CDCl$_3$): δ 7.40–7.30 (8 H, m), 7.21 (2 H, t, J = 8 Hz), 6.70 (1 H, d, J = 8.4 Hz), 6.46 (1 H, dd, J = 8.4, 2.4 Hz), 6.29 (1 H, d, J = 2.4 Hz), 6.02 (1 H, s), 2.74 (2 H, t, J = 6 Hz), 2.32–2.23 (2 H, m), 2.16–2.07 (2 H, m). IR (CHCl$_3$): 3585, 1751, 1710, 1598, 1500, 1297 cm^{-1}. HRMS: calcd 384.1473, found 384.1487. Anal. Calcd for $C_{24}H_{20}N_2O_3$: C, 74.98; H, 5.24; N, 7.25. Found: C, 74.80; H, 5.26; N, 7.31.

Dienone–Phenol Rearrangement of Oxindole 28. The rearrangement of 80 mg (0.30 mmol) of the oxindole dienone **28** was carried out as described above for **7**. Column chromatography of the crude reaction mixture over silica gel using 2:1 chloroform–ethyl acetate gave 73 mg (91% yield) of pure, crystalline tetrahydronaphthol derivative **31**, mp 244–245 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.72 (1 H, br s), 7.20 (1 H, dt, J = 9.6, 1.0 Hz), 7.03–6.93 (3 H, m), 6.87 (1 H, d, J = 8.0 Hz), 6.61 (1 H, dd, J = 8.0, 2.5 Hz), 6.03 (1 H, d, J = 2.5 Hz), 4.93 (1 H, br s), 2.90–2.85 (2 H, m), 2.29–2.14 (2 H, m), 2.02–1.90 (2 H, m). Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.59; H, 5.98; N, 5.55.

Acknowledgment. Partial support of this work by Grant CA-18846, awarded by the National Cancer Institute, is gratefully acknowledged. K.K. thanks the University of Rochester for Sherman Clarke and Hooker Fellowships.

Organobis(cuprates): A New Class of Reagents and Method for Spiroannelation[1]

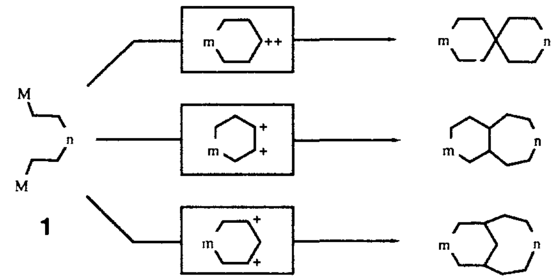
Paul A. Wender* and Alan W. White

Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. Received September 2, 1987

Abstract: A one-step spiroannelation method applicable to the synthesis of the commonly encountered spirocyclic systems is described. The method involves the reaction of 3-halocycloalk-2-enones with a new type of cuprate reagent prepared from organodilithium reagents and copper thiophenoxide and is shown to provide efficient access to spiro[4.4]nonanes, spiro[4.5]decanes, and spiro[5.5]undecanes. The effects of temperature, concentration, and halogen variations on the efficiency of this process are reported for the reactions of 3-halo-5,5-dimethylcyclohex-2-enones **2a–c** with 1,4-bis(CuSPhLi)butane (**3**). Under optimal conditions, chloroenone **2a** reacts with reagent **3** to provide 9,9-dimethylspiro[4.5]decan-7-one (**5**) in 96% yield. The optimized conditions are found to apply generally to variously substituted halocyclopentenones and halocyclohexenones, providing the corresponding spirocyclic products in 76–93% yield. The preparation of new dilithium reagents is also described along with their use in the spiroannelation procedure. The stability of the organobis(cuprates) is found to be influenced by the hybridization of the metal-bearing centers, with alkyl reagents more stable than alkenyl reagents.

Organodimetallic reagents **1** constitute a large and diverse class of important reactive intermediates.[2] From a theoretical and mechanistic viewpoint, these compounds provide the opportunity to study interactions between metal centers in a relatively controllable structural context and to explore how these interactions influence physical properties and reactivity.[2,3] In synthesis, such systems offer service as bis(nucleophiles),[4] by allowing in one operation for the formation of two bonds to a substrate bearing two electrophilic sites. Depending on the disposition of these electrophilic sites, access to spiro, fused, and bridged ring systems is possible (Scheme I). In a preliminary report on this subject,[1b] we described the preparation of the first members of a new class of organodimetallic reagents, the organobis(heterocuprates) (e.g., **3**),[5] in connection with the development of a fundamentally new spiroannelation method (eq 1). A major advantage and unique

Scheme I



---

(1) (a) Taken, in part, from: White, A. W. Ph.D. Dissertation, Harvard University, 1981. (b) For previous work, see: Wender, P. A.; Eck, S. L. *Tetrahedron Lett.* **1977**, 1245.

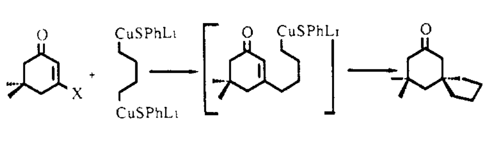
(2) Studies on organodimetallic compounds are extensively documented in current texts. For examples and lead references, see: (a) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. In *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987. (b) Wakefield, B. S. In *The Chemistry of Organolithium Compounds*; Pergamon: Oxford, 1974. (c) For an early review, see: Millar, I. T.; Heaney, H. *Q. Rev., Chem. Soc.* **1957**, *11*, 109.

(3) For lead references and recent representative studies, see: (a) Schleyer, P. v. R.; Kos, A. J.; Kaufman, E. *J. Am. Chem. Soc.* **1983**, *105*, 7617. (b) Negishi, E.-i.; Takahashi, T. *Ibid.* **1986**, *108*, 3402. (c) Brown, K. J.; Murdoch, J. R. *Ibid.* **1984**, *106*, 7843. (d) Bates, R. B.; Hess, B. A.; Ogle, C. A.; Schaad, L. J. *Ibid.* **1981**, *103*, 5052. (e) Agranat, I.; Skancke, A. *Ibid.* **1985**, *107*, 867. (f) Meyers, G. F.; Hall, M. B.; Chin, J. W.; Lagow, R. J. *Ibid.* **1985**, *107*, 1413. (g) Cotton, F. A.; Lahuerta, P.; Sanau, M.; Schwotzer, W. *Ibid.* **1985**, *107*, 8284. (h) Bors, D. A.; Streitweiser, A. *Ibid.* **1986**, *108*, 1397.

(4) For lead references and representative examples, see: (a) Bates, R. B.; Gordon, B.; Highsmith, T. K.; White, J. J. *J. Org. Chem.* **1984**, *49*, 2981. (b) Scott, F.; Mafunda, B. G.; Normant, J. F.; Alexakis, A. *Tetrahedron Lett.* **1983**, *24*, 5767. (c) Takahashi, S.; Suzuki, Y.; Sonogashira, K.; Hagihara, N. *J. Chem. Soc., Chem. Commun.* **1976**, 839. (d) Cabiddu, S.; Floris, C.; Melis, S. *Tetrahedron Lett.* **1986**, *27*, 4625. (e) Hylton, T.; Bockelheide, V. *J. Am. Chem. Soc.* **1968**, *90*, 6887. (f) Canonne, P.; Bernatchez, M. *J. Org. Chem.* **1986**, *51*, 2147. (g) Molander, G. A.; Shubert, D. C. *J. Am. Chem. Soc.* **1987**, *109*, 576.

