Organocalcium Chemistry: Preparation and Reactions of Highly Reactive Calcium

Tse-Chong Wu, Heping Xiong, and R. D. Rieke*

Department of Chemistry, University of Nebraska, Lincoln, Nebraska 68588-0304

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A highly reactive form of calcium was prepared by the reduction of Ca(II) salts with preformed lithium biphenylide. Remarkably, this activated calcium undergoes oxidative addition to organic bromides, chlorides, or even fluorides to form the organocalcium reagents under very mild conditions in high yields. The resulting organocalcium compounds undergo Grignard-type reactions. Transmetalation with Cu(I) salts forms calcium cuprate reagents which undergo a variety of cross-coupling reactions. The activated calcium reacts with 1,3-dienes to yield the corresponding 2-butene-1,4-diylcalcium complexes. These bis-organocalcium reagents can undergo dialkylation reactions with α,ω-alkylene dihalides and dichlorosilanes to form the corresponding 3-, 5-, and 6-membered ring derivatives. Significantly, these reactions are highly stereospecific and regioselective.

We have previously reported that highly reactive magnesium readily reacts with 1,3-dienes to form substituted 2-butene-1,4-diylmagnesium complexes.[1] Reactions of these complexes with organic dihalides yielded 4-, 5-, or 6-membered ring carbocycles. The bis-Grignard reagents can also be reacted with two different electrophiles, yielding polyfunctionalized ketones. Since calcium has a significantly different redox potential as well as a larger ionic radius from that of magnesium, we anticipated that the corresponding calcium metallocycles would behave quite differently with respect to their reactivity and selectivity. In this paper, we report a highly reactive form of calcium, which allows the ready preparation of a wide variety of organocalcium reagents. These reagents in turn can be used to carry out a number of useful transformations.

Highly reactive calcium can be readily prepared by the reduction of calcium halides in tetrahydrofuran solution with preformed lithium biphenylide under an argon atmosphere at room temperature. This colored calcium species seems to be reasonably soluble in THF. However, the reactive calcium complex prepared from preformed lithium naphthalenide was insoluble in THF solution and precipitated out of solution to give a highly reactive black solid. As this lithium naphthalenide generated calcium species was insoluble in most deuterated solvents and reacted with deuterated DMSO and DMF, the exact nature of this black calcium complex has not been determined. Acid hydrolysis of the black material releases naphthalene as well as THF. Accordingly, the most likely structure of the black material is a Ca–naphthalene–THF complex similar in nature to the soluble magnesium–anthracene complex recently reported.[2] A solid-state NMR spectroscopic study of this lithium naphthalenide generated activated calcium complex is currently underway.

Grignard-Type Reactions with Highly Reactive Calcium. The development of organocalcium chemistry has been surprisingly slow with respect to the extensive studies of organometallic reagents of other light metals.[3] The neglect of organocalcium chemistry is due in part to the lack of a facile method of preparing the organocalcium compounds. Direct oxidative addition to calcium has traditionally been limited by the reduced reactivity of calcium metal with organic substrates. This is presumably due to surface poisoning factors. The organocalcium derivatives RCaX were most readily formed when X = I, and the preparation of RCaX (X = Br, Cl) usually required activated calcium. Few examples have been reported, and overall yields tend to be low.[3] Although simple primary and secondary alkyl iodides reacted with calcium in reasonable yields,[4] the tertiary alkyliodocalcium compounds were very difficult to prepare and most workers reported only trace amounts.[5] In contrast, the highly reactive calcium complexes reported in this paper react readily with all of these substrates to generate excellent yields of the corresponding organocalcium compounds.

Highly reactive calcium was prepared by the lithium biphenylide reduction of calcium salts in THF. Both $CaBr_2$ and CaI_2 generated the reactive calcium species. The organocalcium compounds, prepared directly from this calcium complex and organic halides, were found to efficiently undergo Grignard-type reactions. Table I summarizes some examples of our 1,2-addition reactions with cyclohexanone utilizing the reactive calcium. Alkyl bromides and alkyl chlorides rapidly reacted with the calcium complex at temperatures as low as −78 °C. As shown in Table I, 1-bromooctane and 1-bromo-3-phenoxypropane reacted with the calcium complex at −78 °C to form the corresponding alkylbromocalcium reagents which underwent Grignard-type reactions with cyclohexanone to produce the tertiary alcohols in 79% and 75% yields, respectively. Oxidative addition of alkyl chlorides to this calcium species was also very efficient at low temperature (−78 °C). 1-Chlorooctane gave 1-octylcyclohexanol in 83% yield. Similar results were noted for the secondary halides. Bromocyclohexane reacted readily with the calcium species at −78 °C, and the resulting organocalcium reagent underwent carbonyl addition to give the alcohol in 75% yield. Significantly, the highly reactive calcium complex reacted rapidly with tertiary bromides at −78 °C. For example, the Grignard-type reaction for 1-bromoadmantane utilizing the reactive calcium afforded 1-(1-admantyl)cyclohexanol in 80% yield. The direct reaction of 1-bromoadamantane with metals is well known to yield mainly reductive cleavage or dimerization.[6] Ac-

(1) Xiong, H.; Rieke, R. D. *J. Org. Chem.* **1989**, *54*, 3247.
(2) (a) Freeman, P. K.; Hutchinson, L. L. *J. Org. Chem.* **1983**, *48*, 879. (b) Raston, C. L.; Salem, G. *J. Chem. Soc., Chem. Commun.* **1984**, 1702. (c) Harvey, S.; Junk, P. C.; Raston, C. L.; Salem, G. *J. Org. Chem.* **1988**, *53*, 3134. (d) Bogdanovic, B. *Acc. Chem. Res.* **1988**, *21*, 261.
(3) Lindsell, W. E. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergoman Press: Oxford, 1982; Vol. 1, Chapter 4, pp 223–252.
(4) (a) Kawabata, N.; Matsumura, A.; Yamashita, S. *Tetrahedron* **1973**, *29*, 1069. (b) Kawabata, M.; Matsumura, A.; Yamashita, S. *J. Org. Chem.* **1973**, *38*, 4268.
(5) (a) Gowenlock, B. G.; Lindsell, W. E. *J. Organomet. Chem. Library, Organomet. Chem. Rev.* **1977**, *3*, 1. (b) Bogatskii, A. V.; Chumachenko, T. K.; Derkach-Kozkukhova, A. E.; Lyamtseva, L. N.; Suprinovich, E. S. *Zh. Obshch. Khim.* **1977**, *47*, 2297.

