Acknowledgment. M.J.M. thanks the National Science Foundation (USA) for a grant.

Registry No. 1, 127594-76-7; **2**, 127594-78-9; **3**, 127594-79-0; Ph_2C_2, 501-65-5; $[W(CO)(\eta^2\text{-}PhC{\equiv}CPh)(\eta^2\text{-}S_2CNMe_2)_2]$, 98735-58-1; $Sn[CH(SiMe_3)_2]_2$, 41823-72-7; $[W(CO)_3(\eta^2\text{-}S_2CNMe_2)_2]$, 72881-01-7.

Supplementary Material Available: Details of the crystal structure analysis and tables of complete bond angles and distances, anisotropic and isotropic thermal parameters, and fractional atomic coordinates (6 pages); a listing of observed and calculated structure factors (6 pages). Ordering information is given on any current masthead page.

Cyclopropanation with Acyloxy Chromium Carbene Complexes. A Synthesis of (±)-Prostaglandin E_2 Methyl Ester

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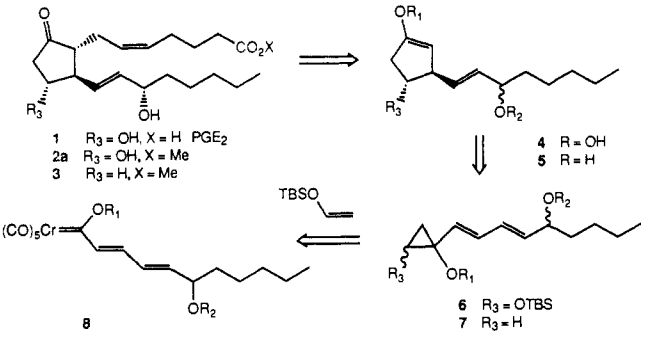
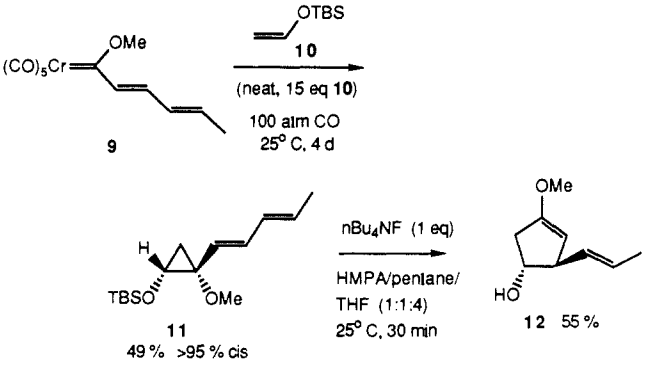
The first reaction of Fischer carbene complexes[2] that was examined for its potential in organic synthesis was the cyclopropanation of olefins; however, the utility of this reaction has yet to be demonstrated in a synthetic application.[3-5] The general strategy for prostaglandin synthesis[7,8] involving a ring expansion of a dienyl cyclopropanone of the type **7** (Scheme I) has only been employed in the synthesis of the C-11 deoxyprostaglandin **3**.[6] Presumably, this approach has been limited due to the lack of methods for the preparation of 1,2-dioxygenated cyclopropanes. We herein report the realization of this strategy for a fully functionalized prostaglandin, a strategy that is highlighted by the development of the cyclopropanation reactions of acyloxy carbene complexes.

Scheme I



In a model study for the synthesis of PGE_2 (**1**), the reaction of the pentadienyl complex **9**[9] and the silyl enol ether **10**[4h] was found to give the cis diastereomer of the cyclopropane **11**.[10] An anionic ring expansion was attempted with the conditions perfected by Danheiser,[11] and it realization for **11** to give *trans*-**12** establishes an alternative to the thermal protocol developed by Salaün[6] for the key ring expansion of **7** to **5** in the synthesis of C-11 deoxy PGE_2 methyl ester **3**.



