with the Lewis acid cocatalyst and develop extensive positive charge at the metal center. Ligand cyclization of **3a**, followed by protonolysis, produced **6a** in 76% yield with complete regioselectivity, as evidenced by the absence of cycloheptane (Table I).[10] Methyl substitution on the tether at the allylic (**b**) or homoallylic (**c**) position gave high yields of dimethylcyclohexane products with 99:1 and 3:97 trans:cis selectivity, respectively. Although the cyclization of **3d** to **6d** did not result in product selectivity (50:50), further increase in the size of the tether substituent (**3e**) produced a 23:77 trans:cis ratio of products **5e**.

The cyclization of substrate **3f**, analogous in substitution pattern to the α, β, and γ carbons of a Ziegler-Natta catalyst with a growing polypropylene chain, differed from those substrates having R^4 = H. Although a trans:cis selectivity of 81:19 was observed, the generation of 3-methyl-1-methylenecyclohexane (**7**), resulting from β-hydride elimination of **5f**, occurred to an extent of 9%. Formation of **7** occurred exclusively from *trans*-**5f**, the product requiring one axial substituent on the cyclohexane ring. Warming the reaction mixture to 0 °C prior to quenching produced a decrease in the amount of *trans*-**6f** and no change in the quantity of *cis*-**6f**. Further, generation of a 3:97 trans:cis mixture of **5c** (**5c** = **5f**) did not produce detectable amounts of **7**. Formation of this common intermediate (**5c**/**f**) from two different substrates (**3c**/**3f**) to give opposite trans:cis preferences demonstrated that alkene insertion was not reversible under these reaction conditions.

With the use of a β-isopropyl substituent, analysis of the cyclization process became more complex. Although Grignard formation from **1g** produced **2g** with only 4% cyclization, subsequent treatment with Cp_2TiCl_2 produced an 83:6:11 ratio of **3g**:*trans*-**5g**:*cis*-**5g**. This unavoidable 17% conversion to cyclic products during transmetalation differed significantly from the 2-4% observed for all other substrates.[12] Treatment of this mixture with $EtAlCl_2$ produced 98% conversion to a 70:19 mixture of *trans*-**6g**:*cis*-**6g**. As was found for **3f**, 9% of the β-hydride elimination product was generated as well. Correcting for the amount of **5** generated prior to the addition of $EtAlCl_2$, the trans selectivity of the ring-forming process promoted by $EtAlCl_2$ was 92:8. The product ratio obtained during transmetalation (6:11), as a result of insertion promoted by MgX_2, was opposite and less selective than that observed for the cyclization promoted by $EtAlCl_2$ (92:8).

In addition to the efficient six-membered-ring formation of unactivated alkenes with sp^3-hybridized carbons,[13] these studies have provided insight into the titanocene-mediated Ziegler-Natta polymerization process through the analysis of monomeric products. As evident from the cyclization of **3d**, a methyl substituent appeared to have little effect on the transition state during the syn coplanar alkene insertion due to the conformational flexibility allowed by the tether. Stereoselectivity observed for the intramolecular insertion of **3b**, **3c**, and **3d** paralleled the intermolecular polymerization of either racemic or optically active α-olefins.[14] In these studies, a high degree of stereoelection was demonstrated through predominant polymerization of similar antipodes of 3-methyl-1-pentene and 4-methyl-1-hexene, while 5-methyl-1-heptene produced low alkene facial selectivity. Conformational control did play a role in the intramolecular insertion of **3f** resulting from β-substituent interaction with the active catalyst species. The resulting 81:19 *trans*-**5f**:*cis*-**5f** product ratio implies that the stereochemical microstructure of poly(1,6-heptadiene) produced by Ziegler-Natta catalysts and alkylaluminum cocatalysts is predominantly trans. The stereoselectivity obtained for formation of poly(1,6-heptadiene) should be much less than that obtained for poly(1,5-hexadiene),[2,4] but could be significantly influenced by the nature of the Lewis acid cocatalyst. This dependence of the resulting stereoselectivity on the Lewis acid cocatalyst ($EtAlCl_2$ or MgX_2) suggests an intimate catalyst-cocatalyst interaction rather than simple generation of a [Cp_2TiR^+] species. Further investigation into the role of the cocatalyst on the chain-end control of propylene polymerization is currently underway.