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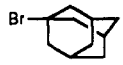
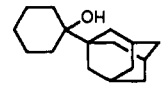
Table I. Grignard-Type Reactions of Organocalcium Reagents with Cyclohexanone

entry	halide	CaX_2[a]	product[b]	% yield[c]
1	$Cl(CH_2)_7CH_3$	CaI_2	$1\text{-}(CH_2)_7CH_3\text{-}1\text{-}OH\text{-}c\text{-}C_6H_{10}$	83
2	$Br(CH_2)_7CH_3$	CaI_2	$1\text{-}(CH_2)_7CH_3\text{-}1\text{-}OH\text{-}c\text{-}C_6H_{10}$	79
3	$Br(CH_2)_3OPh$	$CaBr_2$	$1\text{-}(CH_2)_3OPh\text{-}1\text{-}OH\text{-}c\text{-}C_6H_{10}$	75
4	$Br\text{-}c\text{-}C_6H_{11}$	$CaBr_2$	$1\text{-}c\text{-}C_6H_{11}\text{-}1\text{-}OH\text{-}c\text{-}C_6H_{10}$	75
5		$CaBr_2$		80
6	$BrC_6H_4(m\text{-}CH_3)$	CaI_2	$1\text{-}C_6H_4(m\text{-}CH_3)\text{-}1\text{-}OH\text{-}c\text{-}C_6H_{10}$	76
7	$ClC_6H_4(p\text{-}CH_3)$	CaI_2	$1\text{-}C_6H_4(p\text{-}CH_3)\text{-}1\text{-}OH\text{-}c\text{-}C_6H_{10}$	86
8	FPh	CaI_2	$1\text{-}Ph\text{-}1\text{-}OH\text{-}c\text{-}C_6H_{10}$	85
9	$BrC_6H_4(m\text{-}OCH_3)$	$CaBr_2$	$1\text{-}C_6H_4(m\text{-}OCH_3)\text{-}1\text{-}OH\text{-}c\text{-}C_6H_{10}$	79

[a] Both $CaBr_2$ and CaI_2 generate the highly reactive calcium species. [b] All new substances have satisfactory spectroscopic data including IR, ^1H NMR, ^{13}C NMR, and high-resolution mass spectral data. [c] Isolated yields.

cordingly, this method represents a significant new approach to the 1-metalloadamantane.

Reactions of aryl halides with reactive calcium required slightly higher temperatures, up to −30 °C for aryl bromides and up to −20 °C for aryl chlorides. The aryl calcium compounds are very stable at room temperature. Reactions of *m*-bromotoluene, *m*-bromoanisole, and *p*-chlorotoluene with the activated calcium complex gave the corresponding arylcalcium reagents in quantitative yields based on the GC analyses of reaction quenches. As expected, 1,2-addition of these arylcalcium compounds with ketones gave the alcohols in excellent yields (76%, 79%, and 86%, respectively). Surprisingly, the activated calcium readily reacted with fluorobenzene at room temperature to form the corresponding organometallic compound which underwent an addition reaction with cyclohexanone to give 1-phenylcyclohexanol in 85% yield. Except for highly reactive magnesium prepared by the reduction of magnesium salts,[7] few metals undergo oxidative addition with aryl fluorides to form organometallic compounds.[8] The active calcium species also reacts rapidly with allylic halides; however, the resulting allylcalcium reagent rapidly homocouples with starting allylic halides.

Preparation and Reactions of Calcium Cuprate Reagents. While a wide spectrum of different metal cuprates are known, calcium cuprates have not yet been reported. Addition of copper(I) salts to the organocalcium compounds resulted in a new complex of vastly different chemical reactivity. Presumably, this new complex is a calcium cuprate. Reaction of the organocalcium reagent prepared from an organic halide and the highly reactive calcium, with benzoyl chloride in the absence of a Cu(I) salt, afforded a complex mixture of products. However, in the presence of a Cu(I) salt, high yields of ketone formation were observed. Table II presents some of the ketone formation reactions of the calcium cuprates with benzoyl chloride.

A soluble copper(I) complex, CuCN·2LiBr,[9] was used for the transmetalations with organocalcium reagents to form the assumed copper calcium complexes. Reaction of these calcium cuprate reagents with benzoyl chloride proceeded smoothly at −35 °C to yield ketones in excellent yields. As shown in Table II, the primary alkylcalcium cuprates, *n*-octyl- and (5-phenoxypentyl)calcium cuprate, reacted rapidly with benzoyl chloride at −35 °C to give 1-phenyl-1-nonanone and 1-phenyl-6-phenoxy-1-hexanone in 84% and 76% yield, respectively. The secondary alkylcalcium cuprate, cyclohexyl calcium cuprate, reacted smoothly with benzoyl chloride to form cyclohexylphenylmethanone in 82% yield. Although the tertiary alkylcalcium cuprate was not investigated, it should undergo this transformation. In the aryl cases, 4-methylphenyl and 4-methoxyphenyl cuprate, for example, also reacted with benzoyl chloride to afford (4-methylphenyl)phenylmethanone and (4-methoxyphenyl)-phenylmethanone in 86% and 71% yield, respectively.

Table II. Cross-Coupling Reactions of Calcium Organocuprate Reagents with Benzoyl Chloride[a]

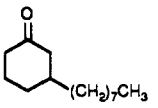
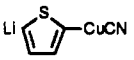
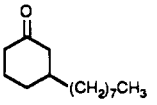
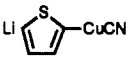
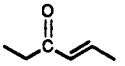
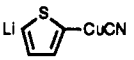
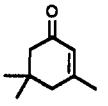
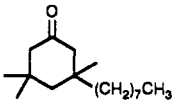
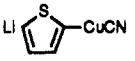
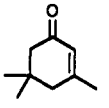
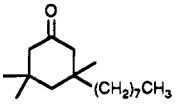
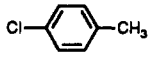
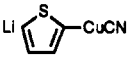
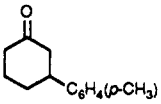
entry	halide	product[b]	% yield[c]
1	$Cl(CH_2)_7CH_3$	$PhC(O)(CH_2)_7CH_3$	84
2	$Br(CH_2)_5OPh$	$PhC(O)(CH_2)_5OPh$	76
3	$Br\text{-}c\text{-}C_6H_{11}$	$PhC(O)\text{-}c\text{-}C_6H_{11}$	82
4	$1\text{-}Cl\text{-}4\text{-}CH_3C_6H_4$	$1\text{-}PhC(O)\text{-}4\text{-}CH_3C_6H_4$	86
5	$1\text{-}Br\text{-}4\text{-}OCH_3C_6H_4$	$1\text{-}PhC(O)\text{-}4\text{-}OCH_3C_6H_4$	71

[a] Active calcium was prepared by the lithium biphenylide reduction of $CaBr_2$ in THF. CuCN·2LiBr was used for transmetalation with organocalcium reagents. [b] Most products were compared with authentic samples. The new substance, 1-phenyl-6-phenoxy-1-hexanone, has satisfactory IR, ^1H NMR, ^{13}C NMR, and high-resolution mass spectral data. [c] Isolated yields.

