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A Novel Class of Tunable Zinc Reagents ($RXZnCH_2Y$) for Efficient Cyclopropanation of Olefins

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A class of zinc reagents ($RXZnCH_2Y$) generated with an appropriate organozinc is very effective for the cyclopropanation of olefins. The reactivity and selectivity of these reagents can be regulated by tuning the electronic and steric nature of the RX group on Zn. A reasonable level of enantioselectivity was obtained for the cyclopropanation of unfunctionalized olefins when a chiral (iodomethyl)zinc species was used, providing a valuable approach for the asymmetric cyclopropanation of unfunctionalized olefins.

The Simmons−Smith reaction is a very powerful method for the cyclopropanation of olefins,[1] and various versions of this reaction have been developed. In Simmons and Smith's original studies, the cyclopropanation reagent $IZnCH_2I$ was generated from CH_2I_2 and Zn−Cu.[2,3] This CH_2I_2−Zn procedure with various modifications[4] has been widely used since then.[1] Wittig showed that cyclopropanation reagents $XZnCH_2X$ or $Zn(CH_2X)_2$ could also be prepared by reacting ZnX_2 with CH_2N_2.[5] In 1966, Furukawa reported that cyclopropanation reagents could be generated by the alkyl exchange between Et_2Zn and CH_2I_2,[6,7] giving active species $EtZnCH_2I$ or $Zn(CH_2I)_2$. In another study, Denmark found that the (chloromethyl)zinc reagent generated from Et_2Zn and $ClCH_2I$ is more reactive than the corresponding (iodomethyl)zinc from Et_2Zn and CH_2I_2.[8] Recently, Charette has reported that bipy·$Zn(CH_2I)_2$ complex can be isolated and stored for an extended period of time in the freezer with little decomposition.[9] This complex can effectively cyclopropanate olefins upon addition of ZnI_2. In addition to (halomethyl)zinc reagents, (acyloxymethyl)zinc species can also cyclopropanate olefins. Wittig reported that bis(benzoyloxymethyl)zinc [$(PhCOOCH_2)_2$-Zn] could cyclopropanate olefins upon activation by ZnI_2.[5d] Very recently, Charette has shown that n-C_4F_9-$COOCH_2ZnEt$ generated from n-$C_4F_9COOCH_2I$ and Et_2Zn is a highly reactive cyclopropanating reagent.[10] Significant progress has also been made in the structural elucidation of various possible reactive cyclopropanating species. Several (halomethyl)zinc compounds or their complexes with other ligands have been investigated and characterized via both X-ray crystallography and NMR spectroscopy by Denmark[11] and Charette.[7b,9,12]

As mentioned above, a (halomethyl)zinc reagent in the Simmons−Smith reaction is generally represented as $XZnCH_2Y$ (**1**)[13] where the X substituent on the Zn is usually limited to halogens, Et, YCH_2, or other alkyl groups[14] depending upon the protocol used (Scheme 1). In 1998, we reported that the cyclopropanation of olefins can be efficiently carried out using a new class of (iodomethyl)zinc species ($RXZnCH_2I$) generated by reacting RXH with an appropriate organozinc reagent (Scheme 2).[15] A wide range of RXH from alcohols to acids can be

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(1) For leading reviews, see: (a) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React*. **1973**, *20*, 1. (b) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev*. **1993**, *93*, 1307. (c) Charette, A. B.; Marcoux, J.-F. *Synlett*, **1995**, 1197. (d) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev*. **1996**, *96*, 49. (e) Charette, A. B.; Beauchemin, A. *Org. React*. **2001**, *58*, 1. (f) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev*. **2003**, *103*, 977.

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

(3) For an earlier report on preparation of $IZnCH_2I$, see: Emschwiller, G. *Compt. Rend*. **1929**, *188*, 1555.

(4) For leading references on various modifications of the reaction using Zn, see: (a) Shank, R.; Shechter, H. *J. Org. Chem*. **1959**, *24*, 1825. (b) LeGoff, E. *J. Org. Chem*. **1964**, *29*, 2048. (c) Rawson, R. J.; Harrison, I. T. *J. Org. Chem*. **1970**, *35*, 2057. (d) Denis, J. M.; Girard, C.; Conia, J. M. *Synthesis* **1972**, 549. (e) Rieke, R. D.; Li, P. T.-J.; Burns, T. P.; Uhm, S. T. *J. Org. Chem*. **1981**, *46*, 4323. (f) Repic, O.; Vogt, S. *Tetrahedron Lett*. **1982**, *23*, 2729. (g) Friedrich, E. C.; Domek, J. M.; Pong, R. Y. *J. Org. Chem*. **1985**, *50*, 4640. (h) Friedrich, E. C.; Lunetta, S. E.; Lewis, E. J. *J. Org. Chem*. **1989**, *54*, 2388. (i) Friedrich, E. C.; Lewis, E. J. *J. Org. Chem*. **1990**, *55*, 2491. (j) Takai, K.; Kakiuchi, T.; Utimoto, K. *J. Org. Chem*. **1994**, *59*, 2671. (k) StenstrØm, Y. *Synth. Commun*. **1992**, *22*, 2801.

(5) (a) Wittig, G.; Schwarzenbach, K. *Angew. Chem*. **1959**, *71*, 652. (b) Wittig, G.; Schwarzenbach, K. *Liebigs Ann. Chem*. **1961**, *650*, 1. (c) Wittig, G.; Wingler, F. *Liebigs Ann. Chem*. **1962**, *656*, 18. (d) Wittig, G.; Jautelat, M. *Liebigs Ann. Chem*. **1967**, *702*, 24.

(6) (a) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett*. **1966**, 3353. (b) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53. (c) Nishimura, J.; Furukawa, J.; Kawabata, N.; Kitayama, M. *Tetrahedron* **1971**, *27*, 1799.

(7) EtZnI could also be used to react with CH_2I_2 to form cyclopropanation reagents; see: (a) Sawada, S.; Inouye, Y. *Bull. Chem. Soc. Jpn*. **1969**, *42*, 2669. (b) Charette, A. B.; Marcoux, J.-F. *J. Am. Chem. Soc*. **1996**, *118*, 4539.

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

(9) Charette, A. B.; Marcoux, J.-F.; Molinaro, C.; Beauchemin, A.; Brochu, C.; Isabel, E. *J. Am. Chem. Soc*. **2000**, *122*, 4508.

(10) Charette, A. B.; Beauchemin, A.; Francoeur, S. *J. Am. Chem. Soc*. **2001**, *123*, 8139.

(11) (a) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc*. **1991**, *113*, 723. (b) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc*. **1992**, *114*, 2592.

(12) Charette, A. B.; Marcoux, J.-F.; Bélanger-Gariépy, F. *J. Am. Chem. Soc*. **1996**, *118*, 6792.

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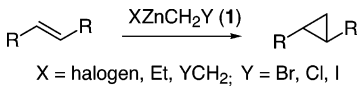
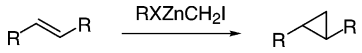
SCHEME 1



SCHEME 2



used to form the (iodomethyl)zinc species,[15,16] and the reactivity of these resulting cyclopropanation reagents can be regulated by changing the electronic and/or steric nature of the modifier RXH. Furthermore, we showed that the asymmetric cyclopropanation of unfunctionalized olefins is possible with a chiral RXH.[15] Herein we wish to report our detailed studies on this subject.