Acknowledgment. We are grateful to the donors of the Petroleum Research Fund, administered by the American Chemical Society, to the National Institutes of Health (GM44163), and to Michigan State University for support of this research.

Registry No. 1a, 4117-09-3; **1b**, 140661-05-8; **1c**, 140661-06-9; **1d**, 140661-07-0; **1e**, 140661-08-1; **1f**, 140661-09-2; **1g**, 140661-10-5; **3a**, 96228-19-2; **3b**, 140661-11-6; **3c**, 140661-12-7; **3d**, 140661-13-8; **3e**, 140661-14-9; **3f**, 140661-15-0; **3g**, 140661-16-1; **5a**, 96228-21-6; **5b**, 140661-17-2; **5c**, 140661-18-3; *trans*-**5d**, 140661-19-4; *cis*-**5d**, 140661-20-7; *trans*-**5e**, 140661-21-8; *cis*-**5e**, 140661-22-9; *trans*-**5g**, 140661-23-0; *cis*-**5g**, 140661-24-1; **6a**, 108-87-2; **6b**, 6876-23-9; **6c**, 638-04-0; *trans*-**6d**, 2207-04-7; *cis*-**6d**, 624-29-3; *trans*-**6e**, 1678-82-6; *cis*-**6e**, 6069-98-3; *cis*-**6f**, 638-04-0; *trans*-**6g**, 17066-66-9; *cis*-**6g**, 17066-65-8; **7**, 3101-50-6.

(12) In the case of substrate **g**, intramolecular insertion could not be avoided during the transmetalation step using either toluene (7-17% **5g**) or CH_2Cl_2 (32% **5g**), and when allowed to proceed, cyclization has reached >90% conversion to **5** when R^4 = alkyl (1:2 ratio of *trans*-**5**:*cis*-**5**). Coincidently, free radical cyclization of **1g** (0.05 M/nBu_3SnH/AIBN/PhH/80 °C) produced 31% conversion to cyclic products composed of the same 10:20 ratio of *trans*-**6g**:*cis*-**6g**.

(13) Other metals have also been reported to mediate stereoselective six-membered-ring formation without evidence of radical intermediates. Lithium: (a) Drozd, V. N.; Ustynyuk, Y. A.; Tsel'eve, M. A.; Dmitriev, L. B. *J. Gen. Chem. USSR* **1969**, *39*, 1951. (b) Bailey, W. F.; Nurmi, T. T.; Patricia, J. J.; Wang, W. *J. Am. Chem. Soc.* **1987**, *109*, 2442. Aluminum: (c) Rienacker, R.; Schwenger, D. *Justus Liebigs Ann. Chem.* **1977**, 1633.

(14) For reviews and leading references in the polymerization of asymmetric 1-alkenes, see: (a) Pino, P. *Adv. Polym. Sci.* **1965**, *4*, 393. (b) Pino, P.; Ciardelli, F.; Zandomeneghi, M. *Annu. Rev. Phys. Chem.* **1970**, *21*, 561. (c) Kissin, Y. V. *Isospecific Polymerization of Olefins with Heterogeneous Ziegler-Natta Catalysts*; Springer-Verlag: New York, 1985; pp 295-306. (d) Ciardelli, F.; Carlini, C.; Altomare, A.; Menconi, F.; Chien, J. C. W. *Transition Metal Catalyzed Polymerizations*; Quirk, R. P., Ed.; Cambridge University Press: Cambridge, 1988; p 25. (e) Vizzini, J.; Ciardelli, F.; Chien, J. C. W. *Macromolecules* **1992**, *25*, 108.

