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Communications to the Editor

Preparation, Solid-State Structure, and Synthetic Applications of Isolable and Storable Haloalkylzinc Reagents

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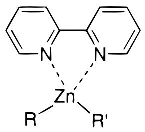
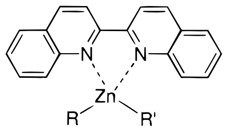
Haloalkylzinc reagents are widely used as cyclopropanating,[1] homologating[2] and alkylating reagents.[3] Recently, ether complexes of these reagents ($Zn(CH_2I)_2$ and $IZnCH_2I$) have been characterized in solution by NMR and in solid-state by X-ray crystallography.[4] These ether complexes are quite weak as they readily dissociate in solution to liberate the electrophilic reagents. Our ongoing interest in this area prompted us to generate more stable complexes that could be isolated and stored but that would also release the electrophilic methylene moiety under specific conditions. Hence, it is well-known that the amine complexes of dialkylzinc are quite stable, but the analogous bipyridine complexes display unique properties.[5] More specifically, the dissociation constant for TMEDA·Zn(*t*-Bu)$_2$ is higher than that measured for TMEDA·ZnMe$_2$.[6] Quite unexpectedly, this trend is oppositive for the related bipy·ZnR$_2$ complexes and the dissociation constant is higher for bipy·ZnMe$_2$ than for bipy·Zn(*t*-Bu)$_2$.[6] The unique stabilizing feature imparted by the bipyridine ligand prompted us to synthesize and study the stability of the complexes generated from bipyridine and haloalkylmetal reagents even though it has been previously reported that amines are generally alkylated by these highly electrophilic reagents.[7] In this contribution, we report the first synthesis, structure determination, and synthetic applications of isolable and storable zinc carbenoid reagents.

A nice and clear dark orange solution was obtained when a 1,1′-bipyridine solution was added to a milky suspension of bis(iodomethyl)zinc in CH_2Cl_2 at −40 °C.[8] A stable, non-pyrophoric yellow solid could be precipitated upon slow addition of hexane, and filtration produced the desired complex in 90% yield. This complex, assigned as bipy·Zn(CH$_2$I)$_2$ (**1**), showed all of the characteristic resonance by ^1H and ^{13}C NMR (Table 1).[9] The iodomethylzinc resonance appearing at 1.49 ppm (and −12.2 ppm by ^{13}C NMR) is consistent with the values reported for the related ether complexes. The elemental analysis is also consistent with the proposed structural formula. The stability of this complex was further confirmed when the elemental analysis of an 8 month-old sample kept in the freezer indicated that very little (if any) decomposition had occurred. Furthermore, this 8 month-old powder was still a very effective cyclopropanating reagent (vide infra). Several other highly colored complexes derived from bipyridine were prepared (**2**−**6**) and they displayed similar spectral properties[10] and reactivities. The relevant ^1H and ^{13}C NMR resonances for the complex are shown in Table 1. The bipyridine complex of $IZnCH_2I$ is less soluble in CH_2Cl_2 than the $Zn(CH_2I)_2$ complex, but both complexes are readily soluble in THF. The bipyridine complex of bis(iodoethyl)zinc (**4**) exists as a 1:1 diastereomeric mixture. We were also able to generate the bipyridine complex of Shi's reagent[11] ($CF_3CO_2ZnCH_2I$), but it appeared to be slightly less stable than those derived from the traditional reagents.



1 R = R' = CH$_2$I
2 R = R' = CH$_2$Cl
3 R = CH$_2$I, R' = I
4 R = R' = CH(Me)I
5 R = CH(Me)I, R' = I
6 R = CH$_2$I, R' = OC(O)CF$_3$



7 R = R' = CH$_2$I
8 R = R' = CH$_2$Cl

After numerous attempts to get suitable crystals of one of the bipyridine complex for X-ray analysis, we eventually succeeded in generating suitable crystals of the 2,2′-biquinoline complex of Wittig's [$Zn(CH_2I)_2$][12] **7** and of the highly reactive Denmark's [$Zn(CH_2Cl)_2$] reagent **8**, which had never been characterized by X-ray crystallography (Figure 1).[13] In these structures, the zinc center displays a distorted tetrahedral geometry. The observed bond lengths and bond angles are consistent with most of those observed for the diether complexes of iodomethylzinc carbenoids.[4] For example, the typical I−CH$_2$−Zn bond angles for analogous diether complexes range from 106.9 to 119.4° depending upon which ligand is used and the typical bond lengths Zn−C is between 1.995 and 2.04 Å for the zinc carbenoids (Table 2).

