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Preparation of a Storable Zinc Carbenoid Species and Its Application in Cyclopropanation, Chain Extension, and [2,3]-Sigmatropic Rearrangement Reactions

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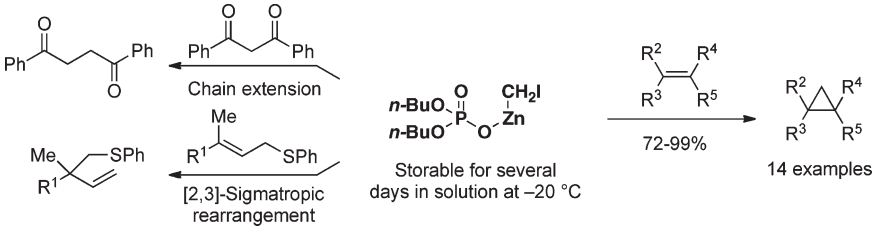
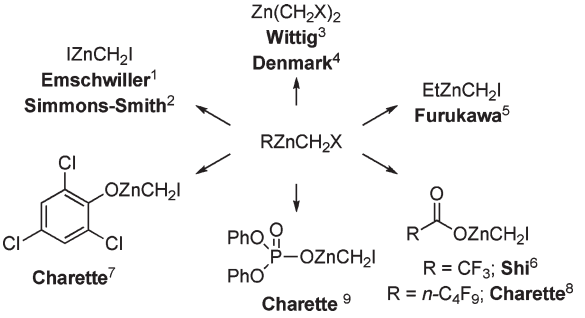


The formation of a new phosphate carbenoid $(n\text{-BuO})_2P(O)OZnCH_2I$ and its application in organozinc-mediated reactions is described. This carbenoid undergoes very slow degradation in solution and can be stored for several weeks at −20 °C. Its reactivity was tested with many representative alkenes and was determined to be a powerful cyclopropanating reagent, giving the corresponding cyclopropanes in 72−99% yield. The use of this carbenoid in the chain extension of 1,3-diketones and [2,3]-sigmatropic rearrangement reactions is also described.

Introduction

Since the preparation of the first zinc carbenoid by Emschwiller[1] in 1929, many related species have been synthesized and have become valuable reagents in a number of organic reactions. One of the most important applications of zinc carbenoids is the Simmons−Smith cyclopropanation reaction.[2] This reaction uses iodomethylzinc iodide ($IZnCH_2I$), which was seminally prepared in 1958 by mixing a zinc/copper couple with CH_2I_2 in ether. Various research groups have since developed variants of this important cyclopropanating reagent, mainly through the replacement of the iodide substituent bonded to the zinc atom with an alternate group (Scheme 1).

SCHEME 1. Different Carbenoids Synthesized



In 1959, Wittig[3] prepared several zinc species bearing two halomethyl substituents by reacting ZnX_2 with diazomethane. Denmark[4] later demonstrated that $Zn(CH_2Cl)_2$ was more effective in cyclopropanation reactions relative to $Zn(CH_2I)_2$. Furukawa[5] also showed that mixing diethylzinc with CH_2I_2 led to the formation of a more practical and reproducible cyclopropanating reagent $EtZnCH_2I$. Although these zinc

(1) Emschwiller, G. *C. R. Hebd. Seance Acad. Sci.* **1929**, *188*, 1555.
(2) (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) *Small Ring Compounds in Organic Synthesis VI*; de Meijere, A., Ed.; Springer: Berlin, Germany, 2000; Vol. 207. (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. (g) Pellissier, H. *Tetrahedron* **2008**, *64*, 7041.
(3) (a) Wittig, G.; Schwarzenbach, K. *Angew. Chem.* **1959**, *71*, 652. (b) Wittig, G.; Schwarzenbach, K. *Liebigs Ann. Chem.* **1961**, *650*, 1.
(4) Denmark, S. E.; Edwards, J. P. *J. Org. Chem.* **1991**, *56*, 6974.
(5) (a) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1966**, *7*, 3353. (b) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53.

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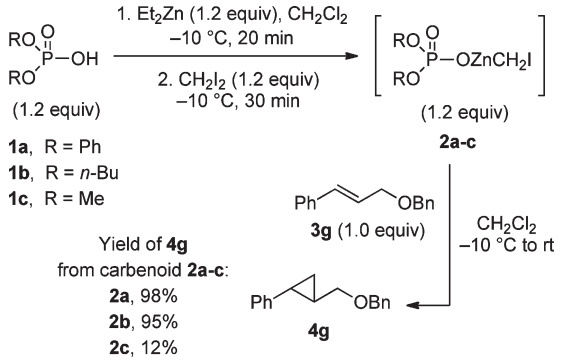
SCHEME 2. Formation of Iodomethylzinc Phosphates and Cyclopropanation Reactions



compounds have proven to be effective for the cyclopropanation of unfunctionalized alkenes, they react much faster with functionalized alkenes containing a directing group, such as allylic alcohols. Recently, several groups have been developing zinc carbenoids that would allow for the rapid cyclopropanation of alkenes without such a directing group. This was achieved by introducing a strongly electron-withdrawing substituent bonded to the zinc. Several examples include carbenoids, such as $CF_3COOZnCH_2I$,[6] $ArOZnCH_2I$,[7] n-C_4F_9-$COOZnCH_2I$,[8] and $(PhO)_2P(O)OZnCH_2I$.[9]

While there are many carbenoid species capable of cyclopropanating alkenes, there still remains a need to develop a "$RZnCH_2I$" reagent that would: (1) be readily produced from cheap and commercially available starting materials, (2) possess an electron-withdrawing R-group in order to increase the electrophilicity of the carbenoid, and (3) be stable and storable for several weeks as a homogeneous solution.[10] Herein, we describe the formation and application of a new zinc carbenoid $(n\text{-BuO})_2P(O)OZnCH_2I$ that addresses these concerns. The versatility of this reagent is demonstrated through its application in cyclopropanation reactions of both functionalized and unfunctionalized alkenes, the chain extension of 1,3-diketones, and [2,3]-sigmatropic rearrangements of sulfonium ylides.