(5) (a) The reagent structures given in this paper follow the convention established for the mono(cuprate) analogues[10] and do not necessarily reflect their structures in solution. For important discussions on the structures of mono(cuprates) and organodimetallic compounds, see: House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59. Ashby, E. C.; Noding, S. A. *J. Org. Chem.* **1979**, *44*, 4371. Schleyer, P. v. R.; Spitznagel, G. W.; Chandrasekhar, J. *Tetrahedron Lett.* **1986**, *27*, 4411; references 3 and 10 and studies cited therein. Related studies on this class of reagents include the following: (*b*) Cyclocuprates: Scott, F.; Mafunda, B. G.; Normant, J. F.; Alexakis, A. *Tetrahedron Lett.* **1983**, *24*, 5767. (c) A coupling process "apparently" proceeding via a bis(cuprate): (House, H. O.; Koepsel, D. G.; Campbell, W. J. *J. Org. Chem.* **1972**, *37*, 1003. Wittig, G.; Klar, G. *Justus Liebigs Ann. Chem.* **1967**, *704*, 91. Kauffmann, T.; Beissner, G.; Sahn, W.; Wottermann, *Angew. Chem., Int. Ed. Engl.* **1976**, *9*, 808. McLoughlin, J. C. R.; Thower, J. *Tetrahedron* **1969**, *25*, 5921. (d) Oxidative coupling of dilithium and dimagnesium reagents through a copper(I) ate complex: Whitesides, G. M.; San Filippo, J.; Casey, C. P.; Panek, E. J. *J. Am. Chem. Soc.* **1967**, *89*, 5302. (e) Copper-catalyzed Michael reactions of dimagnesium alkyls, e.g.: Schisla, R. M.; Hammann, W. C. *J. Org. Chem.* **1970**, *35*, 3224. Reaction of a copper phosphine complex of 1,4-dilithiobutane with CO: Schwartz, J. *Tetrahedron Lett.* **1972**, 2803.

0002-7863/88/1510-2218$01.50/0



(1)

2 3 4 5

a: X=Cl
b: X=Br
c: X=I

96% (X=Cl)

strategic feature[6] of this method is that the spiroannelation (cycloquaternization) of a secondary center is achieved in only one synthetic operation.[7] Alternative methods[6] to accomplish this overall process frequently require three distinct steps, involving sequential attachment of two groups to the secondary center in order to form the necessary quaternary center, and subsequent intramolecular bond formation between these groups to complete the ring. Two-operation strategies are less common but often more efficient and generally involve a process in which the group initially attached to the secondary center incorporates a second functionality that is subsequently activated and deployed for ring closure. The only single-operation strategy that has shown generality for the synthesis of the common spirocyclic systems involves the treatment of cycloalkanones with α,ω-dihaloalkanes in the presence of 2 equiv of base.[7] A notable example of this strategy is found in the synthesis of β-vetivone by Stork, Danheiser, and Ganem.[7]

As described herein, our recent studies on organobis(cuprates) and their use as reagents for spiroannelation have focused on an examination of the factors that influence the synthetic scope and efficiency of this process, including variations in the reagent (hybridization, ligand, tether length), substrate (halogen, ring size, substitution), and reaction conditions. The results of these studies are described for the commonly encountered spiro[4.4], -[4.5], and -[5.5] ring systems. Finally, several new reagents are presented that extend the scope of the current methodology and provide access to other organodimetallic and metallocyclic intermediates of potential synthetic and mechanistic value.[2-5,8]

Results and Discussion

The reaction of organobis(cuprate) **3** with enone **2** served as the starting point for this investigation. The dilithiobutane used in the formation of reagent **3** was easily prepared (70% yield) by reaction of 1,4-dichlorobutane with sodium–lithium alloy (ca. 1% sodium content) in ether solvent.[9] Dilithiobutane obtained in this fashion can be stored as a stock solution for at least 4 months at ≤ -10 °C without decomposition. The preparation of reagent **3** was modeled after procedures developed for the formation of the corresponding mono(cuprates) from organolithium precursors.[10] In general, dilithiobutane (stock solution) was added to a mixture of a copper(I) salt, preferably preformed CuSPh,[11] in THF at -78 °C. The resultant suspension was allowed to warm, generally to -15 °C, during which time most if not all of the initial solid dissolved. Substrate was then added to the reagent solution, and after an appropriate period, the reaction was submitted to a standard workup procedure. The 3-haloenones (**2**) used in this study were found to function superbly as substrates and were easily prepared in good yield from the corresponding 1,3-diones according to the procedures of Piers and Nagakura[12a] and of Heathcock and Clark.[12b] Other 3-substituted enones (e.g., acetoxy, alkoxy, alkylthio) known to react with cuprate reagents were not extensively examined due to the availability and favorable performance of the haloenones.[12d-f]

Table I. Reagent Stability and Temperature and Substituent Effects in the Spiroannelation of Haloenone **2** with Organobis(cuprate) **3**[a]

entry	**2**	**3**, equiv	rxn temp, °C	time (min) at specif temp before addn of **2**	yield[b] of **5**, %
1	**2a**	1.1	−15	10	96
2	**2a**	1.1	−15	70	92
3	**2a**	1.1	0	10	74
4	**2b**	2.0	−78	30	60
5	**2b**	2.0	−35	0	75
6	**2b**	2.0	−15	0	90
7	**2b**	1.1	−15	0	87
8	**2c**	1.1	−15	0	50

[a] The general spiroannelation procedure (see the Experimental Section) was used with modifications indicated by table entries. [b] Yields were determined by internal standard gas chromatographic analysis.

Table I contains only the more synthetically significant results bearing on reagent stability (entries 1–3), the effect of temperature changes (entries 1, 3, 4–6), and the influence of the halogen substituent (entries 1, 7, 8) on the reference reaction. The yields reported in this optimization study were obtained by internal standard gas chromatographic (GC) analysis in order to determine accurately and systematically the effect of changes only in reaction variables and not those arising from transfer and isolation of the somewhat volatile product. For preparative purposes, the yields determined in this fashion were found to be within 10% of the yields obtained through isolation. Comparison of entries 1 and 2, which differ only by the amount of time allowed before addition of substrate **2a**, suggests that little if any change in the reagent occurs over a 1-h period at -15 °C. In contrast, when the reagent

---

(6) For reviews on spiroannelations, see: (a) Marshall, J. A.; Brady, St. F.; Anderson, N. H. *Forschr. Chem. Org. Naturst.* **1974**, *31*, 283. (b) Krapcho, P. A. *Synthesis* **1974**, 383. (c) Krapcho, P. A. *Ibid.* **1976**, 425. (d) Krapcho, P. A. *Ibid.* **1978**, 77. (e) Vandewalle, M.; DeClercq, P. *Tetrahedron* **1985**, *41*, 1767. (f) Trost, B. M. *Pure Appl. Chem.* **1975**, *43*, 563. For a recent discussion on strategies for spirocycle synthesis, see: (g) Martin, J. D.; Perez, C.; Ravelo, J. L. *J. Am. Chem. Soc.* **1986**, *108*, 7801. For a general comparison of spiroannelation methods applied to terpene synthesis, see: (h) Heathcock, C. H.; Graham, S. L.; Pirrung, M. C.; Plavac, F.; White, C. T. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1983; pp 264–313.