As expected, these calcium cuprate compounds also undergo the conjugate 1,4-addition reactions with α,β-unsaturated ketones. Table III presents some examples of conjugate 1,4-addition reactions utilizing these calcium cuprates. In the first case, *n*-octylcalcium cuprate, generated by transmetalation of the *n*-octanocalcium compound with CuCN·2LiBr, reacted with 2-cyclohexenone to give 3-octylcyclohexanone in moderate yield (42% yield). However, a more reactive calcium cuprate species was produced and the yield was greatly improved to 87% when lithium 2-thienylcyanocuprate[10] was used. This cuprate also underwent the conjugate addition with acyclic enones, e.g. 2-hexen-4-one, to give 5-methyl-3-tridecanone in 47% yield. We have not attempted further optimization at this time. Reaction of this calcium cuprate with a sterically hindered enone, for example isophorone, produced less than 3% of the desired compound in 24 h. The isolated yield, however, increased to 84% when the additives BF_3 etherate and chlorotrimethylsilane[11] were used. In the aryl case, *p*-tolylcalcium cuprate also underwent this transformation with 2-cyclohexenone to give 3-(*p*-methyl-

(6) Dubois, J. E.; Bauer, P.; Molle, G.; Daza, J. *C. R. Acad. Sci. Ser. 3* **1977**, *284*, 145.
(7) Rieke, R. D.; Bales, S. E. *J. Am. Chem. Soc.* **1974**, *96*, 1775.
(8) Yu, S. H.; Ashby, E. C. *J. Org. Chem.* **1971**, *36*, 2123 and references cited therein.
(9) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.
(10) Lithium 2-thienylcyanocuprate was purchased from Aldrich Chemical Co. Lipshutz, B. H.; Koerner, M.; Parker, D. A. *Tetrahedron Lett.* **1987**, *28*, 945.
(11) (a) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6019. (b) Alexakis, A.; Berlan, J.; Besace, Y. *Tetrahedron Lett.* **1986**, *27*, 1047.

Table III. Conjugate 1,4-Addition Reactions of Calcium Organocuprate Reagents with Enones

entry	halide	Cu(I) salt	enone	product[a]	% yield[b]
1	$Cl(CH_2)_7CH_3$	CuCN·2LiBr			46
2	$Cl(CH_2)_7CH_3$				87
3	$Cl(CH_2)_7CH_3$			$EtC(O)CH_2CH(CH_3)(CH_2)_7CH_3$	47
4	$Cl(CH_2)_7CH_3$				<3
5	$Cl(CH_2)_7CH_3$	 + TMSCl & BF_3·OEt_2			84
6					68

[a] Most products were compared with authentic samples. The new substance, 3-(*p*-methylphenyl)cyclohexanone, has satisfactory IR, ^1H NMR, ^{13}C NMR, and high-resolution mass spectral data. [b] Isolated yields.

phenyl)cyclohexanone in reasonable yield (Table III). The scope and limitation for the application of these calcium cuprate reagents in the organic synthesis are currently under investigation.

Preparation and Reactions of Calcium Metallocycle. Although magnesium complexes of 1,3-dienes prepared from magnesium and 1,3-dienes have received considerable attention in organometallic syntheses,[12] the corresponding calcium complexes of 1,3-dienes have not yet been reported. We have observed that the calcium complexes can readily be prepared by reaction of the highly reactive calcium with a wide variety of 1,3-dienes. The resulting bis-organocalcium reagents were found to readily undergo alkylation reactions with a variety of electrophiles in a highly regio- and stereospecific manner (Table IV).

The reactivity of the calcium metallocycles was higher than that of the corresponding magnesium analogues. In the 1,4-diphenyl-1,3-butadiene cases, the chemical yields were excellent and generally were higher than the corresponding magnesium analogues. For example, 1,4-diphenyl-1,3-butadiene/calcium complex reacted rapidly with 1,3-dibromopropane and 1,4-dibromobutane to form *trans*-1-phenyl-2-*trans*-β-styrenylcyclopentane and *trans*-1-phenyl-2-*trans*-β-styrenylcyclohexane in 91% and 53% isolated yield, respectively. The stereochemistry of these reactions was always stereospecific.

The observed regiochemistry was basically the same as that reported for magnesium. Reaction of (1,4-diphenyl-2-butene-1,4-diyl)calcium complexes with α,ω-alkylene dihalides usually gave 1,2-addition products while 1,4-addition was always observed in reactions with dichlorosilane. In contrast to the magnesium complex, treatment of (1,4-diphenyl-2-butene-1,4-diyl)calcium complex with 1,2-dibromoethane yielded 7% of the 1,4-addition product, *cis*-3,6-diphenylcyclohexene,[13] along with 72% of the starting material. The yield of the 6-membered ring product was increased to 80%, and the amount of recovered starting material dropped to 8% when 1,2-dichloroethane was used. The higher reduction potential of 1,2-dichloroethane presumably eliminated most of the simple electron transfer pathway. Interestingly, reaction of this calcium complex with dichloromethane afforded only the 1,2-addition product, *trans*-1-phenyl-2-*trans*-β-styrenylcyclopropane,[14] in 47% yield along with 43% of 1,4-diphenyl-1,3-butadiene.

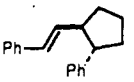
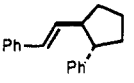
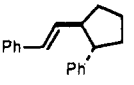
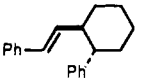
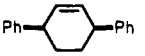
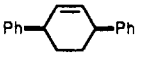
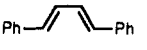
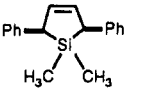
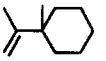
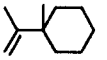
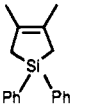
Reduction of 1,4-diphenyl-1,3-butadiene with 2.2 equiv of preformed lithium naphthalenide without the presence of Ca(II) salt, followed by the addition of 1,3-dibromopropane, also yielded the same cyclopentane derivative, but the yield was substantially lower than that obtained in the presence of calcium salts. Also of note is the fact that in the absence of calcium salts over 30% of the starting material was recovered. It is possible that electron transfer from the butadiene dianions to the organic halides was facilitated in the absence of calcium salts, and these resulting radicals and/or anions did not efficiently add to the 1,3-diene. A similar result was also noted in the nonactivated diene system. The yield dramatically decreased from 94% to 25% in the similar experiments using 2,3-dimethyl-1,3-butadiene with 1,3-dichloropropane. In any event, the observed chemistry is dramatically different when the calcium salts are present. Direct reduction of the 1,3-dienes with lithium metal in the absence of electron carriers was also carried out. Reduction of 1,4-diphenyl-

(12) (a) Erker, G.; Kruger, C.; Muller, G. *Adv. Organomet. Chem.* **1985**, *24*, 1. (b) Yasuda, H.; Tasumi, K.; Nakamura, A. *Acc. Chem. Res.* **1985**, *18*, 120. (c) Walther, D.; Pfuetrenreuter, C. *Naturwiss. Reih.* **1985**, *34*, 789.

(13) The stereochemistry of 3,6-diphenylcyclohexane was identified by converting the cyclohexene to 1,2-cyclohexanediol via the epoxide (See Experimental Section for details). Treatment of 3,6-diphenylcyclohex-1-ene with *m*-chloroperbenzoic acid in the presence of K_2CO_3 in CH_2Cl_2 gave only a single product in 60% yield along with 20% of recovered starting material. The fully decoupled ^{13}C NMR spectrum gave only seven peaks which unambiguously proved that two phenyl groups were in cis geometry. Reaction of the epoxide with 6% $HClO_4$ in acetone yielded 1,4-diphenylcyclohexane-2,3-diol in 93% yield. The proton spin–spin coupling constants further verified that the two phenyl groups were cis.