Results and Discussion

We began our study by preparing various carbenoids from the corresponding aryl- and alkylphosphoric acids and by examining the effect of the phosphate group on the efficiency of the corresponding cyclopropanation reactions. Treatment of phosphoric acids **1a**−**c** with 1 equiv of diethylzinc and 1 equiv of diiodomethane at −10 °C, then stirring for 30 min, generated the desired iodomethylzinc phosphate species **2a**−**c**. A solution of *O*-benzyl cinnamyl ether **3g** in CH_2Cl_2 was next added, and the reaction was allowed to warm to room temperature over 20 h (Scheme 2).

CHART 1. Stability of the Carbenoid $(n\text{-BuO})_2P(O)OZnCH_2I$ in Solution at −22 °C

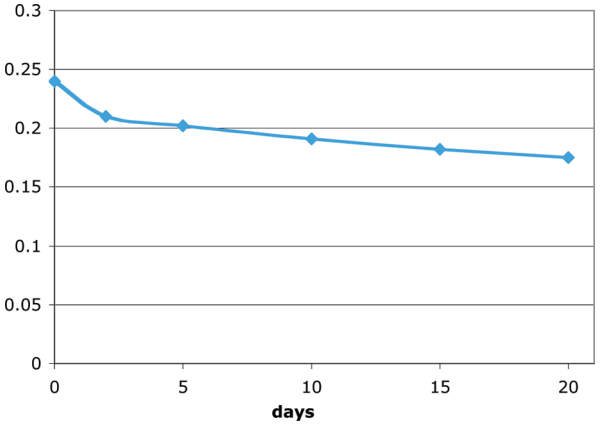
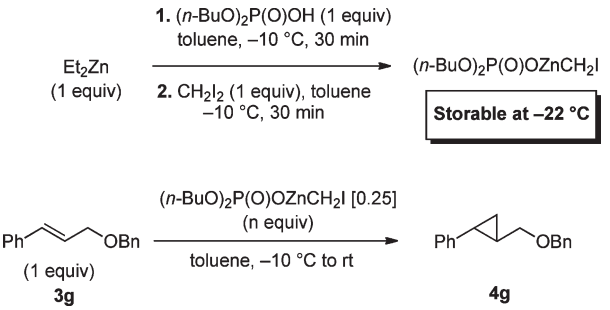


TABLE 1. Reactivity of the Carbenoid $(n\text{-BuO})_2P(O)OZnCH_2I$ in Solution at −22 °C



entry	storage period	n (equiv)	reaction time (h)	yield[a] (%)
1	1 h	1.2	23	>99 (92)
2	6 days	1.2	21	97
3	18 days	1.5	26	96

[a]Determined by ^{1}H NMR. Isolated yield in parentheses.

The carbenoids **2a** and **2b** derived from diphenyl- and dibutylphosphoric acids both gave excellent yields of cyclopropanated product **4g** (98% and 95%, respectively), while the iodomethylzinc dimethylphosphate **2c** resulted in a low 12% conversion. The advantage of dibutyl **2b** compared to diphenylcarbenoid **2a** is that the corresponding dibutylphosphate **1b** precursor is much less expensive relative to the diphenylphosphate **1a**. Furthermore, **2a** precipitates out of the solution upon formation giving rise to a heterogeneous cyclopropanation reaction, while **2b** is completely soluble. This is a significant advantage for carrying out a cyclopropanating processes on larger scale, for storage issues, and manipulations. As the dibutylcarbenoid **2b** proved to be the optimal reagent in terms of reactivity and handling, the remaining studies, including relative stability, solvent screening, and stoichiometry, were conducted with this reagent.

Carbenoid **2b** ($(n\text{-BuO})_2P(O)OZnCH_2I$) prepared in CD_2Cl_2 displays a broad singlet at 1.4 ppm by ^{1}H NMR and a singlet at −23.7 ppm by ^{13}C NMR.[11] These chemical shifts are consistent with those usually observed for similar

(6) (a) Yang, Z. Q.; Lorentz, J. C.; Shi, Y. *Tetrahedron Lett.* **1998**, *39*, 8621. (b) Lorentz, J. C.; Long, J.; Yang, Z.; Xue, S.; Xie, Y.; Shi, Y. *J. Org. Chem.* **2004**, *69*, 327.

(7) Charette, A. B.; Francoeur, S.; Martel, J.; Wilb, N. *Angew. Chem., Int. Ed.* **2000**, *39*, 4539.

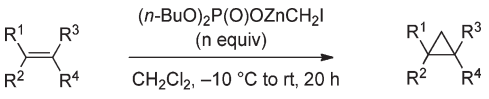
(8) Charette, A. B.; Beauchemin, A.; Francoeur, S. *J. Am. Chem. Soc.* **2001**, *123*, 8139.