Results and Discussions

We began our studies by generating a series of (iodomethyl)zinc species from various modifiers and studying their reactivity. A number of methods are conceivable for the generation of $RXZnCH_2I$ (**3**) from RXH as shown in Scheme 3.[17] In Method A, Et_2Zn is treated with 2 equiv of CH_2I_2 to form $Zn(CH_2I)_2$, which subsequently reacts with RXH (**2**) to generate $RXZnCH_2I$ (**3**). In Method B, Et_2Zn is combined with RXH first to form RXZnEt, which then reacts with 1 equiv CH_2I_2 to generate $RXZnCH_2I$. In method C, Et_2Zn reacts with 1 equiv of CH_2I_2 to form $EtZnCH_2I$ (**4**), which is then treated with RXH to generate $RXZnCH_2I$ (it should be pointed out that the various iodomethylzinc species in Scheme 3 are currently proposed only on the basis of stoichiometry). Methods B and C require 1 equiv of CH_2I_2 less than Method A.

For our initial studies, Method A was used to generate $RXZnCH_2I$ and *trans*-β-methylstyrene was used as the substrate. As shown in Figure 1, the reactivity of $RXZnCH_2I$ was highly dependent upon the RX group. When RXH was EtOH or $ClCH_2CH_2OH$, no reaction occurred after stirring for 24 h at room temperature.[18,19] It was found that, in general, as RXH became more acidic, the reactivity increased. While no cyclopropanation was observed with phenol,[20] cyclopropanation occurred when certain substituted phenols were used (Figure 1).[16] CF_3CO_2H was found to accelerate the cyclopropanation reaction dramatically compared to the standard cyclopropanation conditions (i.e., without RXH). The reaction was complete within 30 min at room temperature for *trans*-β-methylstyrene and was very clean as judged by the ^1H NMR of the crude reaction mixture. To further compare the cyclopropanation reactivities, the Zn reagents generated from a variety of RXH modifiers were tested with *trans*-β-methylstyrene and *trans*-stilbene.[21,22] The reagents generated from halogen-substituted carboxylic acids such as CF_3CO_2H and CCl_3CO_2H were found to be among the most reactive cyclopropanation reagents (Table 1, entries 5, 6, 11, and 12). The reactivity of the generated Zn reagent is also affected by the solubility and stability of the reagent. For example, the relatively poor conversion observed with $CF_3SO_3ZnCH_2I$ (Table 1, entry 2) could be due to its poor solubility in the noncoordinating solvents required for this reaction and/or its instability.

The induction periods displayed in the cases of Cl_2CHCH_2OH and Cl_3CCH_2OH (curves C and D, Figure 1) suggested that the cyclopropanation might be accelerated by the reaction products, possibly ROZnI.[23] In light of this observation, the effects of Lewis acids on the cyclopropanation of unreactive $ClCH_2CH_2OZnCH_2I$ (curve B, Figure 1) were investigated.[24−27] It was found that cyclopropanations proceeded at a reasonable rate when the proper Lewis acid was used (Table 2). Among these Lewis acids, $TiCl_4$, $SnCl_4$, $AlCl_3$, $AlEt_3$, and Et_2AlCl were the best activators. The Lewis acid may accelerate the cyclopropanation in a number of ways.[25−27] One of these is that the Lewis acid may disrupt the aggregate of $ROZnCH_2I$ by complexing to the oxygens (Scheme 4) and generate a vacant orbital on zinc for iodine to coordinate,

(13) For leading references on analogous cyclopropanations using other MCH_2X reagents, see the following. For Al, see: (a) Hoberg, H. *Liebigs Ann. Chem.* **1962**, *656*, 1. (b) Miller, D. B. *Tetrahedron Lett.* **1964**, 989. (c) Maruoka, K.; Fukutani, Y.; Yamamoto, H. *J. Org. Chem.* **1985**, *50*, 4412. For Cd, see: (d) Furukawa, J.; Kawabata, N.; Fujita, T. *Tetrahedron* **1970**, *26*, 243. For Cu, see: (e) Kawabata, N.; Naka, M.; Yamashita, S. *J. Am. Chem. Soc.* **1976**, *98*, 2676. (f) Kawabata, N.; Kamemura, I.; Naka, M. *J. Am. Chem. Soc.* **1979**, *101*, 2139. For Hg, see: (g) Seyferth, D.; Eisert, M. A.; Todd, L. J. *J. Am. Chem. Soc.* **1964**, *86*, 121. For In, see: (h) Maeda, T.; Tada, H.; Yasuda, K.; Okawara, R. *J. Organomet. Chem.* **1971**, *27*, 13. For Mg, see: (i) Fauveau, C.; Gault, Y.; Gault, F. G. *Tetrahedron Lett.* **1967**, 3149. (j) Bolm, C.; Pupowicz, D. *Tetrahedron Lett.* **1997**, *38*, 7349. For Sm, see: (k) Imamoto, T.; Takeyama, T.; Koto, H. *Tetrahedron Lett.* **1986**, *27*, 3243. (l) Imamoto, T.; Takiyama, N. *Tetrahedron Lett.* **1987**, *28*, 1307. (m) Molander, G. A.; Etter, J. B. *J. Org. Chem.* **1987**, *52*, 3942. (n) Molander, G. A.; Harring, L. S. *J. Org. Chem.* **1989**, *54*, 3525. (o) Imamoto, T.; Kamiya, Y.; Hatajima, T.; Takahashi, H. *Tetrahedron Lett.* **1989**, *30*, 5149.

(14) Charette, A. B.; Beauchemin, A.; Marcoux, J.-F. *Tetrahedron Lett.* **1999**, *40*, 33.

(15) For a preliminary report of a portion of this work, see: Yang, Z.; Lorenz, J. C.; Shi, Y. *Tetrahedron Lett.* **1998**, *39*, 8621.

(16) For a related study of $ArOZnCH_2I$ for cyclopropanation recently reported by Charette, see: Charette, A. B.; Francoeur, S.; Martel, J.; Wilb, N. *Angew. Chem., Int. Ed.* **2000**, *39*, 4539.

(17) For references on the generation and studies of RXZnR, see: (a) Noltes, J. G.; Boersma, J. *J. Organomet. Chem.* **1968**, *12*, 425 and references therein. (b) Inoue, S.; Kobayashi, M.; Tozuka, T. *J. Organomet. Chem.* **1974**, *81*, 17 and references therein.

(18) For a discussion on intramolecular cyclopropanation of alkoxy (iodomethyl)zinc formed from unsaturated alcohols, see: (a) Blanchard, E. P.; Simmons, H. E. *J. Am. Chem. Soc.* **1964**, *86*, 1337. (b) Ref 1b. (c) Charette, A. B.; Brochu, C. *J. Am. Chem. Soc.* **1995**, *117*, 11367.

(19) For a related study of $ROZnCH_2I$ for cyclopropanation recently reported by Charette, see: Charette, A. B.; Molinaro, C.; Brochu, C. *J. Am. Chem. Soc.* **2001**, *123*, 12160.

(20) It has been reported that $PhOZnCH_2I$ can undergo ortho methylation of the phenol; see: Lehnert, E. K.; Sawyer, J. S.; Macdonald, T. L. *Tetrahedron Lett.* **1989**, *30*, 5215.

(21) For a recent report on an intramolecular cyclopropanation of allylphosphinoylamino (chloromethyl)zinc, see: Wipf, P.; Kendall, C.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2001**, *123*, 5122.

(22) Since the rate of formation and the reactivity of $RXZnCH_2I$ vary with modifier RXH, it is possible that besides the proposed $RXZnCH_2I$, additional (iodomethyl)zinc species may exist in the reaction mixture and contribute to the cyclopropanation.