All attempts to convert the methyl enol ether in **12** to the corresponding enolate met with disappointment (TMSI destroyed the molecule), and this generated significant concern since all of the cyclopropanation reactions with Fischer carbene complexes that have been reported in the literature with oxygen as the heteroatom have been with alkoxy complexes (R_1 in **8** is alkyl).[3,4] We turned to the investigation of the cyclopropanation of enol ethers with acyloxy carbene complexes (R_1 in **8** is acyl), since according to the synthetic approach outlined in Scheme I, this would deliver the enol acetate **4** and recourse could be made to the standard protocol for its conversion to the corresponding enolate. Acyloxy complexes of the type **15** are thermally unstable but can be generated cleanly[12] at low temperatures from tetraalkylammonium metal acylates of the type **13**[13,14] and acyl halides. The development of the chemistry of acyloxy complexes has been limited to reactions with heteroatomic nucleophiles.[4n,12a,15] As indicated by the data in Table I, a variety of 1,2-dioxygenated cyclopropanes can be obtained from the reactions of enol ethers with in situ generated acyloxy carbene complexes and without high pressures of CO. In a direct comparison to the reaction in entry 1, the methoxyl complex derived from **13a** has been reported to

(1) National Institutes of Health Predoctoral Fellow.

(2) For recent literature, see: (a) Dötz, K. H.; Fischer, H.; Hofmann, P.; Kreissel, F. R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*; Verlag Chemie: Deerfield Beach, FL, 1984. (b) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587. (c) Wulff, W. D. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press Inc.: Greenwich, CT, 1989; Vol. 1. (d) *Advances in Metal Carbene Chemistry*; Schubert, U., Ed.; Kluwer Academic Publishers: 1989.

(3) For reviews, see: (a) Brookhart, M.; Studabaker, W. B. *Chem. Rev.* **1987**, *87*, 411. (b) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919.

(4) For recent articles, see: (ae Reissig, H. U. In *Organometallics in Organic Synthesis 2*; Werner, H., Erker, G., Eds.; Springer-Verlag: Berlin, 1989, p 311. (b) Wienand, A.; Buchert, M.; Hofmann, B.; Reissig, H. U., in ref 2d, p 271. (c) Herndon, J. W.; Tumer, S. U. *Tetrahedron Lett.* **1989**, *30*, 4771. (d) Brookhart, M.; Buck, R. C. *J. Am. Chem. Soc.* **1989**, *111*, 559. (e) Zhao, S. K.; Knors, C.; Helquist, P. *J. Am. Chem. Soc.* **1989**, *111*, 8527. (f) Hoye, T. R.; Rehberg, G. M. *Organometallics* **1989**, *8*, 2070. (g) Wulff, W. D.; Yang, D. C.; Murray, C. K. *J. Am. Chem. Soc.* **1988**, *110*, 2653. (h) Wulff, W. D.; Yang, D. C.; Murray, C. K. *Pure Appl. Chem.* **1988**, *60*, 137. (i) Wienand, A.; Reissig, H. U. *Tetrahedron Lett.* **1988**, *29*, 2315. (j) Buchert, M.; Reissig, H. U. *Tetrahedron Lett.* **1988**, *29*, 2319. (k) Korkowski, P. F.; Hoye, T. R.; Rydberg, D. B. *J. Am. Chem. Soc.* **1988**, *110*, 2676. (l) Parlier, A.; Rudler, H.; Platzer, N.; Fontanille, M.; Soum, A. *J. Chem. Soc., Dalton Trans.* **1987**, 1041. (m) Fischer, H.; Schmid, J.; Zeuner, S. *Chem. Ber.* **1987**, *120*, 583. (n) Casey, C. P.; Hornung, N. L.; Kosar, W. P. *J. Am. Chem. Soc.* **1987**, *109*, 4908.

(5) Fischer, E. O.; Dötz, K. H. *Chem. Ber.* **1972**, *105*, 3966.

(6) Salaün, J.; Ollivier, J. *Nouv. J. Chim.* **1981**, *5*, 587.

