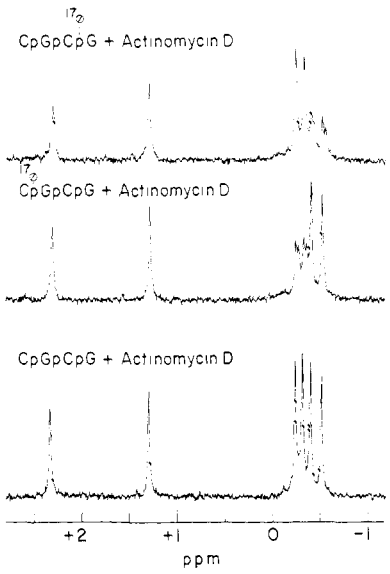

Figure 2. Proton-decoupled ^{31}P NMR spectra at 202.5 MHz and 30 °C of samples of 10 mM d(CpGpCpG) and 5 mM actinomycin D dissolved in D_2O containing 0.1 M sodium cacodylate, pH 7.0, and 2 mM EGTA. The spectra are of the unlabeled sample (bottom), the sample labeled with ^{17}O in the 3′-terminal d(CpG) unit (top), and the sample with ^{17}O in the 5′-terminal d(CpG) unit (middle). Chemical shifts are measured relative to external 85% H_3PO_4.

5′-terminal d(CpG) unit (middle spectrum) demonstrates that the intensity of the upfield resonance is diminished. We note that the naive expectation that the chemical shifts of the external d(CpG) phosphodiester units in the double-helical structure might be similar but different than that of the internal d(GpC) unit is not realized.

The ^{31}P NMR spectra of the unlabeled and labeled oligonucleotides in the presence of actinomycin D (2:1 d(CpGpCpG)–actinomycin D) were also obtained at 202.5 MHz and 30 °C, and these are reproduced in Figure 2. The spectrum of the unlabeled ternary complex (bottom spectrum) is composed of six resonances of equal intensity because all of the ^{31}P nuclei are nonequivalent, and the dissociation of the drug from the complex is slow on the NMR time scale. As expected on the basis of Patel's studies of this complex,[12] two of the resonances are shifted dramatically downfield while the remaining four are found at approximately the same chemical shifts as those of the oligonucleotide in the absence of the drug. The spectra of complexes labeled in the d(CpG) units (top and middle spectra) reveal that the intensities of the upfield resonances are affected by the isotopic labeling, thereby unambiguously establishing that the downfield resonances are associated with the d(GpC) units. These assignments prove Patel's assumption that the phosphodiester groups at the site of intercalation of the drug experience the large downfield changes in chemical shift.[12]

The previously described methods for assigning the ^{31}P NMR resonances of oligonucleotides[2,3] are dependent on the ability to make ^1H NMR assignments. While these spectroscopic methods may be more convenient than the isotopic labeling method described in this communication, it is unlikely that the essential ^1H NMR assignments will always be possible, especially for longer oligonucleotides and oligonucleotides bound to proteins. Thus, our more general isotopic labeling method should permit detailed study of a number of biochemically important problems. Preparation of the required labeled materials can be readily accomplished by any of a variety of procedures now available for the rapid synthesis of oligonucleotides.

The development of general methodology for ^{31}P NMR chemical shift assignments should make ^{31}P NMR a more definitive spectroscopic technique for studying oligonucleotide conformation and dynamics. In addition, sequence-specific ^{17}O labeling of the backbones of oligonucleotides should be useful for ^{17}O NMR studies of dynamics.[15]

The preceding communication describes the application of this method to polynucleotides.[16]

Acknowledgment. We thank Professors Philip H. Bolton and James H. Prestegard for their interest and encouragement. The high-field ^1H and ^{31}P NMR spectra essential to this research were obtained at the NSF Northeast Regional NMR Facility located at Yale University (CHE-7916120). This research was supported by a grant from the National Institutes of Health (GM-30562).

Registry No. ^{17}O, 13968-48-4; d(CpGpCpG), 58927-25-6; actinomycin D, 50-76-0; [$^{17}O_2$]d(CpGpCpG), 88295-83-4.

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1*H*-Cycloprop[*b*]anthracene

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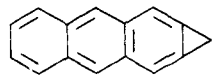
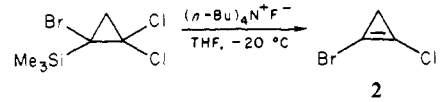
Although cyclopropabenzene[1,2] and both cyclopropanaphthalenes[3,4] have been synthesized and some of their chemical and physical properties investigated, several unsuccessful attempts to prepare parent members of the higher cycloproparenes have been reported.[5-10] We describe here a new approach to the cycloproparenes that we have used to synthesize 1*H*-cycloprop[*b*]anthracene (**1**).[11]



1

A salient feature of this method is the synthesis[12] of the new reagent 1-bromo-2-chlorocyclopropene (**2**) (eq 1).[13] The



(1)

2

cyclopropene can be generated in high yield at −20 °C, transferred in vacuo and stored in tetrahydrofuran at −20 °C for several days.