As expected, these complexes are not good cyclopropanating reagents since their electrophilic character is seriously hampered by the highly basic character of the ligand. For example, if 2 equiv of bipy·Zn(CH$_2$I)$_2$ (**1**) is added to a solution of cinnamyl alcohol in CH_2Cl_2, a 10% yield of the cyclopropane derivative is

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(1) (a) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React. (N.Y.)* **1973**, *20*, 1−131. (b) Charette, A. B. *Cyclopropanation mediated by zinc organometallics*; Knochel, P., Jones, P., Eds.; Oxford University Press: Oxford, 1999; pp 263−283.

(2) Sidduri, A.; Rozema, M. J.; Knochel, P. *J. Org. Chem.* **1993**, *58*, 2694−2713.

(3) For an excellent review on zinc carbenoids, see: Motherwell, W. B.; Nutley, C. J. *Contemp. Org. Synth.* **1994**, *1*, 219−241.

(4) (a) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* **1991**, *113*, 723−725. (b) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* **1992**, *114*, 2592−2602. (c) Charette, A. B.; Marcoux, J. F.; Bélanger-Gariépy, F. *J. Am. Chem. Soc.* **1996**, *118*, 6792−6793. (d) Charette, A. B.; Marcoux, J.-F. *J. Am. Chem. Soc.* **1996**, *118*, 4539−49. (e) Denmark, S. E.; Oconnor, S. P. *J. Org. Chem.* **1997**, *62*, 3390−3401.

(5) Noltes, J. G.; Van Den Hurk, J. W. G. *J. Organomet. Chem.* **1965**, *3*, 222−228.

(6) Noltes, J. G.; Boersma, J. *J. Organomet. Chem.* **1967**, *9*, 1−4.

(7) Wittig, G.; Schwarzenbach, K. *Justus Liebigs Ann. Chem.* **1961**, *650*, 1−21.

(8) Denmark, S. E.; Edwards, J. P. *J. Org. Chem.* **1991**, *56*, 6974−6981.

(9) Although it has been reported that basic nitrogen atoms are readily alkylated by the zinc reagent to generate quaternary ammonium salts, we have not detected any traces of these products. For the synthesis and characterization of *N*-methylbipyridinium iodide and *N,N*-dimethylbipyridinum diiodide, see: Tabushi, I.; Yazaki, A. *Tetrahedron* **1981**, *37*, 4185−4188.

(10) See Supporting Information for complete characterization data.

(11) Yang, Z. Q.; Lorenz, J. C.; Shi, Y. *Tetrahedron Lett.* **1998**, *39*, 8621−8624.

(12) The complex decomposed to the related $IZnCH_2I$ complex upon data collection. See Supporting Information for the X-ray crystal structure and crystallographic data for this complex.

(13) The complex crystallizes as a monomer with two independent conformers in the unit cell. See Supporting Information for the structure of the other conformer.

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Table 1. Selected ^{1}H and ^{13}C Chemical Shifts for Complexes **1**−**6**

complex	ZnCH(R)X ^{1}H	ZnCH(R)X ^{13}C
1	1.49	−12.2
2	2.71	32.9
3	1.64	−14.6
4	3.40, 3.38	23.94, 23.76
5	3.33	19.48
6	1.61	−20.5

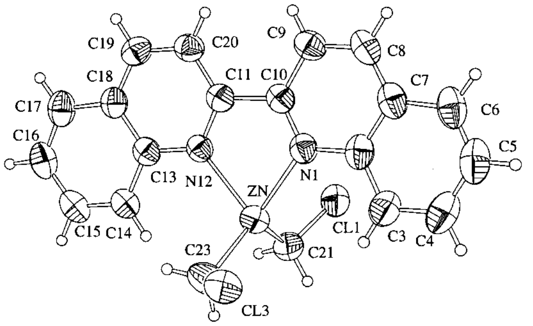
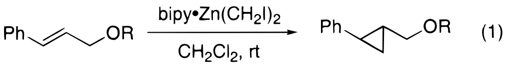


Figure 1. ORTEP drawing of complex **8**. Ellipsoids are drawn at at the 40% probability level.