(7) For reviews, see: (a) *New Synthetic Routes to Prostaglandins and Thromboxanes*; Roberts, S. M., Scheinmann, F., Eds.; Academic Press: London, 1982. (b) Bindra, J.S. In *The Total Synthesis of Natural Products*, ApSimon, J., Ed.; Wiley-Interscience: New York, 1981; Vol. 4, p 353. (c) Mitra, A. *Synthesis of Prostaglandins*; Wiley-Interscience: New York, 1977.

(8) For recent citations, see: (a) Chow, K.; Danishefsky, S. *J. Org. Chem.* **1989**, *54*, 6016. (b) Yanagisawa, A.; Habaue, S.; Yamanoto, H. *J. Org. Chem.* **1989**, *54*, 5198. (c) Danishefsky, S. J.; Cabal, M. P.; Chow, K. *J. Am. Chem. Soc.* **1989**, *111*, 3456. (d) Morita, Y.; Suzuki, M.; Noyori, R. *J. Org. Chem.* **1989**, *54*, 1785.

(9) Casey, C. P.; Anderson, R. L. *J. Organomet. Chem.* **1974**, *77*, 345.

(10) See supplementary material for stereochemical assignment.

(11) Danheiser, R. L.; Martinez-Davila, C.; Auchus, R. J.; Kadonaga, J. T. *J. Am. Chem. Soc.* **1981**, *103*, 2443.

(12) (a) Connor, J. A.; Jones, E. M. *J. Chem. Soc. A* **1971**, 3368. (b) Fischer, E. O.; Selmayr, T.; Kreissl, F. R. *Chem. Ber.* **1977**, *110*, 2947.

(13) The acylate **13c** was prepared in 57% yield from 1-bromocyclohexene according to the Fischer procedure.[14]

(14) Fischer, E. O.; Maasböl, A. *Chem. Ber.* **1967**, *100*, 2445.

(15) (a) Hegedus, L. S.; Schultze, L. M.; Montgomery, J. *Organometallics* **1989**, *8*, 2189. (b) Wulff, W. D.; McCallum, J. S.; Kunng, F. A. *J. Am. Chem. Soc.* **1988**, *110*, 7419. (c) Semmelhack, M. F.; Bozell, J. J.; Keller, L.; Sato, T.; Spiess, E. J.; Wulff, W. D.; Zask, A. *Tetrahedron* **1985**, *41*, 5803. (d) Berke, H.; Härtner, P.; Huttner, G.; Seyerl, J. *J. Organomet. Chem.* **1981**, *219*, 317. (e) Fischer, E. O.; Selmayr, T.; Kreissl, F. R. *Monatsh. Chem.*, **1977**, *108*, 759.

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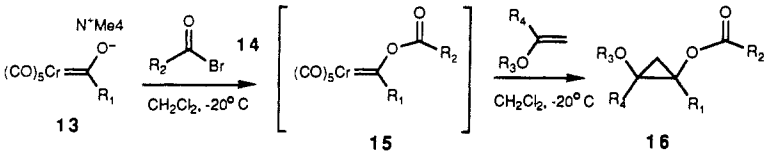
Table I. In Situ Cyclopropanations with Acyloxy Carbene Complexes **15**[a]