^{13}C NMR Spectroscopic Determination of the Magnitude of the β-Silyl Stabilization Effect in 1-Mesitylvinyl Cations

Hans-Ullrich Siehl* and Frank-Peter Kaufmann

Institut für Organische Chemie
Universität Tübingen
D-7400 Tübingen, Germany

Received March 2, 1992

Computational and experimental evidence demonstrates the stabilizing effect of β-silyl groups in carbocations.[1] The hyperconjugational origin of the effect leads to a pronounced dihedral dependence and bond angle distortions. This has recently been proven by dynamic ^{13}C NMR spectroscopy and by IGLO calculations of chemical shifts.[2,3]

Vinyl cations are especially well suited to study β-hyperconjugation. The $C^+{=}C_\beta$ bond is shorter than a single bond, and the σ bond of a β-substituent to C_β is in the plane of the "vacant" 2p orbital on C^+, thus allowing maximum overlap for hyperconjugation. 1-Arylvinyl cations, first postulated in 1964,[4] have been rather elusive toward NMR spectroscopic observation. Heterolytic cleavage of sp^2-C-halogen bonds in 1-arylvinyl halides[5] as well as protonation of alkynes,[6] except for 1-ferrocenylalkynes,[7] has

(1) For a recent review, see: Lambert, J. B. *Tetrahedron* **1990**, *46*, 2677 and references cited.

(2) Siehl, H.-U.; Kaufmann, F.-P.; Apeloig, Y.; Braude, V.; Danovich, D.; Berndt, A.; Stamatis, N. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1479.

(3) (a) In contrast to our findings[2] in a recent study[3b] of 1-adamantyl-2-(trimethylsilyl)allyl cation, no stabilization but some destabilizing influence of a β-silyl substituent was inferred from ^{13}C-NMR data. This is due to the orthogonal alignment of the β-C-Si bond and the "vacant" 2p orbital on C^+ and to steric perturbation of allyl resonance in this cation. (b) Prakash, G. K. S.; Reddy, V. P.; Rasul, G.; Casanova, J.; Olah, G. A. *J. Am. Chem. Soc.* **1992**, *114*, 3076.

(4) Grob, C. A.; Cseh, G. *Helv. Chim. Acta* **1964**, *47*, 194.

(5) Siehl, H.-U.; Hanack, M. *J. Am. Chem. Soc.* **1980**, *102*, 2686.

0002-7863/92/1514-4937$03.00/0

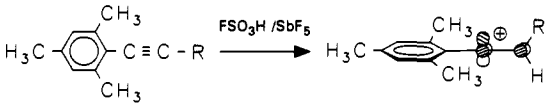
Table I. ^{13}C NMR Spectral Data for Cations **1–10**[a]

no.	α	β	C_1	ortho	meta	para	o-Me; p-Me	other
1	238.5	82.3 (177)	116.6	167.8	133.8 (166)	180.0	21.7; 26.1 (130); (131)	*b*
2	237.3	107.1 (174)	118.4	166.4	133.4 (165)	178.5	21.5; 25.8 (130); (129)	C_q 40.9, Me 30.0 (125)
3	238.7	106.3 (169)	118.7	166.1	133.2 (166)	177.9	21.5; 25.7 (130); (131)	$C_{1'}$ 45.0, $C_{2',8',9'}$ 43.4 (129), $C_{3',5',7'}$ 29.2 (128), $C_{6',4',10'}$ 35.6 (125)
4	206.0	83.6 (183)	113.5	162.7	132.5 (166)	168.5	21.4; 24.4 (131); (129)	SiMe −4.2 (122), CH 16.5 (129), CMe 16.7 (129)
5	206.0	83.2 (182)	113.2	162.3	132.2 (165)	168.2	21.3; 24.2 (127); (124)	SiMe −5.4 (122), C_q 19.8, CMe 24.9 (122)
6	207.3	84.3 (184)	113.5	162.3	132.3 (165)	168.1	21.4; 24.3 (131); (129)	SiMe −2.9 (128), C_q 26.6, C_qMe 17.8 (125), CH 33.6 (156), CHMe 18.0 (132)
7	207.8	81.1 (175)	113.6	162.3	132.6 (166)	168.5	21.8; 24.4 (134); (132)	CH 13.4 (118), Me 17.8 (125)
8	192.2	136.2	119.5	155.7	131.6 (160)	165.3	21.0; 23.7 (129); (130)	C_γ 213.9, Me 34.9 (132)
9	204.3 (154)	27.1 (129)	140.5	166.4 163.9	136.5 134.4 (165) (171)	179.6	26.6; 21.6 25.3 (130); (131) (127)	
10	172.0 (166)		144.1	168.3	135.3 (170)	189.6	20.9; 27.3 (135); (131)	