(23) Denmark reported autocatalytic behavior in the cyclopropanation of allyloxy ethylzinc with $Zn(CH_2I)_2$. Studies showed that ZnI_2 generated from the reaction catalyzed the cyclopropanation. See: (a) Denmark, S. E.; Christenson, B. L.; Coe, D. M.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2215. (b) Denmark, S. E.; Christenson, B. L.; O'Connor, S. P.; Murase, N. *Pure Appl. Chem.* **1996**, *68*, 23. (c) Denmark, S. E.; O'Connor, S. P. *J. Org. Chem.* **1997**, *62*, 3390.

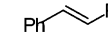
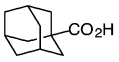
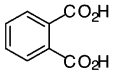
(24) For $TiCl_4$-catalyzed cyclopropanations of alkenes using zinc dust, CuCl, and CH_2X_2, see: ref 4h.

(25) For theoretical studies on Lewis acid acceleration in the Simmons−Smith reaction, see: Nakamura, E.; Hirai, A.; Nakamura, M. *J. Am. Chem. Soc.* **1998**, *120*, 5844.

(26) For Lewis acid-catalyzed intramolecular cyclopropanation of alkoxy (iodomethyl)zinc formed from allylic alcohols, see: (a) Ref 18c. (b) Ref 19. (c) Charette, A. B.; Molinaro, C.; Brochu, C. *J. Am. Chem. Soc.* **2001**, *123*, 12168.

(27) For a related study on Lewis acid-catalyzed intermolecular cyclopropanation of $ROZnCH_2I$, see: ref 19.

TABLE 1. Studies of RXH Effect on Cyclopropanation with $Zn(CH_2I)_2$[a]

		Conv. (%)				 Conv. (%)			
Entry	RXH	1h	2h	6.5h	18h	1h	2h	6.5h	18h
1	none	21	23	34	45	11	19	24	29
2	CF_3SO_3H	47	53	55	58	15	20	25	27
3	*p*-TsOH (anhy.)	23	34	61	86	8	11	18	37
4	F_2CHCO_2H	60	82	89	99	36	51	62	69
5	CF_3CO_2H	100				73	79	81	82
6	$CF_3CF_2CO_2H$	99				61	80	81	84
7	$CF_3(CF_2)_2CO_2H$	98				38	40	42	43
8	$CF_3(CF_2)_3CO_2H$	66	68	70	71	38	39	40	41
9	$ClCH_2CO_2H$	47	74	92	96	10	14	36	61
10	Cl_2CHCO_2H	86	90	96	98	45	60	73	74
11	CCl_3CO_2H	100				53	87	91	91
12	$CClF_2CO_2H$	99				83	87	90	92
13	CH_3CO_2H	24	41	62	86	7	12	29	47
14	$(CH_3)_3CCO_2H$	58	63	70	73	13	19	30	39
15		54	64	71	85	11	25	34	40
16	3,5-F_2PhCO_2H	71	79	89	97	28	42	57	67
17	*o*-NO_2PhCO_2H	30	60	74	79	6	10	16	19
18	*m*-NO_2PhCO_2H	44	49	51	53	6	7	9	9
19	*p*-NO_2PhCO_2H	41	46	49	50	7	9	10	11
20[b]	$(CO_2H)_2$	23	39	68	85	9	18	37	47
21[b]	$HO_2CCH_2CO_2H$	21	38	41	52	14	19	20	23
22[b]	$HO_2C(CH_2)_2CO_2H$	22	24	27	30	9	10	12	13
23[b]		23	29	36	43	8	11	13	17
24	2,6-F_2PhOH	34	48	74	87	4	7	15	31
25	2,6-Cl_2PhOH	11	20	50	75	2	3	14	39
26	2,6-Br_2PhOH	1	5	17	22	<1	1	3	7
27	H_2O	4	8	20	61	1	2	4	22
28[b]	H_2O	5	13	23	45	8	13	20	22
29	CF_3CONH_2	40	67	81	84	15	27	39	47

[a] $RXZnCH_2I$ was generated by treating $Zn(CH_2I)_2$ with RXH (1:1) (Method A), and all reactions were carried out with a 2:1 ratio of Zn/olefin in CH_2Cl_2 at room temperature. The conversion was determined by GC. [b] Performed with 0.5 equiv of RXH relative to $Zn(CH_2I)_2$.

thus activating the methylene group toward cyclopropanation.[28] The complexation of the Lewis acid to the oxygen could also increase the electrophilicity of the methylene group, further accelerating the cyclopropanation.

The high reactivity displayed by $CF_3CO_2ZnCH_2I$ prompted us to examine more substrates to test its scope. As shown in Table 3, a variety of substrates can be converted into cyclopropanes efficiently by this reagent within a short period of time. Having these cyclopropanation reactions proceed with high conversion is operationally beneficial since it is often difficult to separate the starting olefin from the cyclopropane. Considering that many cyclopropanation protocols require refluxing and long reaction times, $CF_3CO_2ZnCH_2I$ and related

(28) Zinc alkoxides ($ROZnR'$) are likely to form aggregates. see: ref 17.

SCHEME 3

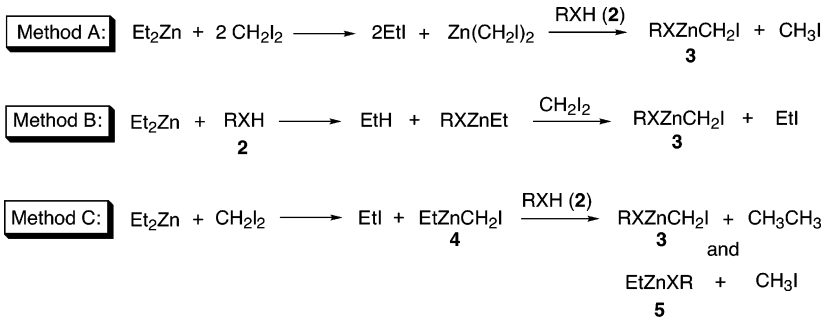
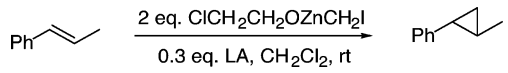


TABLE 2. Effect of Lewis Acids on Cyclopropanation Using $ClCH_2CH_2OZnCH_2I$[a]



Entry	LA	Time (h)	Conversion (%)[b]
1	AgOTf	36	20
2	$Cu(OTf)_2$	36	5
3	$Ti(O^iPr)_4$	45	<1
4	$TiCl_4$	36	76
5	$SnCl_4$	40	73
6	$BF_3{\cdot}OEt_2$	40	54
7	$FeCl_3$	36	41
8	$AlCl_3$	40	70
9	$AlMe_3$	36	59
10	$AlEt_3$	36	97
11	Et_2AlCl	48	100

[a] All reactions were carried out with a 2:1 ratio of Zn/olefin and 0.3 equiv of Lewis acid in CH_2Cl_2 at room temperature. [b] Conversion was determined from the crude reaction mixture by GC.