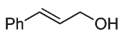
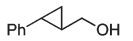
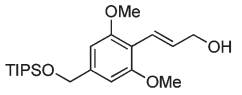
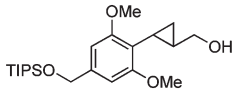
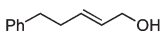
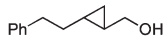
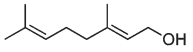
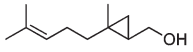
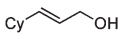
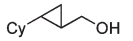
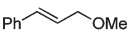
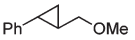
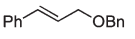
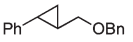
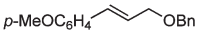
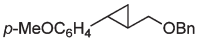
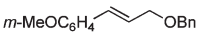
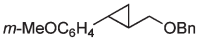
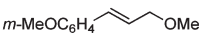
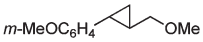
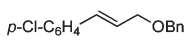
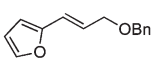
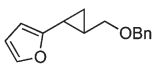
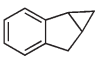
(9) Lacasse, M.-C.; Poulard, C.; Charette, A. B. *J. Am. Chem. Soc.* **2005**, *127*, 12440.

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

(11) See the Supporting Information for NMR spectra.

TABLE 2. Cyclopropanation with $(n\text{-BuO})_2P(O)OZnCH_2I$



entry		substrate		product	n equiv	yield (%)[a]
1	**3a**		**4a**		1.2	86
2	**3b**		**4b**		1.2	96
3	**3c**		**4c**		1.6	88
4	**3d**		**4d**		1.2	93
5	**3e**		**4e**		1.4	76
6	**3f**		**4f**		1.2	72
7	**3g**		**4g**		1.2	95
8	**3h**		**4h**		1.2	91
9	**3i**		**4i**		1.2	98
10	**3j**		**4j**		1.5	99
11	**3k**		**4k**		1.4	93
12	**3l**		**4l**		2.0	85
13	**3m**		**4m**		2.0	>95[b]
14	**3n**		**4n**		2.0	82[b]

[a]Isolated yield. [b]Determined by GC using an internal standard.

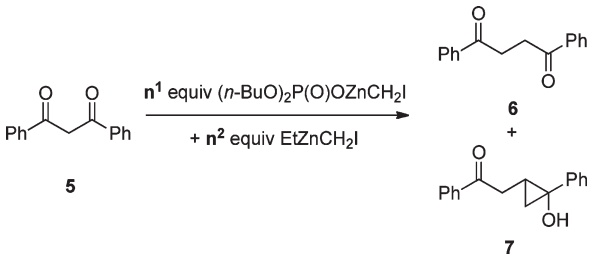
iodomethylzinc carbenoids. The cyclopropanation of *O*-benzyl cinnamyl ether using this species could be achieved with equal efficiency in toluene at the same temperature. The optimal ratio of carbenoid relative to the alkene was 1.2 equiv. This is an added interesting feature of this more stable carbenoid since sometimes a larger excess of other related zinc carbenoid reagents is required for the cyclopropanation to occur quantitatively. The excess is typically required to compensate for the carbenoid decomposition. This observation led us to examine the relative stability of carbenoid **2b** in solution over time. Toluene was chosen as the solvent in order to avoid any significant evaporation and, consequently, any alteration of the solution concentration. Therefore, the carbenoid was generated in toluene at −10 °C, from di-*n*-butylphosphoric acid, diethylzinc, and diiodomethane. The concentration of the solution was evaluated at different times (2, 5, 10, 15, and 20 days) using Knochel's titration method (Chart 1).[12] We were pleased to find that storing the carbenoid solution in the freezer only allows a slow degradation of the carbenoid **2b**. Moreover, this degradation slows down with time, and after 20 days of storage at −22 °C the solution remained over 70% of the initial concentration.

We next tested an "old solution" of the zinc carbenoid to measure its efficiency in cyclopropanation reactions. A carbenoid solution (0.25 M) was generated as previously described. After storage for 1 h at −22 °C under argon, a known quantity of the carbenoid (1.2 equiv relative to the substrate) was placed in a flask at −10 °C followed by the addition of the alkene **3g**. After warming to room temperature over 1 day, complete conversion was observed with a 92% isolated yield (Table 1, entry 1).

The carbenoid was still effective after being stored in the refrigerator at −22 °C for 6 days; the reaction resulted in 97% conversion (Table 1, entry 2). After 18 days, a slight excess of carbenoid was required to obtain high conversion (96%, entry 3), presumably to compensate for the slow degradation of the carbenoid in solution. To the best of our knowledge, this is the first example of a storable carbenoid in solution.

(12) Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, *5*, 890–891.

TABLE 3. Chain Extension of 1,3-Diketones and Synthesis of *trans*-1,2-Disubstitued Cyclopropanols



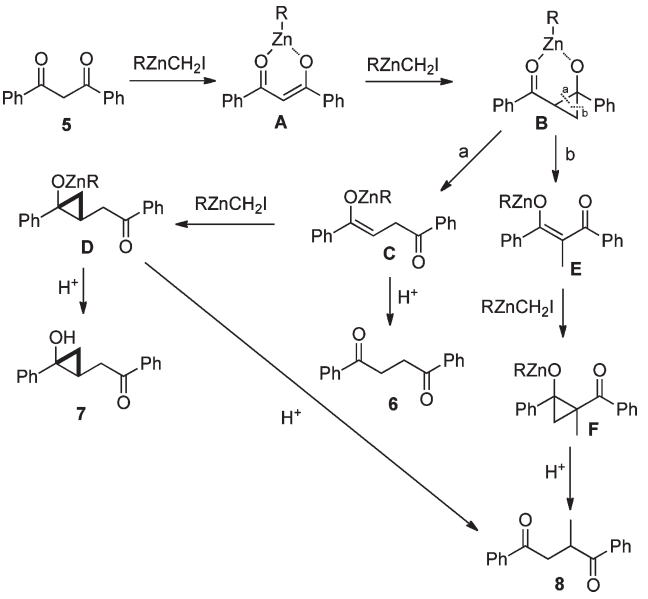
entry	n^1 (equiv)	n^2 (equiv)	time (h)	yield of **6** (%)	yield of **7** (%)
1[a]	2.5		40	52	< 5
2	3.0		32	59	25
3	2.0	2.0	32	17	41
4[b]	2.5	2.0	45	28	42
5	2.0	2.5	45	< 5	73

[a]Unreacted starting material observed. [b]Presence of 1,4-diphenyl-2-methyl-1,4-butanedione **8** in 22% yield.

