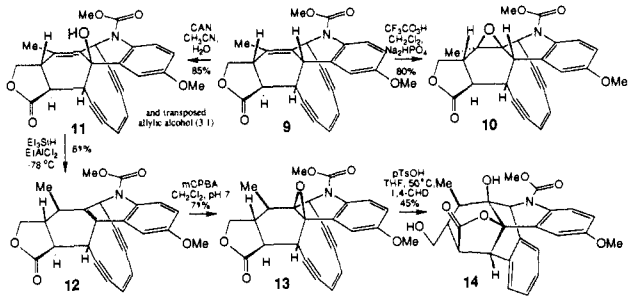
Scheme II



THF) resulted in the trisubstituted dihydroquinoline derivative **6** in 60% overall yield. An X-ray crystallographic analysis of a related heterocycle **6a** (mp 151-152 °C), prepared by a similar reaction sequence, provided evidence for the 2,3,6-trisubstitution pattern and revealed the axial orientation of the acetylene moiety, as anticipated on consideration of allylic ($A^{(1,3)}$) strain[12] that would exist with the equatorially disposed conformer (Figure 1B).[13] Such an orientation was considered desirable for subsequent cyclization reactions. Next, **6** was converted to the cyclization substrates **7** and **8** by carbon-oxygen and carbon-carbon coupling processes, respectively.

Subjection of **7** to the Sonogashira[14] coupling conditions or **8** to the Yamaguchi macrolactonization protocol[15] was hoped to afford the corresponding macrolactone (Figure 1A). Instead, both reactions provided, at room temperature, the product of an apparent transannular Diels-Alder reaction (**9**).[16] Verification of structure followed X-ray crystallographic analysis (Figure 1C) and revealed the bending of the ring acetylenes that is characteristic of the enediyne antibiotics.[13] In contrast to the transannular Diels-Alder reaction, attempted intramolecular Diels-Alder reaction of the methyl ester, *tert*-butyldimethylsilyl ether of **8** failed entirely; slow decomposition occurred instead at temperatures above 180 °C.

Having secured a simple and efficient route to the target dynemicin A model system, we next investigated preliminary functionalization reactions of **9**. An epoxide trigger to the acetylene coupling (Bergman) reaction was installed by the reaction of **9** with anhydrous trifluoroperacetic acid in CH_2Cl_2, which afforded **10** in 80% yield. Translocation of the dynemicin-type epoxide to a calicheamicin-type epoxide (as found in **10**) results in a thermally activatible substrate for the Bergman reaction; the details of this process will be reported elsewhere. In order to examine the positional epoxide isomer found in dynemicin A, isomerization of the tetrasubstituted olefin was required. This was achieved by the oxidation-reduction sequence shown in Scheme II. Benzylic hydroxylation of **9** with ceric ammonium nitrate provided a mixture of **11** and an allylic alcohol isomer (3:1 ratio) in 85% yield. Reaction of either the individual isomers or the 3:1 mixture with Et_3SiH and $EtAlCl_2$ provided a 61% yield of **12** and **9** in an 8:1 ratio. Epoxidation of **12** with mCPBA in a buffered medium resulted in the formation of the stable dynemicin-like epoxide **13**, whose structure was confirmed by X-ray diffractometry (Figure 1D), in 71% yield. Treatment of **13** with pTsOH and 1,4-cyclohexadiene in THF (50 °C, 10 h) resulted in the predominant formation of **14** (45%), which has undergone epoxide ring opening, Bergman aromatization, and translactonization.

The transannular Diels-Alder reaction appears well suited to access structures related to the enediyne family of natural products. Efforts to extend this research are now underway.

Acknowledgment. We thank the NIGMS (GM-40883 awarded to S.L.S.) and the NCI (CA-24487 awarded to J.C.) for financial support and the Division of Organic Chemistry of the American Chemical Society (sponsored by Pfizer, Inc., in support of J.A.P., Jr.) and the NIH (CA-08506, in support of F.J.S.) for fellowships. The assistance of Dr. H. Chikashita is gratefully acknowledged.

Supplementary Material Available: Spectral data (^1H NMR, ^{13}C NMR, IR, and MS) for compounds **9**, **10**, and **12-14** and crystallographic data for compounds **6a**, **9**, and **13** including experimental details, atomic coordinates and thermal parameters, bond distances and angles, and torsional angles (41 pages). Ordering information is given on any current masthead page.