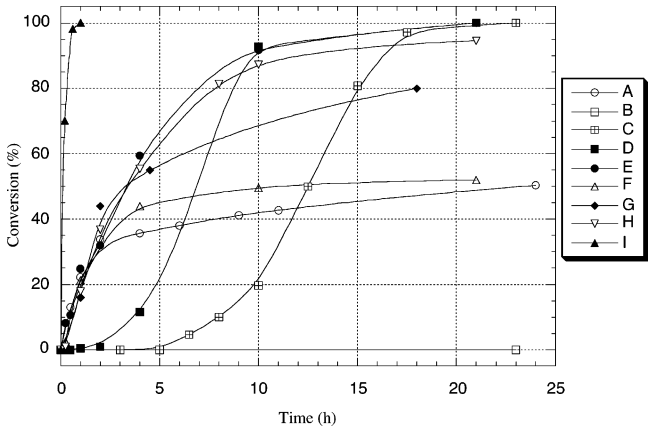
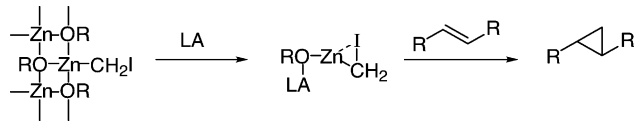


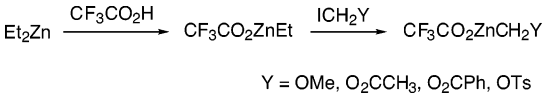
FIGURE 1. Plot of the conversion of *trans*-β-methylstyrene against time (h). The curves presented are: (A) no RXH, (B) EtOH (similar results obtained with $ClCH_2CH_2OH$), (C) Cl_2CHCH_2OH, (D) CCl_3CH_2OH, (E) CF_3CH_2OH, (F) 2-chlorophenol, (G) 2,6-dichlorophenol, (H) $PhCO_2H$, and (I) CF_3CO_2H. The $RXZnCH_2I$ was generated by Method A. All reactions were carried out with a 2:1 ratio of Zn/olefin in CH_2Cl_2 at room temperature.

reagents should provide an attractive alternative, particularly for substrates that are slow to react by other methods.[29] It should be pointed out that better yields are usually obtained if the reaction is stopped as soon as the starting material is consumed since unnecessarily long reaction times could lead to the decomposition of the cyclopropane product.[30]

SCHEME 4



SCHEME 5



In addition to CH_2I_2, other CH_2 sources such as ICH_2Cl, ICH_2OMe, $ICH_2O_2CCH_3$, ICH_2O_2CPh, and ICH_2OTs were also briefly investigated (Scheme 5).[31−33] While $CF_3CO_2ZnCH_2Cl$ generated from ICH_2Cl showed reactivities similar to $CF_3CO_2ZnCH_2I$, $CF_3CO_2ZnCH_2OMe$ showed poor reactivity. When cyclohexene was treated with $CF_3CO_2ZnCH_2OMe$, only trace amounts of cyclopropane were observed in the crude ^1H NMR spectrum after extended reaction times. On the other hand, $CF_3CO_2ZnCH_2O_2CCH_3$, $CF_3CO_2ZnCH_2O_2CPh$, and $CF_3CO_2ZnCH_2OTs$ were found to be active for cyclopropanation, although their reactivities were substantially lower than $CF_3CO_2ZnCH_2I$. For example, 90% conversion was obtained for the cyclopropanation of cyclohexene with $CF_3CO_2ZnCH_2O_2CPh$ at room temperature for 24 h. Interestingly, no cyclopropanation of cyclohexene was observed with Et_2Zn and ICH_2O_2CPh, suggesting that the CF_3CO_2 group greatly enhances the reactivity of the Zn reagent.

Cyclopropanation using metal carbenoids can proceed via [2 + 2] carbometalation (pathway **a**) or concerted [2 + 1] methylene transfer (pathway **b**) (Scheme 6).[1] The preference of the reaction pathway is highly dependent on the nature of the metal. While both pathways may compete in the cyclopropanation with lithium carbenoids,[34] both experimental[35] and theoretical[36] studies

(29) For recent applications of $CF_3CO_2ZnCH_2I$ for cyclopropanation, see: (a) Carter, K. N.; Taverner, T.; Schiesser, C. H.; Greenberg, M. M. *J. Org. Chem*. **2000**, *65*, 8375. (b) Evans, D. A.; Burch, J. D. *Org. Lett*. **2001**, *3*, 503. (c) Rossi, R.; Carpita, A.; Ribecai, A.; Mannina, L. *Tetrahedron* **2001**, *57*, 2847. (d) Carpita, A.; Ribecai, A.; Rossi, R.; Stabile, P. *Tetrahedron* **2002**, *58*, 3673. (e) Charette, A. B.; Lacasse, M.-C. *Org. Lett*. **2002**, *4*, 3351.

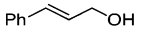
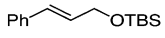
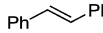
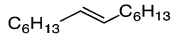
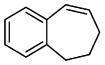
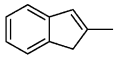
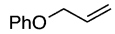
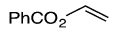
(30) Reaction conditions for the cyclopropanation using $CF_3CO_2ZnCH_2I$ are slightly acidic. Modifiers (RXH) less acidic than CF_3CO_2H may be used if the substrate is acid sensitive.

(31) For earlier studies on the cyclopropanation of $(PhCO_2CH_2)_2Zn$, see: ref 5d.

(32) For a recent report on cyclopropanation using Et_2Zn and n-$C_4F_9CO_2CH_2I$, see: ref 10.

(33) For studies on the Sm-mediated cyclopropanation using ICH_2X, see: ref 13n.

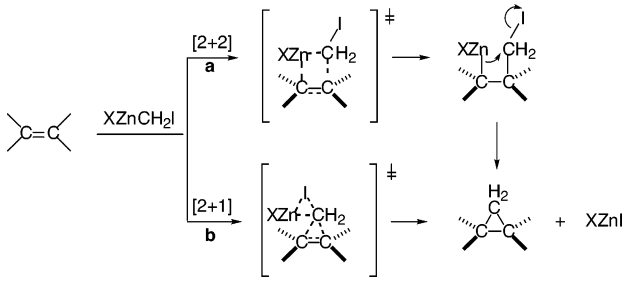
TABLE 3. Cyclopropanation of Representative Olefins Accelerated by CF_3CO_2H[a]

Entry	Substrate	Time (min)	Conv. (%)[b]	Yield (%)[c]
1[d]		30	100	77
2		40	100	80
3		30	100	95
4[d]		60	>90	70
5		40	100	99
6[d]		90	100	76
7[d]		60	nd	72
8		120	100	99
9[e]		240	100	83
10		30	100	78
11		180	100	94
12		240	100	97
13[e]	 X = Et	180	100	93
14	X = Ph	180[f]	100	65
15	X = *p*-MeO-Ph	180	100	98
16	X = *p*-F-Ph	120[g]	100	65
17		25	100	50[h]
18[e]		30	100	69
19		20	100	85
20		30	>97	88
21		150	>90	90

[a] $CF_3CO_2ZnCH_2I$ was generated by Method B except for entry 13, where Method A was used. All reactions were carried out at room temperature with 2 equiv of $CF_3CO_2ZnCH_2I$ unless otherwise noted. For entry 14, 3 equiv of $CF_3CO_2ZnCH_2I$ was used. For entries 4, 7, 13, and 16, 4 equiv of $CF_3CO_2ZnCH_2I$ was used. [b] Conversion was determined from the crude reaction mixture either by GC or ^1H NMR. [c] Isolated yield. [d] *trans*-Olefins gave *trans*-cyclopropanes, and *cis*-olefins gave *cis*-cyclopropanes. [e] Reaction was carried out at 0 °C. [f] Reaction was carried out at 0 °C for 1 h and then at room temperature for 2 h. [g] Reaction was carried out at 0 °C for 1 h and then at room temperature for 1 h. [h] Yield was for the product after desilylation by TBAF.

show that cyclopropanation using zinc carbenoids proceeds by the [2 + 1] pathway, primarily due to the fact that the C−Zn bond is covalent and unpolarized.[36b] The

SCHEME 6



drastic difference in reactivity observed between the traditional zinc carbenoids and the CF_3CO_2H-modified carbenoid prompted us to probe the mechanism of cyclopropanation using *trans*-1,6-diiodo-3-hexene (**6**) (Scheme 7).[37] Cyclopropanation via the [2 + 2] pathway would form both compounds **8** and **9**, while the [2 + 1] pathway leads to **8** exclusively. Subjecting olefin **6** to $CF_3CO_2ZnCH_2I$ at room temperature led to the clean formation of the symmetrical cyclopropane **8** as judged by ^1H and ^{13}C NMR analysis of the crude reaction mixture. This suggests that the modified zinc carbenoid behaves in a manner similar to the typical Simmons−Smith carbenoid by addition in a concerted [2 + 1] fashion. However, full understanding of the reaction pathways requires further studies.