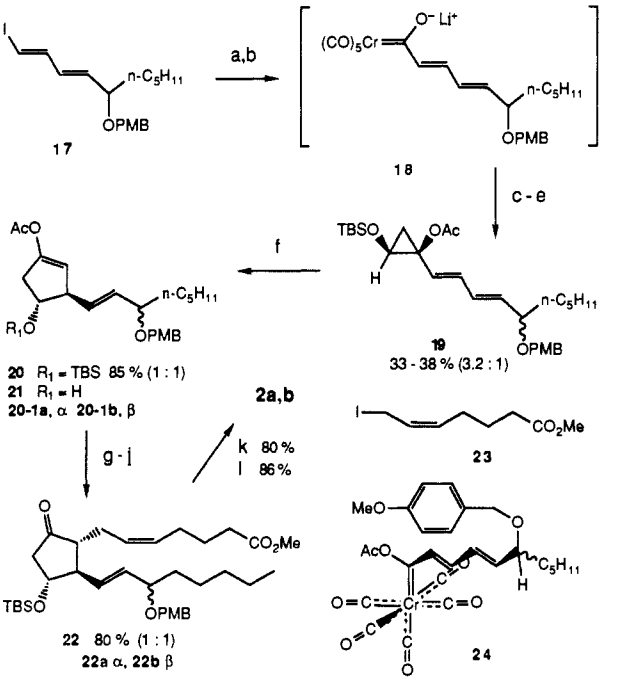
metal acylate	R_1	R_2	R_3	R_4	% yield of **16**[b]	cyclopropane cis:trans
13a	Ph	Me	TBS	H	**16a**, 61	6.4:1.0
13a	Ph	Me	TBS	Ph	**16b**,[c] 90	1.0:4.0
13a	Ph	Me	Et	H	**16c**, 30	6.1:1.0
13b	Me	Me	TBS	Ph	**16d**,[d,e] 78	1.0:1.0
13c	C_6H_9[f]	Me	TBS	H	**16e**,[d,g] 48	cis only
13a	Ph	Ph	TBS	H	**16f**, 60	7.5:1.0

[a] Unless otherwise specified, all reactions were run at 0.5–0.65 M (slurry) in **13** in CH_2Cl_2 at −20 °C by addition of acyl bromide (1 equiv, 60 min), then addition of 3–4 equiv of the enol ether via syringe pump (30–60 min), and stirring at −20 °C for 6–24 h. [b] Isolated yields. [c] Stereochemistry determined by chemical correlation (see supplementary material). [d] Reaction temperature −40 °C. [e] Reaction was 0.065 M in **13**. [f] C_6H_9 = 1-cyclohexenyl. [g] Stereochemistry assigned by NOE experiments (see supplementary material).

react with **10** at 25 °C in 3 days to give a 38% yield of cyclopropane in the absence of CO pressure.[4h] This example illustrates that acyloxy complexes are more reactive than the alkoxy complexes, which is presumably due to the increased electrophilic nature of the carbene carbon that reslts from the more electron withdrawing acyloxy group.

The key carbene complex for the synthesis of PGE_2 was prepared from the dienyl iodide **17**[16] (Scheme II). As we have found to be the situation in general, the lithium acylate **18** would not react cleanly with acetyl halides to generate the acyloxy carbene complex **24**. Furthermore, cation exchange with acylate **18** did not produce a solid tetraalkylammonium salt suitable for isolation. Instead, a methylene chloride solution of **18** was directly treated with nBu_4NF, concentrated, filtered to remove the lithium salts, and then sequentially treated with acetyl bromide and silyl enol ether **10** to give a 38% yield of only the *cis*-dienyl cyclopropane **19**, which was a 3.2:1.0 mixture (stereochemistry not determined) of epimers at C-15. It was surprising to find any stereoselection at C-15 in the formation of **19**, and this could possibly be the result of π stacking[20] of the arene and the diene portions **24**. Anionic ring expansion of the pure major diastereoisomer of **19** (as for **11**) gave a 34% yield of the cyclopentenyl acetate **21** as a 1:1 mixture of epimers at C-15 in addition to a substantial amount of *p*-methoxybenzyl alcohol, and thus in this system at least this reaction is not concerted,[11,17] nor is the thermal ring expansion of **19** concerted[18,19] since **20** is produced as a 1:1 mixture of epimers at C-15 frm either a mixture or the pure major diastereomer of **19**. However, this ring expansion is quite efficient, giving an 85% yield of the *trans*-vinyl cyclopentenyl ether **20** upon thermolysis of **19** in *n*-butyl ether at 190 °C. Installation of the upper side chain via the allyl iodide **23**[21] was achieved in 80% overall yield via the method of Noyori[22] after the enol acetate was converted

