

Preparation and Reactions of New Dialkylzincs Obtained by a Boron-Zinc Transmetalation.

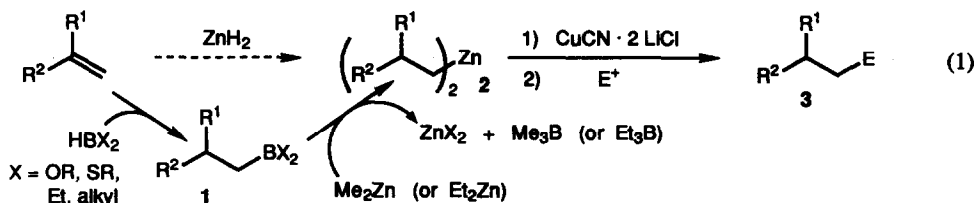
Falk Langer, Jack Waas and Paul Knochel *

Fachbereich Chemie der Philipps-Universität Marburg
Hans-Meerwein-Straße, 35043 Marburg (Germany).

Summary

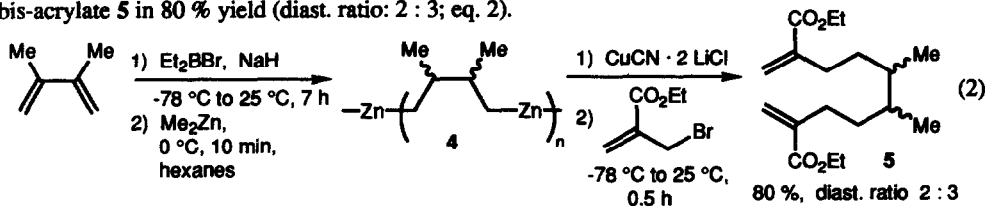
Various aliphatic organoboron derivatives were transmetalated to the corresponding dialkylzincs using diethyl- or dimethyl-zinc. This allows an access to zinc reagents not readily available by standard methods. Didecylzinc obtained by this method adds with good enantioselectivity (83 % ee) to PhCHO in the presence of catalytic amounts of (1R, 2R)-1,2-bis-(trifluorosulfonamido)cyclohexane.

Zinc organometallics have an excellent functional group tolerance and display a good reactivity toward electrophiles in the presence of Cu¹, Pd² or Ti³ catalysts. Most organozinc reagents are prepared by the direct insertion of zinc dust^{1,4} to organic halides or by an iodine-zinc exchange reaction⁵. Herein, we report our preliminary results for the preparation of new organozinc compounds using a boron-zinc transmetalation. Whereas this reaction has proven its utility for the synthesis of allylic⁶ or alkenyl⁷ zinc derivatives, it has not been applied to the preparation of dialkylzincs⁸. The B/Zn transmetalation would be of great synthetic utility since it would be equivalent to the hydrozincation of alkenes⁹ (eq. 1). Our first result shows that an alkylboronic pinacol ester such as **1a** reacts with Et₂Zn (5 equiv., neat, 70 °C, 17 h) and produces, after distilling off the excess of Et₂Zn (0.1 mm Hg, 50 °C), pure Hex₂Zn. After a transmetalation to the corresponding copper species with CuCN · 2 LiCl¹, PhCOCl (0.7 equiv., 0 °C, 2 h) is added, leading