Furthermore, this solution is not pyrophoric, unlike neat diethylzinc or nonstabilized carbenoids, which are known to react vigorously with air and water. The less acidic character of the *n*-butylphosphoric acid ($pK_a = 1.39$ for diethylphosphoric acid[13]) relative to the trifluoroacetic acid ($pK_a = -0.25$) makes **2b** less reactive compared to Shi's carbenoid for the cyclopropanation reactions (evident by the longer reaction times). However, this characteristic is advantageous, since it allows the storage over a long period of time at low temperature.

The scope of the Simmons−Smith cyclopropanation reaction using iodomethylzinc dibutylphosphate was next examined for a wide range of alkenes (Table 2). Both protected and unprotected cinnamyl alcohols **3a**−**l** gave good to excellent yields of the corresponding cyclopropanes (72−99%, entries 1−12). In the case of the alcohol **3a**, only 1.2 equiv of carbenoid was necessary to obtain complete conversion (entry 1). Typically, with other cyclopropanating reagents, 1 equiv is needed for the deprotonation of the alcohol and a second equivalent for the cyclopropanation reaction. Alkyl-substituted alkenes **3c**−**e** were also efficiently cyclopropanated in 88%, 93%, and 76% yields, respectively (entries 3−5). As expected, the cyclopropanation of **3d** was completely regioselective. Substrates **3b**,**h**−**j**, having an electron-donating group at different positions on the aromatic moiety, gave the desired products **4b**,**h**−**j** in excellent yields (91−99% yield, entries 2, 8−10). Even substrate **3k**, substituted by a chlorine atom in the *para* position, gave the corresponding cyclopropane in 93% yield (entry 11). Furylalkene **3l** required 2 equiv of carbenoid for complete conversion (85% yield, entry 12). Finally, the unfunctionalized substrates **3m** and **3n** were cyclopropanated in good yield using 2 equiv of carbenoid (entries 13 and 14).

SCHEME 3. Mechanism Proposed for the Formation of Compounds 6−8



Chain Extension of 1,3-Diketones to 1,4-Diketones and the Synthesis of *trans*-1,2-Disubstitued Cyclopropanols. We next examined the reactivity of zinc carbenoid **2b** in other reactions. It is known that zinc carbenoids are effective in chain extension of 1,3-diketones. Zercher[14] reported a simple approach for the chain extension of β-diketo esters using the Furukawa carbenoid $EtZnCH_2I$. This methodology was also efficient with β-keto amides[15] and β-keto phosphonates.[16] More recently, Xue[17] reported that the use of Shi's carbenoid $CF_3COOZnCH_2I$ gives good results for the chain extension of β-keto esters and acyclic 1,3-diketones. Under our reaction conditions, carbenoid **2b** resulted in the chain extension of 1,3-diketones **5** in 52% yield using 2.5 equiv of zinc carbenoid (Table 3, entry 1). When the amount of **2b** was increased to 3 equiv (entry 2), the yield of the desired compound **6** was increased to 59%, along with the formation of the cyclopropanol **7** in 25% yield. The addition of an excess of the zinc species $EtZnCH_2I$ increased the yield of *trans*-1,2-cyclopropanol **7** (entry 3). Using 2.5 equiv of carbenoid and 2.0 equiv of $EtZnCH_2I$ gives a mixture of three compounds, with the formation of the nonexpected 1,4-diphenyl-2-methyl-1,4-butanedione **8** in 22% yield (entry 4). The use of 2.0 equiv of carbenoid and 2.5 equiv of $EtZnCH_2I$ gave almost exclusively **7** in good yield (73% yield versus 61% with the Shi's carbenoid,[17b] entry 5). When the reaction was conducted with 4 equiv of $EtZnCH_2I$, only 60% conversion was obtained, with a complex mixture of compounds.

Following the seminal work of Zercher,[14] a mechanism for the formation of compounds **6**−**8** is proposed (Scheme 3). After formation of the enolate **A**, a second equivalent of carbenoid reacts with the alkene to obtain the cyclopropyl intermediate **B**. This intermediate can either form **C**, which upon acidic work up would lead to **6**, or form **E** via an

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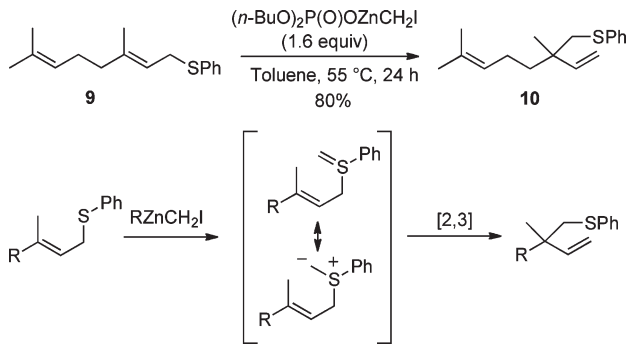
SCHEME 4. [2,3]-Sigmatropic Rearrangement of Sulfonium Ylides



unfavorable cyclopropane ring-opening. Following a second cyclopropanation/ring-opening sequence, compound **8** could be obtained. The cyclopropanation of the enolate **C** followed by an acidic workup gives the product **7**. The intermediate **D** could also be the precursor of compound **8**.