Scheme II[a]



[a] (a) *t*-BuLi (2 equiv)/Et_2O, −78 → 0 °C, 2 h. (b) $Cr(CO)_6$ (1.4 equiv)/Et_2O, −30 → 0 °C, 8 h, 0 → 25 °C, 3 h. (c) Bu_4NF (1.3 equiv/CH_2Cl_2, 25 °C, 1 h, filter. (d) MeCOBr (1.0 equiv/CH_2Cl_2, −40 °C, 1 h. (e) **10** (10 equiv), −40 °C; 42 h. (f) **19** (0.01 M in nBu_2O), 190 °C, 2 h. (g) nBuLi (2 equiv, 0.47 mmol)/THF (2.4 mL), −78 °C, 30 min. (h) HMPA (0.22 mL), −78 °C, 30 min. (i) Ph_3SnCl (2 equiv) in THF (0.5 mL), −78 °C, 30 min. (j) **23** (5 equiv) in HMPA (0.3 mL), −30 °C, 35 h. (k) DDQ (1.5 equiv)/CH_2Cl_2/H_2O, 10 °C, 1 h. (l) HF:pyridine, CH_3CN, 0 → 25 °C, 1.5 h.

to the corresponding enolate.[23] After removal of the protecting groups, the methyl ester of PGE_2 (**2a**) and its C-15 epimer (**2b**) were found to have spectral data identical with those previously reported[21,22,24] and with those of a sample of **2a** kindly provided by Professor Josef Fried.

(16) The dienyl iodide **17** was prepared in four steps from commercially available racemic 1-heptyn-3-ol in 50% overall yield as follows: (1) (i) NaH/DMF: THF, (ii) *p*-methoxybenzyl chloride (83%);[25a] (2) (n-Bu)$_3$SnH, AIBN, 130 °C (94%, 10:1:1 mixture of isomers with the *E*-terminal stannyl alkene as major);[25b] (3) (i) *n*-BuLi, THF, −78 → 0 °C, (ii) DMF, 0 → 25 °C (77%); (4) HCl_3, $CrCl_2$, THF, 0 °C (83%, (*E*,*E*)/(*Z*,*E*) = 8:1).[25c]

(17) (a) Carpenter, B. K.; Zoeckler, M. T. *J. Am. Chem. Soc.* **1981**, *103*, 7661. (b) Cohen, T.; Bhupathy, M.; Matz, J. R. *J. Am. Chem. Soc.* **1983**, *105*, 520.

(18) Gajewski, J. J.; Squicciarini, M. P. *J. Am. Chem. Soc.* **1989**, *111*, 6717.

(19) (a) Hudlicky, T.; Kutchan, T. M.; Naqvi, S. M. *Org. React. (N.Y.)* **1985**, *33*, 247. (b) Goldschmidt, Z.; Crammer, B. *Chem. Soc. Rev.* **1988**, *17*, 229.

(20) (a) Trost, B. M.; O'Krongly, O.; Belletire, J. L. *J. Am. Chem. Soc.* **1980**, *102*, 7595. (b) Siegel, C.; Thornton, E. R. *Tetrahedron Lett.* **1988**, *29*, 5225. (c) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **110**, 1238 and references therein.

(21) Johnson, C. R.; Penning, T. D. *J. Am. Chem. Soc.* **1988**, *110*, 4726.

(22) Suzuki, M.; Yanagiasawa, A.; Noyori, R. *J. Am. Chem. Soc.* **1988**, *110*, 4718.

(23) The C-15 epimers were accompanied with a small amount (<10%) of C-8 isomers as has been seen by Noyori.[20] This problem has more recently been solved.[2b,21]

(24) (a) Cooper, G. F.; Fried, J. *Proc. Natl. Acad. Sci. U.S.A.* **1973**, *70*, 1579. (b) Kukas, G.; Piriou, F.; Gero, S. D.; Van Dorp, D. A. *Tetrahedron Lett.* **1973**, *7*, 515.