(7) This strategy has been the subject of several studies: Mousseroun, M.; Jacquier, R.; Christol, H. *Bull. Soc. Chim. Fr.* **1976**, 346. Stork, G.; Danheiser, R. L.; Ganem, B. *J. Am. Chem. Soc.* **1973**, *95*, 3414 and related studies cited therein and in ref 6. Similar procedures have been developed based on the reactions of cyclopentadienes and dihalides, e.g.: Eck, G.; Julia, M.; Pfeiffer, B.; Rolando, C. *Tetrahedron Lett.* **1985**, *26*. 4725. A one-step spiroannelation of *gem*-dibromocyclopropanes has been reported for the preparation of [*n*.2] spirocycles: Takahashi, S.; Suzuki, Y.; Sonogashira, K.; Hagihara, N. *J. Chem. Soc., Chem. Commun.* **1976**, 839 and ref 5b.

(8) Organodilithium reagents have found considerable use for the preparation of metallocycles. For lead references and examples, see: Chappell, S. D.; Cole-Hamilton, D. J. *Polyhedron* **1982**, *1*, 739. McDermott, J. X.; Wilson, M. E.; Whitesides, G. M. *J. Am. Chem. Soc.* **1976**, *98*, 6529. Whitesides, G. M.; Gutowski, F. D. *J. Org. Chem.* **1976**, *41*, 2882. Negishi, E.-i.; Takahashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 3402. Van de Heisteeg, B. J. J.; Tinga, M. G. M.; Van Den Winkel, Y.; Akkerman, O. S.; Bickelhaupt, F. *J. Organomet. Chem.* **1986**, *316*, 51. Ashe, A. J.; Drone, F. J. *Organometallics* **1985**, *4*, 1478. Normant, H.; Noel, M. *C. R. Acad. Sci.* **1961**, 2237. Masamune, S.; Kim, B. M.; Petersen, J. S.; Sato, T.; Veenstra, S. J. *J. Am. Chem. Soc.* **1985**, *107*, 4549. Barton, T. J.; Wulff, W. D.; Arnold, E. V.; Clardy, J. *Ibid.* **1979**, *101*, 2733. Grubbs, R. H.; Miyashita, A.; Liu, M.; Burk, P. J. *Ibid.* **1978**, *100*, 2418. Eisch, J. J.; Galle, J. E.; Aradi, A. A.; Boleslawsk, M. P. *J. Organomet. Chem.* **1986**, *312*, 399.

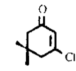
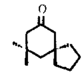
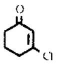
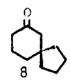
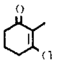
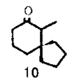
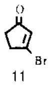
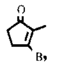
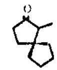
(9) The preparation of 1,4-dilithiobutane and reagents **17**, **25**, and **27** followed a modification of procedures reported by Rochow and Whitesides: West, R.; Rochow, E. G. *J. Org. Chem.* **1953**, *18*, 1739. McDermott, J. X.; Wilson, M. E.; Whitesides, G. M. *J. Am. Chem. Soc.* **1979**, *98*, 6529.

(10) For reviews and lead references on cuprate chemistry, see: Posner, G. H. *Org. React. (N.Y.)* **1972**, *19*, 1. Posner, G. H. *Ibid.* **1975**, *22*, 253. Normant, J. F. *Synthesis* **1972**, 63. Normant, J. F. *Pure Appl. Chem.* **1978**, *50*, 709. Posner, G. H. In *An Introduction to Synthesis Using Organocopper Reagents*; Wiley-Interscience: New York, 1980. Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *40*, 5005. House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59. Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. In *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; pp 682–698. Normant, J. F.; Alexakis, A. In *Current Trends in Organic Synthesis*; Nozaki, H., Ed.; Pergamon: New York, 1983; pp 291–302. Taylor, R. J. K. *Synthesis* **1985**, *364*. Lipshutz, B. H. *Ibid* **1987**, 325.

(11) Posner, G. H.; Whitten, C. E.; Sterling, J. J. *J. Am. Chem. Soc.* **1973**, *95*, 7788. Posner, G. H.; Brunelle, D. J.; Sinoway, L. *Synthesis* **1974**, 662. For a recent example of a new nontransferable ligand, see: Johnson, C. R.; Dhanoa, D. S. *J. Org. Chem.* **1987**, *52*, 1885.

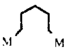
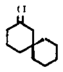
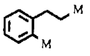
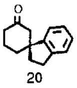
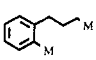
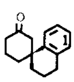
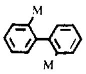
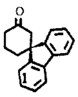
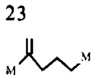
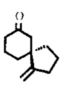
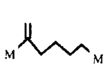
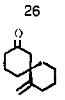
(12) (a) Piers, E.; Nagakura, I. *Synth. Commun.* **1975**, *5*, 193. Piers, E.; Grierson, J. R.; Lau, C. K., Nagakura, I. *Can. J. Chem.* **1982**, *60*, 210. (b) Clark, R. D.; Heathcock, C. H. *J. Org. Chem.* **1976**, *41*, 636. (c) Piers, E.; Nagakura, I. *Ibid.* **1975**, *40*, 2694. (d) Casey, C. P.; Marten, D. F.; Boggs, R. A. *Tetrahedron Lett.* **1973**, 2071. (e) Posner, G. H.; Brunelle, D. J. *J. Chem. Soc., Chem. Commun.* **1973**, 907. (f) Cocchi, S.; Caputo, A.; Misti, D. *Indian J. Chem.* **1974**, *12*, 325.

Table II. Effect of Substrate Variations on Spiroannelation Yields with Reagent **3**

entry	substr[a]	rxn time,[b] h	product	yield,[c] %
1	 2a	1	 5	96
2	 7	1	 8	85
3	 9	1	 10	80
4	9	18	10	93
5	 11	1	 12	87
6	 13	1	 14	76

[a] Prepared from the dione according to the procedure given in ref 12. [b] Time interval between reagent–substrate mixing and workup. [c] Yield determined by internal standard gas chromatographic analysis.

Table III. Effect of Reagent Variations on Spiroannelation Yields with 3-Chloro-2-cyclohexenone (**7**)[a]

entry	reagent (M = CuSPh)	equiv	rxn temp, °C	product	yield,[b] %
1	3	1.1	−15	8	85
2	 17	4.0	−15	 18	74
3	 19	1.2	−20	 20	49
4	 21	3.0	−20	 22	88
5	 23	3.0	−20	 24	39
6	23	10.0	−20	24	94
7	 25	1.1	−20	 26	66
8	 27	4.0	−20	 28	56

[a] The general spiroannelation procedure was used (see the Experimental Section) except that the enone was added over a period of 10 min. [b] Yields were determined by internal standard gas chromatographic analysis except for entries 4–6 where nonvolatile products were isolated and weighed.

is kept at 0 °C for 10 min (entry 3), a lower yield of **5** is obtained, suggesting that the thermal stability of reagent **3** is comparable to that found for the corresponding mono(cuprates).[10,13] Reactions conducted at temperatures much lower than −15 °C (e.g., compare entries 4–6) did not lead to an improvement in yield, presumably due to incomplete reagent formation and/or to the resultant heterogeneity of the reaction.[14] From these and related experiments, it was found that the spiroannelations of chloroenone **2a** and bromoenone **2b** are optimally conducted at approximately −15 °C, at which temperature excellent product yields are obtained. Attempts to extend this optimized procedure to iodoenones (entry 8) were less successful, with the spiroannelated product being formed in only 50% yield. Interestingly, this change in yield as a function of halogen variation is opposite to that reported for the mono(cuprate) reagents.[15] While the basis for this difference requires further study, the higher yield obtained with the chloroenones in this study is synthetically advantageous since these haloenones are generally more stable and more easily prepared.