(11) Prepared by the following reaction sequence: (a) *cis*-1,2-dichloroethylene, $Pd(PPh_3)_4$ (5%), (thexyldimethylsilyl)acetylene, $nPrNH_2$, CuI (15%), benzene, 75%; (b) (trimethylsilyl)acetylene, $Pd(PPh_3)_4$ (5%), $nPrNH_2$, CuI (15%), benzene, 93%; (c) $AgNO_3$, EtOH, H_2O; KCN (80%); (d) BuLi (-78 °C); $MgBr_2$-Et_2O (0 °C).

(12) Johnson, F. *Chem. Rev.* **1968**, 375.

(13) Crystallographic parameters are provided in the supplementary material.

(14) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467.

(15) Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989. High concentrations of DMAP were employed. For example, see: (a) Tone, H.; Nishi, T.; Oikawa, Y.; Kikota, M.; Yonemitsu, O. *Chem. Pharm. Bull.* **1989**, *37*, 1167. (b) Hikota, M.; Tone, H.; Horita, K.; Yonemitsu, O. *J. Org. Chem.* **1990**, *55*, 7.

(16) Selected examples: (a) Cram. D. J.; Knox, G. R. *J. Am. Chem. Soc.* **1961**, *83*, 2204. (b) Wasserman, H. H.; Doumaux, A. R., *J. Am. Chem. Soc.* **1962**, *84*, 4611. (c) Bērubé, G.; Deslongchamps, P. *Can. J. Chem.* **1990**, *68*, 404 and references cited therein.

Synthesis and Characterization of Hexamethyltellurium(VI)

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Peralkylated derivatives of hexavalent transition metals, compounds such as $W(CH_3)_6$ and $Re(CH_3)_6$,[1] have been known for many years; however, the analogous main-group compounds, species like $Te(CH_3)_6$ or $Se(CH_3)_6$, have not been previously reported. Within the main-group elements, $Sb(CH_3)_5$ and $As(CH_3)_5$ have been well characterized[2,3] and a very few perfluoroalkyl and aryl Te(VI) polyfluorides have been prepared,[4] but until the very recent synthesis of $Te(CH_3)_4$,[5] even peralkylated derivatives of Te(IV) were unknown. We report the synthesis, isolation, and characterization of $Te(CH_3)_6$, the first peralkylated hexavalent derivative of one of the representative elements.

Synthesis of $TeF_2(CH_3)_4$.[6] Under an inert atmosphere, XeF_2,[7] 0.359 25 g (2.1220 mmol), was placed into a 10-mL flask that was equipped with a Teflon valve. The flask was degassed, and then $Te(CH_3)_4$, 0.319 65 g (1.7026 mmol), and dry CH_3CN, 5 mL, were added. The solution was stirred at -30 °C for 2 h and then at ambient temperature for 1 h. All of the materials volatile at 0 °C were removed, which left a white solid, $TeF_2(CH_3)_4$, 0.333 05 g (1.4754 mmol), 87%.

The mass spectral and NMR data for this new compound are contained in Tables I and II. Exact mass for the *m/e* 213 ion ($^{130}TeF_2(CH_3)_3^+$): calcd 212.9739, measd 212.9741; $\Delta_m/_m$ = 0.9

(1) Shortland, A. J.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1973**, 872. Galyer, L.; Mertis, K.; Wilkinson, G. *J. Organomet. Chem.* **1975**, *85*, C37. Mertis, K.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1976**, 1488.

(2) Wittig, G.; Torssell, K. *Acta Chem. Scand.* **1953**, *7*, 1293.

(3) Mitschke, K.; Schmidbaur, H. *Chem. Ber.* **1973**, *106*, 3645. Bohra, R.; Roesky, H. W. *Adv. Inorg. Chem. Radiochem.* **1984**, *28*, 203.