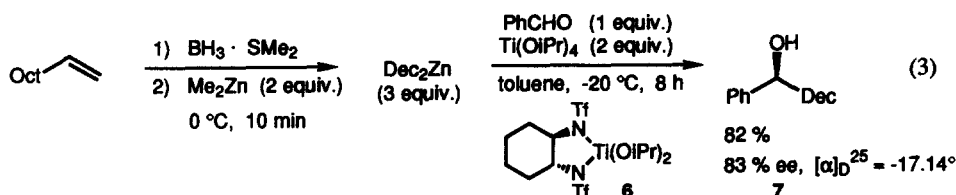


to the expected ketone **3a** in 98 % yield (Table I). It was desirable to use milder reaction conditions for the B/Zn exchange and we found that dithiaborolanes¹⁰ like **1b-1d** (Table I) react with Et₂Zn in hexane within 10 minutes at 0 °C. Some additional functionalities are tolerated in the boron derivatives (*t* BuS, TIPSO) and the corresponding copper reagents react in satisfactory yields with benzylideneacetone and ethyl α-(bromomethyl)acrylate (see **3b-d** of Table I). Further, we found that diethylalkylboranes, which are readily prepared by hydroboration¹¹, undergo a fast transmetalation with Et₂Zn or Me₂Zn. The by-products are highly volatile boranes which are easily removed from the reaction mixture under vacuum. The method allows the conversion of readily available olefins such as (1S)-(-)-β-pinene, (R)-(+)-limonene or (+)-camphene to the valuable zinc reagents **2e-g**. Their reaction with electrophiles such as an iodoalkyne (see **3h** and **3m**), 3-iodocyclohexenone¹² (see **3i** and **3k**), a nitroolefin (see **3j**) or ethyl α-(bromomethyl)acrylate¹³

(see 3I) proceeds in satisfactory yields after a transmetalation with $\text{CuCN} \cdot 2 \text{LiCl}^1$ (Table I). Also, the preparation of 1,*n*-dimetallic reagents is possible¹⁴. Thus, the hydroboration of 2,3-dimethylbutadiene with Et_2BH (-78 °C to 25 °C, 7 h) provides an intermediate 1,4-diboron derivative¹⁵ which after transmetalation with Me_2Zn (6 equiv.) smoothly produces the zinc dimetallic 4 (0 °C, 10 min). The allylation of 4 furnishes the bis-acrylate 5 in 80 % yield (diast. ratio: 2 : 3; eq. 2).



Interestingly, primary trialkylboranes also undergo a fast transmetalation in hexane with Et_2Zn or preferentially Me_2Zn (0 °C, 10 min). All the three alkyl groups are transferred from boron to zinc (Table I). Dialkylzincs prepared in this manner can be added enantioselectively to unsaturated aldehydes. Thus the reaction of Dec_2Zn (3 equiv.) with PhCHO (1 equiv.) in the presence of (1*R*, 2*R*)-1,2-bis-(trifluorosulfonamido)-cyclohexane 6 (8 mol %)^{3,5a} and $\text{Ti}(\text{O}i\text{Pr})_4$ (2 equiv.) provides the benzylic alcohol 7 in 82 % yield and 83 % ee (eq. 3) determined by preparing the corresponding mandelate¹⁶.



In summary, we have shown that various aliphatic organoboron compounds undergo a transmetalation with Et_2Zn or $\text{Me}_2\text{Zn}^{17}$ leading to dialkylzincs which are not always readily available by standard methods¹⁸. We are currently studying the stereochemistry of the transmetalation, its applications to the preparation of polymetallic zinc reagents and the use of the dialkylzincs obtained in asymmetric syntheses.

Acknowledgments

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References and Notes

- (a) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390; (b) Berk, S. C.; Knochel, P.; Yeh, M. C. P. *J. Org. Chem.* **1988**, *53*, 5789; (c) Majid, T. N.; Knochel, P. *Tetrahedron Lett.* **1990**, *31*, 4413; (d) Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1991**, *56*, 1445.
- (a) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340; (b) Negishi, E.; Matsushita, H.; Kobayashi, M.; Rand, C. L. *Tetrahedron Lett.* **1983**, *24*, 3823; (c) Negishi, E.; Takahashi, T.; Baba, S.; Van Horn, D. E.; Okukado, N. *J. Am. Chem. Soc.* **1987**, *109*, 2393; (d) Negishi, E.; Owczarczyk, Z. *Tetrahedron Lett.* **1991**, *32*, 6683; (e) Tamaru, Y.; Ochiai, H.; Nakamura, T.; Yoshida, Z. *Tetrahedron Lett.* **1986**, *27*, 955;
- (a) Takahashi, H.; Kawakita, T.; Ohno, M.; Yoshioka, M.; Kobayashi, S. *Tetrahedron.* **1992**, *48*, 5691; (b) Duthaler, R. O.; Hafner, A. *Chem. Rev.* **1992**, *92*, 807; (c) Brieden, W.; Ostwald, R.; Knochel, P. *Angew. Chem.* **1993**, *105*, 629; *ibid. Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 582.

