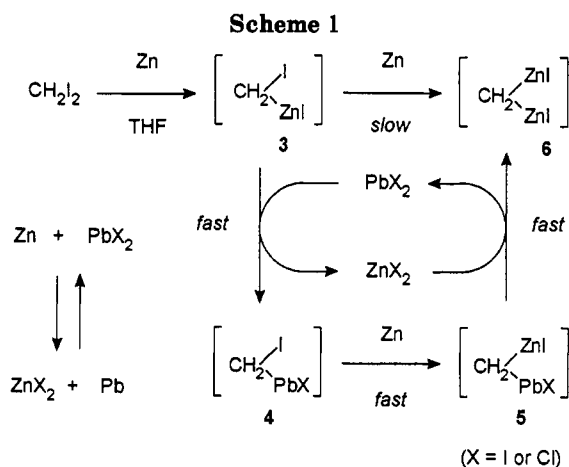
(16) We have found that the Simmons-Smith reaction in ether is inhibited by the presence of a catalytic amount of lead. See the following paper.

(17) (a) Emschwiller, G. *Compt. Rend.* 1929, 188, 1555-1557. (b) Hashimoto, H.; Hida, M.; Miyano, S. *J. Organomet. Chem.* 1967, 10, 518-520. (c) Miyano, S.; Hida, M.; Hashimoto, H. *J. Organomet. Chem.* 1968, 12, 263-268. (b) Harrison, I. T.; Rawson, R. J.; Turnbull, P.; Fried, J. H. *J. Org. Chem.* 1971, 36, 3515-3517.

(18) A geminal dizinc compound called the Nysted reagent (Nysted, L. N. US patent 3 865 848, 1975; *Chem. Abstr.* 1975, 83, 10406q) is commercially available from Aldrich Co. Preparation of the Nysted reagent uses zinc-lead couple or zinc activated with hydrogen chloride.

(19) The amount of the formed $\text{CH}_2(\text{ZnI})_2$ was measured by methane after alcoholysis in aqueous methanol.^{20b} Yields of methane and the amount of PbCl_2 are as follows: PbCl_2 0 mol %, methane <4%; 0.5 mol %, 54%; 1.5 mol %, 62%; 5.0 mol %, 59%; 15 mol %, 22%. Reaction with 1.5 mol % of lead powder instead of PbCl_2 gave methane in 51% yield. Longer reaction time or heating at 50 °C before filtration decreased yields of methane significantly. Such instability of the methylene dianion equivalent could be responsible for the formation of methane around 60% yield.

(20) (a) Eisch, J. J.; Piotrowski, A. *Tetrahedron Lett.* 1983, 24, 2043-2046. (b) Eisch, J. J. *Organometallic Synthesis*; Academic Press: New York, 1981; Vol. 2, p 25.



NMR tube. Upon treatment of a filtered solution derived from CH_2I_2 and zinc in THF with Me_3SnCl at 40 °C for 20 h, $\text{ICH}_2\text{SnMe}_3$ ²¹ was produced in 26% yield along with $\text{CH}_2(\text{SnMe}_3)_2$ ^{3b} in 2% yield. Meanwhile, trapping of the active species in the filtered solution of the lead-containing system with Me_3SnCl and LiI at 40 °C for 20 h furnished $\text{CH}_2(\text{SnMe}_3)_2$ in 26% yield; $\text{ICH}_2\text{SnMe}_3$ was not obtained. The yield of $\text{CH}_2(\text{SnMe}_3)_2$ was increased to 42% by addition of $\text{CuCN}\cdot 2\text{LiCl}$ ^{14c} at -60 °C, before trapping with Me_3SnCl at -60 to 25 °C, over a period of 5 h.²²

The accelerating effect of lead on the reduction of a zinc-carbenoid to a geminal dizinc compound might be explained as shown in Scheme 1. Transmetalation from the zinc-carbenoid 3 with lead(II)²³ produces lead-carbenoid 4,²¹ which is readily reduced by zinc to give geminal lead zinc compound 5.²⁴ Transmetalation from lead to zinc with zinc(II) affords geminal dizinc compound

(21) Seyferth, D.; Andrews, S. B. *J. Organomet. Chem.* 1971, 30, 151-166.

(22) We thank a reviewer for the suggestion to use $\text{CuCN}\cdot 2\text{LiCl}$ before addition of Me_3SnCl in order to increase the nucleophilicity of $\text{CH}_2(\text{ZnI})_2$.

(23) Treatment of lead metal with a solution of zinc(II) iodide in THF at 25 °C furnished lead(II) iodide in our hands.

(24) Direct reduction of the halogen on the zinc-carbenoid 3 with lead metal leading to geminal lead zinc compound 5 could not be negligible. For reduction of active halogen with lead metal formed *in situ* from PbCl_2 and aluminum, see: Tanaka, H.; Yamashita, S.; Hamatani, T.; Ikemoto, Y.; Torii, S. *Synth. Commun.* 1987, 17, 789-794. Dhimane, H.; Tanaka, H.; Torii, S. *Bull. Soc. Chim. Fr.* 1990, 127, 283-291.