(4) Desjardins, C. D.; Lau, C.; Passmore, J. *Inorg. Nucl. Chem. Lett.* **1974**, *10*, 151. Alam, K.; Janzen, A. F. *J. Fluorine Chem.* **1985**, *27*, 467. Wittig, G.; Fritz, H. *Justus Liebigs Ann. Chem.* **1952**, *577*, 39. Cohen, S. C.; Reddy, M. L. N.; Massey, A. G. *J. Organomet. Chem.* **1968**, *11*, 563. $TeI_4(CH_3)_2$ has been shown to be a Te(IV) derivative: Pritzkow, H. *Inorg. Chem.* **1979**, *18*, 311.

(5) Gedridge, R. W.; Harris, D. C.; Higa, K. T.; Nissan, R. A. *Organometallics* **1989**, *8*, 2817.

(6) All manipulations of compounds were carried out either in a glove bag or on a vacuum line. Chemical shifts were measured vs external TMS (^1H and ^{13}C), TFA (^{19}F), or $Te(CH_3)_2$ (^{125}Te).

(7) Williamson, S. M. *Inorg. Synth.* **1968**, *11*, 147.

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Table I. Mass Spectral Data for $Te(CH_3)_6$, $TeF_2(CH_3)_4$, and $Te(CH_3)_4$

$TeMe_6$[a]			TeF_2Me_4[a]			$Te(Me)_4$[a,b]		
mass	ion	% abundance	mass	ion	% abundance	mass	ion	% abundance
206	$TeMe_5H^+$	2.0				175	$TeMe_3^+$	15.6
205	$TeMe_5^+$	55.9	213	$F_2TeMe_3^+$	63.0	160	$TeMe_2^+$	100
176	$TeMe_3H^+$	1.8	209	$FTeMe_4^+$	47.8	146	$TeMeH^+$	5.4
175	$TeMe_3^+$	100	183	F_2TeMe^+	20.8	145	$TeMe^+$	81.3
161	$TeMe_2H^+$	2.1				131	TeH^+	15.6
160	$TeMe_2^+$	61.0	179	$FTeMe_2^+$	100	130	Te^+	18.8
146	$TeMeH^+$	2.5	164	$FTeMe^+$	9.5			
145	$TeMe^+$	29.7	160	$TeMe_2^+$	48.0			
131	TeH^+	6.8	145	$TeMe^+$	37.4			
130	Te^+	5.1	131	TeH^+	6.5			
			130	Te^+	6.8			

[a] Spectra were obtained from an AEI MS-30 instrument at 70 eV. The EI source was operated at ambient temperature. Reported intensities are based upon the ^{130}Te isotope (34.48%). Aside from those reported here, no other ions were detected. [b] Previously unreported.

Table II. Nuclear Magnetic Resonance Data for Alkylated Tellurium Compounds[a]

compd	δ ^{125}Te	δ ^{13}C	δ ^{1}H	δ ^{19}F	$^{2}J_{Te-H}$	$^{1}J_{Te-C}$	$^{1}J_{C-H}$	$^{1}J_{Te-F}$
$Te(CH_3)_2$[b]	0.0	-21.5	1.83		20.8	158.5	140.7	
$Te(CH_3)_4$[b]	-67	20.6	0.99		34.0	127.8	133.4	
$Te(CH_3)_6$[c]	21.7 (m)	37.1 (q)	1.26 (s)		3.0	38.2	131.7	
$TeF_2(CH_3)_4$[c]	592 (t)	36.4 (m)	1.24 (s)	84.0 (s)	43.7	-	-	1830
		25.6 (br)	2.07 (s)		44.3	-		

[a] Chemical shifts in parts per million; coupling constants in hertz; s = singlet, t = triplet, q = quartet, br = broad, m = multiplet. [b] From refs 5 and 10. [c] In C_6D_6.

ppm. Mp (sealed tube): 73 °C.

Synthesis of $Te(CH_3)_6$. Under N_2, *cis*-$TeF_2(CH_3)_4$, 0.233 05 g (1.0324 mmol), was added to a 10-mL flask and degassed, and then $Zn(CH_3)_2$, 0.151 60 g (1.5884 mmol), and diethyl ether, 5 mL, were added. The solution was stirred magnetically for 2 h at 0 °C and then separated. Hexamethyltellurium, 0.153 87 g (0.7064 mmol), 68%, a volatile white solid that is retained at -23 °C, was separated by fractionation. The low-resolution mass spectral and NMR data (Figure 1) are summarized in Tables I and II.