(1) Vogel, E.; Grimme, W.; Korte, S. *Tetrahedron Lett.* **1965**, 3625.
(2) Billups, W. E.; Blakeney, A. J.; Chow, W. Y. *Chem. Commun.* **1971**, 1461.
(3) Billups, W. E.; Chow, W. Y. *J. Am. Chem. Soc.* **1973**, *95*, 4099.
(4) Tanimoto, S.; Schafer, R.; Ippen, J.; Vogel, E. *Angew. Chem., Int. Ed. Engl.* **1976**, *158* 613; *Angew. Chem.* **1976**, *88*, 643 (German version).
(5) Davalian, D.; Garratt, P. J. *Tetrahedron Lett.* **1976**, *32*, 2815.
(6) Billups, W. E. *Acc. Chem. Res.* **1978**, *11*, 245.
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(10) Müller, P.; Rey, M. *Helv. Chim. Acta* **1982**, *65*, 1157.
(11) This name conforms to that used by *Chemical Abstracts*.
(12) Details regarding the synthesis of **2** will be reported elsewhere.
(13) Chan and Massuda have reported the synthesis of 1-bromo- and 1-chlorocyclopropene by treating 1,1-dibromo-2-(trimethylsilyl)cyclopropane and 1,1-dichloro-2-(trimethylsilyl)cyclopropane, respectively, with CsF in diglyme: Chan, T. H.; Massuda, D. *Tetrahedron Lett.* **1975**, 3383. The dichlorocyclopropenes have been prepared in low yield by the reduction of tetrachlorocyclopropene using tri-*n*-butyltin hydride: Breslow, R.; Ryan, G.; Groves, J. T. *J. Am. Chem. Soc.* **1970**, *92*, 988. These workers caution that the dichlorocyclopropenes are explosive and possibly toxic.

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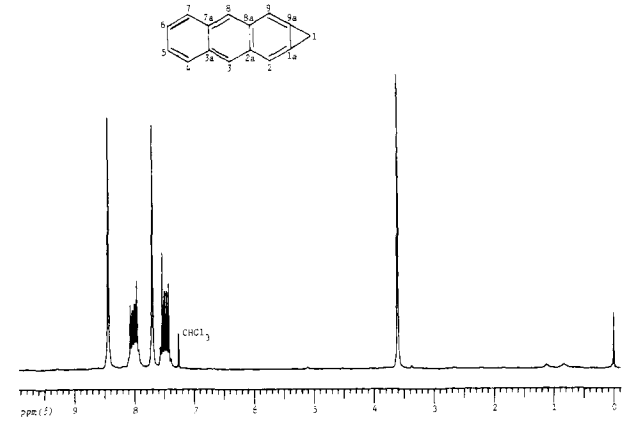
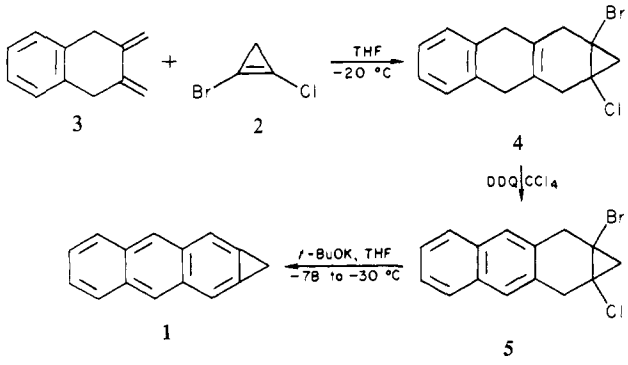


Figure 1. 90-MHz ^1H NMR spectrum of 1*H*-cycloprop[*b*]anthracene in $CDCl_3$.

Scheme I

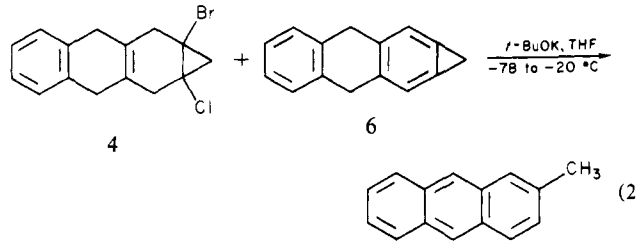


The synthesis of **1** is illustrated in Scheme I. The Diels–Alder addition of **2** to the diene **3**[14] in tetrahydrofuran at −20 °C for 24 h gave the adduct **4**, mp 147–148 °C, in 76% yield.[15] Treatment of **4** (650 mg, 2.1 mmol) with DDQ (715 mg, 3.15 mmol) in CCl_4 at 25 °C for 20 h followed by chromatography on silica gel (CH_2Cl_2) afforded a yellow solid, which was purified by column chromatography using silica gel (hexane, benzene) and then recrystallization from pentane to yield white needles, mp 140–141 °C, in 64% yield.[16] Conversion to **1** was effected by treating **5** (51.5 mg, 0.167 mmol) with potassium *tert*-butoxide (136 mg, 1.2 mmol) at −78 °C in tetrahydrofuran. After warming to −30 °C, the solvent was removed in vacuo and the residue extracted with *n*-pentane to yield 13.2 mg of nearly pure **1** (41.5% yield).

