*J. Am. Chem. Soc.* **1996,** *118,* 4539−4549

# Spectroscopic Characterization of (Iodomethyl)zinc Reagents Involved in Stereoselective Reactions: Spectroscopic Evidence That $IZnCH_2I$ Is Not $Zn(CH_2I)_2 + ZnI_2$ in the Presence of an Ether

**André B. Charette* and Jean-François Marcoux**

*Contribution from the Department of Chemistry, Université de Montréal, Montréal, Québec, Canada H3C 3J7*

*Received April 11, 1995*[⊗]

**Abstract:** We have shown that low-temperature $^{13}C$ NMR spectroscopy is an extremely powerful technique for characterizing the (iodomethyl)zinc-derived reagents involved in the cyclopropanation reactions. This technique has allowed us to spectroscopically characterize and unambigously differentiate the Furukawa reagent ($EtZnCH_2I$), the Simmons−Smith reagent ($IZnCH_2I$), and the Wittig reagent ($Zn(CH_2I)_2$). Unique spectra are obtained for each of these reagents when they are complexed to a chiral diether. We have also demonstrated that $IZnCH_2I$ is not converted into $Zn(CH_2I)_2 + ZnI_2$ in $CD_2Cl_2$ in the presence of a chiral complexing agent. Furukawa's reagent "$EtZnCH_2I$", however, is in equilibrium with $Et_2Zn$ and $Zn(CH_2I)_2$, and it eventually decomposes into PrZnI and EtZnI at room temperature. The decomposition of $Zn(CH_2I)_2$ into $IZnCH_2I$ and of $IZnCH_2I$ into $ZnI_2$ was monitored by NMR. We have also demonstrated that the general trends observed for the various equilibria involving (iodomethyl)zinc-derived reagents follow those observed with ethylzinc-derived organometallic compounds.

## Introduction

The Simmons−Smith cyclopropanation reaction has been the subject of considerable synthetic investigations over the past 35 years.[1] The classical procedure involves treatment of an olefin with Zn/Cu couple and $CH_2I_2$ to produce the corresponding cyclopropane.[2] Several modifications of the original protocol have since been reported. In 1966, Furukawa[3] introduced a remarkable improvement that consisted of replacing the activated zinc by $Et_2Zn$. This procedure resulted in the formation of a more reactive reagent and reproducible results. A great deal of effort has been directed toward the determination of the exact nature of the reagents formed in these reactions, and controversies have appeared in the literature. The formation of zinc carbenoids, generally represented as $RZnCH_2I$,[4] was invoked in all these protocols. Simmons[1a,2] and Rickborn[5] proposed that $Zn(CH_2I)_2{\cdot}ZnI_2$, resulting from the Schlenk equilibrium of $IZnCH_2I$, was the species responsible for the cyclopropanation (eq 1).

$$2IZnCH_2I \rightleftharpoons Zn(CH_2I)_2{\cdot}ZnI_2 \qquad (1)$$

Conversely, Dauben[6] concluded that $IZnCH_2I$, and not $Zn(CH_2I)_2{\cdot}ZnI_2$, was the reactive species since he observed no alkoxide formation when a free alcohol was submitted to the Simmons−Smith conditions. Inouye[7] suggested that $EtZnCH_2I$ or $IZnCH_2I$ was formed when EtZnI was treated with $CH_2I_2$ whereas Furukawa[1b,3] proposed that the same reagent ($EtZnCH_2I$) could be generated from the reaction between $Et_2Zn$ and $CH_2I_2$. He further postulated that the addition of a second equivalent of $CH_2I_2$ produces $Zn(CH_2I)_2$. He stipulated that "the active species may include $EtZnCH_2I$, $IZnCH_2I$ and/or $Zn(CH_2I)_2$ or associated complexes containing these molecules."[1b] A major breakthrough was accomplished recently when Denmark[8] characterized $Zn(CH_2I)_2$ by X-ray crystallography and NMR spectroscopy.

Our interest in the development of new stereoselective cyclopropanation reactions[9,10] compelled us to further characterize these different species. The full characterization and behavior of the various types of zinc carbenoids involved in

---

[⊗] Abstract published in *Advance ACS Abstracts,* April 15, 1996.

[1] (a) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React.* **1973**, *20*, 1−131. (b) Furukawa, J.; Kawabata, N. *Adv. Organomet. Chem.* **1974**, *12*, 83−134. (c) Boersma, J. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon Press: New York, 1984; Vol. 2, Chapter 16, pp 847−848. (d) Zeller, K.-P., Gugel, H. In *Houben-Weyl: Methoden der Organischen Chemie*; Regitz, M., Ed.; Georg Thieme Verlag: Stuttgart, 1989; Band EXIXb, p 195. (e) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307−1370. (f) Motherwell, W. B.; Nutley, C. J. *Contemp. Org. Synth.* **1994**, *1*, 219−241.

[2] (a) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 5323−5324. (b) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, *81*, 4256−4264.

[3] (a) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1966**, 3353−3356. (b) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53−58.

[4] (a) Blanchard, E. P.; Simmons, H. E. *J. Am. Chem. Soc.* **1964**, *86*, 1337−1347. (b) Simmons, H. E.; Blanchard, E. P.; Smith, R. D. *J. Am. Chem. Soc.* **1964**, *86*, 1347−1356. (c) Wittig, G.; Wingler, F. *Chem. Ber.* **1964**, *97*, 2146−2164. (d) Burger, U.; Huisgen, R. *Tetrahedron Lett.* **1970**, 3057−3060. (e) Miyano, S.; Yamashita, J.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1946.

[5] Chan, J. H.-H.; Rickborn, B. *J. Am. Chem. Soc.* **1968**, *90*, 6406−6411.

[6] Dauben, W. G.; Berezin, G. H. *J. Am. Chem. Soc.* **1963**, *85*, 468−472.

[7] Sawada, S.; Inouye, Y. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2669−2672.

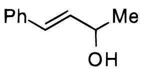
[8] (a) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* **1991**, *113*, 723−725. (b) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* **1992**, *114*, 2592−2602.

[9] Charette, A. B.; Marcoux, J.-F. *Synlett* **1995**, 1197−1207.

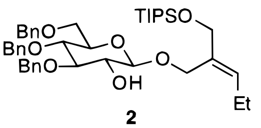
[10] Chiral auxiliaries: (a) Charette, A. B.; Côté, B.; Marcoux, J.-F. *J. Am. Chem. Soc.* **1991**, *113*, 8166−8167. (b) Charette, A. B.; Marcoux, J.-F.; Côté, B. *Tetrahedron Lett.* **1991**, *32*, 7215−7218. (c) Charette, A. B.; Côté, B.; *J. Org. Chem.* **1993**, *58*, 933−936. (d) Charette, A. B.; Marcoux, J.-F. *Tetrahedron Lett.* **1993**, *34*, 7157−7160. (e) Charette, A. B.; Turcotte, N.; Côté, B. *J. Carbohydr. Chem.* **1994**, *13*, 421−432. (f) Charette, A. B.; Turcotte, N.; Marcoux, J.-F. *Tetrahedron Lett.* **1994**, *35*, 513−516. Chiral reagent: (g) Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651−2652. (h) Charette, A. B.; Prescott, S.; Brochu, C. *J. Org. Chem.* **1995**, *60*, 1081−1083. Chiral catalyst: (i) Charette, A. B.; Brochu, C. *J. Am. Chem. Soc.* **1995**, *117*, 11367−11368. Chiral allylic alcohols: (j) Charette, A. B.; Lebel, H. *J. Org. Chem.* **1995**, *60*, 2966−2967.

S0002-7863(95)01171-1 CCC: $12.00

**Table 1.** Effect of the reagents on the diastereoselectivities



**1**



**2**

| entry | substrate | conditions[a] | ds[b] |
|---|---|---|---|
| 1 | **1** | A | 7.0:1 |
| 2 | **1** | B | 3.6:1 |
| 3 | **1** | C | 1.2:1 |
| 4 | **2** | A | 47:1 |
| 5 | **2** | B | 27:1 |
| 6 | **2** | C | 4.6:1 |

[a] The reactions were carried out in $CH_2Cl_2$ either at 0 °C with 4 equiv of reagents (**1**) or at −20 °C with 10 equiv of reagents (**2**). To the zinc alkoxide (prepared from 1ROH + 1$ZnEt_2$) was added (conditions A) a 1:1 stoichiometry of $Et_2Zn/CH_2I_2$, (conditions B) a 1:2 stoichiometry of $Et_2Zn/CH_2I_2$, or (conditions C) a 1:1:1 stoichiometry of $Et_2Zn/I_2/CH_2I_2$. [b] ds = diastereoselectivity. Determined by GC (**1**)/HPLC (**2**) analysis of the crude reaction mixture. Yields were >90% in all the cases.[10a,j]

these reactions are still unsolved issues and are extremely important for the rational design of a chiral catalyst for the $RZnCH_2I$-mediated cyclopropanation of allylic alcohols. Furthermore, the Schlenk equilibrium between the classical Simmons−Smith reagent ($IZnCH_2I$) and $Zn(CH_2I)_2{\cdot}ZnI_2$ is still an open question. In this paper, we report spectroscopic evidence that indicates that the Schlenk equilibrium illustrated in eq 1 appears to lie far to the left (on the side of $IZnCH_2I$) under the conditions generally used for obtaining optimal selectivities in the cyclopropanation reactions.[11] We also report the first spectroscopic studies of Furukawa's reagent, $EtZnCH_2I$.

## Results and Discussion

This study was undertaken following the troubling observation that the cyclopropanation of various chiral substrates led to significantly different diastereoselectivities depending on the reaction conditions. The ethylzinc alkoxides of two model substrates, **1** and **2**, were first submitted to a 1:1 mixture of $ZnEt_2$ and $CH_2I_2$ (5 equiv) (Table 1).

These conditions, which produced mainly $EtZnCH_2I$, were the most efficient, and the desired products were obtained in excellent yields and selectivities (entries 1 and 4). The use of a 1:2 mixture of the reagents to form $Zn(CH_2I)_2$ led to slightly lower selectivities (entries 2 and 5). Finally, the Simmons−Smith reagent ($IZnCH_2I$), prepared by adding sequentially $I_2$ and $CH_2I_2$ to $Et_2Zn$ in $CH_2Cl_2$ to avoid the use of an ethereal solvent,[12] gave much lower diastereoselection (*vide infra*) (entries 3 and 6). These trends have been observed with other substrates and are also followed when only 1 equiv of the reagent is used.[13]

These results are quite intriguing and indicate that different (iodomethyl)zinc reagents ($EtZnCH_2I$, $Zn(CH_2I)_2$, or $IZnCH_2I$) may be involved in the methylene transfer process. Furthermore, the discrepancies between the selectivities observed under conditions B ($Zn(CH_2I)_2$) and C ($IZnCH_2I$) seem to indicate that the Schlenk equilibrium proposed in eq 1 may not be operative under these conditions. The data presented in Table 1 clearly indicate the importance of the stoichiometry of the reagents in Furukawa's protocol, and for the first time, they provide evidence of the unique reactivity of $EtZnCH_2I$. Furthermore, these results raised a number of previously unanswered fundamental questions regarding the structure of these various reagents, the possible equilibria between the reactive species, or the structure of various intermediates involved in these reactions. For these reasons, an extensive NMR study, aimed at characterizing and differentiating spectroscopically all the reagents involved in these reactions, was undertaken.