[a] δ (±0.1 ppm) at −120 °C, in SO_2ClF/SO_2F_2 at 100.6 MHz, internal reference; δ = 53.8 (CD_2Cl_2) or 55.7 (NMe_4^+); $^1J_{CH}$ coupling constants (±1.8 Hz) in parentheses. [b] $(Si(Me)_2CH(Me)_2)OSO_2F$, SiMe −4.5 (122), CH 14.9 (127), CHMe 14.8 (127).

not yet been successful to yield stable vinyl cations.

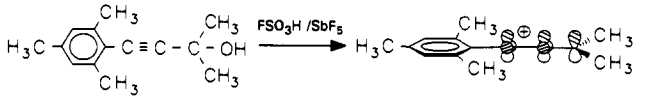
We report here the first NMR spectroscopic characterization of 1-arylvinyl cations with varying β-substituents including alkyl, alkenyl, and silyl groups which allows a comparison of charge distribution and thus a determination of the stabilizing effect of β-silyl groups in these carbocations.



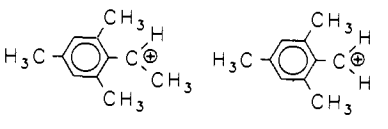
11, R = H
12, R = t-butyl
13, R = 1'-adamantyl
14, R = $Si(Me)_2$ i-pr
15, R = $Si(Me)_2$ t-but
16, R = $Si(Me)_2$ t-hex
17, R = $Si(i\text{-}pr)_3$

1, R = H
2, R = t-butyl
3, R = 1'-adamantyl
4, R = $Si(Me)_2$ i-pr
5, R = $Si(Me)_2$ t-but
6, R = $Si(Me)_2$ t-hex
7, R = $Si(i\text{-}pr)_3$

Protonation of 2-alkyl- or 2-silyl-substituted 1-mesitylalkynes **12–17** with FSO_3H/SbF_5 in SO_2ClF/SO_2F_2 at −130 °C using contemporary experimental techniques[8] yields light colored solutions of the corresponding vinyl cations **2–7**. 1-Mesityl-3,3-dimethylallenyl cation (**8**) was generated in the same way from the tertiary alcohol **18**. For comparison, 1-mesitylethyl cation (**9**) and mesitylmethyl cation (**10**) were prepared from the corresponding alcohol and chloride, respectively.[9]



18 **8**



9 **10**

Atempts to ionize **11** and 1-mesityl-2-(trimethylsilyl)alkyne (**11**, R = $SiMe_3$) to yield the cations **1** and **1**-$SiMe_3$ lead only to complex mixtures. **1** is formed, however, in a clean reaction, when a solution of 1-mesityl-2-(dimethylisopropylsilyl)vinyl cation (**4**) is warmed from −130 to −100 °C for 10 min.

Cations **1–10** were characterized by their ^1H and ^{13}C NMR chemical shifts and coupling constants. Assignments were done using specific ^1H-decoupled ^{13}C NMR spectra and comparison with other vinyl cations[10] and with IGLO calculated ^{13}C NMR shift data of model vinyl cations.[2]

The chemical shifts of the C^+ carbons in **1–8** (239–192 ppm) (Table I) indicate strong shielding (~150–200 ppm) relative to the IGLO calculated chemical shifts of alkylvinyl cations.[2] Comparable shieldings for the C^+ carbon have been observed in vinyl cations stabilized by 2p–π allyl resonance or by hyperconjugation with α- or β-cyclopropyl substituents[10a,b] or with four β-silyl groups.[2] The chemical shift difference for the C^+ position in the β-silyl vinyl cations **4–7** and in the silicon-free analogs **1–3** is 33–30 ppm.