(25) (a) Horita, K.; Yoshioka, T.; Tanaka, T.; Oikawa, Y.; Yonemitsu, O. *Tetrahedron* **1986**, *42*, 3021. (b) Chen, S. M. L.; Schaub, R. E.; Grudzinskas, C. V. *J. Org. Chem.* **1978**, *43*, 3450. (c) Takai, K.; Nitta, K.; Utimoto, K. *J. Am. Chem. Soc.* **1986**, *108*, 7408.

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Supplementary Material Available: Spectral data for compounds **2a,b**, **11**, **12**, **13c**, **16a-f**, **17**, **19a,b**, **20a,b**, **21a,b**, **22a,b**, **26**, and **28** (8 pages). Ordering information is given on any current masthead page.

Approaches to Orthogonally Fused Conducting Polymers for Molecular Electronics[1]

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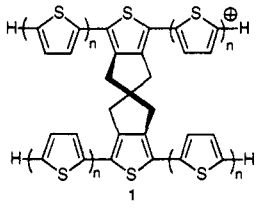
Received April 2, 1990

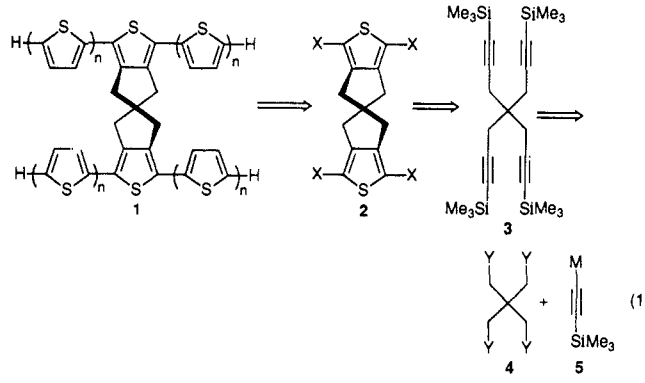
Molecular electronics based computing instruments possess tremendous technological potential. There is the hope of developing single molecules that could each function as a self-contained electronic device. Thus, one can envision computing systems with molecular-sized electronic elements and operational efficiencies far exceeding those of present systems.[3] Recently, Aviram of the IBM Corporation has suggested that molecules that contain a proconducting (nondoped or nonoxidized system, hence insulating) polymer that is fixed at a 90° angle via a nonconjugated σ-bonded network to a conducting (doped or oxidized system) should exhibit properties that would make it suitable for interconnection into future molecular electronic devices.[4] These devices may be useful for memory, logic, and amplification computing systems. Molecule **1** (in doped form) is an example of this proconducting/σ/conducting type of molecule.



1

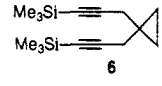
We have undertaken the synthesis of several molecules that fit the structural requirements of this electronic model. From the synthetic standpoint, several aspects are challenging. First, there must be one spiro-fused junction separating two potentially conducting chains with a tetrahedral bonding atom at the center to maintain the 90° angle via a σ-bonded network. Secondly, all four conducting chains originating from the central segment must be *identical* in length. These requirements prohibit the use of any random polymerization methods. Initial reports suggested that conducting chains ~50 Å long (from end to end rather than from end to core) would fulfill the model.[4]

Our initial approach to these systems involved the synthesis of the key spiro core **2** from which we envisioned selective oligomerization to the target molecule **1**. A retrosynthetic analysis is shown in eq 1.