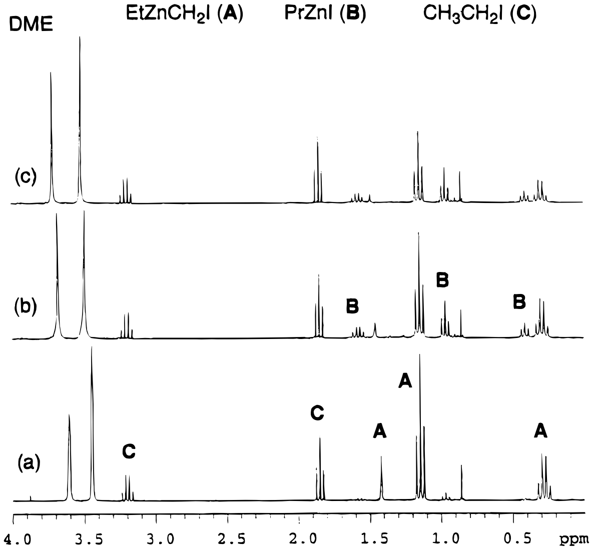


**Figure 1.** $^1H$ NMR spectra of a 1:1:1 mixture of $Et_2Zn/CH_2I_2$/DME in $CD_2Cl_2$ after (a) 5 min, (b) 40 min, and (c) 85 min.

**$EtZnCH_2I{\cdot}DME$ Complex.** The NMR studies were carried out in the presence of an ether (1 or 2 equiv) using $CD_2Cl_2$ as the solvent. These conditions were chosen since they closely simulate those used in the various stereoselective cyclopropanation reactions developed in our laboratories. Coordinating groups, such as ether groups (or alkoxides), are necessary to stabilize the reagents and increase their lifetimes.[14] Furthermore, low-temperature NMR can easily be performed under these conditions. The first surprising result is that the $^1H$ NMR of the reagent prepared from a 1:1 stoichiometry of $Et_2Zn$ and $CH_2I_2$ (conditions A) displayed an unusually high number of resonances after a certain time (Figure 1). The formation of $EtZnCH_2I$ appeared to be extremely rapid as evidenced by the formation of a $ZnCH_2I$ resonance at 1.4 ppm and by the almost complete disappearance of $CH_2I_2$ at 3.9 ppm. However, we observed that "$EtZnCH_2I$" partly underwent a rapid rearrangement at room temperature to produce PrZnI (Figure 1, signals B).[15] This rearrangement occurred in less than 2 h and formed *ca*. 50 mol % PrZnI. On the basis of the integration, the remaining EtZn groups belong to EtZnI (*ca*. 90%) and $EtZnCH_2I$ (10%). This methylene insertion (path B) and the methylene extrusion (path A) seem to be the two major paths for decomposition of $EtZnCH_2I$, and they appear to be fairly important and facile in the absence of an olefin (Scheme 1).

To probe the effect of a zinc alkoxide on the rate of this methylene insertion, 2-methoxy-1-ethanol was treated with 2 equiv of $Et_2Zn$ followed by 1 equiv of $CH_2I_2$. Figure 2 shows that this rearrangement is even faster in the presence of a zinc

---

[11] Presented in part at the 210th ACS National Meeting, Chicago, IL, Aug 20−24, 1995; paper ORGN 186.

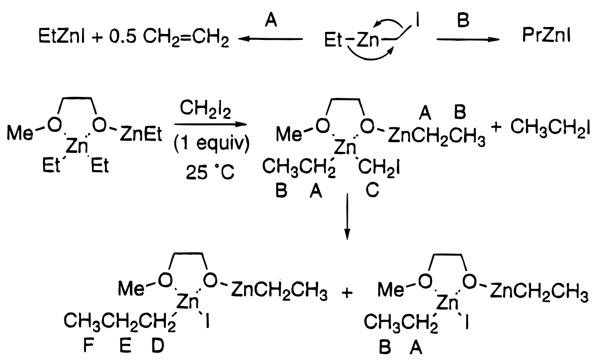
[12] The presence of an ethereal solvent is generally not suitable in these reactions since the reagent is considered to be "delivered" by the proximal hydroxy group (or zinc akoxide). Much lower diastereoselectivities are generally observed when they are carried out in ether, THF, or DME.

[13] It is clear that the nature of the "$ZnCH_2I$" reagent in these reactions can vary as a function of time and of the reaction byproducts (for example, it is conceivable to imagine that $Zn(CH_2I)_2$ is converted into $IZnCH_2I$ after the delivery of a first methylene group or that the aggregation state and nature of the zinc alkoxide may change as the reaction proceeds). The conditions reported in Table 1 that involved an excess of the reagents were chosen to favor a rapid cyclopropanation reaction mediated by mainly one "$ZnCH_2I$"-derived reagent.

[14] Extensive decomposition and formation of a precipitate are observed if these studies are carried out in the absence of a complexing agent.

[15] This correlation was established by comparison with authentic PrZnI prepared from PrI and activated zinc. The singlet at 0.85 ppm corresponds to ethane.

**Scheme 1**



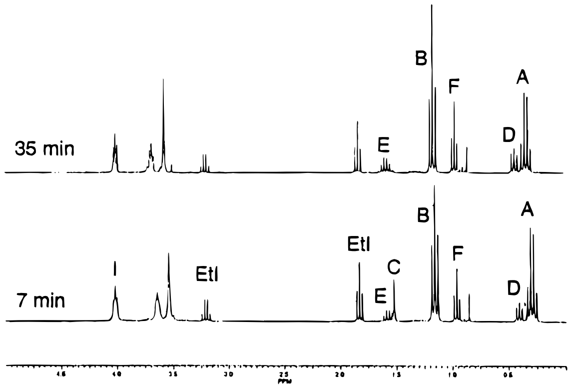
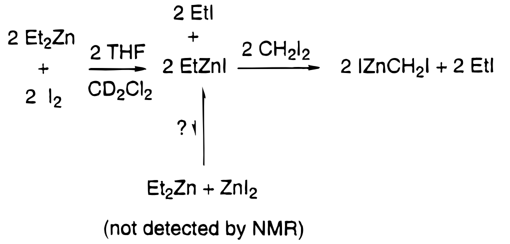


**Figure 2.** $^1$H NMR spectrum of a 1:2:1 mixture of 2-methoxy-1-ethanol/$Et_2Zn$/$CH_2I_2$ at 298 K after (a) 7 min and (b) 35 min.

**Scheme 2**



alkoxide. The signals arising from the formation of PrZnI were already present after only 7 min. Conversely, the $ZnCH_2I$ resonance (C) completely disappeared in less than 35 min (Figure 2b). On the basis of the integration, an equal mixture of the PrZnI and EtZnI was produced. This process is obviously very significant since zinc alkoxides are intermediates in numerous $ZnEt_2$/$CH_2I_2$-mediated stereoselective cyclopropanation reactions.[9]

**$Zn(CH_2I)_2$·THF and $IZnCH_2I$·THF Complexes.** Because of the relatively harsh conditions required to prepared $IZnCH_2I$ using Zn/Cu couple and $CH_2I_2$[1a] and of the little flexibility in the choice of the solvent that can be used (usually ether, THF, or DME), we sought alternative ways to prepare $IZnCH_2I$. The mildest and most flexible method was to generate it from EtZnI and $CH_2I_2$ by an alkyl group exchange. Although this reagent in ether has been used in the cyclopropanation of olefins,[16] the viability of the conversion was initially established independently (Scheme 2). Ethylzinc iodide and iodoethane were produced quantitatively when an equimolar amount of iodine was added to diethylzinc (Figure 3a).[17] It has already been demonstrated by low-temperature NMR spectroscopy that ethylzinc iodide is not converted into a mixture of $Et_2Zn$ and $ZnI_2$ in THF.[18] In a similar way, EtZnI was also produced when equimolar amounts of $Et_2Zn$ and $ZnI_2$ were mixed (Figure 3b). As expected, the addition of a second equivalent of $Et_2Zn$ did not lead to any additional signal even at 223 K (Figure 3c). The $CH_2Zn$ signal is, however, shifted downfield, averaging those of $Et_2Zn$ and EtZnI. These observations are consistent with the postulate that there is a rapid exchange between alkyl groups of the diorganozinc and the organozinc halide.[19] Signal separation began to occur when the temperature was lowered to 178 K, and both signals arising from EtZnI and $Et_2Zn$ were cleanly observed at 163 K (Figure 3d). The spectrum of $Et_2Zn$ is also provided for comparison (Figure 3e). The integration confirmed that the conversion of $ZnI_2$ into EtZnI was quantitative.[20]

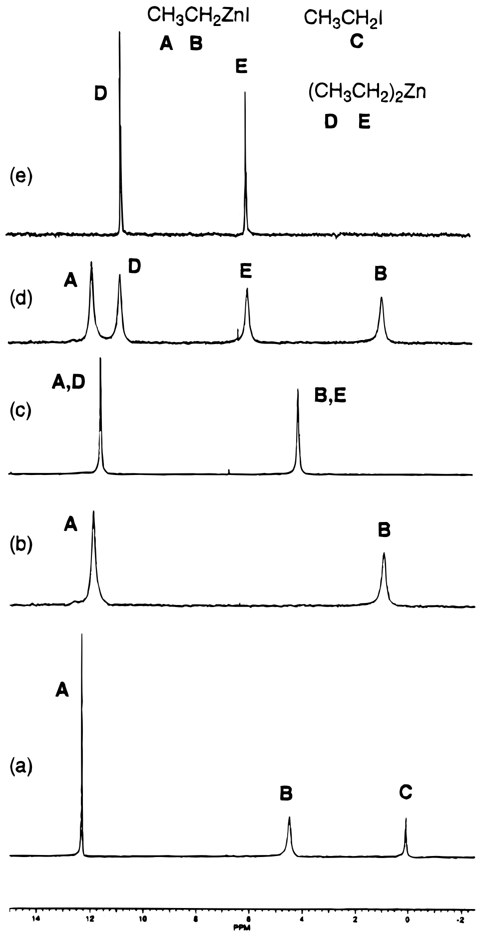


**Figure 3.** $^{13}$C NMR (100 MHz) of the ZnR region of (a) EtZnI·THF at 273 K (obtained from $Et_2Zn$/$I_2$/THF (1:1:1)), (b) EtZnI·THF at 163 K (obtained from $Et_2Zn$/$ZnI_2$/THF (1:1:2)), (c) $Et_2Zn$·THF + $Et_2Zn$/$ZnI_2$/THF (2:1:3)), and (e) $Et_2Zn$·THF.

As expected, subsequent addition of diiodomethane to EtZnI produced (iodomethyl)zinc iodide quantitatively as evidenced by the formation of an additional equivalent of iodoethane (Figure 4, signals C) and a $ZnCH_2I$ signal at 1.35 ppm ($^1$H) and −19 ppm ($^{13}$C) (Figure 4). These observations are, therefore, not consistent with one of the postulates of Inouye stating that EtZnI reacts with $CH_2I_2$ to produce $EtZnCH_2I$ since no EtZn signals could be detected by NMR.

With this information in hand, the $^1$H and $^{13}$C NMR spectra of the reagents prepared from a 1:2 mixture of $Et_2Zn$/$CH_2I_2$ (Zn-

---

[16] For selected examples on the use of EtZnI as the precursor to the Simmons−Smith reagent, see: (a) Paquette, L. A.; Ham, W. H. *J. Am. Chem. Soc.* **1987**, *109*, 3025−3036. (b) Paquette, L. A.; Horn, K. A.; Wells, G. J. *Tetrahedron Lett.* **1982**, *23*, 259−262.

[17] These experiments (Figures 3−7) were carried out in the presence of THF to solubilize EtZnI, $IZnCH_2I$, and $Zn(CH_2I)_2$.

[18] Evans, D. F.; Fazakerley, G. V. *J. Chem. Soc. A* **1971**, 182−183.

[19] Orrell, K. G.; Sik, V. *Annu. Rep. NMR Spectrosc.* **1993**, *27*, 103−171.

[20] In that case, the $^{13}$C NMR spectra were recorded under quantitative conditions with a delay (d1) of 20 s. The absence of a signal indicates that the conversion is ≥98%.