In further studies related to the reference reaction (eq 1), it was found that the reagent obtained from 1 equiv of dilithiobutane and 2 equiv of copper(I) thiophenoxide was superior to those derived from other stoichiometries and from other copper(I) sources. The use of only 1 equiv of copper(I) thiophenoxide/equiv of dilithiobutane, for example, resulted in the formation of complex reaction mixtures. This result is not unexpected, since this reagent stoichiometry [i.e., 1:1 $CuSPh/(CH_2)_4Li_2$] would potentially favor the formation of metallocyclic and/or oligomeric reagents.[5] Other copper(I) sources[10,11] including CuI, $Cu[P(n\text{-}Bu)_3]I$, CuO-*t*-Bu, and pentynylcopper were examined, but these gave lower yields of product. Additionally, substitution of the di-Grignard reagent for 1,4-dilithiobutane or ether for THF as solvent resulted in significantly reduced yields of **5**. *In summary, optimal conditions for the reference reaction have been determined (entry 1), and under these conditions, the spiroannelation product **5** can be obtained in 96% yield.*

With this experimental calibration point, the next goal of our studies was to determine whether the optimized conditions for the reference reaction (eq 1) could be used as a general procedure for the spiropentannelation of other substrates. The results of these studies are summarized in Table II, including the yield response to synthetically important changes in the substrate ring size and substitution variations. Except for entry 4, the reported yields were obtained by using the aforementioned, optimized conditions. In general, good to excellent yields were found for all cases.

It is important to note in examining the data in Tables I and II that the quaternization process,[16] which is an integral element of the spiroannelation, is not observed under comparable conditions for the intermolecular reaction of a β-haloenone with mono(heterocuprate) reagents.[17] For example, reaction of 3-chloro- or 3-bromocyclohex-2-enone with *n*-BuCuSPhLi (2 equiv) is reported to give 3-*n*-butylcyclohex-2-enone (**15**) and none of the quaternized product, 3,3-di-*n*-butylcyclohexanone (**16**). While this result can be replicated when the reagent concentration is ca. 0.1 M, we have found that at much higher reagent concentrations (ca. 1.0 M saturated solution), the disubstituted product **16** is obtained in modest but significant yield (47%). Thus, the high efficiency of the spiroannelation process might be attributed to the higher effective concentration[18] of reactant functionalities, which would serve to drive the intramolecular closure step. Alternatively, a concentration-related change in reagent composition and reactivity could be involved.[10] In either case, the facilitating influence of such concentration effects on ring closure would explain both the absence of any products arising from the coupling of two haloenones to one reagent molecule and the relative

---

[13] While these experiments indicate that the reactive reagent undergoes irreversible transformation at 0 °C, the nature of this change (aggregation, decomposition, etc.) has not been determined for these reagents.

[14] Due to the limited solubility of CuSPh in THF at −78 °C, the preparation of the bis(cuprate) reagents was preferably conducted at higher temperatures (ca. −15 °C). Recooling the solution of the reagent formed in this fashion frequently resulted in the formation of a suspension.

[15] It is noted that "in general, the β-bromoenones appeared superior to the chloro compounds and, compared with the iodo derivatives, were more convenient to prepare and were easier to handle experimentally": Piers, E.; Nagakura, I. *J. Org. Chem.* **1975**, *40*, 2694. Piers, E.; Cheng, K. F.; Nagakura, I. *Can. J. Chem.* **1982**, *60*, 1256.

[16] Martin, S. F. *Tetrahedron* **1980**, *36*, 419.

[17] Reactions of a variety of bromoenones with various mono(cuprates) with a phenylthio ligand are reported to give no detectable product resulting from further addition to the initially formed β-alkylenone (see ref 15).

[18] For a discussion of intramolecular cyclizations, see: Galli, C.; Illuminati, G.; Mandolini, L.; Tamborra, P. *J. Am. Chem. Soc.* **1977**, *99*, 2591.

absence (<1%) of monoaddition products [e.g., 3-*n*-butylcyclohexenone (15)].

The third major goal of this study focused on determining the effect of reagent structural variations on the key reaction, including changes in the number of atoms between the reacting centers of the reagent and in the hybridization along its chain and at its metal-bearing centers. The preparations of the three symmetrical dilithium precursors to reagents **3**, **17**, and **23** (Table III) required for part of this study have been reported.[2,19] However, relatively little information has been reported for the preparation of nonsymmetrical dilithium reagents such as those required to prepare organobis(cuprates) **19**, **21**, **25**, and **27**. Our studies reveal that these new organodimetallic reagents and, presumably, similar nonsymmetrical reagents can be obtained by modifications of conventional procedures involving reductive metalation or lithium–halogen exchange. Thus, the dilithium precursors to **19** and **21** were formed by reactions of 2-(2-bromophenyl)-1-iodoethane and 3-(2-bromophenyl)-1-iodopropane, respectively, with *tert*-butyllithium. The bromo iodide starting materials rather than the dibromides were used in order to facilitate and control the sequence of the exchange reactions.[20] For dilithium precursors to reagents **25** and **27**, the preferred method of preparation involved reaction of the corresponding dihalide in ether at 0 °C with freshly cut lithium wire containing 1% sodium. The resultant dilithium reagents (**25** and **27**; M = Li) were stable for several weeks when stored at −15 °C.

Conversion of the symmetrical or the new dilithium reagents to the corresponding organobis(cuprates) followed the procedure given for the preparation of reagent **3**. For comparison purposes, the efficiencies of the spiroannelations based on these new reagents were then determined by using 3-chloro-2-cyclohexen-1-one (**7**) as a reference substrate. Only the main findings of this study are given in Table III. In general, all of the new reagents were found to provide spirocycles as the major or only substrate-derived product. It was also found that the new cuprate reagents bearing an sp^2 hybridization at a metal-bearing carbon are less stable at −15 °C than the reference reagent **3**. Thus, under the optimum conditions determined for bis(cuprate) **3**, bis(cuprate) **25** gave only a 55% yield of spiroannelation product **26**. This lower yield is, in part, attributable to reagent decomposition, since virtually none of this product (**26**) was obtained when the reagent was held at −15 °C for 1 h before substrate addition. Furthermore, when the reagent was used immediately after its preparation and the total time for substrate addition shortened to 10 min, the product yield increased to 66%. The only byproduct detected in these reactions was 3-thiophenoxycyclohex-2-enone. It was also found that the effect of reagent instability on reaction yield can be ameliorated by conducting the reaction at lower temperature and/or by the use of an excess of reagent. These variations are most dramatically revealed in entries **5** and **6**, where a roughly threefold increase in reagent equivalents results in a yield change from 39% to 94%.

