Improved Preparation of Secondary Zinc Iodides by 1,2-Migration of sp^3 Carbenoids

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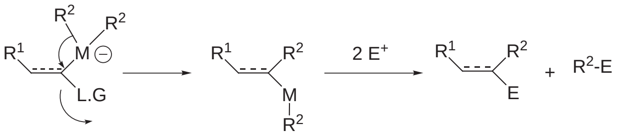
Dedicated fondly to Professor J. F. Normant on the occasion of his 65th birthday

Abstract: R_2Zn in the presence of NMP or LiBr promotes the intramolecular rearrangement of 1,1-diiodoalkanes via the formation of sp^3 secondary zinc carbenoid.

Key words: dialkylzinc, zincate, 1,1-diiodoalkane, secondary organozinc iodide, sp^3 carbenoid, homologation

The intermolecular reaction between a nucleophilic organometallic and an electrophilic carbon center represents one of the widest classes of carbon-carbon bond forming reaction nowadays. Far less common are intramolecular variants in which both the nucleophilic and electrophilic partners are bound to the same metal (intramolecular rearrangement of carbenoid). When the metal bears a negative charge, such reactions are defined as 1,2-metallate rearrangements and are relatively well known for the migration of alkyl groups to sp^3-, sp^2- and sp-hybridized carbons.[1] Particularly attractive is the rearrangement of α-halo-triorganozincate[2] (M = Zn) as well as α-alkoxy-alkenyl lithio cuprate (M = Cu, Scheme 1).[3]

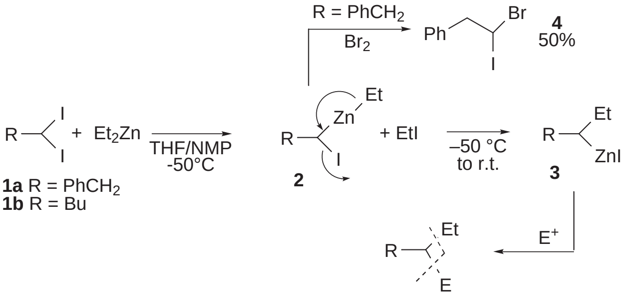


Scheme 1

However, an excess of electrophile is usually required to compensate the excess of alkyl groups attached to the metal. When the metal is not negatively charged, no intramolecular rearrangement is observed and only intermolecular reaction occurs between carbenoid and organometallic derivative[4] to give the alkylated and rearranged organometallics as products.[5]

It was reported recently by one of us that a polar cosolvent like *N*-methylpyrrolidinone (NMP) permitted the 1,4-addition of R_2Zn to enones in the absence of any copper or transition metal catalyst; named as the uncatalyzed conjugate addition reaction.[6] R_2Zn alone did not react with any of these enones. The origin of this reaction rate increase in NMP may result from the ionization of the diorganozinc by the NMP providing a more reactive pseudozincate.[7] So, we wished to use this efficient and economic new form of activated dialkylzinc (equivalent of zincate derivatives)[8] for several different synthetic purposes, and we report here that these derivatives can be successfully used for the intramolecular rearrangement of sp^3 carbenoids.[9]

Indeed, treatment of 1,1-diiodoalkane[10] **1** with 1.2 equivalents of Et_2Zn in THF in the presence of NMP allows iodine-zinc exchange at –50 °C to form the corresponding sp^3 secondary zinc carbenoid **2**. Then, by warming the reaction mixture to room temperature, the carbenoid **2** undergoes an intramolecular nucleophilic rearrangement into the secondary organozinc iodide derivative **3** which can react with different electrophiles in good overall yields (Scheme 2 and Table).

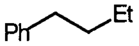
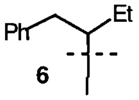
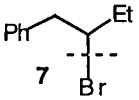
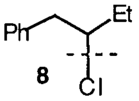
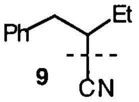
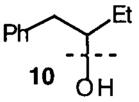
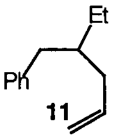
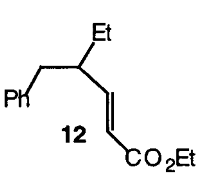
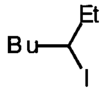


Scheme 2

In order to prove the stepwise mechanism, intermediate zinc carbenoid **2** was trapped with Br_2 at -50 °C to get **4**. Although, the α,α'−bromo iodo derivative **4** was isolated in a promising 50% yield, minor amounts of dibromoalkanes were always present in the crude reaction mixture (probably formed by degradation of the carbenoid **2** into carbene and subsequent reaction with Br_2).

The formation of a secondary organozinc halide **3** was checked by halogenolysis (entries 2 to 4 and entry 9), oxidation[11] (entry 6) and, finally, by allylation and 1,4-addition reactions after transmetallation of the organozinc halide into an organocopper derivative (entries 7 and 8).[12] The presence of NMP is absolutely necessary for the reaction to proceed[13] since in pure THF, no homologation was observed.