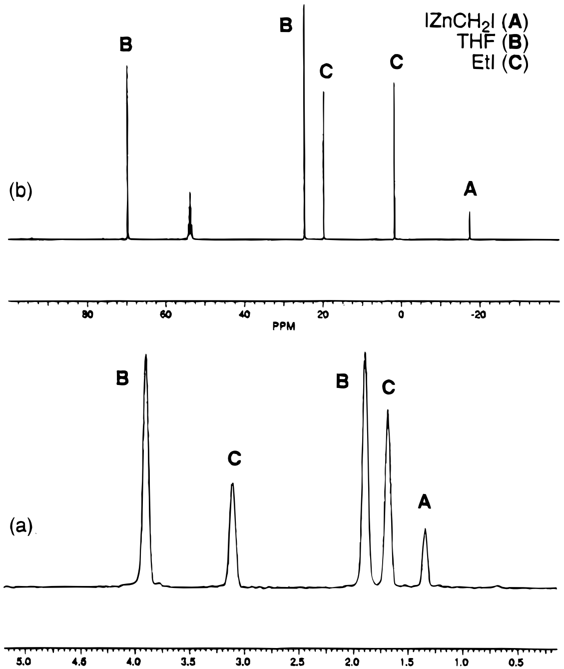


**Figure 4.** (a) $^1$H and (b) $^{13}$C NMR spectra at 158 K of $IZnCH_2I{\cdot}2THF$ in $CD_2Cl_2$ obtained from $Et_2Zn/I_2/CH_2I_2/THF$ (1:1:1:2).

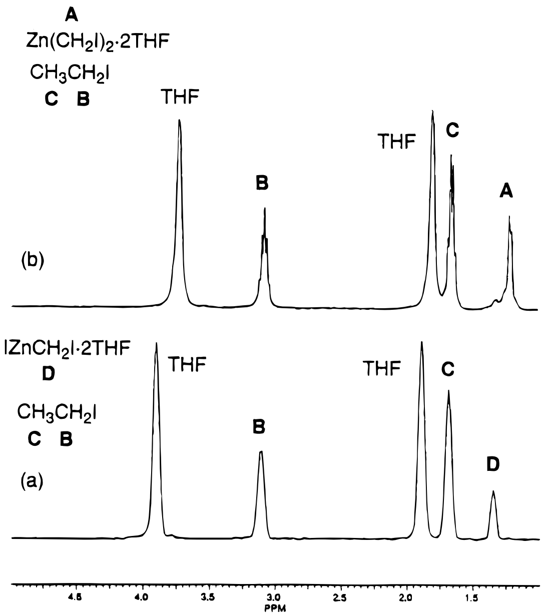


**Figure 5.** $^1$H NMR spectra of (a) $IZnCH_2I{\cdot}2THF$ and (b) $Zn(CH_2I)_2{\cdot}$2THF at 158 K.

$(CH_2I)_2$) and from a 1:1 mixture of $EtZnI/CH_2I_2$ ($IZnCH_2I$) were recorded and compared. We found that the differentiation of the reagents by this NMR experiment was inconclusive on the basis of this data (Figures 5 and 6). Comparison of the $^1$H and $^{13}$C spectra of both reagents did not allow any differentiation of the two species. Furthermore, a single broad signal for both $ZnCH_2I$ resonances was observed by $^{13}$C NMR at 163 K if both preformed species were mixed in the presence of THF (Figure 7). Moreover, low-temperature NMR of the THF and DME complexes of the two crucial reagents ($IZnCH_2I$ vs $Zn(CH_2I)_2$) did not allow separation of the NMR signals, and unambiguous differentiation could not be established.

Finally, nothing could be concluded about the possible Schlenk-type conversion of $IZnCH_2I$ into $Zn(CH_2I)_2$ and $ZnI_2$. To differentiate the species, their complexation with a non-$C_2$-symmetric chiral diether, (1*R*)-*exo,exo*-2,3-dimethoxy-1,7,7-trimethylbicyclo[2.2.1]heptane (**3**),[8] was studied by low-temperature NMR.

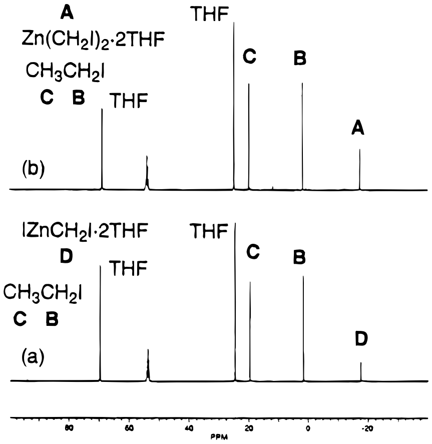


**Figure 6.** $^{13}$C NMR spectra of (a) $IZnCH_2I{\cdot}2THF$ and (b) $Zn(CH_2I)_2{\cdot}$-2THF at 158 K.

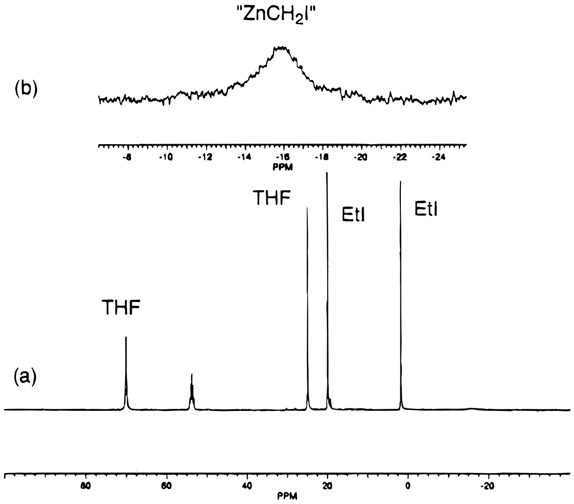
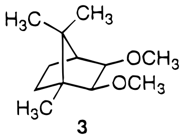
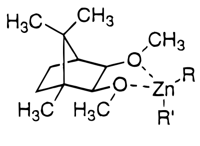


**Figure 7.** (a) $^{13}$C NMR spectrum of a 1:1 mixture of $Zn(CH_2I)_2{\cdot}THF$ and $IZnCH_2I{\cdot}THF$ at 163 K. (b) Expansion of the $ZnCH_2I$ region.



**3**

**$Zn(CH_2I)_2$·Chiral Diether 3 and $IZn(CH_2)I$·Chiral Diether 3 Complexes.** In his extensive spectroscopic investigation of $Zn(CH_2I)_2$, Denmark has studied the behavior of the **3**·$Zn(CH_2I)_2$ complex **7** by $^{13}$C NMR in $C_6D_6$ and found that the two methylene groups displayed a single signal.[8] In that respect, low-temperature NMR might allow us to slow the rapid equilibrium between the complexed and uncomplexed species and lead to a signal separation for the two diastereotopic $CH_2$ groups in **7**. Each one of the complexes **4**−**9** should display a unique spectrum at low temperature, thereby allowing their



**4** R = R' = I
**5** R = R' = Et
**6a** R = I, R' = Et
**6b** R = Et, R' = I
**7** R = R' = $CH_2I$
**8a** R = $CH_2I$, R' = I
**8b** R = I, R' = $CH_2I$
**9a** R = Et, R' = $CH_2I$
**9b** R = $CH_2I$, R' = Et

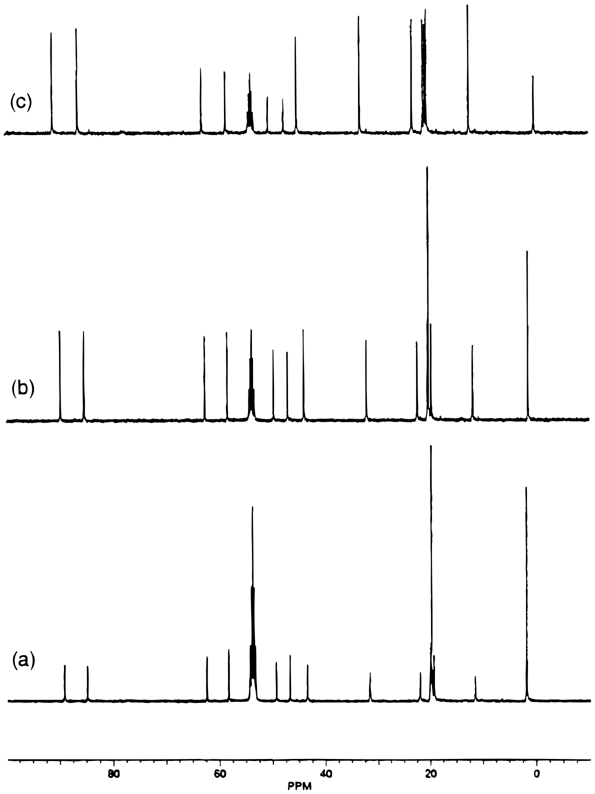


**Figure 8.** $^{13}$C NMR spectra of **3**·ZnI$_2$ (**4**) at (a) 163 K, (b) 193 K, and (c) 300 K.

differentiation. In the cases where R = R′, only one complex is expected (**4**, **5**, **7**). Furthermore, the two diastereotopic groups (R, R′) might be separable at low temperature in the case of complexes **5** and **7** only if the complexation−decomplexation equilibrium is slow on the NMR time scale.[19] Conversely, two diastereomeric complexes should be observed when R ≠ R′ (**6**, **8**, **9**).

The $^{13}$C NMR spectra of **3**·ZnI$_2$ (**4**) and the related complexes **5** and **6** were also recorded in CD$_2$Cl$_2$ at various temperatures ranging from 25 to −100 °C. (Figures 8−10).[21] The **3**·ZnI$_2$ complex was prepared by treating the analogous Et$_2$Zn complex with 2 equiv of iodine. The $^{13}$C NMR displayed the appropriate number of carbon signals for the chiral ligand (12) along with EtI (produced as a byproduct)[22] (Figure 8). As expected, the spectra recorded at various temperatures were very similar.

The variable temperature $^{13}$C NMR spectra of **3**·ZnEt$_2$ (**5**) and **3**·EtZnI (**6**) are shown in Figures 9 and 10. Complex **5** displayed the appropriate number of signals, and more importantly, the resonances corresponding to the diastereotopic ethyl groups of diethylzinc did not split even at 163 K. Lowering the temperature induced an upshield shift of *ca.* 5 ppm of the ZnCH$_2$ signal whereas the CH$_3$ signal overlaps with one of the CH$_3$ (ligand) resonances (*ca.* 12 ppm).[23]