Conclusions

A new, one-operation spiroannelation method has been developed based on the reaction of β-halocycloalkenones with a novel class of reagents, the organobis(cuprates). The method uniquely[7] allows for the efficient synthesis of the most commonly encountered spirocyclic systems, i.e., spiro[4.4]nonanes, spiro[4.5]decanes, and spiro[5.5]undecanes. The spiroannelation process can be efficiently accomplished with variously substituted β-haloenones and with functionalized organobis(cuprates).[21] The stability of the organobis(cuprates) is influenced by the hybridization of the metal-bearing centers, with alkyl reagents being more stable than alkenyl reagents. Finally, several new organodilithium reagents have been prepared. These and other dilithium reagents provide relatively stable (storable) precursors to the organobis(cuprates) and to other novel organometallic compounds.

Experimental Section

General Procedures. All oxygen- or moisture-sensitive reactions were performed in flame- or oven-dried glassware under a positive pressure of prepurified nitrogen. Air-sensitive liquids and solutions were transferred by syringe or cannula and were introduced into reaction flasks through rubber septa. Air- or moisture-sensitive solids were transferred in a dry glovebag under nitrogen or through a funnel over which a rapid nitrogen flow was maintained. All reaction solutions were dried by shaking with anhydrous sodium sulfate or magnesium sulfate. Temperatures are given in degrees Centigrade. Unless noted otherwise, commercial solvents and reagents were used without further purification. Ether and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl before use.[22] *n*-Butyllithium (ca. 2.4 M in hexanes), methyllithium (ca. 1.4 M in ether, low chloride concentration), and *tert*-butyllithium (ca. 1.5 M in pentane) were purchased from Aldrich Chemical Co. and Alfa/Ventron. The concentrations of alkyllithium and organodilithium reagents were determined by Gilman's method of double titration based on dibromoethane,[23a] by titration of a standard alcohol solution using 1,10-phenanthroline or triphenylmethane as indicator,[23b] and/or by reaction with benzaldehyde and isolation of the resultant product.[23c] Copper thiophenoxide was prepared according to the procedure of Posner[11] and stored in a sealed container between uses. Flash column chromatography[24] was performed with either Woelm silica (32–63 μm) or Merck silica gel 80 (40–63 μm). Dry-column chromatography[25] was done with Woelm silica (63–200 μm). Boiling points (bp) are uncorrected. Melting points (mp) were taken on a Thomas-Hoover capillary melting point apparatus and are corrected. IR spectra were measured on a Perkin-Elmer Model 137 spectrometer. NMR spectra were determined with Varian HFT-80 and Varian A-60 spectrometers. Chemical shifts are reported (δ) relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; qn, quintet; m, multiplet; and br, broad signal. Coupling constants (*J*) are reported in hertz. An AEI-MS9 double-focusing mass spectrometer was used to determine the high- and low-resolution mass spectral data. Ultraviolet spectra were measured on a Perkin-Elmer Model 202 instrument. A Varian 920 gas chromatograph with a thermal conductivity detector was used for all GLC analyses. GLC analyses were precalibrated by using mixtures of products and internal standard of known (weighed) composition. Column A is a 20 ft × $^1/_4$ in. 3% OV-210 on Anakrom Q (90/100 mesh) column. Combustion analyses were performed by Galbraith Laboratories, Knoxville, TN.

1,4-Dilithiobutane. The procedure used in the preparation of this reagent is a modification of that published by Rochow.[9] A dry, 250-mL, one-necked flask was equipped with a large magnetic stir bar and glass beads (2–3-mm diameter). Lithium wire (0.9% Na, 2.3 g), prewashed with pentane, was held with forceps over the flask and cut into pieces (approximately 2-mm length) under a rapid flow of dry nitrogen. The flask was equipped with a pressure-equalizing addition funnel and was immersed in a 0 °C bath. Approximately one-tenth of a solution of 1,4-dichlorobutane (7.2 mL, 0.65 mol) in ether (55 mL) was added to the flask, and the reaction was initiated by vigorous stirring. The remainder of the solution was added over a 2-h period. The gray suspension was rapidly stirred for an additional 7 h at 0 °C and then stored overnight at −10 °C. The mixture was most conveniently filtered through a coarse (25–50-μm) sintered glass frit covered with a thin layer of anhydrous lithium chloride. It is recommended that the temperature of the resulting clear solution be maintained below 0 °C. The solution was stable for several months when stored at −10 °C under nitrogen. The concentration of 1,4-dilithiobutane (0.53 M), which was determined by titration of *tert*-butyl alcohol using triphenylmethane as indicator,[23b] indicated a yield of approximately 70%.[26]

General Procedure for Spiroannelations Using Bis(cuprate) 3. The following preparation of 9,9-dimethylspiro[4.5]decan-7-one (**5**) is rep-

---

[19] For a comprehensive treatment of these and other organodilithium preparations, see: Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon: Oxford, 1974. Mueller, E. *Methoden der Organischen Chemie* (Houben-Weyl); Georg Thieme Verlag: Stuttgart, 1973; Vol. 13/2a.

[20] Treatment of the dibromide with *tert*-butyllithium at −100 °C is reported to give the monolithio product resulting from exchange of the aryl bromide: Parham, W. E.; Bradsher, C. K.; Hunt, D. A. *J. Org. Chem.* **1978**, *43*, 1606.

[21] It is expected that the organobis(heterocuprates) would tolerate other functional groups that have been used in the corresponding mono(cuprates).

[22] For a discussion of the effectiveness of various drying methods, see: Burfield, D. R.; Smithers, R. H. *J. Org. Chem.* **1978**, *43*, 3966.

[23] (a) Gilman, H.; Cartledge, F. K. *J. Organomet. Chem.* **1964**, *2*, 447. (b) Watson, S. C.; Eastham, J. F. *Ibid.* **1967**, *9*, 165. (c) We have found that this procedure serves as an excellent independent and direct assay for dilithium content and offers the advantage of providing an isolable product.

[24] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

[25] Loev, B.; Goodman, M. M. *Chem. Ind.* (*London*) **1967**, 2026.

[26] Higher yields have been reported.[9]

resentative of the procedure used to prepare the spirocyclic compounds reported in Tables I and II.

To a mixture of CuSPh[11] (0.290 g, 1.65 mmol) and dry tetrahydrofuran 10 mL) at −78 °C was added 1,4-dilithiobutane (1.6 mL of an 0.53 M solution, 0.83 mmol) over a 2-min period. The mixture was then allowed to warm to −15 °C over a 20-min period, during which time the initial yellow color changed to red and the majority of the solid dissolved. After 10 min, 3-chloro-5,5-dimethylcyclohex-2-en-1-one[12] (0.120 g, 0.75 mmol) in THF (10 mL) was added over a 1-h period (syringe pump). After an additional 30 min, the reaction was allowed to warm to room temperature and was then poured into saturated NH_4Cl solution. This mixture was diluted with ether (50 mL) and stirred for 15 min. The resulting mixture was filtered, and the layers were separated. The aqueous layer was reextracted with Et_2O, and the combined organic layers were then washed with saturated $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. Gas chromatographic analysis of the crude reaction mixture, conducted on column A using ethyl phthalate as an internal standard, indicated a yield of 96% of **5** based on chloroenone **2a**. Pure samples of **5** (colorless oil) were obtained by preparative gas chromatography or, for large scale reactions, by simple distillation.

5: ^1H NMR ($CDCl_3$) δ 1.01 (s, 6 H), 1.4–1.7 (m, 8 H), 1.66 (s, 2 H), 2.08 (s, 4 H); IR (film) 2925, 1710, 1232, 1272 cm^{-1}; MS, *m/e* 83 (base); calcd for $C_{12}H_{20}O$ 180.1514, found 180.1504. Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.84; H, 11.21.