Ir (in CCl_4): 2994 (s), 2909 (s), 2786 (w), 2391 (w), 2337 (m), 1630 (w), 1472 (w), 1406 (m), 1185 (s), 807 (s), and 469 (s) cm^{-1}. Exact mass for the *m/e* 205 ion ($^{130}Te(CH_3)_5^+$): calcd 205.0241, measd 205.0238; $\Delta m/m$ = 1.5 ppm. Exact mass for the *m/e* 203 ion ($^{128}Te(CH_3)_5^+$): calcd 203.0221, measd 203.0220; $\Delta m/m$ = 0.5 ppm.

Reaction of $Te(CH_3)_6$ with Br_2. Under N_2, $Te(CH_3)_6$, 0.024 95 g (0.1146 mmol), was placed in a reactor and degassed, and then bromine, 1.406 60 g (8.8018 mmol), was added. The vessel was held at -78 °C for 0.5 h and warmed to ambient temperature for 0.5 h, and then the contents were separated by fractionation. Methyl bromide, 0.065 20 g (0.6868 mmol), was identified by ^1H NMR data and by mass spectrometry. The $TeBr_4$ that was generated was reacted with excess HNO_3 at 140 °C, and then the TeO_2 formed, 0.018 25 g (0.1144 mmol), was dried and weighed. The experimental Te/CH_3 ratio in $Te(CH_3)_6$ is 1.00/6.00. Analysis for Te in $Te(CH_3)_6$: calc 58.6%, found 58.5%.

Thermal Stability of $Te(CH_3)_6$. A sample consisting of $Te(CH_3)_6$, 10% in C_6D_6, was heated in a sealed Pyrex vessel to 140 °C for 4.5 h. Proton NMR spectra indicated that the $Te(CH_3)_6$ was unchanged.

The first reaction described above demonstrates that XeF_2 cleanly oxidizes $Te(CH_3)_4$ to $TeF_2(CH_3)_4$ in high yields. Gaseous Xe is the only other product observed. The NMR data unequivocally indicate that the fluorine ligands are cis in the difluoride. Tetramethyltellurium(VI) difluoride is a sublimable white solid that is stable for several days in the absence of air. The 70-eV mass spectra (Table I) do not contain molecular ions, but both the $TeF_2(CH_3)_3^+$ and the $TeF(CH_3)_4^+$ ions are reasonably prominent in the spectrum. The relative intensities of hydride-containing ions, e.g., TeH^+, present in the 70-eV spectrum can be easily decreased by a reduction of the electron voltage.

If $TeF_2(CH_3)_4$ is not separated from the reaction mixture for several hours, a second Te-containing species, $TeF_3(CH_3)_3$, is generated by the reaction of $TeF_2(CH_3)_4$ with the HF formed from

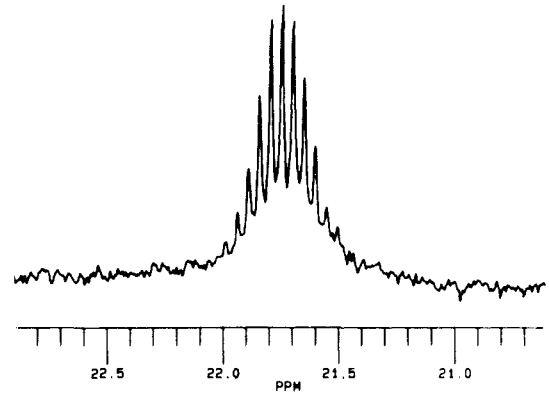

Figure 1. The ^{125}Te NMR spectrum of $Te(CH_3)_6$. The $^{2}J_{Te-H}$ coupling constant is 3.0 Hz. Only 11 of the anticipated 19 lines are evident in the ^{125}Te spectrum, but these 11 lines contain 99.247% of the total intensity of the Te resonance.

XeF_2 and the solvent, CH_3CN. The ^{19}F NMR data for the trifluoride (100.3 (t) ppm, 1 F, J_{Te-F} = 2677 Hz; 10.0 (d) ppm, 2 F, J_{Te-F} = 1752 Hz, J_{F-F} = 40 Hz) clearly indicate the meridional stereochemistry.