The discovery that zinc reagents modified by a covalent ligand ($RXZnCH_2I$) are effective for cyclopropanation prompted us to investigate whether a chiral (iodomethyl)zinc species (R^*XZnCH_2I) could induce enantioselectivity. Thus, a number of chiral alcohols were tested using *trans*-β-methylstyrene as a substrate. Generally, cyclopropanations with these R^*OZnCH_2I reagents were very sluggish but accelerated by the addition of a catalytic amount of Lewis acid. As shown in Table 4, 51% ee was obtained for the cyclopropane product using the fructose-derived alcohol **15** as a modifier.

Great progress has been made in the area of asymmetric Simmons−Smith reactions. Efficient asymmetric cyclopropanations using a variety of chiral auxiliaries have been reported.[38−41] Recently, highly enantioselective cyclopropanations of allylic alcohols have been achieved using either chiral reagents or catalysts.[42,43] On the other hand, the direct asymmetric cyclopropanation of unfunctionalized olefins by transferring a methylene group from a (halomethyl)zinc reagent is an unsolved problem. Prior

(34) Stiasny, H. C.; Hoffmann, R. W. *Chem. Eur. J.* **1995**, *1*, 619.
(35) Wittig, G.; Wingler, F. *Chem. Ber.* **1964**, *97*, 2146.

(36) (a) Bernardi, F.; Bottoni, A.; Miscione, G. P. *J. Am. Chem. Soc.* **1997**, *119*, 12300. (b) Hirai, A.; Nakamura, M.; Nakamura, E. *Chem. Lett.* **1998**, 927. (c) Zhao, C.; Wang, D.; Phillips, D. L *J. Am. Chem. Soc.* **2002**, *124*, 12903.
(37) Similar probe using 1,6-dichloro-3-hexene was reported by Wittig; see: ref 35.
(38) For leading references on chiral ketal-based asymmetric cyclopropanations, see: (a) Arai, I.; Mori, A.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 8254. (b) Mash, E. A.; Nelson, K. A. *J. Am. Chem. Soc.* **1985**, *107*, 8256. (c) Mori, A.; Arai, I.; Yamamoto, H.; Nakai, H.; Arai, Y. *Tetrahedron* **1986**, *42*, 6447. (d) Kang, J.; Lim, G. J.; Yoon, S. K.; Kim, M. Y. *J. Org. Chem.* **1995**, *60*, 564. (e) Mash, E. A.; Gregg, T. M.; Kaczynski, M. A. *J. Org. Chem.* **1996**, *61*, 2743. (f) Kaye, P. T.; Molema, W. E. *Chem. Commun.* **1998**, 2479.
(39) For leading references on chiral allylic ether-based asymmetric cyclopropanations, see: (a) Charette, A. B.; Côté, B.; Marcoux, J.-F. *J. Am. Chem. Soc.* **1991**, *113*, 8166. (b) Charette, A. B.; Côté, B. *J. Org. Chem.* **1993**, *58*, 933. (c) Charette, A. B.; Marcoux, J.-F. *Tetrahedron Lett.* **1993**, *34*, 7157. (d) Charette, A. B.; Turcotte, N.; Marcoux, J.-F. *Tetrahedron Lett.* **1994**, *35*, 513. (e) Charette, A. B.; Côté, B. *J. Am. Chem. Soc.* **1995**, *117*, 12721.

SCHEME 7

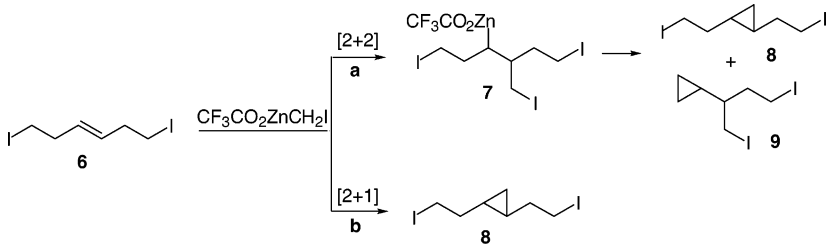
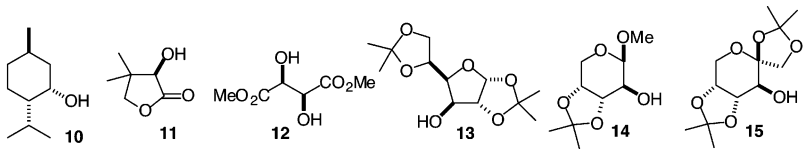


TABLE 4. Cyclopropanation of *trans*-β-Methylstyrene Using Chiral R*OZnCH$_2$I[a]



entry	R*OH	LA	time (h)	conversion (%)[b]	ee (%)[c]
1	**10**	Et_2AlCl	44	85	8
2	**11**	Et_2AlCl	45	91	17[d]
3	**12**	Et_2AlCl	36	4	nd
4	**13**	$TiCl_4$	64	6	8[d]
5	**14**	Et_2AlCl	45	19	20
6	**15**	Et_2AlCl	44	74	51

[a] R*OZnCH$_2$I was generated by Method A, and all reactions were carried out with olefin (0.5 mmol), R*OZnCH$_2$I (1.0 mmol), and Lewis acid (0.15 mmol) in CH_2Cl_2-hexane at room temperature. [b] Conversion was determined from the crude reaction mixture by GC. [c] Enantioselectivity was determined by chiral GC (Chiraldex GTA). [d] Opposite configuration was obtained.

to our earlier studies,[15] only two reports appeared in the literature for asymmetric cyclopropanation of unfunctionalized olefins using (halomethyl)zinc reagents. In one case, (−)-menthol was used as a chiral inducer, and <4% ee was obtained for a number of test substrates.[44a] In the other case, L-leucine was used as the chiral inducer, and an optical rotation of −0.77 was reported for *cis*-1-ethoxy-2-isopropylethylene (no ee was mentioned).[44b] Although only moderate ee has been obtained, the current study provides a valuable approach toward asymmetric cyclopropanation of unfunctionalized olefins. Also, since the cyclopropanation of RXZnCH$_2$I is greatly facilitated by addition of a Lewis acid, it is possible that the addition of a catalytic amount of the proper chiral Lewis acid might further introduce asymmetry into the reaction. Such an approach is currently under investigation.

In summary, we have developed a novel class of zinc reagents (RXZnCH$_2$Y) that can efficiently cyclopropanate olefins. These reagents provide the opportunity to regulate the reactivity and selectivity of cyclopropanations by tuning the electronic and/or steric nature of the RX group on Zn. A reasonable level of enantioselectivity was obtained for the cyclopropanation of unfunctionalized olefins with a chiral (iodomethyl)zinc species. Further studies to expand the scope of these modified zinc reagents and develop an effective enantioselective cyclopropanation of unfunctionalized olefins are currently underway.

Experimental Section

General Methods. Dichloromethane was distilled from calcium hydride.