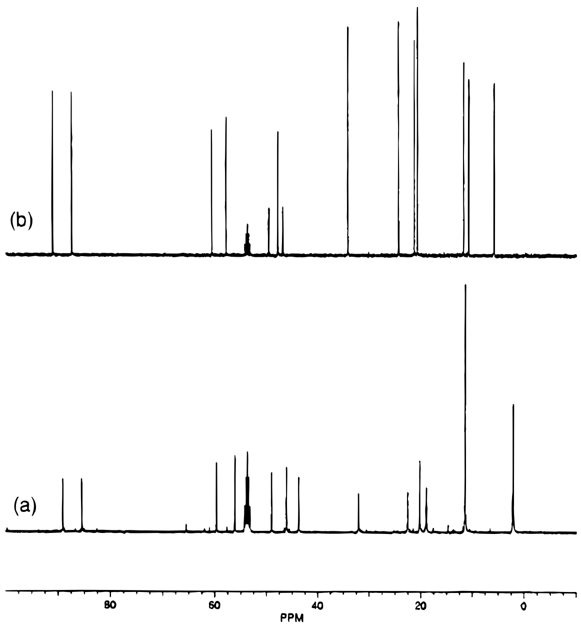


**Figure 9.** $^{13}$C NMR spectra of **3**·Et$_2$Zn (**5**) at (a) 163 K and (b) 298 K.

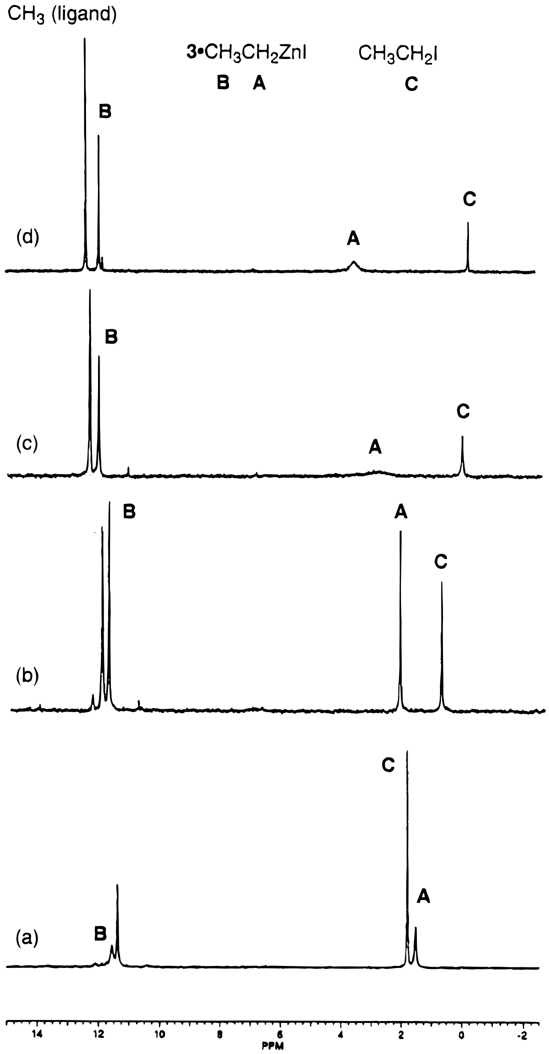


**Figure 10.** $^{13}$C NMR spectra of **3**·EtZnI (**6**) at (a) 163 K, (b) 223 K, (c) 273 K, and (d) 298 K.

The $^{13}$C NMR spectra derived from complex **6** are rather interesting (Figure 10). In this case, we have the possible formation of two diastereomeric complexes **6a** and **6b**. The spectrum recorded at 298 K shows the appropriate number of signals. Quite interestingly, the ZnCH$_2$ signal was relatively broad at 298 and 273 K, indicating a possible equilibrium between several species (possibly between **3**·EtZnI and **3** + EtZnI). This signal became very sharp at 223 K, and it shifted upfield by *ca.* 2 ppm. More importantly, only one of the two possible diastereomeric complexes **6a** and **6b** (>90%) appeared

---

[21] Full-scale $^{1}$H (+9 to −0.5 ppm) and/or $^{13}$C (+120 to −30 ppm) NMR spectra are provided in the supporting information.

[22] It is interesting to note not only that the intensity of the EtI signals increased at lower temperature but also that small upshield shifts of the signals were observed.

[23] This upshield shift may be the result of the increasing concentration of [**3**·Et$_2$Zn] relative to [**3**] and [Et$_2$Zn]. This equilibrium is however too rapid to be observed by NMR: see ref 19.

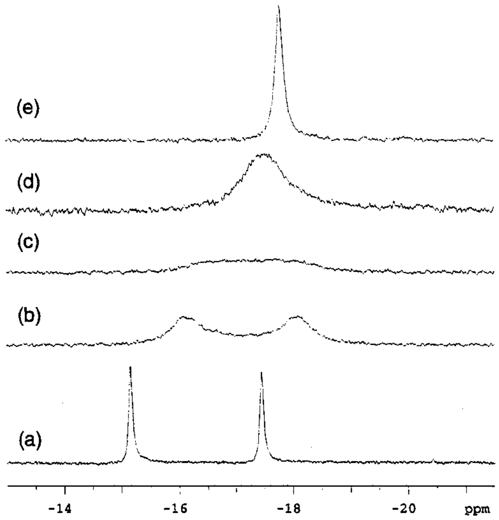


**Figure 11.** Expansion of the $^{13}$C NMR spectrum of **3**·$Zn(CH_2I)_2$ (**7**) in $CD_2Cl_2$ at (a) 173 K, (b) 213 K, (c) 223 K, (d) 233 K, and (e) 253 K ($ZnCH_2I$ region).

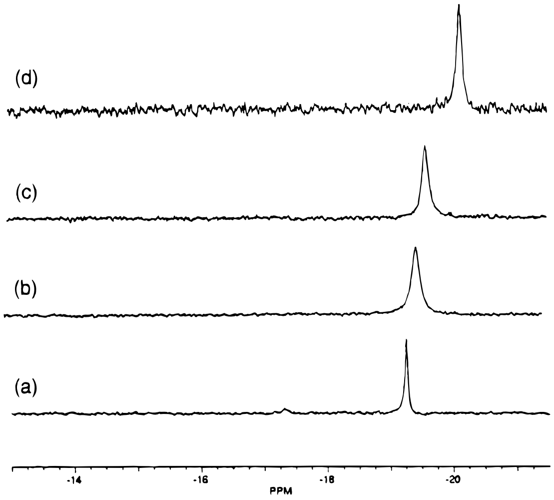


**Figure 12.** Expansion of the $^{13}$C NMR spectrum of **3**·$IZnCH_2I$ (**8**) in $CD_2Cl_2$ at (a) 163 K, (b) 193 K, (c) 233 K, and (d) 273 K ($ZnCH_2I$ region).

to be formed at low temperature.[24] The formation of only one complex may be due to the presence of nonbonded interactions between the *gem*-dimethyl groups of the chiral ligand and the RZn group when different R and R′ groups are present. The formation of two complexes would be expected when both groups (R and R′) are of comparable sizes (*vide infra*).

With these data in hand, the NMR study of the cyclopropanating reagents was undertaken. Gratifyingly, low-temperature $^{13}$C NMR of the complex **7** in $CD_2Cl_2$ confirmed that coalescence occurred at 223 K. Two sharp singlets, resulting from the two diastereotopic $CH_2$ groups, were subsequently obtained at 173 K (Figure 11).[25] Furthermore, the chiral ligand resonances were not split at that temperature. This observation is consistent with the presence of a unique complex (Figure 11).

Conversely, the $^{13}$C NMR of the $IZnCH_2I$ complex displayed a single signal for the "$ZnCH_2I$" resonance under a wide range of temperatures (Figure 12). No trace of the related $Zn(CH_2I)_2$ or $ZnI_2$ complex (**7** or **4**) could be detected by NMR even at temperatures as low as 163 K,[26] *indicating that the Schlenk equilibrium (Scheme 3) lies on the side of $IZnCH_2I$ and not $Zn(CH_2I)_2 + ZnI_2$ under these conditions.*[27−29]

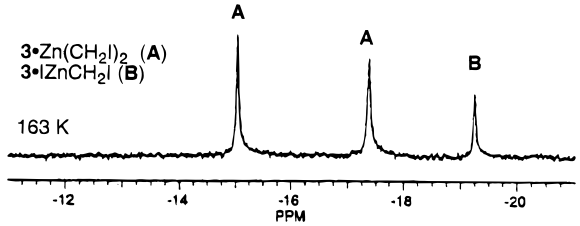
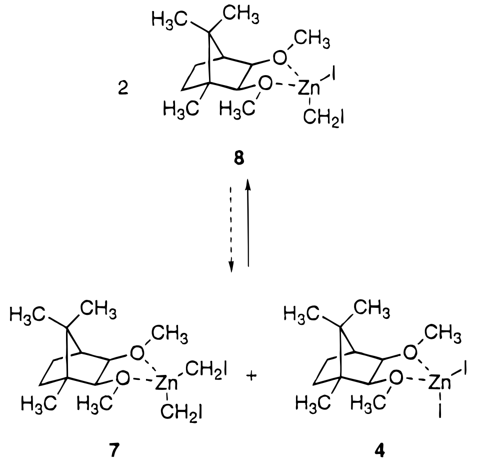


**Figure 13.** Expansion of the $^{13}$C NMR spectrum of a mixture of **3**·$Zn(CH_2I)_2$ (**7**) and **3**·$IZnCH_2I$ (**8**) (7:3) in $CD_2Cl_2$ at 163 K ($ZnCH_2I$ region).

**Scheme 3**



Moreover, these two species (**7** and **8**) are both viable simultaneously and could be differentiated by low-temperature NMR (Figure 13). Addition of 0.3 equiv of complex **8** to a solution of complex **7** produced the two expected distinct signals at low temperature for both complexes.[30]

Finally, the quantitative formation of **3**·$IZnCH_2I$ (**8**) was observed if stoichiometric amounts of **3**·$Zn(CH_2I)_2$ (**7**) and **3**·$ZnI_2$ (**4**) were mixed (Figure 14).[31] These results are all consistent with the fact that the Schlenk equilibrium favors the formation of $IZnCH_2I$ instead of $Zn(CH_2I)_2$ and $ZnI_2$ under these conditions.

**$EtZnCH_2I$·Chiral Diether 3 Complex.** The spectroscopic studies of Furukawa's reagent, "$EtZnCH_2I$", prepared by mixing stoichiometric amounts of $Et_2Zn$ and $CH_2I_2$ in the presence of the chiral ligand **3**, were then undertaken. The low-temperature $^{13}$C NMR showed many additional resonances than those

---

[24] None of the chiral ligand signals were split upon cooling which is also consistent with the presence of only one diastereomeric complex.

[25] The downfield shift of the signal (or the average of the split signals) is consistent with the fact that the concentration of the complexed species increases upon cooling due to entropic reasons. This behavior has been observed with all the complexes studied.

[26] Freezing of the solution occurred below that temperature.

[27] For discussion of the Schlenk equilibria of alkylzinc halide species, see: (a) Garrett, A. B.; Sweet, A.; Marshall, W. L.; Riley, D.; Touma, A. *Rec. Chem. Prog.* **1952**, *13*, 155. (b) Dessy, R. E.; Coe, G. R. *J. Org. Chem.* **1963**, *28*, 3592−3593. (c) Boersma, J.; Noltes, J. G. *Tetrahedron Lett.* **1966**, 1521−1525. (d) Abraham, M. H.; Rolfe, P. H. *J. Organomet. Chem.* **1967**, *7*, 35−43. (e) Evans, D. F.; Wharf, I. *J. Chem. Soc. A* **1968**, 783−787. (f) Evans, D. F.; Fazakerley, G. V. *J. Chem. Soc. A* **1971**, 182−183.

[28] It is sowewhat surprising to observe a single resonance for $ZnCH_2I$ in this spectrum. We think that a single diastereomeric complex, **8**, is formed with $IZnCH_2I$ since none of the chiral ligand resonances are split upon decreasing the temperature. This is probably due to the large difference in the steric bulk of the two groups attached to the zinc. This phenomenon has also been observed with the related EtZnI·**3** (**6**) complex.

[29] A small peak at −17.2 ppm appeared at 163 K, but it is not clear at this point whether this is the other diastereomeric complex or other related species (such as the monodentate ether complex).

[30] Obviously, this does not imply that the three $CH_2I$ groups are not exchangeable at higher temperature.

[31] The signal at −20.3 ppm corresponds to $CH_3I$ formed either by decomposition of the reagents or by the reaction between the reagents and traces of moisture.