[2,3]-Sigmatropic Rearrangement. We next turned our attention to the use of carbenoid $(n\text{-BuO})_2P(O)OZnCH_2I$ in [2,3]-sigmatropic rearrangement of sulfonium ylides. In the literature, only two examples that utilize iodomethylzinc carbenoids for the formation of allylic sulfonium ylide have been reported.[10,18] Using only 1.6 equiv of the carbenoid, complete conversion was obtained with an 80% isolated yield of the desired product **10** (Scheme 4).

In Cohen's original studies,[18] 2 equiv of Et_2Zn and 3 equiv of CH_2I_2 were necessary to obtain complete conversion. The use of a samarium carbenoid[19] required 3 equiv of CH_2I_2 and 6 equiv of SmI_2. As expected, no cyclopropanation of the two alkenes present in the molecule was observed as it is known that the alkenes were less reactive than the sulfide toward the zinc carbenoid.[20]

Conclusion

In summary, we have synthesized a new phosphate carbenoid $(n\text{-BuO})_2P(O)OZnCH_2I$, which shows very slow degradation at −22 °C and can be used several weeks after its synthesis. Its reactivity as a powerful cyclopropanating reagent was demonstrated with many representative substrates. Protected and unprotected allylic alcohols, styrenic substrates with electron-donating or electron-withdrawing substituents on the aromatic ring, and unfunctionalized alkenes all gave the desired products with excellent yields. Application to the chain extension of 1,3-diketones and [2,3]-sigmatropic rearrangement of allylic sulfides also gave good results. We are currently examining the development of a chiral version of this reagent for its use in asymmetric cyclopropanation.

Experimental Section

General Procedure for the Storable Solution of $(n\text{-BuO})_2P(O)OZnCH_2I$. To a solution of $ZnEt_2$ (1,02 mL, 10 mmol, 1.0 equiv) in toluene (30 mL) at −10 °C was added dropwise a solution of freshly distilled $(n\text{-BuO})_2P(O)OH$ (1.96 mL, 10 mmol, 1.0 equiv) in toluene (10 mL). This solution was stirred at −10 °C for 20 min after which CH_2I_2 (805 μL, 10 mmol, 1.0 equiv) was added. This solution was stirred for an additional 30 min at −10 °C and stored at −22 °C.

General Procedure for the Cyclopropanation Using *n*-Butyl Phosphate. To a solution of $ZnEt_2$ (37 μL, 0.36 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) at −10 °C was added dropwise a solution of $(n\text{-BuO})_2P(O)OH$ (76 mg, 0.36 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL). This solution was stirred for 15 min after which CH_2I_2 (29 μL, 0.36 mmol, 1.2 equiv) was added. This solution was stirred for an additional 30 min. A solution of substrate (0.30 mmol, 1.0 equiv) in CH_2Cl_2 (0.5 mL) was added, and the resulting solution was stirred for 20 h. The reaction was quenched with saturated NH_4Cl solution, washed with saturated aqueous NaCl, dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by flash chromatography to afford the pure desired cyclopropane derivative.

(2-Phenylcyclopropyl)methanol (4a).[21,22] The cyclopropanation of the commercially available (*E*)-cinnamyl alcohol **3a** (40 mg, 0.30 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (10% EtOAc/hexanes) to produce the desired cyclopropane (38 mg, 86%): R_f 0.46 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.25 (m, 2H), 7.20−7.16 (m, 1H), 7.11−7.06 (m, 2H), 3.65−3.58 (m, 2H), 2.05 (s, 1H), 1.86−1.80 (m, 1H), 1.49−1.43 (m, 1H), 1.00−0.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 128.4, 125.9, 125.7, 66.5, 25.3, 21.4, 14.0; IR ν_{max} 3339, 3026, 2870, 1604, 1497, 1461, 1265, 1090, 1032, 1018, 736, 696 cm^{-1}.

(*E*)-3-(2,6-Dimethoxy-4-((triisopropylsilyloxy)methyl)phenyl)-prop-2-en-1-ol (3b): R_f 0.51 (30% EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.85 (d, J = 16.2 Hz, 1H), 6.73 (dt, J = 16.2, 5.7 Hz, 1H), 6.57 (s, 2H), 4.80 (s, 2H), 4.27 (d, J = 5.1 Hz, 2H), 3.80 (s, 6H), 2.10−2.00 (m, 1H), 1.30−1.00 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 142.4, 132.0, 121.9, 112.2, 101.0, 65.5, 65.0, 55.6, 18.1, 12.1; IR ν_{max} = 3383, 2940, 2864, 2243, 1607, 1577, 1456, 1417, 1367, 1231, 1198, 1124, 974, 909, 882, 732, 682, 647 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{37}O_4Si$ $[M + H]^+$ 381.2455, found 381.2451.

(2-(2,6-Dimethoxy-4-((triisopropylsilyloxy)methyl)phenyl)cyclopropyl)methanol (4b). The cyclopropanation of (*E*)-3-(2,6-dimethoxy-4-((triisopropylsilyloxy)methyl)phenyl)prop-2-en-1-ol **3b** (76 mg, 0.20 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (10% EtOAc/hexanes) to produce the desired cyclopropane (76 mg, 96%): R_f 0.59 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56 (s, 2H), 4.79 (s, 2H), 3.95 (dd, J = 10.8, 10.5 Hz, 1H), 3.80 (s, 6H), 3.12 (dd, J = 10.5, 10.2 Hz, 1H), 2.50 (bs, 1H), 1.40 (m, 1H), 1.30−1.00 (m, 23H), 1.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 141.7, 115.0, 101.3, 68.0, 65.0, 55.7, 23.1, 18.2, 12.4, 12.1, 11.7; IR ν_{max} = 3437, 2941, 2865, 1610, 1580, 1455, 1416, 1227, 1119, 1013, 971, 881, 818, 736, 681, 656 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{39}O_4Si$ $[M + H]^+$ 395.2612, found 395.2607.