Representative Procedure for the Effect of RXH on Cyclopropanation (Method A) (Figure 1). To a solution of Et_2Zn (1.0 M in hexane) (1.0 mL, 1.0 mmol) in CH_2Cl_2 (1 mL) at −78 °C under N_2 was added a solution of CH_2I_2 (0.53 g, 2.0 mmol) in CH_2Cl_2 (0.5 mL). After the reaction mixture was stirred at −15 °C for 30 min, a solution of RXH (1.0 mmol) in CH_2Cl_2 (0.5 mL) was added. After an additional 30 min of

(40) For leading references on chiral enol ether-based asymmetric cyclopropanations, see: (a) Sugimura, T.; Futagawa, T.; Tai, A. *Tetrahedron Lett.* **1988**, *29*, 5775. (b) Sugimura, T.; Koguro, K.; Tai, A. *Tetrahedron Lett.* **1993**, *34*, 509. (c) Sugimura, T.; Yoshikawa, M.; Mizuguchi, M.; Tai, A. *Chem. Lett.* **1999**, 831. (d) Sugimura, T.; Futagawa, T.; Yoshikawa, M.; Katagiri, T.; Miyashige, R.; Mizuguchi, M.; Nagano, S.; Sugimori, S.; Tai, A.; Tei, T.; Okuyama, T. *Tetrahedron* **2001**, *61*, 7495.

(41) For leading references on chiral vinyl boronic ester-based asymmetric cyclopropanations, see: (a) Imai, T.; Mineta, H.; Nishida, S. *J. Org. Chem.* **1990**, *55*, 4986. (b) Luithle, J. E. A.; Pietruszka, J. *Liebigs Ann./Recueil* **1997**, 2297.

(42) For leading references on chiral reagent-based asymmetric cyclopropanations of allylic alcohols, see: (a) Ukaji, Y.; Nishimura, M.; Fujisawa, T. *Chem. Lett.* **1992**, 61. (b) Denmark, S. E.; Edwards, J. P. *Synlett* **1992**, 229. (c) Ukaji, Y.; Sada, K.; Inomata, K. *Chem. Lett.* **1993**, 1227. (d) Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651. (e) Charette, A. B.; Prescott, S.; Brochu, C. *J. Org. Chem.* **1995**, *60*, 1081. (f) Kitajima, H.; Aoki, Y.; Ito, K.; Katsuki, T. *Chem. Lett.* **1995**, 1113. (g) Charette, A. B.; Juteau, H.; Lebel, H.; Deschênes, D. *Tetrahedron Lett.* **1996**, *37*, 7925. (h) Kitajima, H.; Ito, K.; Aoki, Y.; Katsuki, T. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 207. (i) Charette, A. B.; Lemay, J. *Angew. Chem., Int. Ed.* **1997**, *36*, 1090. (j) Charette, A. B.; Juteau, H.; Lebel, H.; Molinaro, C. *J. Am. Chem. Soc.* **1998**, *120*, 11943.

(43) For leading references on chiral catalyst based asymmetric cyclopropanations of allylic alcohols, see: (a) Takahashi, H.; Yoshioka, M.; Ohno, M.; Kobayashi, S. *Tetrahedron Lett.* **1992**, *33*, 2575. (b) Imai, N.; Takahashi, H.; Kobayashi, S. *Chem. Lett.* **1994**, 177. (c) Imai, N.; Sakamoto, K.; Takahashi, H.; Kobayashi, S. *Tetrahedron Lett.* **1994**, *35*, 7045. (d) Ref 23a. (e) Denmark, S. E.; Christenson, B. L.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2219. (f) Takahashi, H.; Yoshioka, M.; Shibasaki, M.; Ohno, M.; Imai, N.; Kobayashi, S. *Tetrahedron* **1995**, *51*, 12013. (g) Ref 18c. (h) Denmark, S. E.; O'Connor, S. P. *J. Org. Chem.* **1997**, *62*, 584. (i) Imai, N.; Sakamoto, K.; Maeda, M.; Kouge, K.; Yoshizane, K.; Nokami, J. *Tetrahedron Lett.* **1997**, *38*, 1423. (j) Ref 23c. (k) Balsells, J.; Walsh, P. J. *J. Org. Chem.* **2000**, *65*, 5005. (l) Ref 26c.

(44) (a) Sawada, S.; Oda, J.; Inouye, Y. *J. Org. Chem.* **1968**, *33*, 2141. (b) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1968**, 3495. (c) Ref 16. (d) For recent progress on asymmetric Simmons−Smith cyclopropanation of unfunctionalized olefins, see: Long, J.; Yuan, Y.; Shi, Y. *J. Am. CHem. Soc.* **2003**, *125*, 13632.

stirring, a solution of *trans*-β-methylstyrene (0.06 g, 0.5 mmol) in CH_2Cl_2 (0.5 mL) was added. The reaction mixture was then stirred at room temperature. Samples were taken over the course of the reaction and analyzed by GC to determine the conversion.

Representative Cyclopropanation Procedure Using $CF_3CO_2ZnCH_2I$ (Method B). To freshly distilled CH_2Cl_2 (20 mL) was added Et_2Zn (1.0 M in hexanes) (20.0 mL, 20.0 mmol) under N_2 (it is best to use an inlet adapter for the nitrogen line since needles often become clogged). The solution was cooled in an ice bath and a solution of trifluoroacetic acid (1.54 mL, 20.0 mmol) in CH_2Cl_2 (10 mL) was then dripped *very slowly* into the reaction mixture via syringe. Upon stirring for 20 min, a solution of CH_2I_2 (1.61 mL, 20.0 mmol) in CH_2Cl_2 (10 mL) was added. After an additional 20 min of stirring, a solution of the TBS ether of cinnamyl alcohol (2.60 g, 10.0 mmol) in CH_2Cl_2 (10 mL) was added, and the ice bath was removed. After an additional 30 min of stirring, the reaction mixture was quenched with 0.1 N HCl (50 mL) (alternatively with saturated aqueous NH_4Cl or Et_3N followed by saturated aqueous $NaHCO_3$) and hexanes (25 mL), and the layers were separated. The aqueous layer was extracted with hexanes. The combined organic layers were washed with saturated $NaHCO_3$, H_2O, and brine and then dried (Na_2SO_4), filtered, concentrated, and purified by column chromatography (hexanes/ether = 50/1) to yield the cyclopropane product (2.61 g, 95%).

Representative Procedure for Lewis Acid-Catalyzed Cyclopropanation (Table 2). To a solution of Et_2Zn (1.0 M in hexane) (1.0 mL, 1.0 mmol) in CH_2Cl_2 (1 mL) at −78 °C under N_2 was added a solution of CH_2I_2 (0.53 g, 2.0 mmol) in CH_2Cl_2 (0.5 mL). After the reaction mixture was stirred at −15 °C for 1−2 h, a solution of $ClCH_2CH_2OH$ (0.079 g, 1.0 mmol) in CH_2Cl_2 (1 mL) was added. After 30−45 min of stirring, a solution of *trans*-β-methylstyrene (0.06 g, 0.5 mmol) in CH_2Cl_2 (0.5 mL) was added. After an additional 15 min of stirring, Lewis acid (0.15 mmol) was added. The reaction mixture was then stirred at room temperature for the indicated time, poured into diluted HCl, extracted with hexanes, washed with saturated $NaHCO_3$, H_2O, brine, dried (Na_2SO_4), and concentrated. The crude product was then analyzed by GC and/or ^1H NMR to determine the conversion.

***trans*-1-Methyl-2-phenylcyclopropane (Table 3, Entry 1):**[2b,8] IR (film) 1605, 1495, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27−7.20 (m, 2H), 7.15−7.08 (m, 1H), 7.05−7.00 (m, 2H), 1.56 (dt, J = 8.8, 4.6 Hz, 1H), 1.18 (d, J = 5.7 Hz, 3H), 1.04 (m, 1H), 0.88 (m, 1H), 0.73 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.3, 128.4, 125.7, 125.4, 24.6, 19.3, 18.2, 17.8.