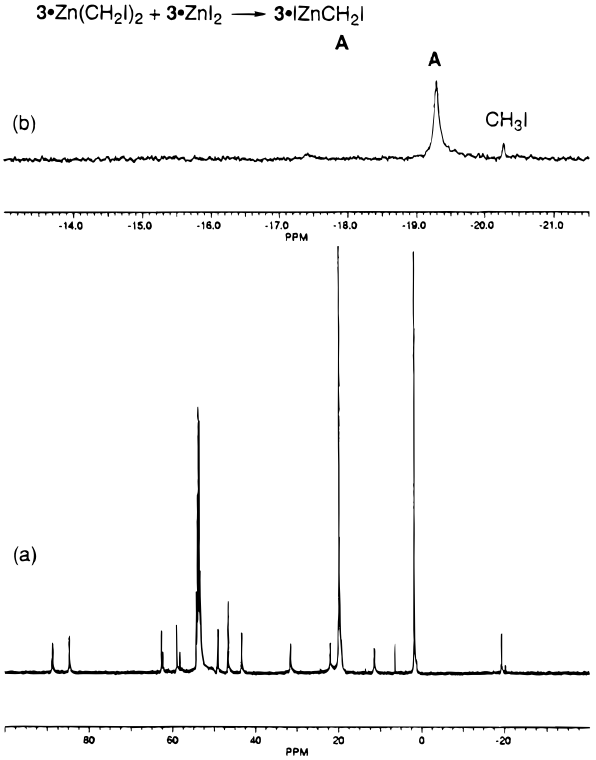


**Figure 14.** (a) $^{13}C$ NMR spectrum of **3**·$IZnCH_2I$ (**8**) prepared from **3**·$Zn(CH_2I)_2$ (**7**) and **3**·$ZnI_2$ (**4**) (1:1) at 163 K. (b) Expansion of the $ZnCH_2I$ region.

expected for $EtZnCH_2I$ (Figure 15). It was clear that a significant amount is of **3**·$Zn(CH_2I)_2$ (Figure 15, signals C) and **3**·$Et_2Zn$ (Figure 15, signals D) were also present and obviously formed via the equilibrium shown in eq 2. Coalescence occurred

$$2EtZnCH_2I \rightleftharpoons Zn(CH_2I)_2 + Et_2Zn \qquad (2)$$

at *ca.* 180 K for the $EtZnCH_2I$ complexes. The signals at −1.0 and −3.0 ppm correspond to the methyl groups in $EtZnCH_2I$, whereas those at −12.0 and −14.0 ppm are consistent for both $ZnCH_2I$ resonances. The coalescence temperature of the $EtZnCH_2I$ complexes was lower than that of the related $Zn(CH_2I)_2$ complex which is consistent with the former's weaker Lewis acidity.

The addition of the **3**·$ZnEt_2$ complex to the related $Zn(CH_2I)_2$ complex produced the same pattern of NMR signals as that obtained in Figure 15 (Figure 16). This control experiment further confirms the equilibrium shown in eq 2.

**Decomposition of 3·Zn(CH$_2$I)$_2$ and 3·IZnCH$_2$I.** Since it is fairly well-established that these very reactive $ZnCH_2I$ species decompose on standing, we felt that we should be able to monitor that decomposition by NMR spectroscopy using this system.[32] It is expected that **3**·$Zn(CH_2I)_2$ should initially decompose into **3**·$IZnCH_2I$ (Scheme 4). In the same way, **3**·$IZnCH_2I$ should eventually decompose into **3**·$ZnI_2$ upon standing at room temperature.

## Scheme 4

$$\mathbf{3}\cdot Zn(CH_2I)_2\ (\mathbf{7}) \rightarrow \mathbf{3}\cdot IZnCH_2I\ (\mathbf{8}) \rightarrow \mathbf{3}\cdot ZnI_2\ (\mathbf{4})$$

This clean decomposition could easily be followed by NMR simply by leaving a solution of **8** at room temperature for a certain time and by recooling it to 163 K to record the NMR spectrum. Figure 17 shows that complex **7** was completely converted into a mixture of complex **8** and **4** after 5 h at room temperature. Conversely, complex **8** quantitatively decomposed into complex **4** in less than 1 h at 313 K (Figure 18).[33] These experiments further demonstrate that the chemistry of $ZnCH_2I$-derived reagents is relatively simple and that the presence of all these different species can be easily monitored by low-temperature $^{13}C$ NMR spectroscopy.

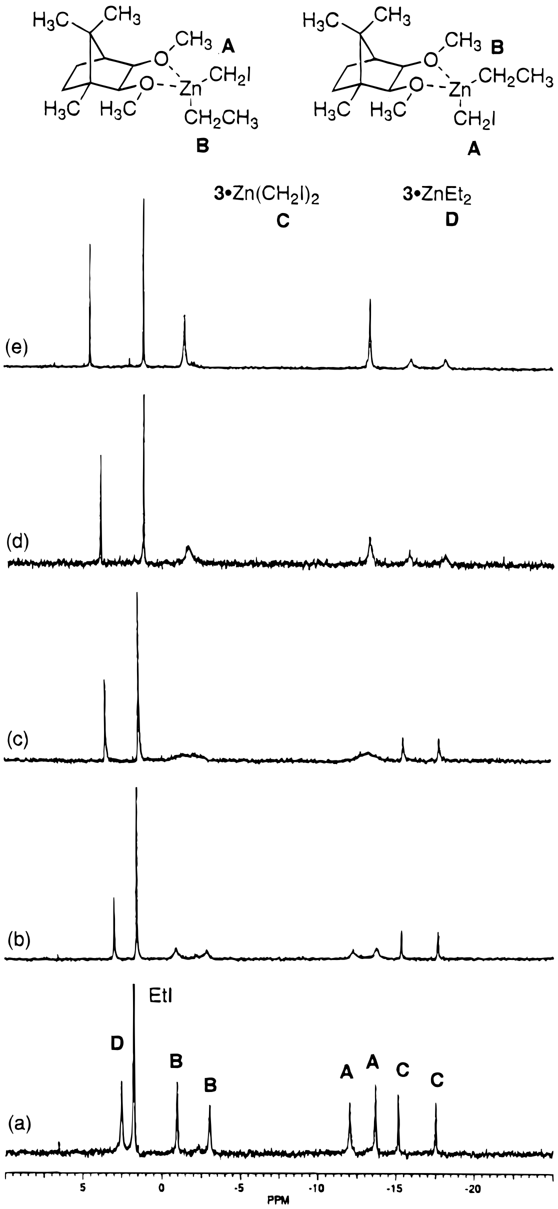


**Figure 15.** $^{13}C$ NMR spectra (100 MHz) of a 1:1:1 mixture of **3** $Et_2Zn/CH_2I_2$ at (a) 163 K, (b) 173 K, (c) 183 K, (d) 193 K, and (e) 203 K (expansion of the RZn region).

## Conclusion

In conclusion, we have spectroscopically characterized $EtZnCH_2I$ and $IZnCH_2I$, two reagents that display unique reactivities in stereoselective reactions. Futhermore, we have shown that the Schlenk equilibrium, illustrated in eq 1, appears to lie heavily on the side of $IZnCH_2I$ and that none of the related $ZnI_2$ or $Zn(CH_2I)_2$ could be detected by $^{13}C$ NMR spectroscopy in the presence of a chiral ether. It should be emphasized that the position of this equilibrium is obviously solvent-dependent.[27] The conditions chosen in this study were those that reflected best the one used in the various stereoselective cyclopropanation

---

[32] The decomposition of $Zn(CH_2I)_2$ into $IZnCH_2I$ was monitored by NMR (relative integration of the $ZnCH_2I$ signal), and the resulting species gave an elemental analysis consistent with a $IZnCH_2I$ complex (see ref 8b).

[33] The signal at 6 ppm is probably due to the presence of ethane arising from the decomposition of these species.

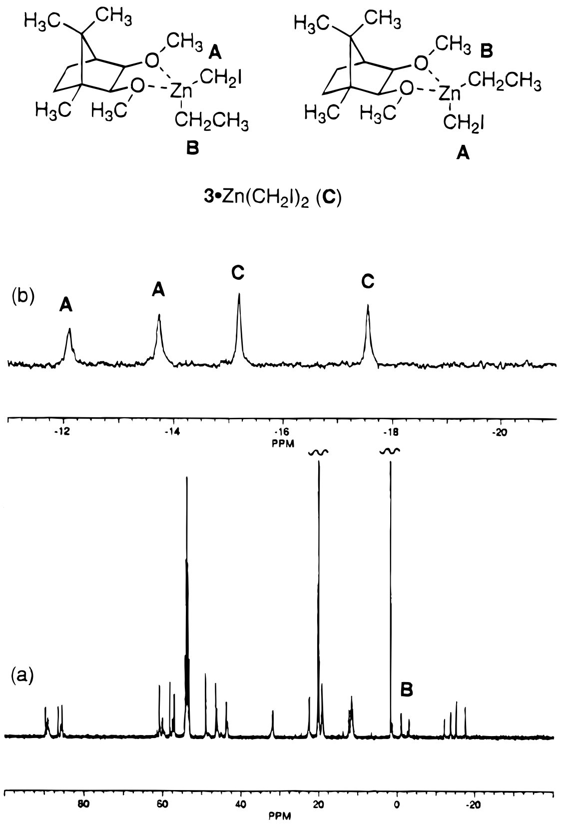


**Figure 16.** (a) $^{13}$C NMR spectra (100 MHz) of a 1:1 mixture of **3**$\cdot$Zn$(CH_2I)_2$ and **3**$\cdot Et_2Zn$ at 163 K in $CD_2Cl_2$. (b) Expansion of the $ZnCH_2I$ region.

reactions developed in our laboratories. We have also demonstrated that the general trends observed in the various equilibria involving (iodomethyl)zinc-derived reagents follow those observed with ethylzinc-derived organometallic compounds.

These fundamental results will certainly be very useful in the elaboration of transition state models for the stereoselective cyclopropanation reactions.

## Experimental Section

**General Procedures.** All cyclopropanation reactions and NMR experiments were carried out under argon, using anhydrous, freshly distilled $CH_2Cl_2$ (dried over $CaH_2$), THF, and DME (dried over acetophenone ketyl). The diethylzinc was used neat, as received from Akzo Nobel Inc. and manipulated under argon with gas-tight syringes. The deuterated dichloromethane was used as received by MSD Isotopes. The cyclopropanation reactions were performed under nitrogen or argon. $^1$H and $^{13}$C NMR spectra and variable temperature NMR experiments were performed on a Brucker AMX-300 or Brucker ARX-400 spectrometer in $CDCl_3$ or $CD_2Cl_2$.

**Cyclopropanation of (*E*)-4-Phenyl-3-buten-2-ol (1) with $EtZnCH_2I$ (Table 1, Entry 1, Conditions A).** To a solution of **1** (113 mg, 0.77 mmol) in anhydrous $CH_2Cl_2$ (7.65 mL) at 0 °C was slowly added $Et_2Zn$ (395 $\mu$L, 3.85 mmol).[34] After 5 min of stirring, $CH_2I_2$ (248 $\mu$L, 3.82 mmol, 4.0 equiv) was slowly added, and the reaction mixture was stirred for 1 h at 0 °C and 6 h at room temperature. The mixture was diluted with ether, washed with aqueous HCl (10%), brine, and aqueous $NaHCO_3$, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The diastereomeric ratios were determined by $^1$H NMR (300 MHz) and GC analysis of the acetate derived from (*E*)-1-(1-hydroxyethyl)-2-phenylcyclopropane[10j] (capillary GC: DB-1701 (0.25 mm × 30 m; pressure, 25 psi; 140 °C isotherm) $T_{r(major)}$ 11.3 min, $T_{r(minor)}$ 10.2 min) to give a *syn*:*anti* ratio of 7.0:1. *Syn* isomer: $R_f$ 0.30 (25% AcOEt/75% hexane); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.30−7.06 (m, 5H), 3.39 (dq, $J$ = 8, 6 Hz, 1H), 1.85−1.79 (m, 1H), 1.67 (br s, 1H), 1.36 (d, $J$ = 6 Hz, 3H), 1.33−1.24 (m, 1H), 1.05−0.93 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 142.6, 128.4, 126.0, 125.6, 71.3, 30.7, 22.8, 20.7, 13.9; IR (film) 3360 (br), 3080, 3030, 3000, 2980, 2930, 1600, 1500, 1470, 1410, 1370, 1100, 1080, 975, 940, 750, 690 cm$^{-1}$. *Anti* isomer: $R_f$ 0.55 (25% EtOAc/75% hexane); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.30−7.08 (m, 5H), 3.40 (dq, $J$ = 8, 6 Hz, 1H), 1.95−1.89 (m, 1H), 1.68 (s, 1H), 1.34 (d, $J$ = 6 Hz, 3H), 1.34−1.25 (m, 1H), 0.98−0.90 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 142.6, 128.2, 125.7, 125.5, 71.7, 30.7, 22.3, 21.2, 13.2; IR (film) 3360 (br), 3060, 3000, 2960, 2920, 1600, 1490, 1440, 1410, 1210, 1100, 1070, 1020, 970, 930, 740, 680 cm$^{-1}$.