The following spirocyclic compounds presented along with reaction yields in Table II were prepared by the above procedure.

Spiro[4.5]decan-7-one (8): ^1H NMR ($CDCl_3$) δ 1.3–2.0 (m, 12 H), 2.22 (s, 2 H), 2.27 (m, 2 H); IR (film) 2930, 1710, 1435, 1220 cm^{-1}; MS, *m/e* 152 (M^+), 109 (base); calcd for $C_{10}H_{16}O$ 152.1201, found 152.1201. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.70; H, 10.39.

6-Methylspiro[4.5]decan-7-one (10): ^1H NMR ($CDCl_3$) δ 1.02 (d, 3 H, *J* = 7 Hz), 1.3–2.0 (m, 12 H), 2.2–2.5 (m, 3 H); IR (film) 2940, 1710, 1460 cm^{-1}; MS, *m/e* 166 (M^+), 94 (base); calcd for $C_{11}H_{18}O$ 166.1358, found 166.1358. Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.25; H, 10.94.

Spiro[4.4]nonan-2-one (12): ^1H NMR ($CDCl_3$) δ 1.60 (br s, 8 H), 1.75–2.50 (m, 4 H), 2.15 (s, 2 H); IR (film) 2940, 1738, 1440, 1395, 1150 cm^{-1}; MS, *m/e* 138 (M^+), 109, 67 (base); calcd for $C_9H_{14}O$ 138.1046, found 138.1045. Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.09; H, 10.33.

1-Methylspiro[4.4]nonan-2-one (14): ^1H NMR ($CDCl_3$) δ 0.99 (d, 3 H, *J* = 7 Hz), 1.67 (br s, 10 H), 2.0–2.5 (m, 3 H); IR (film) 2940, 1735, 1450, 1405, 1370, 1155, 1042, 975 cm^{-1}; MS, *m/e* 152 (M^+), 69 (base); calcd for $C_{10}H_{16}O$ 152.1201, found 152.1205. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 79.19; H, 10.72.

3,3-Di-*n*-butylcyclohexanone (16). To a mixture of CuSPh[11] (1.73 g, 10 mmol) and THF (7.0 mL) was added *n*-BuLi (4.25 mL of 2.35 M in hexane, 10 mmol) over a 5-min period. The reaction was allowed to warm to −15 °C over 15 min. 3-Chlorocyclohex-2-en-1-one[12] (0.130 g, 1.0 mmol) was added neat over a 10-min period, and the reaction was subsequently maintained at −15 °C for 27 h. The reaction was then allowed to warm to room temperature and was submitted to the standard workup (see the general procedure). Gas chromatographic analysis of the crude material indicated a 3:1 ratio of **16** to **15**.[27] Dry-column chromatography on silica gel with ether/hexanes (1:5) (R_f 0.35) afforded 99 mg (47% yield) of **16** as a colorless oil: ^1H NMR ($CDCl_3$) δ 0.89 (br t, 6 H), 1.21 (br s, 12 H), 1.4–2.0 (m, 4 H), 2.15 (br s, 2 H) 2.27 (br t, 2 H); IR (film) 2900, 1708, 1460, 1230 cm^{-1}; MS, *m/e* 210 (M^+), 153 (base). Anal. Calcd for $C_{14}H_{26}O$: C, 80.05; H, 12.86. Found: C, 79.94; H, 12.46.

1,5-Dilithiopentane (17; M = Li). Lithium wire (0.24 mmol) containing 1% Na was freshly cut and added to a predried flask. 1,5-Dibromopentane (6.90 g, 30.0 mmol) in anhydrous ether (40 mL) was then added to the lithium alloy over 2 h at −5 °C. The reaction was stirred for an additional 1 h and then filtered through sintered glass. Double titration of the resultant solution using dibromoethane[23a] indicated that the concentration of dilithium reagent was 0.53 M (~88% yield).

Spiro[5.5]undecan-8-one (18). Copper thiophenoxide[11] (0.69 g, 4.0 mmol) in THF (10 mL) was cooled to −78 °C, and 1,5-dilithiopentane (3.8 mL) of 0.53 M, 2.0 mmol) was added over 5 min. The yellow mixture was allowed to warm to −15 °C over 20 min. After an additional 10 min, 3-chlorocyclohex-2-enone (**7**;[12] 0.065 g, 0.5 mmol) in THF (4 mL) was added to the light red solution over a 10-min period. Stirring was continued for 1 h at −15 °C. The reaction was then allowed to warm to room temperature, after which it was submitted to the standard workup (see the general procedure). GC analysis on column A using ethyl phthalate as internal standard indicated the yield of **18** was 74%.

Preparative gas chromatography on column A yielded pure **17** as a colorless oil: ^1H NMR ($CDCl_3$) δ 1.39 (br s, 10 H), 1.5–2.0 (m, 4 H), 2.20 (s, 2 H), 2.28 (m, 2 H); IR (film) 2900, 1710, 1450, 1330 cm^{-1}; MS, *m/e* 166 (M^+), 123 (base); calcd for $C_{11}H_{18}O$ 166.1357, found 166.1361. Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.21; H, 10.92.

2-(2-Bromophenyl)-1-iodoethane and 3-(2-Bromophenyl)-1-iodopropane. Methyl iodide (2.13 g, 15.0 mmol), triphenyl phosphite (3.41 g, 11.0 mmol), and 2-(2-bromophenyl)ethan-1-ol[28] (2.00 g, 10.0 mmol) were mixed at room temperature and then heated under reflux for 24 h.[29] The temperature of the oil bath increased from 75 to 130 °C over the 24-h period. The reaction was allowed to cool, and the crude material was taken up in ether. The ether layer was extracted with 5% NaOH (three times), and the combined extracts were dried (K_2CO_3). The solvent was removed in vacuo. The crude material was distilled at 110 °C (0.25 Torr), during which time some decomposition occurred. The distilled material was filtered through basic alumina with pentane. After the solvent was removed in vacuo, a colorless oil (2.30 g, 74% yield) remained: ^1H NMR ($CDCl_3$) δ 3.25 (s, 4 H), 7.22 (m, 3 H), 7.55 (m, 1 H); IR (film) 3070, 2970, 1465, 1435, 1175, 1038, 752 cm^{-1}; MS, *m/e* 312, 310 (M^+); 185, 183 (base), 104; UV, λ_{max} (EtOH) 257 nm (log ϵ 3.0); calcd for $C_8H_8{}^{79}BrI$ 309.8861, found 309.8857.

3-(2-Bromophenyl)-1-iodopropane was prepared (in 55% yield) from 3-(2-bromophenyl)propan-1-ol[30] in a fashion similar to the above procedure: ^1H NMR ($CDCl_3$) δ 2.14 (br qn, 2 H), 2.87 (t, 2 H, *J* = 7.5 Hz), 3.21 (t, 2 H, *J* = 6.9 Hz), 7.0–7.3 (m, 3 H), 7.5–7.6 (m, 1 H); IR (film) 3050, 2920, 1440, 1435, 1215, 1170, 1025, 748 cm^{-1}; MS, *m/e* 326, 324 (M^+); 171, 169 (base); UV, λ_{max} (EtOH) 259 nm (log ϵ 2.8); calcd for $C_9H_{10}{}^{79}BrI$ 323.9013, found 323.9020.