The signal for the sp^2 hybridized β-carbon in **1–7** (107–82 ppm, $^1J_{CH}$ = 184–169 Hz) was assigned by specific decoupling of the vinylic protons (7.06–6.69 ppm). The chemical shift of C_β in **1–7** is in accord with that in other vinyl cations[7,10] and with IGLO calculations.[2] Comparing **2** and **3** with **4–7** shows the different effect of alkyl and silyl substituents on the shift of C_β ($\Delta\delta \sim -24$ ppm).

The large shielding effect of 20–30 ppm for the aromatic C_1 position in **1–8** relative to **9** and **10** is due to the adjacent C^+ carbon, which is sp or sp^2 hybridized, respectively. The equivalent two ortho and two meta positions in the vinyl cations **1–7** and in the allenyl cation **8** as compared to the 1-mesitylethyl cation (**9**) give direct proof for linear cation structures **1–8** with the "vacant" 2p orbital on C^+ in the plane with the aryl π system.

The chemical shift of the C^+ carbon in **1–8** is not only dependent on the charge density but also influenced by a substituent effect on the chemical shift from the different substituents at C_β. The para carbon position is sufficiently remote from C_β so that substituent effects on the chemical shift are negligible. It is thus a better choice to monitor the electronic demand of the carbocation center in **1–10** and to evaluate the effect of a β-silyl group on a

(6) (a) Olah, G. A.; Spear, R. J. *J. Am. Chem. Soc.* **1975**, *97*, 1845. (b) van der Höut-Lodder, A. E.; de Haan, J. W.; van de Ven, L. J. M.; Buck, H. M. *Recl. Trav. Chim.* **1973**, *92*, 1040. (c) Olah, G. A.; Mayr, H. *J. Am. Chem. Soc.* **1976**, *98*, 7333. (d) Olah, G. A.; Staral, J. S.; Spear, R. J.; Liang, G. *J. Am. Chem. Soc.* **1975**, *97*, 5489.

(7) Koch, E.-W.; Siehl, H.-U.; Hanack, M. *Tetrahedron Lett.* **1985**, *26*, 1493.

(8) Lenoir, D.; Siehl, H.-U. In *Houben-Weyl Methoden der Organischen Chemie*; Hanack, M., Ed.; Thieme: Stuttgart, 1990; Vol. E19c, pp 26–32.

(9) (a) Olah, G. A.; Porter, R. D.; Kelly, P. *J. Am. Chem. Soc.* **1971**, *93*, 464. (b) Bollinger, J. M.; Comisarow, M. B.; Cupas, C. A.; Olah, G. A. *J. Am. Chem. Soc.* **1967**, *89*, 5687.

(10) (a) Siehl, H.-U.; Koch, E.-W. *J. Org. Chem.* **1984**, *49*, 575. (b) Siehl, H.-U. *J. Chem. Soc., Chem. Commun.* **1984**, 635. (c) Siehl, H.-U.; Mayr, H. *J. Am. Chem. Soc.* **1982**, *104*, 909.

positive charge. The more stabilizing a β-substituent, the less is the demand for charge delocalization into the aromatic ring.

The para carbon chemical shifts in 1-mesitylvinyl cation (**1**) (181.0 ppm) and 1-mesitylethyl cation (**9**) (179.6 ppm) are similar. The electron demand is thus about the same, demonstrating that both cations are stabilized by σ bond interaction with the β-substituent as compared to mesitylmethyl cation (**10**) (189.6 ppm), which lacks a β-substituent.