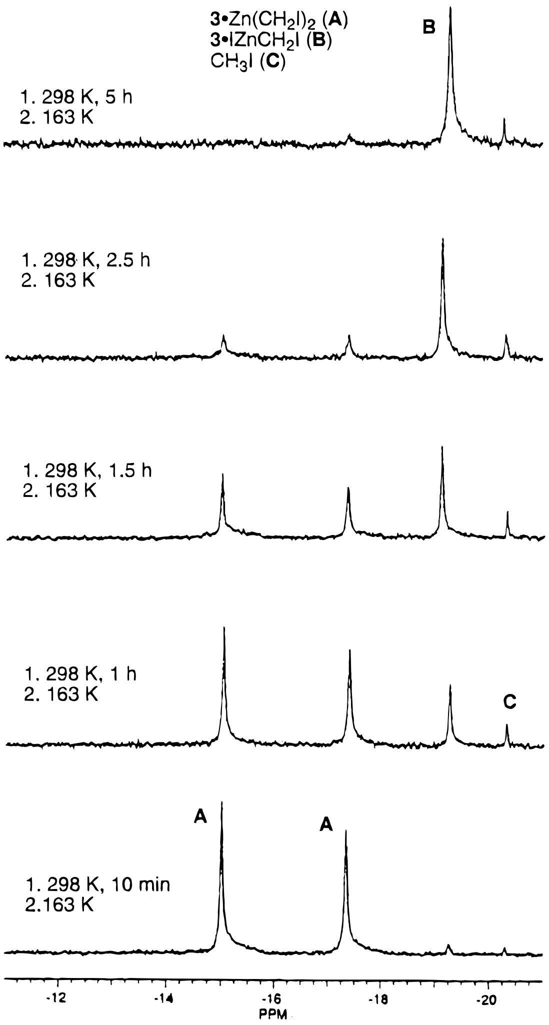


**Figure 17.** $^{13}$C NMR spectra (100 MHz) of the decomposition of **3**$\cdot$Zn$(CH_2I)_2$ (**7**) as a function of time (163 K).

**Cyclopropanation of (*E*)-4-Phenyl-3-buten-2-ol (1) with Zn$(CH_2I)_2$ (Table 1, Entry 2, Conditions B).** To a solution of **1** (109 mg, 0.73 mmol) in anhydrous $CH_2Cl_2$ (7.30 mL) at 0 °C was slowly added $Et_2Zn$ (375 $\mu$L, 3.66 mmol). After 5 min of stirring at that temperature, $CH_2I_2$ (475 $\mu$L, 5.90 mmol) was then slowly added, and the reaction mixture was stirred for 1 h at 0 °C and 6 h at room temperature. The mixture was diluted with ether, washed with aqueous HCl (10%), brine, and aqueous $NaHCO_3$, dried over $MgSO_4$, and concentrated under reduced pressure. The GC analysis of the acetylated products with the conditions described above gave a *syn*:*anti* diastereomeric ratio of 3.6:1.

**Cyclopropanation of (*E*)-4-Phenyl-3-buten-2-ol (1) with Zn$(CH_2I)_2$ (Table 1, Entry 3, Conditions C).** To a solution of **1** (100 mg, 0.68 mmol) in anhydrous $CH_2Cl_2$ (6.80 mL) at 0 °C was added iodine (696 mg, 2.74 mmol) followed by $Et_2Zn$ (350 $\mu$L, 3.41 mmol). After the iodine was completely consumed, $CH_2I_2$ (220 $\mu$L, 2.73 mmol) was slowly added, and the reaction mixture was stirred for 1 h at 0 °C and 6 h at room temperature. The mixture was then diluted with ether, washed with aqueous HCl (10%), brine, and aqueous $NaHCO_3$, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The GC analysis of the acetylated products with the conditions described above gave a *syn*:*anti* diastereomeric ratio of 1.2:1.

---

(34) The formation of the zinc alkoxide and ethane is instantaneous at that temperature as observed by low-temperature NMR: Côté, B. Ph.D. Thesis, Université de Montréal, 1994.

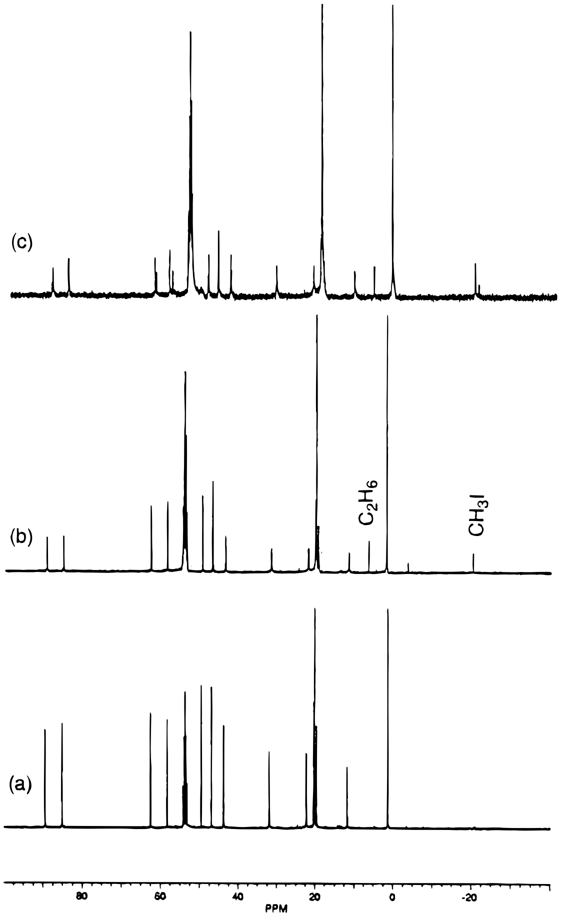


**Figure 18.** $^{13}$C NMR spectra of (a) **3**·ZnI$_2$ (**4**), (b) **3**·IZnCH$_2$I (**8**) after 3.5 h at 298 K and 1 h at 313 K, and (c) **3**·IZnCH$_2$I (**8**) after 1.5 h at 298 k.

**Cyclopropanation of 1-*O*-[2′-[[(Triisopropylsilyl)oxy]methyl]-2′-penten-1′-yl]-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranose (2) with EtZnCH$_2$I (Table 1, entry 4, conditions A).** To a solution of **2** (54 mg, 0.077 mmol) in anhydrous CH$_2$Cl$_2$ (640 $\mu$L) at room temperature was slowly added Et$_2$Zn (87 $\mu$L, 0.85 mmol). After 5 min of stirring at 0 °C, the solution was cooled to −20 °C. A solution of CH$_2$I$_2$ in CH$_2$Cl$_2$ (450 $\mu$L, 1.71 M, 0.77 mmol) was then slowly added, and the reaction mixture was stirred at −20 °C for 16 h. The mixture was diluted with ether, washed with aqueous HCl (10%), brine, and aqueous NaHCO$_3$, dried over anhydrous MgSO$_4$, and concentrated under reduced pressure. The diastereomeric ratios were determined by $^1$H NMR (300 MHz) and HPLC analysis of the crude mixture (HPLC: 4 $\mu$m NOVA-PAK (8 × 200 mm; 8% EtOAc/hexane.; 1 mL/min) $T_{\mathrm{r(major)}}$ 15.7 min, $T_{\mathrm{r(minor)}}$ 20.4 min) to give a ratio of 47:1. Major isomer: $R_f$ 0.3 (10% EtOAc/hexane); [α]$_D$ −11.7° (*c* 1.95, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.44−7.21 (m, 15H), 5.02 (d, $J$ = 11 Hz, 1H), 4.89 (d, $J$ = 11 Hz, 1H), 4.86 (d, $J$ = 11 Hz, 1H), 4.65 (d, $J$ = 12 Hz, 4H), 4.60 (d, $J$ = 11 Hz, 1H), 4.58 (d, $J$ = 12 Hz, 1H), 4.36 (d, $J$ = 7 Hz, 1H), 3.95 (d, $J$ = 11 Hz, 1H), 3.82−3.72 (m, 4H), 3.66−3.59 (m, 3H), 3.50 (d, $J$ = 10 Hz, 1H), 3.52−3.49 (m, 1H), 2.53 (s, 1H), 1.53−1.36 (m, 2H), 1.17−1.05 (m, 21H), 1.02 (t, $J$ = 7 Hz, 3H), 0.81−0.76 (m, 1H), 0.71 (dd, $J$ = 9, 5 Hz, 1H), 0.23 (t, $J$ = 5 Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 138.7, 138.2, 138.1, 128.2, 128.2, 128.2, 127.8, 127.8, 127.6, 127.5, 127.4, 127.4, 102.5, 84.4, 77.5, 75.2, 74.9, 74.9, 74.8, 73.4, 69.6, 68.9, 67.4, 26.4, 22.8, 22.0, 17.9, 14.7, 14.2, 11.9; IR (film) 3460 (br), 3020, 2940, 2860, 1490, 1450, 1360, 1100 (br), 875, 780, 740, 690 cm$^{-1}$.

**Cyclopropanation of 1-*O*-[2′-[[(Triisopropylsilyl)oxy]methyl]-2′-penten-1′-yl]-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranose (2) with Zn(CH$_2$I)$_2$ (Table 1, Entry 5, Conditions B).** To a solution of **2** (48 mg, 0.068 mmol) in anhydrous CH$_2$Cl$_2$ (570 $\mu$L) at room temperature was slowly added Et$_2$Zn (42 $\mu$L, 0.41 mmol), and after 5 min of stirring, the solution was cooled to −20 °C. A solution of CH$_2$I$_2$ in CH$_2$Cl$_2$ (400 $\mu$L, 1.7 M, 0.68 mmol) was then slowly added, and the reaction mixture was stirred for 16 h at −20 °C. The mixture was diluted with ether, washed with aqueous HCl (10%), brine, and aqueous NaHCO$_3$, dried over anhydrous MgSO$_4$, and concentrated under reduced pressure. The analysis of the crude mixture by HPLC with the conditions described above gave a diastereomeric ratio of 27:1.

**Cyclopropanation of 1-*O*-[2′-[[(Triisopropylsilyl)oxy]methyl]-2′-penten-1′-yl]-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranose (2) with IZnCH$_2$I (Table 1, Entry 6, Conditions C).** To a solution of **2** (51 mg, 0.073 mmol) in anhydrous CH$_2$Cl$_2$ (600 $\mu$L) at −20 °C was added iodine (185.0 mg, 0.73 mmol) followed by Et$_2$Zn (82 $\mu$L, 0.80 mmol). After the iodine was completely consumed, a solution of CH$_2$I$_2$ in CH$_2$Cl$_2$ (425 $\mu$L, 1.7 M, 0.73 mmol) was slowly added, and the reaction mixture was stirred for 16 h at −20 °C. The mixture was diluted with ether and washed with aqueous HCl (10%), brine, and aqueous NaHCO$_3$, dried over anhydrous MgSO$_4$, and concentrated under reduced pressure. The analysis of the crude mixture by HPLC with the conditions described above gave a diastereomeric ratio of 4.6:1.

**Preparation and NMR Study of EtZnCH$_2$I·DME (Figure 1).** In a vacuum-dried NMR tube sealed with a septum and Teflon tape and purged several times with argon were placed CD$_2$Cl$_2$ (0.70 mL), dimethoxyethane (25 $\mu$L, 0.32 mmol), and Et$_2$Zn (33 $\mu$L, 0.32 mmol). The NMR tube was cooled to −40 °C, and a solution of CH$_2$I$_2$ (23.0 $\mu$L, 0.29 mmol, 0.90 equiv) in CD$_2$Cl$_2$ (0.70 mL) was then slowly added in five portions with shaking of the tube between each addition. The NMR spectra were then recorded and are shown in Figure 1: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.61 (br s, 4H), 3.44 (br s, 6H), 1,42 (br s, 2H), 1.04 (t, $J$ = 11 Hz), 0.29 (q, $J$ = 11 Hz).