2-(2-Phenylethyl)cyclopropylmethanol (4c).[22] The cyclopropanation of (*E*)-5-phenyl-2-pentenol **3c**[22] (49 mg, 0.30 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (25% EtOAc/hexanes) to produce the desired cyclopropane (47 mg, 88%): R_f 0.49 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.22 (m, 2H), 7.20−7.13 (m, 3H), 3.40 (dd, J = 11.4, 7.2 Hz, 1H), 3.34 (dd, J = 10.8, 6.9 Hz, 1H),

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2.75−2.65 (m, 2H), 1.68−1.48 (m, 2H), 1.45 (s, 1H), 0.90−0.75 (m, 1H), 0.65−0.55 (m, 1H), 0.40−0.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 128.6, 128.4, 125.9, 67.1, 36.0, 35.4, 21.5, 17.0, 9.9; IR ν_{max} = 3326, 2995, 2920, 2855, 1603, 1495, 1454, 1061, 1032, 1016, 742, 698, 631 cm^{-1}.

(2-Methyl-2-(4-methylpent-3-enyl)cyclopropyl)methanol (4d).[22] The cyclopropanation of the commercially available geraniol **3d** (46 mg, 0.30 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (25% EtOAc/hexanes) to produce the desired cyclopropane (47 mg, 93%): R_f 0.65 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.12−5.05 (m, 1H), 3.69 (dd, J = 11.2, 6.6 Hz, 1H), 3.47 (dd, J = 11.2, 8.4 Hz, 1H), 2.10−1.98 (m, 2H), 1.66 (s, 3H), 1.63 (s, 1H), 1.60 (s, 3H), 1.40−1.32 (m, 1H), 1.18−1.10 (m, 1H), 1.08 (s, 3H), 0.95−0.85 (m, 1H), 0.48 (dd, J = 8.8, 4.8 Hz, 1H), 0.11 (t, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.4, 124.7, 64.0, 41.2, 26.3, 25.8, 25.6, 20.0, 17.75, 17.69, 17.1; IR ν_{max} = 3370, 2968, 2920, 1452, 1383, 1265, 1032, 738, 628 cm^{-1}.

(2-Cyclohexylcyclopropyl)methanol (4e).[22] The cyclopropanation of (*E*)-3-cyclohexylprop-2-en-1-ol **3e**[22] (36 mg, 0.26 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (40% Et_2O/hexanes) to produce the desired cyclopropane (30 mg, 76%): R_f 0.39 (40% Et_2O/hexane)s; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.40 (dd, J = 11.2, 7.2 Hz, 1H), 3.36 (dd, J = 10.8, 6.8 Hz, 1H), 1.80−1.64 (m, 4H), 1.62−1.52 (m, 2H), 1.20−0.95 (m, 5H), 0.89−0.78 (m, 1H), 0.60−0.48 (m, 1H), 0.44−0.35 (m, 1H), 0.34−0.26 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 67.4, 42.0, 33.2, 32.9, 26.6, 26.4, 24.1, 20.1, 8.8; IR ν_{max} = 3329, 2919, 2849, 1447, 1049, 1028, 1013, 962, 868, 664 cm^{-1}.

(2-(Methoxymethyl)cyclopropyl)benzene (4f).[9] The cyclopropanation of (*E*)-(3-methoxyprop-1-enyl)benzene **3f**[23,24] (44 mg, 0.30 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (10% EtOAc/hexanes) to produce the desired cyclopropane (35 mg, 72%): R_f 0.55 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.24 (m, 2H), 7.17 (tt, J = 7.6, 1.2 Hz, 1H), 7.12−7.07 (m, 2H), 3.46 (dd, J = 10.2, 6.6 Hz, 1H), 3.40 (s, 3H), 3.39 (dd, J = 10.4, 6.8 Hz, 1H), 1.83 (dt, J = 8.4, 4.8 Hz, 1H), 1.49−1.40 (m, 1H), 1.03−0.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 128.4, 125.9, 125.7, 76.2, 58.5, 22.5, 21.5, 14.1; IR ν_{max} = 3030, 2924, 2815, 1602, 1498, 1463, 1200, 1105, 913, 748, 697 cm^{-1}.

(2-(Benzyloxymethyl)cyclopropyl)benzene (4g).[9] The cyclopropanation of (*E*)-(3-(benzyloxy)prop-1-enyl)benzene **3g**[9] (67 mg, 0.30 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (5% EtOAc/hexanes) to produce the desired cyclopropane (68 mg, 95%): R_f 0.61 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.28 (m, 7H), 7.21 (tt, J = 7.6, 1.2 Hz, 1H), 7.15−7.11 (m, 2H), 4.62 (s, 2H), 3.60 (dd, J = 10.4, 6.4 Hz, 1H), 3.49 (dd, J = 10.0, 6.8 Hz, 1H), 1.85 (dt, J = 9.2, 4.8 Hz, 1H), 1.55−1.50 (m, 1H), 1.10−0.95 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 138.6, 128.5, 128.4, 127.8, 127.7, 125.9, 125.7, 73.6, 72.6, 22.7, 21.6, 14.3; IR ν_{max} = 3060, 3027, 2855, 1604, 1497, 1454, 1359, 1094, 1078, 909, 735, 696 cm^{-1}.