The reaction of $TeF_2(CH_3)_4$ with $Zn(CH_3)_2$ in diethyl ether results in $Te(CH_3)_6$, a colorless volatile solid. As was found for $Te(CH_3)_4$ and $TeF_2(CH_3)_4$, Table I, the molecular ions for $Te(CH_3)_6$ are not observed in the low-resolution mass spectrum,[8] but the exact mass data prove the attachment of five CH_3 groups to the Te atom, and the bromination reaction shows that the sixth ligand is also a methyl group. All of the currently available evidence is consistent with octahedral coordination of the ligands about the Te(VI) centers in each of the new compounds discussed here.

The reactivity of hexavalent tellurium compounds is currently under intensive investigation, but one of the more interesting aspects, the stability of the Te(VI) alkyl derivatives, is already evident. Methyl for F ligand exchanges and their reverse occur easily without concurrent reduction. In addition, Gedridge[5] has

(8) Molecular ions are also unobserved in the 70-eV mass spectra of TeF_6, $TeBrF_5$,[9] and $W(CH_3)_6$.[1]

(9) Fraser, G. W.; Peacock, R. D.; Watkins, P. M. *J. Chem. Soc., Chem. Commun.* **1968**, 1257.

(10) Pfisterer, G.; Dreeskamp, H. *Ber. Bunsen-Ges. Phys. Chem.* **1969**, *73*, 654.

shown that $Te(CH_3)_4$ completely decomposed after 4 h at 120 °C. Since, as shown above, the $Te(CH_3)_6$ sample in C_6D_6 survived for 4.5 h at 140 °C unchanged, $Te(CH_3)_6$ is clearly much more thermally stable than $Te(CH_3)_4$.

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A Novel Regio- and Stereocontrolled Synthesis of Diol Epoxide and *trans*-Dihydrodiol Metabolites of Polycyclic Aromatic Hydrocarbons. An Application to the Synthesis of the Bay-Region *syn*- and *anti*-Diol Epoxides of the Carcinogen 1,4-Dimethylphenanthrene†

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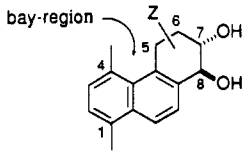
Carcinogenic polycyclic aromatic hydrocarbons (PAHs) require metabolic activation in order to exert their tumorigenic activity, typically to the diol epoxides[1] as predicted by the bay-region concept.[2] While a number of synthetic methods toward these

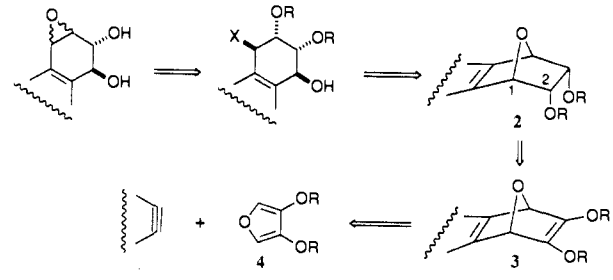


1a 5β,6β-epoxide (*syn*-diol epoxide)
1b 5α,6α-epoxide (*anti*-diol epoxide)
1c 5,6-ene

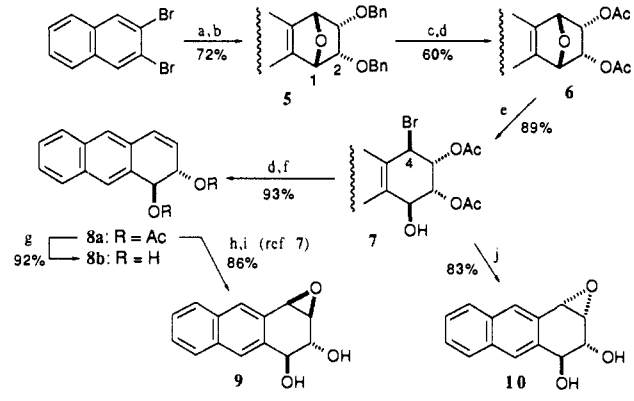
diol epoxides are described in the literature,[3] it was felt that a new, entirely different approach may be needed that achieves regio- and stereochemically controlled synthesis of these metabolites, particularly the bay-region analogues. In the following we delineate a generally applicable, efficient synthesis of PAH diol epoxides and *trans*-dihydrodiols and its application to the first synthesis of the putative active metabolites, the bay-region diol epoxides of the carcinogen 1,4-dimethylphenanthrene (1,4-DMPh).[4]