**Preparation and NMR Study of CH$_3$OCH$_2$CH$_2$OZnEt·EtZnCH$_2$I (Figure 2).** To a vacuum-dried NMR tube sealed with a septum and Teflon tape and purged several times with argon were added at room temperature CD$_2$Cl$_2$ (0.70 mL), 2-methoxyethanol (25 $\mu$L, 0.32 mmol), and Et$_2$Zn (65 $\mu$L, 0.64 mmol). After 10 min at room temperature, the NMR tube was cooled to −40 °C. A solution of CH$_2$I$_2$ (23.0 $\mu$L, 0.29 mmol) in CD$_2$Cl$_2$ (0.70 mL) was then slowly added in five portions, and the tube was shaken between each addition. The NMR tube was then directly transferred into the NMR probe for the analysis shown in Figure 2: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.04−4.00 (m, 2H), 3.66−3.60 (m, 2H), 3.53 (br s, 3H), 1,52 (br s, 2H), 1.16 (t, $J$ = 8 Hz, 6H), 0.29 (q, $J$ = 8 Hz, 4H).

**Formation and NMR Study of the EtZnI·THF Complex (Figure 3).** In a vacuum-dried NMR tube was placed iodine (122 mg, 0.48 mmol), and the tube was sealed with a septum and Teflon tape and was purged several times with argon. CD$_2$Cl$_2$ (0.70 mL) and THF (39.0 $\mu$L, 0.48 mmol) were added via a syringe. The solution was cooled to −40 °C, and Et$_2$Zn (49.0 $\mu$L, 0.48 mmol) was added. The solution was allowed to reach 0 °C in order to completely consume the iodine. The NMR tube was then directly transferred to the precooled NMR probe for the study shown in Figure 3a: $^1$H NMR (400 MHz, CD$_2$Cl$_2$, 273 K) $\delta$ 4.02−3.98 (m, 4H, THF), 3.18 (q, $J$ = 7 Hz, 2H, EtI), 2.00−1.96 (m, 4H, THF), 1.80 (t, $J$ = 7 Hz, 3H, EtI), 1.08 (t, $J$ = 8 Hz, 3H), 0.31 (q, $J$ = 8 Hz, 3H); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$, 273 K) $\delta$ 70.3 (THF), 25.5 (THF), 20.7 ($C$H$_3$CH$_2$I), 12.3, 4.5, 0.07 (CH$_3$$C$H$_2$I); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$, 163 K) $\delta$ 69.6 (THF), 24.9 (THF), 19.9 ($C$H$_3$CH$_2$I), 12.0, 2.6, 1.69 (CH$_3$$C$H$_2$I). In the case of Figure 3b, the NMR tube was prepared as described above except that Et$_2$Zn (45 $\mu$L, 0.44 mmol) was mixed with ZnI$_2$ (140 mg, 0.44 mmol). In the case of Figure 3c,d, an additional equivalent of Et$_2$Zn (45 $\mu$L, 0.44 mmol) was added.

**Preparation and NMR Study of the Et$_2$Zn·THF Complex (Figure 3e).** The NMR tube was prepared as described for the EtZnI·THF complex except that it was done at 0 °C and that the addition of iodine was omitted: $^1$H NMR (400 MHz, CD$_2$Cl$_2$, 298 K) $\delta$ 3.77−3.73 (m, 4H, THF), 1.84−1.88 (m, 4H, THF), 1.15 (t, $J$ = 8 Hz, 3H), 0.24 (q, $J$ = 8 Hz, 3H); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$, 298 K) $\delta$ 68.3 (THF), 26.0 (THF), 10.7, 6.0.

**Formation and NMR Study of the IZnCH$_2$I·THF Complex (Figures 4, 5a, and 6a).** In a vacuum-dried NMR tube was placed iodine (225 mg, 0.89 mmol), and the tube was sealed with a septum and Teflon tape, and purged several times with argon. CD$_2$Cl$_2$ (1.30 mL) and THF (142 $\mu$L, 1.75 mmol) were added via a syringe. The solution was cooled to −40 °C, and Et$_2$Zn (90 $\mu$L, 0.88 mmol) was added. The NMR tube was shaken, and the solution was allowed to reach 0 °C to completely consume the iodine. The clear solution was then cooled to −78 °C, and CH$_2$I$_2$ (71 $\mu$L, 0.88 mmol) was then slowly added. The NMR tube was then directly transferred to the precooled

NMR probe for the study shown in Figures 4, 5a, and 6a: $^1$H NMR (400 MHz, $CD_2Cl_2$, 158 K) $\delta$ 3.95−3.83 (m, 8H, THF), 1.95−1.84 (m, 8H, THF), 1.34 (br s, 2H); $^{13}$C NMR (100 MHz, $CD_2Cl_2$, 158 K) $\delta$ 69.7 (THF), 24.7 (THF), 19.8 (*C*$H_3CH_2I$), 1.8 ($CH_3$*C*$H_2I$), −17.4.

**Formation and NMR Analysis of the $Zn(CH_2I)_2$·THF Complex (Figures 5b and 6b).** To a vacuum-dried NMR tube sealed with a septum and Teflon tape and purged several times with argon were added at room temperature $CD_2Cl_2$ (1.30 mL), THF (142 $\mu$L, 1.75 mmol), and $CH_2I_2$ (142.0 $\mu$L, 1.76 mmol). The NMR tube was cooled to −78 °C, and $Et_2Zn$ (90 $\mu$L, 0.88 mmol) was then slowly added. The tube was then warmed to room temperature for about 20 s to dissolve the white precipitate and then cooled back to −78 °C. The NMR tube was then directly transferred to the precooled NMR probe for the study shown in Figures 5b and 6b: $^1$H NMR (400 MHz, $CD_2Cl_2$, 158 K) $\delta$ 3.81−3.65 (m, 8H), 1.88−1.74 (m, 8H), 1.33−1.18 (m, 4H); $^{13}$C NMR (100 MHz, $CD_2Cl_2$, 158 K) $\delta$ 68.7 (THF), 24.8 (THF), 19.8 (*C*$H_3CH_2I$), 1.8 ($CH_3$*C*$H_2I$), −17.3.

**Formation of a Mixture of $IZnCH_2I$·THF and $Zn(CH_2I)_2$·THF (Figure 7).** The complexes were independently prepared as described above and were transferred into a dry NMR tube via a Teflon cannula under argon at −78 °C. The NMR tube was then directly transferred to the precooled NMR probe for the study shown in Figure 7.

**Formation and NMR Analysis of the (1*R*)-*exo,exo*-2,3-Dimethoxy-1,7,7-trimethylbicyclo[2.2.1]heptane·Zinc Iodide Complex (4) (Figure 8).** Diether **3** (68 mg, 0.35 mmol) and iodine (175 mg, 0.69 mmol) were placed in a vacuum-dried NMR tube. The tube was then sealed with a septum and Teflon tape and purged with argon. $CD_2Cl_2$ (1.30 mL) was added via a dried syringe, and the NMR tube was cooled to −78 °C. Neat $Et_2Zn$ (35.0 $\mu$L, 0.35 mmol) was then slowly added, and the tube was allowed to reach room temperature until there was a complete disappearance of iodine. The solution was then placed in the NMR probe for analysis: $^1$H NMR (400 MHz, $CD_2Cl_2$, 298 K) $\delta$ 3.89 (d, $J$ = 7 Hz, 1H), 3.75 (s, 3H), 3.70 (d, $J$ = 7 Hz, 1H), 3.56 (s, 3H), 2.09 (d, $J$ = 5 Hz, 1H), 1.85−1.74 (m, 1H), 1.52 (dt, $J$ = 5, 12 Hz, 1H), 1.10 (t, $J$ = 8 Hz, 3H), 1.07 (s, 3H), 1.03 (s, 3H), 0.88−1.02 (m, 2H), 0.82 (s, 3H), 0.24 (q, $J$ = 8 Hz, 2H); $^{13}$C NMR (100 MHz, $CD_2Cl_2$, 298 K) $\delta$ 90.8, 86.5, 62.3, 58.0, 50.3, 47.4, 45.3, 23.4, 20.1, 13.4, 3.9.

**NMR Spectra of the (1*R*)-*exo,exo*-2,3-Dimethoxy-1,7,7-trimethylbicyclo[2.2.1]heptane·Diethylzinc Complex (5) (Figure 9).** Diether **3** (98 mg, 0.49 mmol) was placed in a vacuum-dried NMR tube sealed with a septum and Teflon tape and purged with argon. $CD_2Cl_2$ (1.30 mL) and $Et_2Zn$ (50 $\mu$L, 0.49 mmol) were added via a dried syringe. The solution was then placed in the NMR probe for analysis: $^1$H NMR (400 MHz, $CD_2Cl_2$, 298 K) $\delta$ 3.45−3.22 (m, 1H), 3.43 (br s, 3H), 3.37 (s, 3H), 3.21 (d, $J$ = 7 Hz, 1H), 1.87 (d, $J$ = 5 Hz, 1H), 1.74−1.66 (m, 1H), 1.49 (dt, $J$ = 4, 12 Hz, 1H), 1.15 (br t, $J$ = 8 Hz, 6H), 1.11−0.88 (m, 2H), 1.09 (s, 3H), 0.94 (s, 3H), 0.81 (s, 3H), 0.25 (q, $J$ = 4, 8 Hz, 4H); $^{13}$C NMR (100 MHz, $CD_2Cl_2$, 298 K) $\delta$ 91.2, 87.5, 60.7, 57.9, 49.7, 47.8, 46.9, 34.2, 24.4, 21.3, 20.7, 11.8, 10.7, 5.8.

**NMR Spectra of the (1*R*)-*exo,exo*-2,3-Dimethoxy-1,7,7-trimethylbicyclo[2.2.1]heptane·Ethylzinc Iodide Complex (6) (Figure 10).** Diether **3** (123 mg, 0.62 mmol) and iodine (157 mg, 0.62 mmol) were placed in a vacuum-dried NMR tube. The tube was then sealed with a septum and Teflon tape and purged with argon. $CD_2Cl_2$ (1.00 mL, 0.62 M) was added via a dried syringe, and the NMR tube was cooled to −78 °C. Neat $Et_2Zn$ (49 $\mu$L, 0.48 mmol) was then slowly added, and the tube was allowed to reach room temperature until there was a complete disappearance of the iodine to form a homogeneous, colorless solution. The solution was then placed in the NMR probe for analysis: $^1$H NMR (400 MHz, $CD_2Cl_2$, 298 K) $\delta$ 3.80 (d, $J$ = 7 Hz, 1H), 3.66 (br s, 3H), 3.61 (d, $J$ = 7 Hz, 1H), 3.50 (br s, 3H), 2.05 (d, $J$ = 5 Hz, 1H), 1.80−1.70 (m, 1H), 1.50 (dt, $J$ = 5, 12 Hz, 1H), 1.09 (t, $J$ = 8 Hz, 3H), 1.06 (s, 3H), 1.03 (s, 3H), 1.02−0.91 (m, 2H), 0.82 (s, 3H), 0.23 (q, $J$ = 8 Hz, 2H); $^{13}$C NMR (100 MHz, $CD_2Cl_2$, 298 K) $\delta$ 90.8, 86.5, 62.3, 58.0, 50.3, 47.4, 45.3, 23.4, 21.2, 20.8, 20.1, 13.4, 12.0, 3.9. −0.3; $^{13}$C NMR (100 MHz, $CD_2Cl_2$) $\delta$ (Zn*C*$H_2CH_3$) (223 K) 2.8 (br), (223 K) 2.1, (163 K) 1.5; $\delta$ ($ZnCH_2$*C*$H_3$) (223 K) 12.0, (223 K) 11.8, (163 K) 11.6.