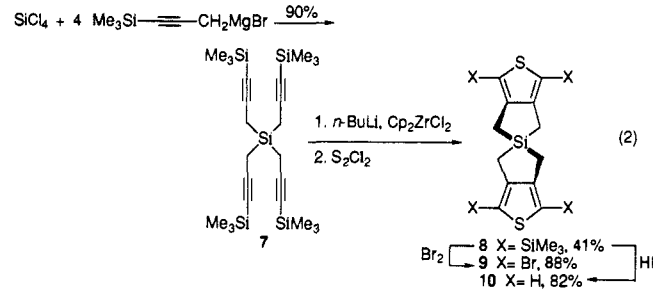
1 **2** **3** **4** **5** (1)

Though substitutions on pentaerythrityl tetrahalides involve reactions on a neopentyl system, exhaustive substitution has been accomplished using oxygen, nitrogen, and sulfur nucleophiles.[5] Attempted formation of **3** using 1-metallo-2-(trimethylsilyl)-acetylenes **5** and pentaerythrityl tetrahalides and tosylates **4** proved to be very difficult even though we tried numerous coupling procedures (M = MgBr, Li, ZnCl, Cu, and AlR_2 with and without Pd and Ni catalysis). In several cases, we obtained the cyclopropyl system **6**.[6] In an effort to overcome these difficulties while



6

maintaining the required σ-bonded tetrahedral spiro junction, we turned our attention to the use of silicon as the central atom. Accordingly, treatment of $SiCl_4$ with the silyl-protected propargyl Grignard reagent cleanly afforded the tetraalkyne **7**.[6] Treatment of **7** with a zirconocene equivalent, generated in situ from zirconocene dichloride and butyllithium, and quenching with sulfur monochloride afforded the trimethylsilyl spiro core **8** (eq 2).[6,7]



7 **8** X = $SiMe_3$, 41% **9** X = Br, 88% **10** X = H, 82% (2)

To our knowledge, use of this group IVA coupling procedure for a bisbicyclization has never before been demonstrated. The trimethylsilyl core (**8**) was converted to the tetrabromide (**9**) and parent core (**10**) under electrophilic substitution conditions.[6,8] Remarkably, no attack on the pseudoallylic central silicon atom was observed.

Likewise, we have synthesized another key core segment based on a *p*-polyphenylene[9] conducting unit which fits the general

(1) Presented at the 199th National Meeting of the American Chemical Society, Boston, MA, April 1990; Polymer Division.

(2) Recipient of the Office of Naval Research Young Investigator Award (1989-1992).

(3) (a) Bowden, M. J. In *Electronic and Photonic Applications of Polymers*; Bowden, M. J., Turner, S. R., Eds.; Advances in Chemistry 218; American Chemical Society: Washington, DC, 1988. (b) *Molecular Electronic Devices*; Carter, F. L., Ed.; Marcel Dekker: New York, 1982. (c) *Molecular Electronic Devices II*; Carter, F. L., Ed.; Marcel Dekker: New York, 1984. (d) Third International Symposium on Molecular Electronic Devices, Washington, DC, Oct 1986. Roland Etvos Physical Society, Satellite Symposium on Molecular Electronics, Budapest, Hungary, Aug 1987.

(4) Aviram, A. *J. Am. Chem. Soc.* **1988**, *110*, 5687 and references therein.

(5) (a) Padias, A. B.; Hall, H. K., Jr.; Tomalia, D. A.; McConnell, J. R. *J. Org. Chem.* **1987**, *52*, 5305. (b) Fujihara, H.; Imaoka, K.; Furukawa, N. *J. Chem. Soc., Perkin Trans. 1* **1986**, 465.

(6) All new compounds were fully characterized spectroscopically, and the elemental composition was established by high-resolution mass spectrometry and/or combustion analysis. All reported yields pertain to isolated homogeneous materials which were purified by recrystallization or chromatography.

(7) (a) Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336. (b) Fagan, P. J.; Nugent, W. A. *J. Am. Chem. Soc.* **1988**, *110*, 2310. (c) Buchwald, S. L.; Nielsen, R. B. *Chem. Rev.* **1988**, *88*, 1047.

(8) (a) Chan, T. H.; Fleming, I. *Synthesis* **1979**, 761. (b) Utimoto, K.; Kitai, M.; Nozaki, H. *Tetrahedron Lett.* **1975**, 2825.

0002-7863/90/1512-5662$02.50/0