The ^1H NMR spectrum of **1** (Figure 1) displays the expected pattern with singlets at δ 3.56 (bridging CH_2), 7.67 (H_2, H_9), 8.41 (H_3, H_8), and an AA'BB' system at 7.34–7.60 (H_5, H_6) and 7.86–8.12 (H_4, H_7). The ^{13}C NMR spectrum ($CDCl_3$) shows signals at 18.6 (C1), 111.6 (C2, C9), 123.3 (C1a, C9a), 125.3 (C5, C6), 126.6 (C4, C7), 128.1 (C3, C8), 131.7 (C3a, C7a), and 135.2 (C2a, C8a). The ultraviolet spectrum (*n*-hexane) exhibits a maximum at 252 nm (ϵ 117 000) with other absorptions at 320 (ϵ 1500), 334 (ϵ 3500), 351 (ϵ 5300), and 371 (ϵ 4700). The IR spectrum showed the characteristic benzene "double bond" at 1678 cm^{-1}. Elemental composition was provided by high-resolution mass spectrometry: calcd for $C_{15}H_{10}$ *m/e* 190.0783, found *m/e* 190.0781.

The ease of synthesis of **1** using the method described here and the absence of unusual spectral properties indicate that the failure to form **1** using other routes cannot be attributed to a greater degree of bond fixation (and thus destabilization) as previously suggested.[5,7] The determination of exact bond lengths in **1** by X-ray analysis is under investigation.

Other cycloproparenes can also be prepared readily from Diels–Alder adducts of **2**. Thus treatment of **4** with potassium *tert*-butoxide in tetrahydrofuran (eq 2) results in nearly quantitative conversion to a 77:23 mixture (NMR) of 3,8-dihydro-1*H*-cycloprop[*b*]anthracene (**6**)[17] and 2-methylanthracene, respectively.[18] Compound **6** exhibits NMR singlets at δ 3.27 (bridging CH_2), 3.95 (H_3, H_8), and aromatic signals extending from ~7.0 to 7.5.



(2)

Finally, this route promises to be extremely useful for the synthesis of other cycloproparenes. We are currently pursuing these studies.

Acknowledgment. We gratefully acknowledge the Robert A. Welch Foundation (Grant C-490) for support of this work.

Registry No. 1, 287-03-6; **2**, 88180-95-4; **3**, 65957-27-9; **4**, 88180-96-5; **5**, 88180-97-6; **6**, 88180-98-7; 1-bromo-2,2-dichloro-1-(trimethylsilyl)-cyclopropane, 88180-99-8; 2-methylanthracene, 613-12-7.

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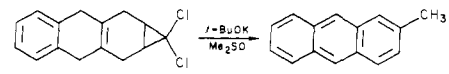
(15) NMR ($CDCl_3$) δ 1.24–1.68 (m, 2 H), 2.60–3.36 (m, 8 H), 7.13 (s, 4 H). Anal. Calcd for $C_{15}H_{14}BrCl$: *m/e* 307.9967. Found: *m/e* 307.9973.

(16) NMR ($CDCl_3$) δ 1.34 (s, 2 H), 3.5–4.0 (m, 4 H), 7.25–7.6 (m, 2 H), 7.53 (s, 2 H) 7.6–7.9 (m, 2 H). Anal. Calcd for $C_{15}H_{12}BrCl$: *m/e* 305.9811. Found: *m/e* 305.9813.

(17) This material decomposes at −20 °C after ~36 h.

(18) A previous attempt[5,7] to synthesize this compound by treating i with potassium *tert*-butoxide in dimethyl sulfoxide yielded only 2-methylanthracene.



i

Unprecedented Asymmetric Induction from a Chiral Acetate Enolate Equivalent. The Condensation of $(\eta\text{-}C_5H_5)Fe(CO)(PPh_3)(COCH_3)$ with Imines

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Various organic complexes of the $(\eta\text{-}C_5H_5)Fe(CO)(PPh_3)$ fragment, **1**, have found applications in organic synthesis because

of the unique reactivity imparted by the metal on the organic residue R.[2] Although mechanistic studies using the chirality in

(1) Fellow of the Alfred P. Sloan Foundation, 1983–1985.

(2) Recent articles by leading practitioners: (a) Chang, T. C. T.; Rosenblum, M. *Tetrahedron Lett.* **1983**, 695–698. (b) Lennon, P.; Rosenblum, M. *J. Am. Chem. Soc.* **1983**, *105*, 1233–1241. (c) Bucheister, A.; Klemarczyk, P.; Rosenblum, M. *Organometallics* **1982**, *1*, 1679–1684. (d) Reger, D. L.; McElligott, P. J. *J. Am. Chem. Soc* **1980**, *102*, 5924–5926. (e) Baker, R.; Rao, V. B.; Erdik, E. *J. Organomet. Chem.* **1983**, *243*, 451–460.

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