**NMR Spectra of the (1*R*)-*exo,exo*-2,3-Dimethoxy-1,7,7-trimethylbicyclo[2.2.1]heptane·Bis(iodomethyl)zinc Complex (7) (Figure 11).** Diether **3** (78 mg, 0.39 mmol) was placed in a NMR tube, and the tube was sealed with a septum and Teflon tape and purged several times with argon. $CD_2Cl_2$ (0.70 mL) and $CH_2I_2$ (64 $\mu$L, 0.78 mmol) were successively added via a syringe. The NMR tube was cooled to −78 °C, and $Et_2Zn$ (40 $\mu$L, 0.39 mmol) was then slowly added. The tube was warmed to room temperature (*ca.* 20 s) to completely dissolve the white precipitate and was cooled back to −78 °C. The NMR tube was then directly transferred to the precooled NMR probe for analysis: $^1$H NMR (400 MHz, $CD_2Cl_2$, 273 K) $\delta$ 3.79 (d, $J$ = 7 Hz, 1H), 3.59 (s, 3H), 3.56−3.53 (m, 1H), 3.53 (s, 3H), 1.97 (d, $J$ = 5 Hz, 1H), 1.72−1.61 (m, 1H), 1.45 (dt, $J$ = 4, 12 Hz, 1H), 1.38−1.32 (m, 4H), 1.05−0.86 (m, 2H), 0.98 (s, 3H), 0.97 (s, 3H), 0.75 (s, 3H); $^1$H NMR (400 MHz, $CD_2Cl_2$, 173 K) $\delta$ 3.86−3.81 (m, 1H), 3.55 (s, 3H), 3.56−3.50 (m, 1H), 3.51 (s, 3H), 1.95−1.93 (m, 1H), 1.64−1.54 (m, 1H), 1.45−1.32 (m, 3H), 1.17−1.11 (m, 2H), 1.14 (s, 3H), 1.00−0.80 (m, 2H), 0.93 (s, 3H), 0.85 (s, 3H); $^{13}$C NMR (100 MHz, $CD_2Cl_2$, 253 K) $\delta$ 90.9, 87.1, 61.6, 58.5, 49.8, 46.9, 45.2, 33.1, 23.4, 21.0 (*C*$H_3CH_2I$), 20.6, 19.9, 11.9, 0.4 ($CH_3$*C*$H_2I$), −17.8; $^{13}$C NMR (100 MHz, $CD_2Cl_2$, 173 K) $\delta$ 89.8, 86.5, 61.0, 58.2, 49.2, 46.5, 43.8, 31.8, 22.5, 20.3, 20.0 (*C*$H_3CH_2I$), 19.2, 11.4, 11.9, 1.7 ($CH_3$*C*$H_2I$), −15.1, −17.4; $^{13}$C NMR (100 MHz, $CD_2Cl_2$) $\delta$ (Zn(*C*$H_2I)_2$) (173 K) −15.1, −17.4, (193 K) −15.6, −17.8, (203 K) −15.8 (br), −18.0, (br), (213 K) −16.1 (br), −18.1 (br), (223 K) −17.4 (coalescent), (233 K) −17.5 (br), (253 K) −17.8.

**NMR Spectra of (1*R*)-*exo,exo*-2,3-Dimethoxy-1,7,7-trimethylbicyclo[2.2.1]heptane·(Iodomethyl)Zinc Iodide (8) (Figure 12).** Diether **3** (95 mg, 0.48 mmol) and iodine (122 mg, 0.48 mmol) were placed in a vacuum-dried NMR tube. The tube was then sealed with a septum and Teflon tape and purged with argon. $CD_2Cl_2$ (0.70 mL) was added via a dried syringe, and the NMR tube was cooled to −78 °C. Neat $Et_2Zn$ (49 $\mu$L, 0.48 mmol) was then slowly added, and the tube was allowed to reach room temperature until there was a complete disappearance of the iodine to form a colorless solution. $CH_2I_2$ (39 $\mu$L, 0.48 mmol) was then added at −78 °C. The NMR tube was directly transferred to the precooled NMR probe for analysis: $^1$H NMR (400 MHz, $CD_2Cl_2$, 273 K) $\delta$ 3.84 (d, $J$ = 7 Hz, 1H), 3.73 (s, 3H), 3.66 (d, $J$= 7 Hz, 1H), 3.60 (s, 3H), 2.07 (d, $J$ = 5 Hz, 1H), 1.84−1.70 (m, 1H), 1.51 (dt, $J$ = 4, 12 Hz, 1H), 1.42 (br s, 2H), 1.06 (s, 3H), 1.03 (s, 3H), 0.98−0.79 (m, 2H), 0.81 (s, 3H); $^1$H NMR (400 MHz, $CD_2Cl_2$, 163 K) $\delta$ 3.72 (br d, $J$ = 7 Hz, 1H), 3.64 (br s, 3H, 3.58 (br d, $J$ = 7 Hz, 1H,), 3.53 (br s, 3H), 2.05−2.00 (m, 1H), 1.70−1.59 (m, 1H), 1.45−1.32 (m, 3H), 1.05−0.70 (m, 2H), 0.98 (br s, 3H), 0.88 (br s, 3H), 0.70 (br s, 3H); $^{13}$C NMR (100 MHz, $CD_2Cl_2$, 163 K) $\delta$ 88.7, 84.9, 62.7, 59.0, 49.1, 46.6, 43.4, 31.6, 22.0, 19.9 (*C*$H_3CH_2I$), 19.6, 11.5, 1.9 ($CH_3$*C*$H_2I$), −19.3; $^{13}$C NMR (100 MHz, $CD_2Cl_2$) $\delta$ (Zn*C*$H_2I$) (163 K) −19.3, (193 K) −19.5, (233 K) −19.6, (273 K) −19.8.

**Preparation of a Mixture of 3·$IZnCH_2I$ and 3·$Zn(CH_2I)_2$ (Figure 13).** The complexes **3**·$IZnCH_2I$ and **3**·$Zn(CH_2I)_2$ were independently prepared as described above and were transferred into a dry NMR tube via a Teflon cannula under argon at −78 °C. The NMR tube was then directly transferred to the precooled NMR probe for analysis.

**Preparation of 3·$IZnCH_2I$ from 3·$Zn(CH_2I)_2$ and 3·$ZnI_2$ (Figure 14).** The complexes **3**·$Zn(CH_2I)_2$ and **3**·$ZnI_2$ were independently prepared as described above, and equimolar amounts were transferred into a dry NMR tube via a Teflon cannula under argon at −78 °C. The NMR tube was then directly transferred to the precooled NMR probe for analysis.

**NMR Spectra of (1*R*)-*exo,exo*-2,3-Dimethoxy-1,7,7-trimethylbicyclo[2.2.1]heptane·(Iodomethyl)ethylzinc (9) (Figure 15).** Diether **3** (79 mg, 0.40 mmol) was placed in a vacuum-dried NMR tube sealed with a septum and Teflon tape and purged with argon. $CD_2Cl_2$ (0.70 mL) and $CH_2I_2$ (32 $\mu$L, 0.40 mmol) were then successively added via purged syringes. The NMR tube was cooled to −78 °C, and neat $Et_2Zn$ (41 $\mu$L, 0.40 mmol) was then slowly added. The white precipitate was allowed to dissolve by shaking the tube at room temperature for about 20 s, and it was then cooled back to −78 °C. The NMR tube was directly transferred to the precooled NMR probe for analysis: $^1$H NMR (400 MHz, $CD_2Cl_2$, 273 K) $\delta$ 3.66−3.62 (m, 1H), 3.53 (br s, 3H), 3.47−3.39 (m, 1H), 3.46 (s, 3H), 1.97−1.92 (m, 1H), 1.74−1.64 (m, 1H), 1.46 (dt, $J$ = 4, 12 Hz, 1H), 1.38 (dd, $J$ = 11, 14 Hz, *ca.* 1H), 1.33 (m, *ca.* 1H), 1.10 (br t, $J$ = 8 Hz, 3H), 1.05−0.86 (m, 2H), 1.01 (s, 3H), 0.97 (s, 3H), 0.77 (s, 3H), 0.35−0.01 (m, 2H); $^{13}$C NMR (100 MHz, $CD_2Cl_2$, 203 K) $\delta$ 89.9, 86.1, 60.1, 57.4, 49.2, 46.5, 44.5, 32.6, 23.0, 20.6, 20.0 (*C*$H_3CH_2I$), 19.4, 12.3, 11.7, 11.3, 4.5, 1.1 ($CH_3$*C*$H_2I$), −1.5, −13.3, −16.0, −18.1; $^{13}$C NMR (100 MHz, $CD_2Cl_2$, 163 K) $\delta$

89.7, 89.3, 89.1, 86.5, 85.8, 85.5, 60.9, 60.7, 60.1, 58.2, 57.5, 57.1, 49.1, 46.5, 46.2, 43.8, 43.7, 43.5, 31.9, 31.8, 22.5, 20.8, 20.3, 20.2, 20.0 ($\mathit{C}H_3CH_2I$), 19.1, 19.0, 12.3, 11.6, 11.5, 2.5, 1.8 ($CH_3\mathit{C}H_2I$), −1.0, −3.0, −12.0, −13.7, −15.1, −17.5; $^{13}C$ NMR (100 MHz, $CD_2Cl_2$) $\delta$ ($(CH_3\mathit{C}H_2)_2Zn$) (163 K) 2.5, (173 K) 3.0, (183 K) 3.5, (193 K) 4.0, (203 K) 4.5; $\delta$ ($CH_3CH_2Zn\mathit{C}H_2I$) (163 K) −12.0, −13.7, (173 K) −12.2 (br), −13.7 (br), (183 K) −13.3 (coalescent), (193 K) −13.2 (br), (203 K) −13.3; $\delta$ ($CH_3\mathit{C}H_2ZnCH_2I$) (163 K) −1.0, −3.0, (173 K) −0.9 (br), −2.8 (br), (183 K) −2.2 (coalescent), (193 K) −1.5 (br), (203 K) −1.5; $\delta$ ($Zn(\mathit{C}H_2I)_2$) (163 K) −15.1, −17.5, (173 K) −15.3, −17.7, (183 K) −15.6, −17.9, (193 K) −15.8 (br), −18.1 (br), (203 K) −16.0 (br), −18.1 (br).

**Formation of 3·EtZnCH$_2$I from 3·Zn(CH$_2$I)$_2$ and 3·Et$_2$Zn (Figure 16).** The complexes **3**·$Zn(CH_2I)_2$ and **3**·$Et_2Zn$ were independently prepared as described above, and equimolar amounts were transferred into a dry NMR tube via a Teflon cannula under argon at −78 °C. The NMR tube was then directly transferred to the precooled NMR probe for analysis.

**Decomposition of 3·Zn(CH$_2$I)$_2$ and 3·IZnCH$_2$I (Figures 17 and 18).** A solution of **3**·$Zn(CH_2I)_2$ or **3**·$IZnCH_2I_2$ in $CD_2Cl_2$ was prepared in a NMR tube as described above. The solution was kept at room temperature for the specified time and was placed in the NMR probe precooled to 163 K for analysis. The tube was then kept at room temperature for a another specified time before the next analysis.

**Acknowledgment.** This research was supported by the NSERC (Canada), FCAR (Québec), Merck Frosst Canada, Eli Lilly, Servier, and the Université de Montréal. J.F.M. thanks NSERC and FCAR for postgraduate fellowships. We are also grateful to the Centre Régional de Spectroscopie NMR for their assistance in carrying out NMR experiments. We would like to thank Dr. Martine Monette for many helpful discussions.

**Supporting Information Available:** Figures showing full-scale $^{13}C$ NMR spectra of the various complexes for which only expansions were shown (21 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

JA951171K