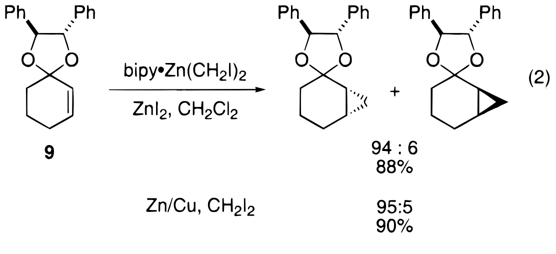
observed after 6 h at room temperature (eq 1). The yield of



R = H, no additive, 6h	<10%
R = ZnEt, no additive, 6h	75%
R = H, ZnI$_2$, 6 h	>95%
R = Bn, ZnI$_2$, 16 h	>95%

cyclopropanation is increased to 75% if the more basic zinc alkoxide is used. Conversely, we found that it is possible to release or activate the reagent by adding freshly prepared ZnI$_2$.[14] The reaction of the benzyl ether proceeded in very good yield (>95%) with only 1 equiv of the reagent and 1 equiv of ZnI$_2$.

Reagent **1** is also quite effective in stereoselective processes. For example, the cyclopropanation of the cyclohexene acetal **9** proceeded in 88% and produced a 96:4 diastereomeric mixture with complex **1** (eq 2). These results are comparable to those

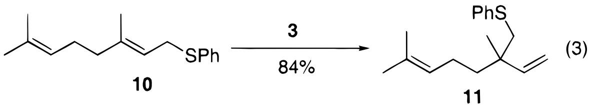


reported by Mash using the zinc−copper couple and diiodomethane.[15]

Table 2. Selected Bond Lengths (Å) and Angles (deg) for Complex **7** and **8**

bond lengths	**7**	**8**
Zn−C(21)	2.015(8)	2.013(5)
Zn−C(23)	2.082(9)	2.054(6)
Zn−Cl(1)		3.222(2)
Zn−Cl(2)		3.168(2)
Zn−I	3.477(4)	
Zn−I	3.551(7)	
Zn−N(1)	2.135(7)	2.117(4)
Zn−N(12)	2.141(6)	2.137(4)
bond angles	**7**	**8**
C(22)−Zn−C(21)	125.5(3)	127.7(3)
Zn−C(21)−I(1)	113.5(3)	
Zn−C(23)−I(2)	116.0(5)	
Cl(1)−C(21)−Zn		115.8(3)
Cl(2)−C(22)−Zn		115.3(4)
N(12)−Zn−N(1)	76.8(2)	77.02(15)

The complex bipy•IZnCH$_2$I (**3**) can also be used in methylation reactions. One example is to use it as a sulfur alkylating agent for the synthesis of the precursor in the [2,3]-sigmatropic rearrangement of sulfonium ylides. Treatment of thioether **10** with 2 equiv of bipy•IZnCH$_2$I produced the desired [2,3]-sigmatropic rearrangement product **11** in 84% yield (eq 3).[16]



In conclusion, we have shown that the bipyridine complexes of haloalkylzinc reagents are fully characterized and quite stable reagents that can be stored and used in haloalkylzinc mediated processes. The use of these reagents in catalytic asymmetric processes will be reported in due course.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of all the complexes. Description of the structure determination and tables of X-ray crystallographic data for the various complexes including atomic coordinates, anisotropic thermal parameters, and fixed atom coordinates; listing of observed and calculated structure factors for the various complexes (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Several Lewis acids were tested and ZnI$_2$ is by far superior to others. At this time, it is not clear what is the exact mechanism by which the reagent is released. For a theoretical study on the Lewis acid activation of halomethylzinc reagents, see: Nakamura, E.; Hirai, A.; Nakamura, M. *J. Am. Chem. Soc.* **1998**, *120*, 5844−5845.

(15) Mash, E. A.; Hemperly, S. B.; Nelson, K. A.; Heidt, P. C.; Van Deusen, S. *J. Org. Chem.* **1990**, *55*, 2045−2055.

(16) Kosarych, Z.; Cohen, T. *Tetrahedron Lett.* **1982**, *23*, 3019−3022.