Table I. Products Obtained by the Reaction of Dialkylzincs Prepared by a Boron-Zinc Transmetalation with Electrophiles in the Presence of $\text{CuCN} \cdot 2 \text{LiCl}$.

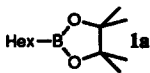
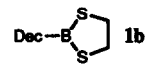
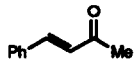
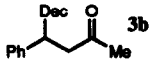
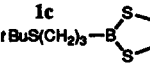
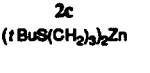

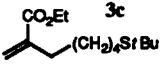
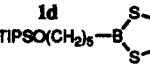
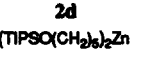

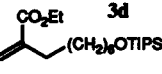

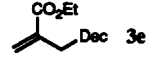

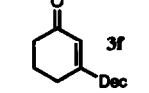

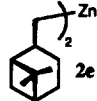
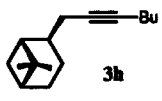

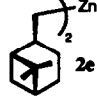

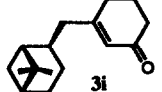
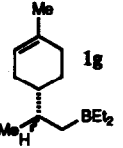
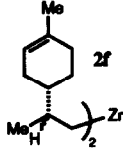

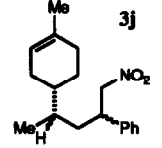
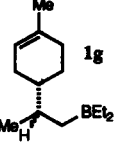
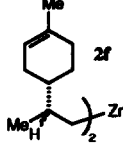

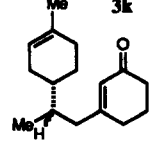
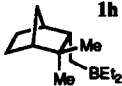


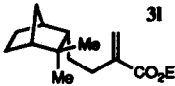
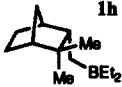
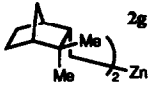


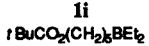
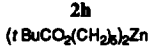

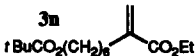

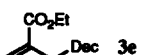
Boron Reagent 1	Zinc Reagent 2	Electrophile	Product 3	Yield (%) ^a
 1a	Hex ₂ Zn 2a	PhCOCl	PhCOHex 3a	98
 1b	Dec ₂ Zn 2b		 3b	85
 1c	 2c		 3c	78
 1d	 2d		 3d	83
DecBEt ₂ 1e	Dec ₂ Zn 2b		 3e	75
DecBEt ₂ 1e	Dec ₂ Zn 2b		 3f	81
DecBEt ₂ 1e	Dec ₂ Zn 2b	Bu—C≡C—I	Bu—C≡C—Dec 3g	78
 1f	 2e	Bu—C≡C—I	 3h	70
 1f	 2e		 3i	75
 1g	 2f		 3j	97
 1g	 2f		 3k	94

Table I. (continued)

				91
				89
				82
Dec ₃ B 1j	Dec ₂ Zn 2b			86 ^b , 91 ^c

a) Isolated yields of analytically pure products characterized by IR, ¹H and ¹³C-NMR, mass spectra and elementary analysis. b) B/Zn exchange performed with Et₂Zn. c) B/Zn exchange performed with Me₂Zn.