(14) Lomonosov, M. V. *Zhurnal Organicheskoi Khimii* **1977**, *13*, 63.

Table IV. Reactions of 1,3-Diene/Calcium Complex with Organic Dihalides[a]

entry	diene	Li/Ar	CaX_2	electrophile	product[b]	% yield[c]
1		Li/Biph	CaI_2	$Br(CH_2)_3Br$		91
2		Li/Np	-	$Br(CH_2)_3Br$		51[d]
3		Li/-	CaI_2	$Br(CH_2)_3Br$		74[e]
4		Li/Biph	CaI_2	$Br(CH_2)_4Br$		53
5		Li/Biph	CaI_2	$Br(CH_2)_2Br$		7[f]
6		Li/Biph	CaI_2	$Cl(CH_2)_2Cl$		80[g]
7		Li/Biph	CaI_2	$ClCH_2Cl$		47[h]
8		Li/Biph	CaI_2	$(CH_3)_2SiCl_2$		-[i]
9		Li/Biph	CaI_2	$Cl(CH_2)_3Cl$		(98)[j]
10		Li/Biph	-	$Cl(CH_2)_3Cl$		(25)
11		Li/Biph	CaI_2	$Cl(CH_2)_4Cl$		(36)[j]
12		Li/Biph	CaI_2	$Br(CH_2)_4Br$		(54)[j]
13		Li/Biph	CaI_2	Ph_2SiCl_2		(89)[k]

[a] The active calcium was prepared from 2.05 equiv of preformed lithium biphenylide and 1.0 equiv of CaI_2. [b] The known products were compared with the authentic sample. All new substances have satisfactory spectroscopic data including IR, ^1H NMR, ^{13}C NMR, and high-resolution mass spectral data. [c] Isolated yields. GC yields are given in parentheses. [d] 31% starting material was recovered. [e] No starting material was recovered. [f] 72% starting material was recovered. [g] 8% starting material was recovered. [h] 43% starting material was recovered. [i] Isolation was difficult because of overlapping with biphenyl. [j] Product was isolated by distillation. [k] Product was isolated by reverse-phase thin-layer chromatography.

1,3-butadiene with 2.5 equiv of lithium metal in THF, followed by the sequential addition of 2.0 equiv of CaI_2 and 1,3-dibromopropane, yielded the same 5-membered ring product in 74% yield along with a small amount of unidentified high molecular weight material. Significantly, no starting material was found in the reaction workup. While the exact structures of the organometallic species involved have not yet been determined, the requirement and involvment of calcium ions is unequivocal. The crystal structure of the magnesium analogue of the 1,4-diphenyl-1,3-butadiene complex has been reported.[15] Crystallization and spectroscopic studies are underway to fully establish the structures of these calcium/diene complexes.

This chemistry can also be extended to 2,3-dimethyl-1,3-butadiene, which is a molecule that is much more difficult to reduce. The calcium complex was readily prepared by reacting freshly distilled 2,3-dimethyl-1,3-butadiene with either the biphenylide complex or the calcium naphthalenide complex. Reaction of the resulting complex with 1,3-dichloropropane and 1,4-dichlorobutane gave the 5-membered ring product and 6-membered ring product in 94% and 36% yield, respectively. For the latter reaction, the yield was improved to 54% when 1,4-dibromobutane was used. The regiochemistry of the 2,3-dimethyl-1,3-butadiene/calcium complexes again paralleled that of the corresponding magnesium complexes. Similarly, treatment of (2,3-dimethyl-2-butene-1,4-diyl)-calcium complex with dichlorodiphenylsilane yielded the 1,4-addition adduct in 89% yield. Efforts to effect stepwise electrophilic additions to 2,3-dimethyl-1,3-butadiene/calcium complex with two different electrophiles are currently underway.

In summary, a highly reactive form of calcium has been prepared by the lithium biphenylide or lithium naphthalenide reduction of calcium salts. This calcium will rapidly undergo an effective oxidative addition reaction with alkyl or aryl halides to yield the corresponding or-

(15) The molecular formula in the solid state is $Mg(THF)_3$(*s-cis*-PhCH=CHCH=CHPh). Kai, Y.; Kanehisa, N.; Miki, K.; Kasai, N.; Mashima, K.; Yasuda, H.; Nakamura, A. *Chem. Lett.* **1982**, 1277.

ganocalcium compounds. These organocalcium compounds have been found to undergo Grignard-type additions to ketones. Addition of copper(I) salts leads to new complexes which are presumed to be the corresponding calcium cuprates. These calcium cuprates will undergo clean cross-coupling with acid chlorides to generate ketones as well as undergo conjugate 1,4-additions to α,β-unsaturated ketones. The activated calcium will react with 1,3-dienes to yield (2-butene-1,4-diyl)calcium complexes. These bis-organocalcium reagents can undergo dialkylation reactions with α,ω-alkylene dihalides and dichlorosilanes to form 3-, 5-, and 6-membered ring derivatives. Significantly, these reactions are stereospecific and are highly regioselective. Studies to delineate the synthetic significance of organocalcium reagents generated by this approach are currently underway.

Experimental Section

Melting points were determined on a Thomas-Hoover melting point apparatus or an Electrothermal melting point apparatus and are corrected. IR spectra were taken on an Analect RFX-30 FTIR spectrophotometer neat between NaCl or KBr plates or as KBr disks. ^{1}H NMR spectra were recorded on a Nicolet NT-360 (360 MHz) or on a Varian VXR-200 (200 MHz) spectrometer. All chemical shifts are reported in parts per million (δ) downfield from internal tetramethylsilane. Fully decoupled ^{13}C NMR spectra and DEPT experiments were recorded on a Varian VXR-200 (50 MHz) spectrometer. The center peak of $CDCl_3$ (77.0 ppm) was used as the internal reference. Two-dimensional COSY spectra were recorded on a Nicolet NT-360 (360 MHz) spectrophotometer. High-resolution mass spectra were performed by the Midwest Center for Mass Spectrometry at the University of Nebraska–Lincoln using a Kratos MS-80 mass spectrometer. Elemental analyses were performed by Oneida Research Services, Inc., Whitesboro, NY. Gas chromatography analysis was done on a Hewlett-Packard 5890A chromatograph using stainless steel columns (12 ft × $^1/_8$ in.) packed with OV-17 (3%) on 100/120 Chromosorb G-AW or SE-30 (5%) on 100/120 Chromosorb G-NAW. Analytical thin-layer chromatography was performed using Merck 5735 (0.2 mm thickness) indicating plates. Preparative thin-layer separations were performed using Analtech silica gel GF (1 or 2 mm thickness) preparative plates or using Whatman PLKC 18F linear-K reversed phase (1 mm thickness) preparative plates. Low-temperature reactions were performed utilizing a Neslab endocal ULT-80 refrigerated circulating bath or utilizing dry ice/acetone baths. All manipulations were carried out on a dual manifold vacuum/argon system. The Linde prepurified grade argon was further purified by passing it through a 150 °C catalyst column (BASF R3-11), a phosphorus pentoxide column, and a column of granular potassium hydroxide. Lithium and naphthalene were weighed out and charged into reaction flasks under argon in a Vacuum Atmospheres Co. drybox. Tetrahydrofuran was freshly distilled under argon from sodium/potassium alloy. Anhydrous calcium(II) iodide and calcium(II) bromide were purchased from Cerac, Inc. 2,3-Dimethyl-1,3-butadiene was distilled prior to use. Other commercially available reagents were used as received unless specially noted.