A pronounced upfield shift of the para carbon (10–12 ppm) is observed for the β-silyl vinyl cations **4–7** relative to the silyl-free cations **1–3**, indicating a decrease in electron demand when the β-substituent is changed from β-H or β-alkyl to a β-silyl group. This shows that β-C–Si hyperconjugation is more efficient than β-C–H or β-C–C hyperconjugation. In fact the similar para carbon shift of the silyl-substituted cations **4–7** (168–170 ppm) to that of the 1-mesitylallenyl cation **8** (165.9 ppm), which in addition to α-aryl conjugation enjoys β-allyl resonance stabilization, shows that hyperconjugative interaction of a β-C–Si σ bond with the "vacant" 2p orbital on C^+ in **4–7** is about as efficient in dispersing the positive charge as β-π conjugation in **8**.

In conclusion we have prepared the first persistent α-aryl vinyl cations by protonation of alkynes in superacids. The NMR spectroscopic data of the β-silyl-substituted vinyl cations give experimental proof for the hyperconjugative charge delocalizing ability of β-silyl groups, and the comparison with silyl-free analogs demonstrates the magnitude of the β-silyl effect. The results are in accord with IGLO chemical shift calculations on model cations.

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

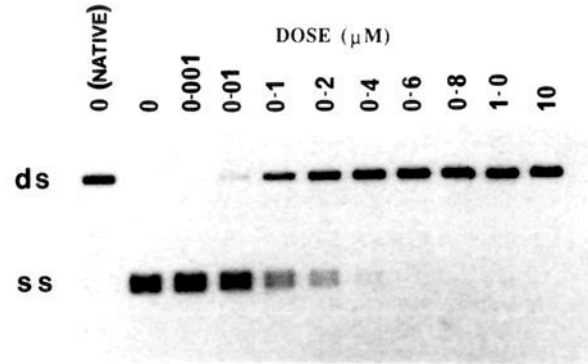


Figure 1. Autoradiograph of a neutral agarose gel showing DNA interstrand cross-linking by **7** in linear ^{32}P end-labeled pBR322 DNA. Drug reactions (2 h at 37 °C) were in 25 mM triethanolamine/1 mM EDTA pH 7.2 buffer with 10 ng of DNA in a final volume of 50 μL. Reaction was terminated by addition of an equal volume of 0.6 M sodium acetate, 20 mM EDTA, and 100 μg/mL tRNA, and the DNA precipitated with ethanol. Dried pellets were taken up in strand separation buffer (30% w/w DMSO in 1mM EDTA). Denaturation for 2 min at 90 °C was followed by immediate chilling in an ice–water bath. Electrophoresis was carried out on 0.8% w/v submerged horizontal agarose gels at 40 V for 16 h with tris-acetate running buffer. Double-stranded (ds) and single-stranded (ss) DNA were quantitated by laser densitometry.

Table I. In Vitro Cytotoxicity of **7** and **8**[a]

IC_{50} (μM)	L1210	ADJ/PC6	CH1
7 (DSB-120)	0.01	0.0005	0.003
8 (DC-81)	0.38	0.33	0.1

[a] IC_{50} is the dose (μM) for 50% growth inhibition compared to solvent controls. Drugs were dissolved in DMSO to provide a final concentration of 0.05% DMSO. Incubation times (37 °C) were as follows: L1210, 3 days; ADJ/PC6, 4 days; CH1, 9 days.

Rational Design of a Highly Efficient Irreversible DNA Interstrand Cross-Linking Agent Based on the Pyrrolobenzodiazepine Ring System

D. Subhas Bose,[†] Andrew S. Thompson,[†] Jingshan Ching,[†] John A. Hartley,[‡] Mark D. Berardini,[‡] Terence C. Jenkins,[§] Stephen Neidle,[§] Laurence H. Hurley,[∥] and David E. Thurston*[,†]

School of Pharmacy and Biomedical Sciences
University of Portsmouth, King Henry I Street
Portsmouth PO1 2DZ, U.K.
Department of Oncology
University College and Middlesex School of Medicine
91 Riding House Street, London W1P 8BT, U.K.
CRC Biomolecular Structure Unit
Institute of Cancer Research
Sutton, Surrey SM2 5NG, U.K.
College of Pharmacy
University of Texas at Austin
Austin, Texas 78712