(*trans*-2-Phenylcyclopropyl)methanol (Table 3, Entry 2):[43f,h] IR (film) 3341, 1604, 1497, 1020, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (m, 2H), 7.15 (m, 1H), 7.06 (m, 2H), 3.63 (dd, J = 11.4, 6.6 Hz, 1H), 3.59 (dd, J = 11.4, 6.6 Hz, 1H), 1.82 (dt, J = 8.4, 4.8 Hz, 1H), 1.56 (m, 1H), 1.45 (m, 1H), 0.96 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7, 128.6, 126.1, 125.9, 66.8, 25.5, 21.5, 14.1.

***trans*-1-[(*tert*-Butyldimethylsiloxy)methyl]-2-phenylcyclopropane (Table 3, Entry 3):** IR (film) 1606, 1497, 1097, 836, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.28−7.03 (m, 5H), 3.72 (dd, J = 10.8, 5.7 Hz, 1H), 3.62 (dd, J = 10.8, 6.3 Hz, 1H), 1.80 (dt, J = 8.5, 5.0 Hz, 1H), 1.33 (m, 1H), 0.98−0.89 (m, 2H), 0.90 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.3, 128.5, 126.1, 125.6, 66.1, 26.2, 25.5, 21.0, 18.7, 13.9, −4.9. Anal. Calcd for $C_{16}H_{26}OSi$: C, 73.22; H, 9.98. Found: C, 73.19; H, 9.71.

***trans*-1,2-Diphenylcyclopropane (Table 3, Entry 4):**[45] IR (film) 1603, 1498, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32−7.12 (m, 10H), 2.16 (dd, J = 7.5, 6.9 Hz, 2H), 1.45 (dd, J = 7.5, 6.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8, 128.6, 126.0, 126.0, 28.3, 18.5.

***trans*-1,2-Dihexylcyclopropane (Table 3, Entry 5):** IR (film) 1465, 1458 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.38−1.14 (m, 20H), 0.88 (t, J = 6.7 Hz, 6H), 0.38 (m, 2H), 0.13 (t, J = 6.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.6, 32.2, 29.9, 29.5, 23.0, 19.0, 14.4, 12.0. Anal. Calcd for $C_{15}H_{30}$: C, 85.63; H, 14.37. Found: C, 85.76; H, 14.13.

***cis*-1-Methyl-2-Phenylcyclopropane (Table 3, Entry 6):**[46] IR (film) 1497 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29−7.12 (m, 5H), 2.08 (td, J = 8.7, 6.3 Hz, 1H), 1.17−1.07 (m, 1H), 0.97 (td, J = 8.7, 4.8 Hz, 1H), 0.80 (d, J = 6.3 Hz, 3H), 0.58 (q, J = 5.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.6, 129.4, 127.9, 125.7, 21.4, 13.9, 13.0, 11.2.

***cis*-1,2-Diphenylcyclopropane (Table 3, Entry 7):**[47] IR (film) 1602, 1497, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.10−6.92 (m, 10H), 2.48 (dd, J = 8.6, 6.2 Hz, 2H), 1.46 (td, J = 8.6, 5.4 Hz, 1H), 1.37 (td, J = 6.2, 5.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 129.2, 127.9, 125.8, 24.6, 11.6.

Benzo[2,3]bicyclo[3.1.0]hexane (Table 3, Entry 8).[4i] IR (film) 1475 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31−7.26 (m, 1H), 7.16−7.02 (m, 3H), 3.19 (dd, J = 16.8, 6.6 Hz, 1H), 2.95 (d, J = 16.8 Hz, 1H), 2.38−2.28 (m, 1H), 1.88−1.78 (m, 1H), 1.05 (td, J = 8.1, 4.5 Hz, 1H), 0.06 (q, J = 3.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.1, 142.0, 126.0, 125.54, 125.46, 123.5, 35.7, 24.2, 17.0, 16.3. Anal. Calcd for $C_{10}H_{10}$: C, 92.26; H, 7.74. Found C, 92.12; H, 7.89.

Benzo[2,3]bicyclo[5.1.0]octane (Table 3, Entry 9):[48] IR (film) 1450 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.28 (m, 1H), 7.19−7.09 (m, 2H), 7.06−7.00 (m, 1H), 3.35 (td, J = 12.6, 7.2 Hz, 1H), 2.54 (dd, J = 13.2, 5.7 Hz, 1H), 2.08−1.91 (m, 2H), 1.90−1.77 (m, 1H), 1.58−1.44 (m, 1H), 1.12−0.86 (m, 2H), 0.54−0.37 (m, 1H), 0.27−0.18 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.9, 130.8, 128.2, 126.6, 126.5, 31.5, 27.1, 24.2, 17.6, 12.5, 12.4. Anal. Calcd for $C_{12}H_{14}$: C, 91.08; H, 8.92. Found: C, 90.88; H, 9.07.

1-Phenylbicyclo[4.1.0]heptane (Table 3, Entry 10):[49] IR (film) 1601, 1494, 1448, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27−7.24 (m, 4H), 7.14 (m, 1H), 2.12−1.86 (m, 3H), 1.66 (m, 1H), 1.50−1.18 (m, 5H), 0.93 (dd, J = 9.3, 4.5 Hz, 1H), 0.62 (dd, J = 5.4, 4.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.9, 128.4, 127.7, 125.6, 31.8, 24.8, 24.3, 22.0, 21.9, 19.2, 18.6. Anal. Calcd for $C_{13}H_{16}$: C, 90.64; H, 9.36. Found: C, 90.46; H, 9.30.

Benzo[3,4]-1-methylbicyclo[3.1.0]hexane (Table 3, Entry 11):[50] IR (film) 1477 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.22−7.17 (m, 1H), 7.11−6.98 (m, 3H), 3.01 (d, J = 16.8 Hz, 1H), 2.93 (d, J = 16.8 Hz, 1H), 2.06 (ddd, J = 7.8, 3.3, 0.9 Hz, 1H), 1.37 (s, 3H), 0.95 (dd, J = 7.8, 4.2 Hz, 1H), 0.23 (dd, J = 4.2, 3.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.0, 142.6, 125.9, 125.3, 125.2, 123.1, 41.8, 31.2, 24.3, 24.0, 22.0.

Benzo[2,3]-1-phenylbicyclo[3.1.0]hexane (Table 3, Entry 12):[51] IR (film) 1477 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48−7.02 (m, 9H), 3.40 (dd, J = 16.8, 6.6 Hz, 1H), 3.03 (d, J = 16.8 Hz, 1H), 2.05−1.94 (m, 1H), 1.77 (dd, J = 8.1, 4.5 Hz, 1H), 0.59 (dd, J = 4.8, 4.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.1, 142.0, 141.3, 129.2, 128.4, 126.5, 126.1, 125.8, 125.6, 123.9, 39.8, 35.8, 26.7, 22.0. Anal. Calcd for $C_{16}H_{14}$: C, 93.16; H, 6.84. Found: C, 92.90; H, 6.68.

Benzo[2,3]-1-ethylbicyclo[4.1.0]heptane (Table 3, Entry 13): IR (film) 1491 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, J = 7.8 Hz, 1H), 7.21−7.12 (m, 1H), 7.08−6.99 (m, 2H), 2.68−2.36 (m, 3H), 2.06−1.94 (m, 1H), 1.90−1.74 (m, 1H), 1.33−1.23 (m, 1H), 1.21−1.04 (m, 1H), 0.95 (t, J = 6.9 Hz, 3H),

(45) (a) Hildebrand, J. P.; Marsden, S. P. *Synlett* **1996**, 893. (b) Zhou, S.-M.; Deng, M.-Z.; Xia, L.-J.; Tang, M.-H. *Angew. Chem., Int. Ed.* **1998**, *37*, 2845. (c) Yao, M.-L.; Deng, M.-Z. *Synthesis* **2000**, 1095.