Typical Procedure for Preparation of Active Calcium. Lithium (9.0 mmol) and biphenyl (9.8 mmol) in freshly distilled THF (20 mL) were stirred under argon until the lithium was completely consumed (ca. 2 h). To a well-suspended solution of CaI_2 or $CaBr_2$ in freshly distilled THF (20 mL), the preformed lithium biphenylide was transferred via a cannula at room temperature. The reaction mixture was stirred for 1 h at room temperature prior to use. [Note: Excess calcium salt was used in the oxidative addition reactions with organic halides. Details are described later in this section.]

Typical Grignard-Type Reaction. Activated calcium (3.07 mmol), prepared from lithium biphenylide (6.15 mmol) and excess CaI_2 (4.91 mmol) in THF (30 mL), was cooled to −78 °C. The color turned green upon cooling. *p*-Chlorotoluene (324 mg, 2.56 mmol) was added via a disposable syringe at −78 °C, and the reaction mixture was allowed to warm to −20 °C and stirred at −20 °C for 30 min. The reaction mixture was cooled back to −35 °C, and excess cyclohexanone (510 mg, 5.20 mmol) was added via a disposable syringe at −35 °C. The resulting mixture was gradually warmed to room temperature and was stirred at room temperature for 30 min. The reaction mixture was recooled to −35 °C and neutral H_2O (20 mL) was added at −35 °C. After being warmed to room temperature, the reaction mixture was filtered through a small pad of Celite and was washed with Et_2O (50 mL). The aqueous layer was extracted with Et_2O (3 × 30 mL), and the combined organic phases were washed with H_2O (15 mL) and dried over anhydrous $MgSO_4$. Removal of solvent and flash-column chromatography on silica gel (100 g, 230–400 mesh, eluted sequentially with 20:1 hexanes/EtOAc, 15:1 hexanes/EtOAc, 10:1 hexanes/EtOAc) afforded 1-(*p*-methylphenyl)cyclohexanol (417 mg, 86% yield) as white crystals:[16] mp 53–55 °C; IR (KBr) 3419, 3030, 2935, 2843, 1514, 1446, 1392, 1134, 1036, 964, 810 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.35–7.45 (m, 2 H), 7.10–7.20 (m, 2 H), 2.33 (s, 3 H), 1.55–1.85 (m, 11 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 146.5, 136.2, 128.9, 124.5, 72.9, 38.9, 25.5, 22.2, 20.9.

1-Octylcyclohexanol[17] (83% yield): IR (neat) 3379, 2929, 2856, 1448, 1259, 968 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.15–1.65 (m, 25 H), 0.88 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 71.4, 42.5, 37.5, 31.9, 30.3, 29.6, 29.3, 25.9, 22.9, 22.7, 22.3, 14.1; MS (EI) m/e (relative intensity) 212 (M^+, 1.2), 194 (5.8), 183 (1.5), 169 (23.5), 141 (11.4), 127 (10.9), 109 (13.6), 99 (100.0), 81 (67.0); HRMS calcd for $C_{14}H_{28}O$ m/e 212.2140, found m/e 212.2137.

1-Phenylcyclohexanol (85% yield): mp 62–63 °C (lit.[18] mp 62–63 °C); IR (KBr) 3336, 3059, 3030, 1444, 1381, 1259, 1134, 1032, 974, 756, 696 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.20–7.55 (m, 5 H), 1.20–1.92 (m, 11 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.4, 128.2, 126.7, 124.6, 73.1, 38.8, 25.5, 22.2.

1-(*m*-Methylphenyl)cyclohexanol[19] (76% yield): IR (neat) 3406, 3024, 2931, 2856, 1606, 1446, 1259, 1167, 1132, 1036, 972, 783, 704 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.02–7.35 (m, 4 H), 2.36 (s, 3 H), 1.57–1.88 (m, 11 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.4, 137.7, 128.1, 127.4, 125.3, 121.6, 73.1, 38.8, 25.5, 22.2, 21.6.

1-Cyclohexylcyclohexanol[20] (75% yield): IR (KBr) 3469, 2929, 2850, 1446, 1254, 1165, 1132, 960 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.80–1.90 (m, 22 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 73.0, 48.2, 34.3, 26.9, 26.6, 26.5, 26.0, 21.9.

1-(3-Phenoxypropyl)cyclohexanol (75% yield): IR (neat) 3433, 2931, 2858, 1601, 1587, 1496, 1246, 754, 690 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.20–7.32 (m, 2 H), 6.84–6.97 (m, 3 H), 3.96 (t, 2 H, J = 6.3 Hz), 1.15–1.95 (m, 15 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 158.9, 129.3, 120.5, 114.5, 71.0, 68.3, 38.6, 37.4, 25.8, 23.0, 22.2; MS (EI) m/e (relative intensity) 234 (M^+, 1.4), 216 (0.7), 191 (1.2), 141 (52.5), 123 (32.1), 120 (34.7), 99 (42.0), 94 (90.9), 81 (100.0); HRMS calcd for $C_{15}H_{22}O_2$ m/e 234.1620, found m/e 234.1625. Anal. Calcd: C, 76.88; H, 9.46. Found: C, 76.57; H, 9.55.

1-(*m*-Methoxyphenyl)cyclohexanol[21] (79% yield): IR (neat) 3437, 2933, 2854, 1601, 1583, 1483, 1448, 1431, 1288, 1265, 1248, 1049, 781, 698 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.75–7.31 (m, 4 H), 3.81 (s, 3 H), 1.40–1.90 (m, 11 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 159.6, 151.3, 129.2, 117.0, 111.8, 110.7, 73.1, 55.2, 38.8, 25.5, 22.2.

1-(1-Admantyl)cyclohexanol (80% yield): mp 166–168 °C; IR (KBr) 3465, 2931, 2902, 2844, 1448, 1344, 980, 955, 935 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.95–2.05 (m, 26 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 74.6, 39.1, 37.3, 35.8, 29.8, 28.7, 26.0, 21.9; MS (EI) m/e (relative intensity) 234 (M^+, 0.2), 135 (26.0), 98 (100.0); HRMS calcd for $C_{16}H_{26}O$ m/e 234.1984, found m/e 234.1982. Anal. Calcd: C, 81.99; H, 11.18. Found: C, 82.13; H, 11.41.

Typical Ketone Formation Reaction. The organocalcium reagent (2.72 mmol) was prepared from *p*-chlorotoluene (344 mg, 2.72 mmol) and highly reactive calcium (3.15 mmol) as described above. CuCN·2LiBr in THF (10 mL) was added via a cannula at −35 °C, and the reaction mixture was stirred at −35 °C for 30 min. Benzoyl chloride (950 mg, 6.76 mmol) was added via a

(16) Known compound: IR, see *Sadtler* 36367; ^{1}H NMR, see *Sadtler* 21529; ^{13}C NMR, see *Sadtler* 5269.