- (a) Gaudemar, M. *Bull. Soc. Chim. Fr.* **1962**, 974; (b) Tamaru, Y.; Ochiai, H.; Nakamura, T.; Tsubaki, K.; Yoshida, Z. *Tetrahedron Lett.* **1985**, 26, 5559.
- (a) Rozema, M. J.; AchyuthaRao, S.; Knochel, P. J. *J. Org. Chem.* **1992**, 57, 1956. (b) Tucker, C. E.; Majid, T. N.; Knochel, P. J. *Am. Chem. Soc.* **1992**, 114, 3983.
- (a) Thiele, K.-H.; Zdunneck, P. *J. Organomet. Chem.* **1965**, 4, 10; (b) Thiele, K.-H.; Engelhardt, G.; Köhler, J.; Arnstedt, M. *J. Organomet. Chem.* **1967**, 9, 385.
- (a) Oppolzer, W.; Radinov, R. N. *Helv. Chim. Acta.* **1992**, 75, 170; (b) Oppolzer, W.; Radinov, R. N. *J. Am. Chem. Soc.* **1993**, 115, 1593; (c) Srebnik, M. *Tetrahedron Lett.* **1991**, 32, 2449.
- Zakharkin, L. I.; Okhlobystin, O. Y. *Z. Obsc. Chim.* **1960**, 30, 2134; *engl.* 2109; *Chem. Abst.* **1961**, 55, 9319.
- Dzhemilev, U. M.; Vostrikova, O. S.; Tolstikov, G. A. *J. Organomet. Chem.* **1986**, 304, 17.
- Thaisrivongs, S.; Wuest, J. D. *J. Org. Chem.* **1977**, 42, 3243.
- (a) Pelter, A.; Rowe, K.; Sharrocks, K. N.; Smith, K.; Subrahmanayam, C. *J. Chem. Soc., Dalton* **1976**, 2087. (b) Pelter, A.; Rowe, K.; Smith, K. *J. Chem. Soc. Chem. Comm.* **1975**, 532.
- Piers, E.; Nagakura, I. *Synth. Commun.* **1975**, 5, 193.
- Villieras, J.; Rambaud, M. *Synthesis* **1982**, 924.
- (a) AchyuthaRao, S.; Knochel, P. *J. Org. Chem.* **1991**, 56, 4591; (b) Xiong, H.; Rieke, R. D. *J. Org. Chem.* **1989**, 54, 3247.
- Köster, R.; Griasnow, G.; Larbig, W.; Binger, P. *Liebigs. Ann. Chem.* **1964**, 672, 1.
- Parker, D. *J. Chem. Soc., Perkin Trans.* **1983**, 2, 83.
- Krug, R. C.; Tang, P. J. C. *J. Am. Chem. Soc.* **1954**, 76, 2262
- Typical procedure:** Preparation of 3k (see Table I): A 25 mL Schlenk-flask equipped with a rubber septum was charged under argon with the borane 1g (522 mg, 2.53 mmol) in hexane (5 mL) and cooled to 0 °C. Me₂Zn¹⁶ (1.43 g, 1.48 mL, 15 mmol) was added at once via syringe and the solution was stirred at 0 °C for 10 min. The solvent, the excess Me₂Zn and the formed BMe₃ were pumped off carefully at 0 °C. The resulting zinc compound 2f was left at room temperature under vacuum for 1 h, dissolved in THF (5 mL) and cooled to -60 °C (liquid N₂/ether bath). CuCN (448 mg, 5.0 mmol) and LiCl (424 mg, 10.0 mmol) in THF (5 mL) were added slowly, leading to an orange solution. After warming up to 0 °C for 10 sec (affording a black solution) and cooling back to -60 °C, 3-iodocyclohexenone (495 mg, 2.23 mmol, 0.88 equiv.) was added. The reaction mixture was slowly warmed up to -10 °C within 2 h and worked up as usual. The crude product was purified by flash chromatography (hexanes/ether 19:1), yielding 3k (554 mg, 94 % yield) as a clear, colorless oil.