Spiro[cyclohexane-1,1′-indan]-3-one (20). 2-(2-Bromophenyl)iodoethane (0.200 g, 0.640 mmol) was dissolved in anhydrous ether (2 mL) and cooled to −78 °C. *t*-BuLi[31] (1.15 mL of 1.60 M in pentane, 1.80 mmol) was then added over 2 min, and the mixture was stirred at −78 °C for 15 min. THF (3 mL) and copper thiophenoxide (0.210 g, 1.20 mmol) were then added. The temperature was increased to −15 °C over 15 min. 3-Chlorocyclohex-2-enone (**7**,[12] 0.065 g, 0.50 mmol) in THF (5 mL) was added over 10 min. After being stirred for 1 h at −15 °C and warming to room temperature, the reaction was submitted to the usual workup (see the general procedure). The crude material was analyzed on column A with ethyl phthalate as an internal standard. The yield of **20** was determined to be 49%. Silica gel column chromatography using ether/hexanes (1:3) (R_f 0.44) followed by preparative gas chromatography on column A provided an analytical sample of **20** as a viscous, colorless oil: ^1H NMR ($CDCl_3$) δ 1.6–2.2 (m, 6 H), 2.3–2.5 (m, 4 H), 2.91 (t, 2 H, *J* = 7.2 Hz), 7.18 (s, 4 H); IR (film) 1705, 1470, 1310, 774, 758 cm^{-1}; MS, *m/e* 200 (M^+), 143 (base), 130; UV, λ_{max} (EtOH) 265 nm (log ϵ 2.60), 272 (2.60); calcd for $C_{14}H_{16}O$ 200.120, found 200.1204. Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.76; H, 8.07.

3′,4′-Dihydrospiro[cyclohexane-1,1′(2′*H*)-naphthalen]-3-one (22). To a solution of 3-(2-bromophenyl)-1-iodopropane (0.241 g, 0.75 mmol) in ether (1.5 mL) at −78 °C was added *t*-BuLi (1.30 mL of 1.70 M in pentane, 2.25 mmol) over 2 min. The resulting suspension was stirred for 30 min. THF (3 mL) and CuSPh[11] (0.26 g, 1.5 mmol) were then added. The reaction was then allowed to warm from −78 to −20 °C, during which time the yellow suspension changed to a red solution. 3-Chlorocyclohex-2-enone (**7**,[2] 0.032 g, 0.25 mmol) in THF (4 mL) was added over 10 min at −20 °C. After 2 h at −20 °C, the reaction was allowed to warm to room temperature and was subjected to the standard workup (see the general procedure). The crude material was purified by dry-column chromatography on silica gel (6:1 hexanes/ether) to produce 47.0 mg of **22** (88% yield) as a colorless, viscous oil (R_f 0.24): ^1H NMR ($CDCl_3$) δ 1.60–2.10 (m, 8 H), 2.25–2.45 (m, 3 H), 2.60–2.80 (m, 3 H), 7.00–7.45 (m, 4 H); IR (film) 2900, 1710, 1495, 1460, 1330, 790, 730 cm^{-1}; MS, *m/e* 214 (M^+), 157, 144, 129 (base), 128; UV, λ_{max} (CCl_4) 266 nm (log ϵ 2.70), 273 (2.71); calcd for $C_{15}H_{18}O$ 214.1359. Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 83.82;, H, 8.61.

Sprio[cyclohexane-1,9′-fluoren]-3-one (24). 2,2′-Dibromobiphenyl (0.624 g, 2.00 mmol) was dissolved in ether (2 mL) and cooled to −78 °C. *t*-BuLi (2.35 mL of 1.70 M in pentane, 4.00 mmol) was added over 2 min at −78 °C and allowed to stir for an additional 15 min. THF (6 mL) and CuSPh[11] (0.690 g, 4.00 mmol) were then added. The yellow

---

[27] Authentic samples of **15** and **16** were prepared for identification purposes based on the literature procedures.[15]

[28] Sontag, D. *Ann. Chim. (Paris)* **1934**, *1*, 359. Uyeo, S.; Mizutani, T.; Yoshitake, A.; Ito, A. *Yakugaku Zasshi* **1964**, *84*, 458.

[29] Landauer, S. R.; Rydon, H. N. *J. Chem. Soc.* **1953**, 2224.

[30] Beeby, M. H.; Mann, F. G. *J. Chem. Soc.* **1951**, 411.

[31] This lithium–halogen exchange proceeded in >80% yield.[23a,c] Attempts to prepare reagents **19** and **21** by reaction of the corresponding dichlorides with lithium–sodium alloy (1% sodium) were unsuccessful.

suspension dissolved and a red solution developed when the reaction was allowed to warm to −20 °C over 15 min. 3-Chlorocyclohex-2-enone (**7**,[12] 0.026 g, 0.200 mmol) in ether (2 mL) was added at −20 °C over 10 min, and the solution was then stirred for 2 h. The reaction was allowed to warm to room temperature and was then submitted to the standard workup (see the general procedure). Dry-column silica gel chromatography using hexanes/ether (6:1) provided 48.0 mg (94%) of chromatographically pure material (R_f 0.22). Recrystallization from ether/hexanes gave an analytical sample of **24**: (mp 192–193 °C; ^{1}H NMR ($CDCl_3$) δ 1.75–2.00 (m, 2 H), 2.28 (br qn, 2 H), 2.61 (s, 2 H), 2.69 (br t, 2 H, $J \cong 6$ Hz), 7.2–7.5 (m, 6 H), 7.6–7.8 (m, 2 H); IR (CH_2Cl_2) 3030, 2940, 1708, 1478, 1445, 1325, 765, 735 cm^{-1}; MS, *m/e 248* (M^+), 191, 178 (base); UV, λ_{max} (CCl_4) 271 nm (log ϵ 4.17), 292 (3.82), 304 (3.89); calcd for $C_{18}H_{16}O$ 248.1203, found 248.101. Anal. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.45. Found: C, 86.81; H, 6.53.

4-Chloro-4-penten-1-ol. To a suspension of lithium aluminum hydride (15.0 g, 400 mmol) in anhydrous ether (500 mL) was added 4-chloro-4-pentenoic acid[32] (28.0 g, 0.210 mmol) in anhydrous ether (100 mL) at such a rate that gentle reflux was maintained. After the reaction had stirred an additional 3 h at room temperature, it was quenched by adding consecutively H_2O (15 mL), 15% NaOH (15 mL), and H_2O (45 mL). The resultant suspension was filtered and and the precipitate washed with dry ether. The solvent was removed at reduced pressure. Distillation afforded 24.3 g of 4-chloro-4-penten-1-ol (99%) as a colorless oil: bp 61.5–62.5 °C (3.1 Torr); ^{1}H NMR (CCl_4) δ 1.77 (br qn, 2 H), 2.43 (br t, 2 H, $J \cong 7$ Hz), 3.60 (br t, 2 H, $J \cong 6$ Hz), 4.01 (br s, OH), 5.13 (s, 2 H); IR (film) 3300, 2940, 1638, 1050, 885 cm^{-1}; MS, *m/e* 122, 120 (M^+), 67 (base); calcd for $C_5H_9{}^{37}ClO$ 122.0312, found 122.0312.