(17) The spectral data are identical to the authentic sample which is prepared from Grignard reaction. Mukherjee, S. N.; Majee, R. N. *J. Inst. Chem.* **1981**, *53*, 300.

(18) Fieser, L. F.; Szmuszkovicz, J. *J. Am. Chem. Soc.* **1948**, *70*, 3352.

(19) Known compound: ^{1}H NMR, see *Sadtler* 33855.

(20) Signaigo, F. K.; Cramer, P. L. *J. Am. Chem. Soc.* **1933**, *55*, 3326.

(21) Askan, V.; Bailey, D. *J. Chem. Soc.* **1965**, 3872.

disposable syringe at −35 °C, and the resulting mixture was gradually warmed to room temperature. Saturated aqueous NH_4Cl solution (20 mL) was added at room temperature. The reaction mixture was then filtered through a small pad of Celite and was washed with Et_2O (50 mL). The aqueous layer was extracted with Et_2O (2 × 30 mL), and the combined organic phases were washed with H_2O (3 × 15 mL) and dried over anhydrous $MgSO_4$. Removal of solvent and flash column chromatography on silica gel (100 g, 230–400 mesh, eluted sequentially with 20:1 hexanes/EtOAc, 15:1 hexanes/EtOAc, and 10:1 hexanes/EtOAc) yielded (4-methylphenyl)phenylmethanone[22] (458 mg, 86% yield): IR (neat) 3058, 3027, 2921, 1658, 1606, 1446, 1317, 1278, 1178, 937, 924, 835, 787, 730, 700 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.24–7.82 (m, 9 H), 2.43 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 196.4, 143.2, 137.9, 134.8, 132.1, 130.3, 129.9, 128.9, 128.2, 21.6.

(4-Methoxyphenyl)phenylmethanone (71% yield): mp 60–61 °C (lit.[22] mp 60–61 °C); ^1H NMR (200 MHz, $CDCl_3$) δ 7.42–7.87 (m, 7 H), 6.92–7.01 (m, 2 H), 3.89 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 195.4, 163.2, 138.3, 132.5, 131.9, 130.2, 129.7, 128.2, 113.5, 55.5.

1-Phenyl-1-nonanone[23] (84% yield): ^1H NMR (200 MHz, $CDCl_3$) δ 7.90–8.02 (m, 2 H), 7.38–7.62 (m, 3 H), 2.96 (t, J = 7.4 Hz, 2 H), 1.14–1.74 (m, 12 H), 0.88 (t, J = 6.5 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 200.5, 137.2, 132.7, 128.5, 128.0, 38.6, 31.8, 29.4, 29.4, 29.1, 24.4, 22.6, 14.0.

1-Phenyl-6-phenoxy-1-hexanone (76% yield): mp 53.5–54.5 °C; IR (KBr) 3059, 2941, 2900, 2869, 1678, 1599, 1498, 1475, 1244, 752, 729, 687 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.92–8.00 (m, 2 H), 7.19–7.60 (m, 5 H), 6.84–6.98 (m, 3 H), 3.97 (t, J = 6.4 Hz, 2 H), 3.00 (t, J = 7.3 Hz, 2 H), 1.48–1.93 (m, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 200.2, 159.0, 137.0, 132.9, 129.4, 128.5, 128.0, 120.5, 114.4, 67.5, 38.4, 29.2, 25.8, 24.0; MS (EI) m/e (relative intensity) 268 (M^+, 3.2), 175 (45.3), 105 (100.0), 94 (20.3), 77 (30.0); HRMS calcd for $C_{18}H_{20}O_2$ m/e 268.1463, found m/e 268.1459. Anal. Calcd: C, 80.56; H, 7.51. Found: C, 80.63; H, 7.69.

Cyclohexylphenylmethanone[24] (82% yield): mp 54–56 °C; IR (KBr) 2927, 2850, 1668, 1595, 1577, 1444, 1252, 1209, 974, 703 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.90–8.00 (m, 2 H), 7.38–7.60 (m, 3 H), 3.16–3.35 (m, 1 H), 1.14–1.97 (m, 10 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 203.8, 136.3, 132.7, 128.5, 128.2, 45.6, 29.4, 25.9, 25.8.

Typical Conjugate 1,4-Addition Reaction. The organocalcium reagent (2.66 mmol) was prepared from 1-chlorooctane (395 mg, 2.66 mmol) and highly reactive calcium (3.10 mmol) as described above. Lithium 2-thienylcyanocuprate (0.25 M in THF, 14 mL, 3.50 mmol) was added via a syringe at −50 °C, and the reaction mixture was gradually warmed to −35 °C over a 30-min period. The reaction mixture was cooled back to −50 °C, and 2-cyclohexen-1-one (210 mg, 2.18 mmol) was added via a disposable syringe at −50 °C. The resulting mixture was gradually warmed to room temperature. Saturated aqueous NH_4Cl solution (20 mL) was added at room temperature. The reaction mixture was then filtered through a small pad of Celite and was washed with Et_2O (50 mL). The aqueous layer was extracted with Et_2O (2 × 30 mL), and the combined organic phases were washed with H_2O (3 × 15 mL) and dried over anhydrous $MgSO_4$. Removal of solvent and flash column chromatography on silica gel (70 g, 230–400 mesh, eluted sequentially with 50:1 hexanes/EtOAc and 10:1 hexanes/EtOAc) gave 3-octylcyclohexanone[23] (401 mg, 87% yield): IR (neat) 2954, 2925, 2854, 1714, 1458, 1225 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.10–2.50 (m, 23 H), 0.88 (t, J = 6.4 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.0, 48.2, 41.5, 39.1, 36.6, 31.8, 31.3, 29.7, 29.5, 29.2, 26.6, 25.3, 22.6, 14.1.

5-Methyl-3-tridecanone (42% yield): IR (neat) 2958, 2927, 2856, 1718, 1460, 1414, 1376 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.90–2.47 (m, 5 H), 1.10–1.40 (m, 14 H), 1.04 (t, J = 7.3 Hz, 3 H), 0.88 (t, J = 6.4 Hz, 3 H), 0.88 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.6, 49.9, 37.0, 36.4, 31.8, 29.7, 29.6, 29.3, 29.3, 26.9, 22.6, 19.8, 14.0, 7.7.

3-(*p*-Methylphenyl)cyclohexanone (70% yield): IR (neat) 3020, 2935, 2864, 1712, 1516, 1446, 1421, 1313, 1248, 1223, 806 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.01–7.32 (m, 4 H), 2.88–3.06 (m, 1 H), 2.32 (s, 3 H), 1.66–2.67 (m, 8 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 210.9, 141.4, 136.1, 129.3, 126.4, 49.0, 44.3, 41.1, 32.8, 25.5, 20.9; MS (EI) m/e (relative intensity) 188 (M^+, 60.8), 173 (4.4), 145 (19.8), 131 (100.0), 118 (31.1), 105 (14.9), 91 (13.5); HRMS calcd for $C_{13}H_{16}O$ m/e 188.1201, found m/e 188.1209. Anal. Calcd: C, 82.94; H, 8.57. Found: C, 82.83; H, 8.60.