1-(2-(Benzyloxymethyl)cyclopropyl)-4-methoxybenzene (4h).[25] The cyclopropanation of (*E*)-1-(3-(benzyloxy)prop-1-enyl)-4-methoxybenzene **3h**[9] (64 mg, 0.25 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (5% EtOAc/hexanes) to produce the desired cyclopropane (61 mg, 91%): R_f 0.46 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.25 (m, 5H), 7.00 (dt, J = 9.0, 2.1 Hz, 2H), 6.79 (dt, J = 8.7, 2.1 Hz, 2H), 4.55 (s, 2H), 3.76 (s, 3H), 3.52 (dd, J = 10.2, 6.6 Hz, 1H), 3.41 (dd, J = 10.2, 6.9 Hz, 1H), 1.80−1.71 (m, 1H), 1.43−1.31 (m, 1H), 0.95−0.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 138.6, 134.7, 128.5, 127.8, 127.7, 127.1, 113.9, 73.8, 72.6, 55.4, 22.2, 20.9, 13.8; IR ν_{max} = 2985, 2306, 1515, 1455, 1265, 1177, 1033, 909, 754, 704, 630 cm^{-1}.

1-(2-(Benzyloxymethyl)cyclopropyl)-3-methoxybenzene (4i). The cyclopropanation of (*E*)-1-(3-(benzyloxy)prop-1-enyl)-3-methoxybenzene **3i**[26] (76 mg, 0.30 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (10% EtOAc/hexane) to produce the desired cyclopropane (79 mg, 98%): R_f 0.46 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.27 (m, 5H), 7.19 (t, J = 7.8 Hz, 1H), 6.75−6.63 (m, 3H), 4.58 (s, 2H), 3.80 (s, 3H), 3.56 (dd, J = 10.2, 6.3 Hz, 1H), 3.44 (dd, J = 10.2, 6.6 Hz, 1H), 1.85−1.77 (m, 1H), 1.55−1.42 (m, 1H), 1.05−0.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 144.5, 138.6, 129.4, 128.5, 127.8, 127.7, 118.4, 111.8, 110.9, 73.5, 72.6, 55.2, 22.8, 21.6, 14.3; IR ν_{max} = 3002, 2936, 2855, 1602, 1582, 1494, 1454, 1264, 1206, 1154, 1094, 1072, 1046, 773, 735, 694 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{21}O_2$ $[M + H]^+$ 269.1536, found 269.1525.

(*E*)-1-Methoxy-3-(3-methoxyprop-1-enyl)benzene (3j). The methylation of (*E*)-3-(3-methoxyphenyl)prop-2-en-1-ol (253 mg, 1.54 mmol) was performed according to a previously described procedure using NaH 60% (1.2 equiv) and MeI (1.2 equiv) in THF (10 mL). Classical work up following by a purification by flash chromatography on silica gel (10% EtOAc/hexanes) produce the desired product **1f** (230 mg, 84%): R_f 0.42 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (dd, J = 8.1, 7.8 Hz, 1H), 6.97 (d, J = 7.5 Hz, 1H), 6.92 (d, J = 2.4 Hz, 1H), 6.78 (dd, J = 8.1, 2.4 Hz, 1H), 6.57 (d, J = 15.9 Hz, 1H), 6.26 (dt, J = 15.9, 6.0 Hz, 1H), 4.07 (dd, J = 6.0, 5.7 Hz, 1H), 3.79 (s, 3H), 3.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 138.2, 132.3, 129.6, 126.4, 119.2, 113.4, 111.8, 73.1, 58.1, 55.2; IR ν_{max} = 2926, 2821, 1598, 1598, 1579, 1489, 1453, 1379, 1289, 1258, 1154, 1119, 1041, 967, 771, 689, 630 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{14}O_2Ag$ $[M + Ag]^+$ 285.0039, found 285.0037.

1-Methoxy-3-(2-(methoxymethyl)cyclopropyl)benzene (4j). The cyclopropanation of (*E*)-1-methoxy-3-(3-methoxyprop-1-enyl)-benzene **3j** (53 mg, 0.30 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (10% EtOAc/hexanes) to produce the desired cyclopropane (57 mg, 99%): R_f 0.39 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dd, J = 8.0, 7.6 Hz, 1H), 6.75−6.60 (m, 3H), 3.79 (s, 3H), 3.45−3.30 (m, 5H), 1.84−1.77 (m, 1H), 1.47−1.40 (m, 1H), 1.02−0.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 144.4, 129.4, 118.4, 111.8, 110.9, 76.1, 58.5, 55.2, 22.6, 21.6, 14.2; IR ν_{max} = 2926, 2834, 1603, 1582, 1493, 1455, 1264, 1200, 1155, 1103, 1046, 773, 694 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{16}O_2Ag$ $[M + Ag]^+$ 299.0195, found 299.0185.

1-(2-(Benzyloxymethyl)cyclopropyl)-4-chlorobenzene[25] **(4k).** The cyclopropanation of (*E*)-1-(3-(benzyloxy)prop-1-enyl)-4-chlorobenzene **4k** (66.5 mg, 0.257 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (5% Et_2O/hexane) to produce the desired cyclopropane (65 mg, 93%): R_f = 0.40 (10% Et_2O/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.29 (m, 5H), 7.24 (d, J = 8.4 Hz, 2H), 7.02 (d, J = 8.4 Hz, 2H), 4.58 (s, 2H), 3.53 (dd, J = 10.4, 6.8 Hz, 1H), 3.50 (dd, J = 10.0, 6.4 Hz, 1H), 1.85−1.78 (m, 1H), 1.50−1.40 (m, 1H), 0.98 (dd, J = 7.2, 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 138.5, 131.2,

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128.51, 128.45, 127.8, 127.7, 127.3, 73.4, 72.7, 22.9, 21.1, 14.3; IR ν_{max} = 3028, 2855, 1495, 1454, 1360, 1092, 1013, 823, 736, 698 cm^{-1}.