1,4-Dichloro-4-pentene. 4-Chloro-4-penten-1-ol (12.0 g, 0.100 mmol) and triphenylphosphine (31.5 g, 0.120 mmol) were dissolved in CCl_4 (80 mL).[33] The reaction was heated under reflux for 40 min [*Caution*—a controllable exotherm occurred when the bath initially reached 80 °C] and subsequently cooled to room temperature, diluted with pentane (80 mL), and filtered. The solvent was removed at reduced pressure. 1,4-Dichloro-4-pentene (9.1 g, 66% yield) was obtained as a colorless oil by distillation at 58–60 °C (20 mm): ^{1}H NMR (CCl_4) δ 2.05 (br qn, 2 H), 2.55 (br t, 2 H, $J \cong 6$ Hz), 3.51 (t, 2 H, $J \cong 7$ Hz), 5.18 (br s, 2 H); IR (film) 2940, 1638, 890, 795 cm^{-1}; MS, *m/e* 142, 140, 138 (M^+), 40 (base); calcd for $C_5H_8{}^{37}Cl_2$ 141.9941, found 141.9943.

1,4-Dilithio-4-pentene and 1,5-Dilithio-5-hexene. Lithium wire (1.7 g, 0.24 mmol) containing 0.9% Na was cut under a rapid flow of dry nitrogen and allowed to fall into a predried flask. Anhydrous ether (10 mL) was added to the flask, and the mixture was cooled to 0 °C. 1,4-Dichloro-1-pentene (7.0 g, 0.050 mmol) in anhydrous ether (15 mL) was then added over 1.5 h at 0 °C. After an additional 2 h at 0 °C, the reaction was stored overnight at −15 °C. The mixture was then filtered through sintered glass (25–50 μm), which was covered with a thin layer of anhydrous LiCl. This procedure provided a clear orange solution determined to be 1.07 M in dilithium reagent by double titration with dibromoethane[23a] (~84% yield). Titration of the stock solution after it was stored for 6 weeks at −15 °C indicated that less than 10% reagent decomposition had occurred. 1,5-Dilithio-5-hexene was prepared in the same manner from 1,5-dibromo-5-hexene,[34] albeit in lower yield (~45%).

1-Methylenespiro[4.5]decan-7-one (26). To a suspension of CuSPh[11] (0.190 g, 1.10 mmol) in THF (5 mL) at −70 °C was added 1,4-dilithio-4-pentene (0.83 mL of 0.67 M, 0.55 mmol) over 10 min. The reaction was quickly warmed (10 min) to −20 °C, and 3-chlorocyclohex-2-enone (**7**,[12] 0.065 g, 0.50 mmol) in THF (3 mL) was immediately added over 10 min. After 30 min at −20 °C, the reaction was allowed to warm to room temperature and was submitted to the usual workup (see the general procedure). Analysis of the crude reaction mixture on column A using ethyl phthalate as internal standard indicated that the yield of **26** was 66%. 3-Thiophenoxycyclohex-2-en-1-one (ca. 10–30% depending on addition times) was also obtained.[35] An analytical sample of **26** was prepared by silica gel column chromatography ($CHCl_3$; R_f 0.50) followed by preparative gas chromatography on column A. **26** was obtained as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.50–1.75 (m, 8 H), 2.25 (br s, 6 H), 4.78 (t, 1 H, $J = 2.4$ Hz), 4.92 (t, 1 H, $J = 2.0$ Hz); IR (film) 2920, 1710, 1650, 1440, 1305, 1225, 885 cm^{-1}; MS, *m/e* 164 (M^+), 95 (base), 79; calcd for $C_{11}H_{16}O$ 164.1198, found 164.1201. Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.16; H, 9.53.

1-Methylenespiro[5.5]undecan-8-one (28). Spirocycle **28** was prepared by the same procedure used for **26**. When 1.1 equiv of bis(cuprate) **27** (M = CuSPhLi) was used, a 45% yield of **28** was isolated by silica gel chromatography (ether/hexanes, 1:6; R_f 0.22). When 4.0 equiv of bis(cuprate) **27** (M = CuSPhLi) was used, a 56% yield of **28** was obtained as determined by gas chromatography on column A by using ethyl phthalate as an internal standard: ^{1}H NMR ($CDCl_3$) δ 1.3–1.9 (m, 8 H), 1.9–2.6 (m, 8 H), 4.59 (s, 1 H), 4.79 (d, 1 H, $J = 1.0$ Hz); IR (film) 2920, 1710, 1640, 1440, 1330, 905, 885 cm^{-1}; MS, *m/e* 178 (M^+, base), 109, 97, 79, 67, 55; calcd for $C_{12}H_{18}O$ 178.1358, found 178.1344. Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.61; H, 10.13.

Acknowledgment. The National Science Foundation (Grant CHE-8319020) is acknowledged for their support of this research.

Registry No. **2a**, 17530-69-7; **2b**, 13271-49-3; **2c**, 56671-85-3; **3**, 63856-63-3; **5**, 63858-64-0; **7**, 5682-75-7; **8**, 62788-60-7; **9**, 35155-66-9; **10**, 113163-13-6; **11**, 51865-32-8; **12**, 34177-18-9; **13**, 56671-87-5; **14**, 84966-72-3; **16**, 51756-28-6; **17**, 2223-58-7; **18**, 1781-81-3; **20**, 113163-14-7; **22**, 113163-15-8; **24**, 113163-16-9; **26**, 113163-17-0; **28**, 113163-18-1; $Cl(CH_2)_4Cl$, 110-56-5; CuSPh, 1192-40-1; $Br(CH_2)_5Br$, 111-24-0; MeI, 74-88-4; 1,4-dilithiobutane, 2123-72-0; 3-*n*-butylcyclohex-2-enone, 6301-49-1; 2-(2-bromophenyl)-1-iodoethane, 113163-19-2; 3-(2-bromophenyl)-1-iodopropane, 113163-20-5; 2-(2-bromophenyl)ethan-1-ol, 1074-16-4; 3-(2-bromophenyl)propan-1-ol, 52221-92-8; triphenyl phosphite, 101-02-0; 2,2′-dibromobiphenyl, 13029-09-9; 4-chloro-4-penten-1-ol, 1647-18-3; 1,4-dichloro-4-pentene, 58568-26-6; 1,4-dilithio-4-pentane, 61354-42-5; 1,5-dilithio-5-hexene, 113218-90-9; 4-chloro-4-pentenoic acid, 58435-01-1; 1,5-dibromo-5-hexene, 87280-36-2; 3-thiophenoxy-2-cyclohexen-1-one, 75717-39-4.

---

[32] Drouin, J. Ph.D. Thesis, Universite de Paris Sud, Centre d'Orsay, 1976. A related procedure is given by: Boatman, S.; Hauser, C. R. In *Organic Synthesis*; Wiley: New York, 1973; Collect. Vol. V, p 767.

[33] Tomoskozi, I.; Gruber, L. Radus, L. *Tetrahedron Lett.* **1975**, 2473. Aneja, R.; Davies, A. P.; Knaggs, J. A. *Ibid.* **1975**, 67.

[34] Colonge, J.; Lasfarques, P. *Bull. Soc. Chim. Fr.* **1962**, 177. Rydon, H. N. *Spec. Publ. Chem. Soc.* **1957**, *n8*, 61. Verheyden, J. O. H.; Moffatt, J. G. *J. Am. Chem. Soc.* **1966**, *88*, 5684.

[35] Bakuzis, P.; Bakuzis, M. L. F. *J. Org. Chem.* **1981**, *46*, 235.