3,5,5-Trimethyl-3-octylcyclohexanone[23] (84% yield): IR (neat) 2954, 2927, 2856, 1714, 1466, 1281, 1226 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.04–2.24 (m, 4 H), 1.63 (d, J = 14.2 Hz, 1 H), 1.49 (d, J = 14.2 Hz, 1 H), 1.16–1.38 (m, 14 H), 1.05 (s, 3 H), 1.04 (s, 3 H), 0.99 (s, 3 H), 0.88 (t, J = 6.5 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.5, 54.3, 53.2, 49.0, 44.8, 38.7, 36.0, 32.2, 31.8, 30.7, 30.3, 29.5, 29.3, 27.5, 23.7, 22.6, 14.1. Anal. Calcd for $C_{17}H_{32}O$: C, 80.89; H, 12.78. Found: C, 80.50; H, 12.80.

Typical Reaction of the Calcium Complex of 1,3-Diene. Highly reactive calcium (5.02 mmol) was prepared from CaI_2 (5.02 mmol) and lithium biphenylide (10.30 mmol) in THF (20 mL) as described above. To this calcium solution was added *trans,trans*-1,4-diphenyl-1,3-butadiene (0.863 g, 4.18 mmol) in THF (10 mL) at room temperature. (An internal standard *n*-dodecane was added with starting material for the GC analyses in the cases of 2,3-dimethyl-1,3-butadiene.) After being stirred at room temperature for 30 min, the reaction mixture was cooled to −78 °C and excess 1,3-dibromopropane (1.020 g, 5.05 mmol) was added via a disposable syringe at −78 °C. The reaction was monitored by GC (OV-17 column). (In the cases of 2,3-dimethyl-1,3-butadiene, GC yields were reported based on the analyses of reaction quenches by an OV-17 column.) The reaction mixture was gradually warmed to −60 °C and stirred at −60 °C for 1 h. Saturated NH_4Cl aqueous solution (20 mL) was then added to −40 °C. The reaction mixture was filtered through a small pad of Celite and was washed with Et_2O (30 mL). The aqueous layer was extracted with Et_2O (2 × 30 mL). The combined organic phases were washed with H_2O and brine and dried over anhydrous $MgSO_4$. Removal of solvent and flash column chromatography on silica gel (200 g, 230–400 mesh, eluted sequentially with hexanes and 1% Et_2O/hexanes) afforded *trans*-1-phenyl-2-*trans*-β-styrenylcyclopentane[1] (940 mg, 91% yield): IR (neat) 3080, 3059, 3024, 2952, 2868, 1599, 1495, 1448, 964, 744, 694 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.01–7.33 (m, 10 H), 6.06–6.27 (m, 2 H), 2.57–2.88 (m, 2 H), 1.99–2.66 (m, 2 H), 1.55–1.95 (m, 4 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.5, 137.4, 133.5, 129.2, 128.4, 128.2, 127.5, 126.7, 126.0, 125.9, 52.7, 51.6, 35.0, 33.2, 24.2. Anal. Calcd for $C_{19}H_{20}$: C, 91.88; H, 8.12. Found: C, 91.87; H, 8.22.

***trans*-1-Phenyl-2-*trans*-β-styrenylcyclohexane**[1] (53% yield): IR (neat) 3082, 3059, 3026, 2924, 2850, 1601, 1495, 1446, 962, 744, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.02–7.30 (m, 10 H), 6.11 (d, J = 15.9 Hz, 1 H), 5.82–5.98 (m, 1 H), 2.28–2.47 (m, 2 H), 1.25–2.02 (m, 8 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 146.0, 138.0, 135.0, 128.8, 128.3, 128.2, 127.6, 126.6, 125.9 (2C), 50.6, 46.4, 35.4, 33.3, 26.7, 26.1. Anal. Calcd for $C_{20}H_{22}$: C, 91.55; H, 8.45. Found: C, 91.37; H, 8.10.

***cis*-3,6-Diphenyl-1-cyclohexene**[25] (80% yield): IR (neat) 3080, 3059, 3024, 2931, 2856, 1601, 1493, 1450, 754, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.16–7.36 (m, 10 H), 5.98 (d, J = 1.3 Hz, 2 H), 3.45–3.55 (m, 2 H), 1.87–2.07 (m, 2 H), 1.60–1.79 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 145.9, 131.1, 128.3, 127.9, 126.1, 41.2, 29.3; MS (EI) m/e (relative intensity) 234 (M^+, 15.4), 206 (2.7), 143 (10.8), 130 (100.0), 115 (25.3), 104 (24.8), 91 (21.1), 77 (6.3); HRMS calcd for $C_{18}H_{18}$ m/e 234.1409, found m/e 234.1409.

***trans*-1-Phenyl-2-*trans*-β-styrenylcyclopropane**[12] (47% yield): IR (neat) 3080, 3059, 3024, 2966, 2929, 1647, 1605, 1496, 1460, 1448, 958, 750, 739, 694 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.04–7.35 (m, 10 H), 6.47 (d, J = 15.8 Hz, 1 H), 5.90 (dd, J = 15.8, 8.6 Hz, 1 H), 2.03 (ddd, J = 8.8, 5.5, 4.3 Hz, 1 H), 1.82 (ddt, J = 8.6, 5.6, 4.3 Hz, 1 H), 1.31 (dt, J = 8.5, 5.4 Hz, 1 H), 1.21 (dt, J = 8.8, 5.4 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 142.1, 137.5, 132.8, 128.5 (2C), 128.4, 128.2, 126.8, 125.7 (2C), 27.4, 25.7, 17.1; MS (EI) m/e (relative intensity) 220 (M^+, 30.6), 142 (8.0), 129 (100.0), 115 (25.1), 103 (3.6), 91 (28.8), 77 (9.5); HRMS calcd for

(22) Nishida, S. *J. Org. Chem.* **1967**, *32*, 2692.
(23) Wehmeyer, R. M., Ph.D. Dissertation, University of Nebraska, Lincoln, Nebraska, 1988.
(24) The spectral data are identical to the authentic sample. Commercially available compound (from Aldrich) has mp = 55–57 °C.
(25) Mandrou, A.-M.; Potin, P.; Wylde-Lachazette, R. *Bull. Soc. Chim. Fr.* **1962**, 1546.

$C_{17}H_{16}$ m/e 220.1252, found m/e 220.1252.

***cis*-1,1-Dimethyl-2,5-diphenylsilacyclopent-3-ene:**[1] IR (neat) 3078, 3059, 3020, 2954, 2895, 2850, 1599, 1495, 1250, 1061, 858, 802, 746, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.00–7.30 (m, 10 H), 6.11 (s, 2 H), 3.27 (s, 2 H), 0.39 (s, 3 H), –0.67 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 143.4, 135.0, 128.3, 126.4, 124.3, 39.9, –2.8, –6.8.