6. Reduction of the lead-carbenoid **4** with zinc could proceed faster than that of the zinc-carbenoid **3**, since the lead-carbon bond is more covalent than the zinc-carbon bond.²⁵

The Wittig-type olefination of carbonyl compounds can be accomplished with geminal dimetallic compounds ($L_nM^1CHR^2L_m$)^{12,13} or the Schrock-type metal-alkylidene complexes ($L_nM=CHR$).²⁶ The present reagent derived from $RCHX_2$, $TiCl_4$, zinc, and a catalytic amount of $PbCl_2$ has the following features, which are typical for titanium-based reactive species:^{27,28} (i) the methylenation reagent is effective for highly enolizable ketones^{3c} and (ii) olefination of carboxylic acid derivatives proceeds under mild conditions.⁴ We are tempted to assume that the key intermediate of the methylenation is the Tebbe-type complex (**9** or **10**)^{29,30} or a titanium-containing geminal dimetallic compound (**7** or **8**),³¹ which is produced by transmetalation from the geminal dizinc compound **6** (Scheme 2).

Effects of a catalytic amount of lead on other zinc-mediated reactions are under investigation.

Acknowledgment. The authors thank Prof. Ryoji Noyori, Dr. Hsiao Yi, Prof. Robert K. Boeckman, Jr., Dr.

(25) For facile reduction of a boron-carbenoid with zinc under mild conditions, see: Knochel, P. *J. Am. Chem. Soc.* **1990**, *112*, 7431-7433.

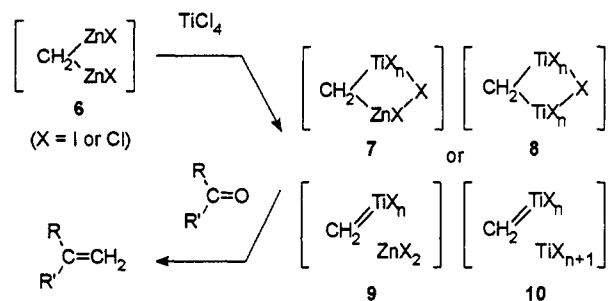
(26) (a) Ta: Schrock, R. R. *J. Am. Chem. Soc.* **1976**, *98*, 5399-5400. Schrock, R. R.; Fellmann, J. D. *J. Am. Chem. Soc.* **1978**, *100*, 3359-3370. (b) Zr: Hartner, F. W., Jr.; Schwartz, J.; Clift, S. M. *J. Am. Chem. Soc.* **1983**, *105*, 640-641. Clift, S. M.; Schwartz, J. *J. Am. Chem. Soc.* **1984**, *106*, 8300-8301. (c) W: Aguero, A. Kress, J.; Osborn, J. A. *J. Chem. Soc., Chem. Commun.* **1986**, 531-533.

(27) Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer-Verlag: Berlin, Heidelberg, 1986.

(28) Pine, S. H. *Org. React.* **1993**, *43*, 1-91.

(29) (a) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611-3613. (b) Pine, S. H.; Zahler, R.; Evans, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 3270-3272. (c) Pine, S. H.; Pettit, R. J.; Geib, G. D.; Cruz, S. G.; Gallego, C. H.; Tijerina, T.; Pine, R. D. *J. Org. Chem.* **1985**, *50*, 1212-1216. (d) Petasis, N. A.; Bzowej, E. I. *J. Am. Chem. Soc.* **1990**, *112*, 6392-6394.

Scheme 2



Alan T. Johnson, and Prof. Jeremiah P. Freeman, who kindly informed us of the results of their attempts to reproduce the alkyldienation and thus initiated these studies in a fruitful manner. We also thank Prof. Hiroshi Takatsuki and Mr. Yoshiji Honda of Environment Reservation Center of Kyoto University for the analysis of fluorescent X-ray. Financial supports from the Ministry of Education, Science, and Culture of Japan and Asahi Glass Foundation for Sciences are gratefully acknowledged.

Supplementary Material Available: Typical procedure for methylenation of 4-decanone (eq 1) and pentyldienation of ethyl benzoate (eq 2) and ¹H NMR spectra of ICH_2ZnI and $CH_2(ZnI)_2$ in THF-*d*₈ (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(30) In 1983, J. J. Eisch reported the Tebbe-type reagent, $Cp_2Ti(CH_2)ZnX_2$, prepared by treatment of Cp_2TiCl_2 with $CH_2(ZnI)_2$ in THF.^{20a} See also: Bruin, J. W.; Schat, G.; Akkerman, O. S.; Bickelhaupt, F. *Tetrahedron Lett.* **1983**, *24*, 3935-3936.

(31) Reported stereoselectivities of carboxylic acid derivatives with Schrock-type metal-alkylidene complexes are moderate.²⁶ In contrast, alkyldienation of carbonyl compounds with geminal dimetallic compounds proceeds under high stereocontrol.^{18b,c} Because the alkyldienation of ester carbonyl groups with the $RCHBr_2-TiCl_4-Zn-TMEDA$ system produces *Z*-isomers of alkenyl ethers stereoselectively, the possibility of geminal dimetallic compounds **7** and **8** could not be neglected.