Table Reaction of 1,1-Diiodoalkanes **1** with Et_2Zn in THF/NMP

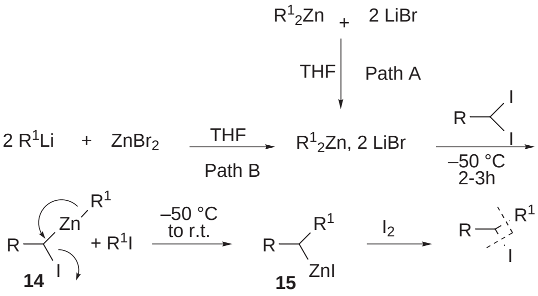
Entry	R	E⁺	Products	Yields (%)[a]
1	$PhCH_2$ **1a**	H_3O^+	 **5**	75
2	$PhCH_2$ **1a**	I_2	 **6**	80
3	$PhCH_2$ **1a**	Br_2	 **7**	70
4	$PhCH_2$ **1a**	TosCl	 **8**	71
5	$PhCH_2$ **1a**	TosCN	 **9**	60
6	$PhCH_2$ **1a**	Air	 **10**	60
7	$PhCH_2$ **1a**	AllylCl CuCN	 **11**	65
8	$PhCH_2$ **1a**	Ethyl Propiolate CuCN	 **12**	63
9	Bu **1b**	I_2	 **13**	60

[a] Isolated yields after purification by chromatography on silica gel.

Moreover, as we have reported recently that lithium halides may also modify the Lewis character of the zinc atom,[14] probably via a zincate species,[15] we wanted to check the behavior of the combination of R_2Zn/LiBr in this intramolecular rearrangement.

Indeed, addition of R^1_2Zn and 2LiBr in THF to **1a** at –50 °C also led to the formation of carbenoid **14**, which rearranged cleanly into the secondary zinc iodide **15** and, after addition of iodine, **6** was isolated in 75% yield (path A, Scheme 3).

As the combination R^1_2Zn, 2LiBr was also successful for the intramolecular rearrangement, the direct preparation of this complex was performed by treatment of BuLi with $ZnBr_2$ in THF at 0 °C to room temperature (path B, Scheme 3). Then, a solution of **1a** or **1b** was added at –50 °C and the reaction mixture was warmed to room temperature to furnish the homologated product, which was classically isolated as iodide **16** and **17** in 75% and 82% yield, respectively (Scheme 3).[16]



6 R PhCH₂, R¹ = Et 75%
16 R = PhCH₂, R¹ = Bu 75%
17 R = Bu, R¹ = Bu 82%

Scheme 3

Here again, the mechanism of the reaction is divided into two steps; formation of the carbenoid and its intramolecular rearrangement. The same result was obtained by the reaction of Bu_2Zn, $2MgBr_2$ ($2BuMgBr$ with $ZnBr_2$) and **1a** to furnish **16** in 75% yield.

In conclusion, we have reported a unique and straightforward intramolecular 1,2-rearrangement by the combination of R_2Zn either in the presence of 2 equivalents of NMP[17] or in the presence of 2 equivalents of LiBr[18] (or $MgBr_2$) with 1,1-diiodoalkane. We believe that the reactive species is an activated form of R_2Zn (as zincate) but in which only two alkyl groups are linked to the metal. The reactivity of these derivatives with different systems are currently being studied in our laboratory.

Acknowledgement

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(16) The combination Bu_2Zn, 2LiBr undergoes the 1,4-addition to cyclohexenone, in the presence of TMSCl, in a non-optimized 50% yield.

(17) *Typical experimental procedure for Et_2Zn in THF/NMP.* To a solution of 1,1-diodo-2-phenylethane (716 mg, 2 mmol) in THF (10 mL) and NMP (0.19 mL, 2mmol) cooled to −50 °C was slowly added Et_2Zn (1.0 M in hexane, 2.4 mmol, 1.2 equiv). The reaction mixture was stirred for 3 hours at −50 °C and then was allowed to warm to 0 °C for 1 hour. The secondary alkyl zinc iodide formed **3** was then cooled to −50 °C and a solution of I_2 (508 mg, 4 mmol, 2 equiv) in THF (3 mL) was added and then slowly warmed to room temperature. A saturated solution of NH_4Cl (20 mL) was added and the aqueous layer was extracted with ether. The combined organic layers were washed with $Na_2S_2O_3$ (10 mL) and the organic phases are then stirred for 3 hours in the presence of few Na_2S crystals. The organic layer was once more extracted with ether and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by chromatography silica gel (solvent; hexane) to give 416 mg of **6** (80% yield).

(18) *Typical experimental procedure for R_2Zn, 2LiBr in THF.* To a solution of $ZnBr_2$ (495 mg, 2 mmol) in 10 mL of THF was slowly added n-BuLi (1M solution in hexane, 4.4 mmol, 2.2 equiv) at −40 °C. The reaction mixture was allowed to warm to room temperature and 1,1-diodo-2-phenylethane (716 mg, 2 mmol) in THF (3mL) was added at −50 °C. After stirring for 1 hour at −40 °C, the reaction mixture was warmed to 0 °C for an hour. Reaction with electrophiles as well as subsequent treatment is the same as that the one described in the previous experimental procedure.

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