1,1-Diphenyl-3,4-dimethylsilacyclopent-3-ene[26] (89% GC yield): IR (neat) 3066, 3049, 2976, 2906, 2871, 1427, 1174, 1117, 773, 731, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.27–7.62 (m, 10 H), 1.87 (s, 4 H), 1.77 (s, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 136.4, 134.7, 130.7, 129.3, 127.8, 24.2, 19.3.

1-Methyl-1-(2-propenyl)cyclopentane[1] (94% GC yield): IR (neat) 2958, 2871, 1639, 1452, 1369, 889 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.65–4.73 (m, 2 H), 1.76 (dd, J = 1.3, 0.7 Hz, 3 H), 1.35–1.73 (m, 8 H), 1.05 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 153.3, 107.6, 48.0, 37.7, 26.0, 23.7, 20.2.

1-Methyl-1-(2-propenyl)cyclohexane[1] (54% GC yield): ^1H NMR (200 MHz, $CDCl_3$) δ 4.72–4.82 (m, 2 H), 1.71 (dd, J = 1.4, 0.7 Hz, 3 H), 1.20–1.75 (m, 10 H), 0.98 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 152.6, 109.1, 38.8, 36.4, 27.1, 26.4, 22.6, 19.5.

1,2-Epoxy-3,6-diphenylcyclohexane. 3,6-Diphenylcyclohexene (50 mg, 0.21 mmol), *m*-chloroperbenzoic acid (55%, 200 mg, 0.64 mmol), and K_2CO_3 (150 mg, 1.09 mmol) were stirred in CH_2Cl_2 (10 mL) for 24 h. The reaction mixture was filtered and washed with CH_2Cl_2 (40 mL). The filtrate and aqueous $Na_2S_2O_3$ solution (10%, 10 mL) were stirred for 2 h. The organic phase was washed with saturated $NaHCO_3$ solution and H_2O and dried over anhydrous magnesium sulfate. Preparative thin-layer chromatography (silica gel, 2 mm, developed with 10:1 hexane-/EtOAc) gave 1,2-epoxy-3,6-diphenylcyclohexane (32 mg, 60% yield) as a colorless oil along with recovery of starting material (10 mg, 20%). 1,2-Epoxy-3,6-diphenylcyclohexane:[25] ^1H NMR (200 MHz, $CDCl_3$) δ 7.20–7.45 (m, 10 H), 3.45 (s, 2 H), 3.37 (t, J = 6.4 Hz, 2 H), 1.67–1.88 (m, 2 H), 1.37–1.58 (m, 2 H); ^{13}C NMR (50 MHz) δ 143.2, 128.6, 128.0, 126.5, 56.2, 39.9, 25.0.

3,6-Diphenylcyclohexane-1,2-diol. 1,2-Epoxy-3,6-diphenylcyclohexane (32 mg, 0.13 mmol) was dissolved in acetone (10 mL). $HClO_4$ (6%, 10 mL) was added, and the mixture was stirred at room temperature for 24 h. The reaction solution was neutralized with Na_2CO_3, and the reaction mixture was reduced to approximately half volume under reduced pressure. Extraction with CH_2Cl_2 and removal of the solvent yielded crude product (93% yield) as a white solid. Based upon the analyses of NMR spectra of crude and recrystallized product, reaction gave a single product. Recrystallization from hexane/CH_2Cl_2 gave pure product as a white crystalline solid: mp 134–135 °C; IR (KBr) 3303, 3086, 3059, 3026, 2935, 2858, 1603, 1495, 1454, 1041, 760, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.20–7.60 (m, 10 H), 4.08 (t, J = 9.8 Hz, 1 H), 3.95 (dd, J = 9.5, 5.5 Hz, 1 H), 3.56 (m, 1 H), 2.67 (ddd, J = 11.7, 9.9, 4.3 Hz, 1 H), 1.65–2.39 (m, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 142.3, 140.8, 129.7, 128.8, 128.4, 127.8, 126.9, 126.5, 76.8, 74.6, 50.6, 44.7, 29.9, 29.2; MS (EI) m/e (relative intensity) 268 (M^+, 61.9), 250 (12.9), 237 (11.5), 219 (7.3), 146 (30.1), 131 (94.9), 117 (55.4), 104 (100.0), 91 (73.6), 77 (15.3); HRMS calcd for $C_{18}H_{20}O_2$ m/e 268.1463, found m/e 268.1464.

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(26) Filleux-Blanchard, M. L.; An, N.-D.; Manuel, et G. *J. Organomet. Chem.* **1977**, *137*, 11.

Hydroboration. 87. Controlled and Sequential Hydroboration of Simple Representative Alkenes with Methylborane in Tetrahydrofuran. An Examination of the Directive Effects in the First and Second Stages of Hydroboration

Morris Srebnik,[1a] Thomas E. Cole,[1b] and Herbert C. Brown*

H. C. Brown and R. B. Wetherill Laboratories of Chemistry, Purdue University, West Lafayette, Indiana 47907

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Methylborane ($MeBH_2$), the simplest of the monoalkylboranes, possesses extraordinary hydroborating characteristics in tetrahydrofuran. In this solvent $MeBH_2$ selectively hydroborates all important classes of alkenes, hindered and nonhindered, to yield the methylalkylboranes MeRBH. These dialkylboranes are readily converted into and isolated as their borinic esters, MeRBOR′, which in turn can be transformed into methyl ketones, thus providing a simple and highly regio- and stereoselective synthesis of the latter. The addition of a second equivalent of another alkene to the methyalkylborane gives a sequential hydroboration product, MeR^AR^BB. This mixed trialkylborane is readily converted into the corresponding tertiary alcohol via carbonylation–oxidation. The ability to hydroborate an alkene in consecutive stages enables the regioselectivity of the first and second stages of hydroboration to be determined. Thus, the first hydroboration of 1-hexene gives a C-1/C-2 ratio of 98.5:1.5, similar to values obtained with 9-BBN and Sia_2BH. The second hydroboration of *cis*-4-methyl-2-pentene occurs with complete regioselectivity, i.e., 100:0, surpassing the values obtained with the two aforementioned hydroborating agents. $MeBH_2$ is the first example of a sterically nonhindered monoalkylborane capable of stepwise hydroborations of all classes of alkenes.

Investigation of the chemical properties of methylborane ($MeBH_2$) the simplest of the monoalkylboranes has been hampered by lack of suitable synthetic methodology. The method of preparing this compound has changed little over the years, employing the redistribution of trimethylborane—a highly pyrophoric gas—with diborane.[2] These routes are experimentally tedious, difficult to carry out on large-scale preparations, and give a mixture of products that must be carefully fractionated at low temperatures.

(1) (a) Present address: Department of Chemistry, The University of Toledo, Toledo, OH 43606-3390. (b) Present address: Department of Chemistry, San Diego State University, San Diego, CA 92182-0328.

(2) (a) Schlesinger, H. I.; Walker, A. O. *J. Am. Chem. Soc.* **1935**, *57*, 621. (b) Schlesinger, H. I.; Flodin, N. W.; Burg, A. B. *Ibid.* **1939**, *61*, 1078.

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