(46) Casey, C. P.; Polichnowski, S. W.; Shusterman, A. J.; Jones, C. R. *J. Am. Chem. Soc.* **1979**, *101*, 7282.

(47) Kawabata, N.; Kamemura, I.; Naka, M. *J. Am. Chem. Soc.* **1979**, *101*, 2139.

(48) Hahn, R. C.; Howard, P. H.; Kong, S.-M.; Lorenzo, G. A.; Miller, N. L. *J. Am. Chem. Soc.* **1969**, *91*, 3558.

(49) Balsamo, A.; Battistini, C.; Crotti, P.; Macchia, B.; Macchia, F. *J. Org. Chem.* **1975**, *40*, 3233.

(50) O'Leary, M. A.; Wege, D. *Tetrahedron* **1981**, *37*, 801.

(51) Lamberts, J. J. M.; Laarhoven, W. H. *J. Org. Chem.* **1983**, *48*, 2202.

0.88 (t, J = 5.1 Hz, 1H), 0.72 (dd, J = 8.1, 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1, 135.4, 128.8, 126.2, 126.0, 124.5, 30.3, 27.2, 22.9, 22.0, 20.6, 17.3, 11.5. Anal. Calcd for $C_{13}H_{16}$: C, 90.64; H, 9.36. Found: C, 90.80; H, 9.19.

Benzo[2,3]-1-phenylbicyclo[4.1.0]heptane (Table 3, Entry 14):[52] mp 49−50 °C; IR (film) 1487 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.22 (m, 5H), 7.10−6.94 (m, 3H), 6.76−6.71 (m, 1H), 2.82−2.54 (m, 2H), 2.24−2.10 (m, 1H), 2.07 (tdd, J = 12.6, 5.8, 2.7 Hz, 1H), 1.76−1.62 (m, 1H), 1.43 (dd, J = 8.4, 5.1 Hz, 1H), 1.26 (t, J = 5.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.4, 141.7, 134.1, 130.7, 128.6, 128.4, 126.5, 126.0, 124.8, 28.7, 26.8, 24.2, 19.9, 15.3. Anal. Calcd for $C_{17}H_{16}$: C, 92.68; H, 7.32. Found: C, 92.44; H, 7.21.

Benzo[2,3]-1-(*p*-methoxyphenyl)bicyclo[4.1.0]heptane (Table 3, Entry 15): mp 64−65 °C; IR (film) 1514, 1244 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32−7.26 (m, 2H), 7.08−6.94 (m, 3H), 6.92−6.86 (m, 2H), 6.77 (m, 1H), 3.82 (s, 3H), 2.80−2.54 (m, 2H), 2.23−2.12 (m, 1H), 2.06−1.92 (m, 1H), 1.72−1.66 (m, 1H), 1.37 (dd, J = 8.4, 5.1 Hz, 1H), 1.24 (t, J = 5.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 142.1, 137.7, 134.1, 131.8, 128.6, 128.5, 125.9, 124.8, 113.8, 55.5, 27.9, 26.8, 24.3, 19.9, 15.4. Anal. Calcd for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.50; H, 7.40.

Benzo[2,3]-1-(*p*-fluorophenyl)bicyclo[4.1.0]heptane (Table 3, Entry 16): mp 55−56 °C; IR (film) 1510, 1220 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.30 (m, 2H), 7.12−6.98 (m, 5H), 6.72 (d, J = 7.2 Hz, 1H), 2.80−2.54 (m, 2H), 2.24−2.13 (m, 1H), 2.06−1.92 (m, 1H), 1.74−1.64 (m, 1H), 1.42−1.34 (m, 1H), 1.30−1.23 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 159.9, 141.5, 141.22, 141.16, 134.1, 132.3, 132.2, 128.7, 128.4, 126.0, 125.0, 115.4, 115.1, 27.9, 26.7, 24.3, 19.8, 15.4. Anal. Calcd for $C_{17}H_{15}F$: C, 85.68; H, 6.34. Found: C, 85.89; H, 6.43.

Benzo[2,3]bicyclo[4.1.0]heptan-1-ol (Table 3, Entry 17).[53] The crude cyclopropanation product was desilyled with TBAF to give an alcohol: IR (film) 3292, 1488, 1223, 1206, 752, 740 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (dd, J = 7.8, 1.3 Hz, 1H), 7.26 (m, 1H), 7.13 (td, J = 7.3, 1.3 Hz, 1H), 7.07 (m, 1H), 2.64 (m, 1H), 2.42−2.29 (m, 2H), 1.99 (m, 1H), 1.80−1.70 (m, 2H), 1.23 (dd, J = 9.6, 5.7 Hz, 1H), 1.07 (t, J = 5.7 Hz, 1H); ^{13}C NMR (75 MHZ, $CDCl_3$) δ 140.8, 133.1, 128.4, 126.6, 125.8, 124.3, 54.8, 26.3, 24.8, 18.6, 16.6. Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.60; H, 7.68.

***cis*-2-Methyl-1-phenyl-1-(trimethylsiloxy)cyclopropane (Table 3, Entry 18):** IR (film) 1497, 1251 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−7.14 (m, 5H), 1.32 (dd, J = 9.9, 6.0 Hz, 1H), 1.23 (d, J = 6.3 Hz, 3H), 1.03−0.94 (m, 1H), 0.74 (dd, J = 6.6, 6.0 Hz, 1H), 0.09 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.0, 128.1, 126.0, 124.8, 61.2, 23.2, 22.4, 13.2, 1.5; HRMS calcd for $C_{13}H_{20}OSi$ (M^+) 220.1283, found 220.1279.

Phenylcyclopropane (Table 3, Entry 19):[2b,6b] IR (film) 1604, 1496, 1464, 1260, 751, 696 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28−7.05 (m, 5H), 1.89 (tt, J = 8.4, 5.1 Hz, 1H), 0.95 (m, 2H), 0.70 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.2, 128.5, 125.8, 125.6, 15.6, 9.4.

(Phenoxymethyl)cyclopropane (Table 3, Entry 20):[54] IR (film) 1600, 1496, 1243 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (m, 2H), 6.90 (m, 3H), 3.79 (d, J = 7.0 Hz, 2H), 1.27 (m, 1H), 0.63 (m, 2H), 0.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 129.6, 120.8, 114.8, 72.9, 10.5, 3.4.

Cyclopropyl Benzoate (Table 3, Entry 21): IR (film) 1725, 1273 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (m, 2H), 7.55 (m, 1H), 7.42 (m, 2H), 4.36 (m, 1H), 0.84−0.82 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 133.2, 130.3, 129.7, 128.6, 49.6, 5.5. Anal. Calcd for $C_{10}H_{10}O_2$: C, 74.06; H, 6.21. Found: C, 74.06; H, 6.20.

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(52) Klemm, L. H.; Lee, D. H.; Santhanam, P. S.; White, D. V.; Shabtai, J.; Olson, D. R. *J. Org. Chem.* **1972**, *37*, 2043.

(53) (a) Rubottom, G. M.; Lopez, M. I. *J. Org. Chem.* **1973**, *38*, 2097. (b) Murai, S.; Aya, T.; Sonoda, N. *J. Org. Chem.* **1973**, *38*, 4354. (c) Imamoto, T.; Takiyama, N. *Tetrahedron Lett.* **1987**, *28*, 1307.

(54) Durandetti, S.; Sibille, S.; Périchon, J. *J. Org. Chem.* **1991**, *56*, 3255.