Received December 18, 1991

Many DNA cross-linking agents with significant antitumor activity[1] are GC site-specific, which may contribute to their potency, as it has been established that a number of oncogenes, including c-Ha-*ras*, contain highly GC-rich regions.[2] Most known cross-linking agents are of sufficient size to recognize only two or three base pairs, and extension of this limited sequence recognition is of interest, as such agents may have the potential to produce irreparable cross-links at precisely defined genomic locations.[3] Furthermore, clinically-useful cross-linking agents such as the nitrogen mustards alkylate within the major groove of DNA whereas, with few exceptions,[4–6] the biological consequences of minor groove cross-linking have been relatively unexplored. We report here the synthesis of a pyrrolo[2,1-*c*][1,4]benzodiazepine (PBD) bifunctional alkylating agent, DSB-120 (**7**), that forms an irreversible interstrand cross-link between two guanine bases within the minor groove via their exocyclic N2 atoms.[7] According to molecular modeling and NMR studies, it spans six base pairs, actively recognizing a central 5′-GATC sequence. It is one of the most efficient DNA cross-linking agents known and is significantly cytotoxic toward tumor cells in vitro.

The PBD antitumor antibiotics monoalkylate the exocyclic N2 of guanine in the minor groove of DNA via their electrophilic

[†] University of Portsmouth.
[‡] University College and Middlesex School of Medicine.
[§] Institute of Cancer Research.
[∥] University of Texas at Austin.

(1) (a) Kohn, K. W. In *Molecular Aspects of Anticancer Drug Action*; Neidle, S., Waring, M. J., Eds.; Macmillan Press: London, 1983; pp 315–361. (b) Pratt, W. B.; Ruddon, R. W. *The Anticancer Drugs*; Oxford University Press: New York, 1979. (c) Chabner, B., Ed. *Pharmacological Principles of Cancer Treatment*; W. B. Saunders and Co.: Philadelphia, 1982.
(2) Mattes, W. B.; Hartley, J. A.; Kohn, K. W.; Matheson, D. W. *Carcinogenesis* **1988**, *9*, 2065–2072.
(3) (a) Hopkins, P. B.; Millard, J. T.; Woo, J.; Weidner, M. F.; Kirchner, J. J.; Sigurdsson, S. Th.; Raucher, S. *Tetrahedron* **1991**, *47*, 2475–2489. (b) Millard, J. T.; Weidner, M. F.; Kirchner, J. J.; Ribeiro, S.; Hopkins, P. B. *Nucleic Acids Res.* **1991**, *19*, 1885–1891. (c) Thurston, D. E.; Thompson, A. S. *Chem. Br.* **1990**, *26*, 767–772.
(4) Tomasz, M.; Lipman, R.; Chowdary, D.; Pawlak, J.; Verdine, G. L.; Nakanishi, K. *Science* **1987**, *235*, 1204–1208.
(5) (a) Mitchell, M. A.; Johnson, P. D.; Williams, M. G.; Aristoff, P. A. *J. Am. Chem. Soc.* **1989**, *111*, 6428–6429. (b) Mitchell, M. A.; Kelly, R. C.; Wicnienski, N. A.; Hatzenbuhler, N. T.; Williams, M. G.; Petzold, G. L.; Slightom, J. L.; Siemieniak, D. R. *J. Am. Chem. Soc.* **1991**, *113*, 8994–8995. (c) Lee, C.-S.; Gibson, N. W. *Cancer Res.* **1991**, *51*, 6586–6591.
(6) (a) Farmer, J. D.; Rudnicki, S. M., Jr.; Suggs, J. W. *Tetrahedron Lett.* **1988**, *29*, 5105–5108. (b) Farmer, J. D., Jr.; Gustafson, G. R.; Conti, A.; Zimmt, M. B.; Suggs, J. W. *Nucleic Acids Res.* **1991**, *19*, 899–903.
(7) British Patent Application No. 9205051.7 (9 March, 1992).

0002-7863/92/1514-4939$03.00/0