2-(2-(Benzyloxymethyl)cyclopropyl)furan (4l). The cyclopropanation of (*E*)-2-(3-(benzyloxy)prop-1-enyl)furan **1l**[27] (43 mg, 0.20 mmol) was performed according to the previously described procedure. The residue was purified by flash chromatography on silica gel (10% EtOAc/hexanes) to produce the desired cyclopropane (39 mg, 85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.24 (m, 6H), 6.27 (dd, J = 3.2, 2.0 Hz, 1H), 5.97 (dd, J = 3.2, 0.5 Hz, 1H), 4.57 (s, 2H), 3.51−3.42 (m, 2H), 1.84 (dt, J = 9.2, 4.8 Hz, 1H), 1.50 (m, 1H), 1.05 (ddd, J = 8.4, 5.2, 3.2 Hz, 1H), 0.86 (ddd, J = 8.4, 5.2, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 140.6, 138.5, 128.5, 127.8, 127.7, 110.4, 103.8, 72.9, 72.6, 20.2, 14.8, 11.8; IR ν_{max} = 3028, 2923, 2856, 1599, 1508, 1496, 1453, 1359, 1073, 1009, 728, 696, 597 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{16}O_2Na$ $[M + Na]^+$ 251.1042, found 251.1030.

1,4-Diphenylbutane-1,4-dione (6). Compound **6** was prepared according to a known literature procedure[17b] starting from the commercially available 1,4-diphenylbutane-1,4-dione **5** (67 mg, 0.30 mmol) to afford the desired compound as a white solid in 52% yield after flash chromatography on silica gel (20% Et_2O/hexanes): R_f 0.37 (30% Et_2O/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dt, J = 7.2, 1.5 Hz, 2H), 7.55 (tt, J = 7.5, 1.2 Hz, 1H), 7.50−7.42 (m, 2H), 3.45 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 136.9, 133.3, 128.7, 128.2, 32.7; IR ν_{max} = 3026, 2906, 1677, 1594, 1578, 1446, 1354, 1223, 1180, 991, 775, 737, 693 cm^{-1}.

2-(2-Hydroxy-2-phenylcyclopropyl)-1-phenylethanone (7). The compound **7** was prepared according to a known literature procedure[17b] starting from the commercially available 1,4-diphenylbutane-1,4-dione **5** (67 mg, 0.30 mmol) to afford the desired compound as a white solid in 73% yield after flash chromatography on silica gel (20% Et_2O/hexanes): R_f 0.41 (50% Et_2O/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, J = 7.2, 1.2 Hz, 2H), 7.63−7.56 (m, 1H), 7.52−7.31 (m, 6H), 7.27−7.21 (m, 1H), 3.70 (dd, J = 17.2, 5.2 Hz, 1H), 3.24 (s, 1H), 3.03 (dd, J = 17.2, 8.8 Hz, 1H), 1.62−1.52 (m, 1H), 1.40−1.30 (dd, J = 9.6, 6.0 Hz, 1H), 1.15−1.10 (t, J = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.3, 144.6, 136.8, 133.5, 128.8, 128.5, 128.4, 126.7, 125.2, 58.9, 37.8, 23.6, 22.4 IR ν_{max} = 3399, 3060, 1682, 1598, 1496, 1449, 1216, 1032, 752, 737, 698 cm^{-1}.

2-Methyl-1,4-diphenylbutane-1,4-dione (8): R_f 0.55 (40% Et_2O/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06−8.01 (m, 2H), 8.00−7.92 (m, 2H), 7.60−7.40 (m, 6H), 4.16 (ddq, J = 8.4, 7.2, 4.8 Hz, 1H), 3.72 (dd, J = 18.0, 8.4 Hz, 1H), 3.10 (dd, J = 18.0, 4.8 Hz, 1H), 1.27 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.6, 198.6, 136.8, 136.2, 133.3, 133.1, 128.8, 128.72, 128.67, 128.2, 42.5, 36.4, 18.1; IR ν_{max} = 2981, 2906, 1675, 1594, 1578, 1446, 1394, 1371, 1346, 1238, 1212, 999, 975, 729, 706, 689 cm^{-1}.

(2,6-Dimethyl-2-vinylhept-5-enyl)(phenyl)sulfane (10). To a solution of $ZnEt_2$ (33 μL, 0.325 mmol, 1.6 equiv) in toluene (1.0 mL) at 0 °C was added dropwise a solution of $(n\text{-BuO})_2P(O)OH$ (68 mg, 0.33 mmol, 1.6 equiv) in toluene (1.0 mL). This solution was stirred for 15 min after which CH_2I_2 (27 μL, 0.33 mmol, 1.6 equiv) was added. This solution was stirred for an additional 15 min. A solution of (*E*)-(3,7-dimethylocta-2,6-dienyl)(phenyl)sulfane **9**[28] (50 mg, 0.20 mmol, 1.0 equiv) in toluene (0.5 mL) was added, and the resulting solution was stirred for 22 h at 50 °C. The reaction was cooled to rt, and acetaldehyde (290 μL) was added to the solution. After the mixture was stirred for 25 min, the crude was poured into a separatory funnel, and Et_2O and saturated NH_4Cl solution were aded. The aqueous layer was washed twice with ether, and the combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (10% EtOAc/hexanes) to afford the pure desired compound **10**.

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Supporting Information Available: ^{1}H and ^{13}C spectra for products **1f**,**g**, **2a**−**k**, **4**, **5**, and **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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