Our strategy is illustrated in Scheme I in the form of retrosynthetic analysis. This approach entails (1) the initial cycloaddition between an aryne and a 3,4-dialkoxyfuran, (2) the stereoselective hydrogenation of the cycloadduct **3** from the exo side, and (3) the regioselective ether-bridge opening of **2** with a stereocontrolled incorporation of an appropriate nucleophile. It should be noted that the trans relationship between the two oxygen groups at C-1 and -2 in **2** forms the basis of our synthetic strategy toward these PAH metabolites.

Scheme I

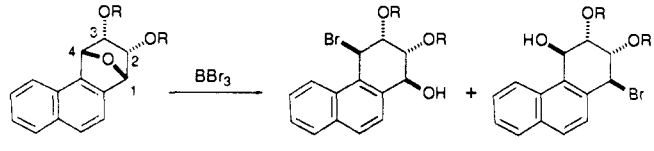


Scheme II[a]



[a] Conditions: (a) **4** [R = Bn (ref 5); 2.5 equiv], *n*-BuLi (1.1 equiv)/THF, −78 °C → room temperature, 12 h; (b) H_2/PtO_2, benzene/EtOH, room temperature, 4 h; (c) $BF_3{\cdot}Et_2O$ (4.2 equiv), EtSH (70 equiv)/CH_2Cl_2, 0 °C, 6 h; (d) Ac_2O/pyridine, room temperature, overnight; (e) BBr_3 (1.5 equiv)/CH_2Cl_2, 0 °C, 30 min; (f) $Cr(ClO_4)_2$, ethylenediamine/DMF, 0 °C, 20 min (ref 6); (g) NH_3/MeOH, 0 °C → 10 °C, 3 h; (h) *N*-bromoacetamide (NBA)/20% aqueous THF, 0 °C, 4 h; (i) NaOMe (1.2 equiv)/THF, MeOH, room temperature, 2 h; (j) same as (i), 1 h.

Scheme III[a]



12a/b **13a/b** **14a/b**

[a] a series, R = Ac; b series, R = O(C=O)O.

In an effort to assess the feasibility of this approach, the synthesis of the diol epoxides and *trans*-dihydrodiols of the linear PAHs naphthalene and anthracene was probed. Interestingly, the synthesis of the diol epoxides of anthracene has not been reported in the literature, presumably due to the lack of tumorigenic activity of anthracene. These derivatives of both naphthalene and anthracene can be efficiently synthesized, as summarized in Scheme II for the anthracene series, under complete stereochemical control based on the aryne 3,4-bis(benzyloxy)furan cycloaddition approach. Thus, the synthesis of *syn*-**9** and *anti*-diol epoxides **10** and 1,2-*trans*-dihydrodiol **8b** of anthracene has been efficiently achieved from 2,3-dibromonaphthalene in 31, 32, and 33% overall yields, respectively.[8]

Unlike the examples described above, the physiologically more potent PAH diol epoxides have the epoxide group in the bay region. Therefore, the application of the present methodology in the

† Dedicated to Professor Koji Nakanishi on the occasion of his receipt of the 1990 Cope Award from the American Chemical Society and the 1990 Imperial Prize of Japan Academy.

(1) *Polycyclic Hydrocarbons and Carcinogenesis*; ACS Monograph 283; Harvey, R. G., Ed.; American Chemical Society, Washington, DC, 1985.

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(3) (a) Harvey, R. G. In: Reference 1, pp 35-62. (b) Harvey, R. G. *Synthesis* **1986**, 605.

(4) (a) LaVoie, E. J.; Tulley-Freiler, L.; Hoffmann, D. *Cancer Res.* **1981**, *41*, 3441. (b) LaVoie, E. J.; Bedenko, V.; Tulley-Freiler, L.; Hoffmann, D. *Ibid.* **1982**, *42*, 4045. (c) LaVoie, J. E.; Tulley-Freiler, L.; Bedenko, V.; Hoffmann, D. *Mutat. Res.* **1983**, *116*, 91. (d) Hecht, S. S.; Amin, S.; Melikian, A. A.; LaVoie, E. J.; Hoffmann, D. In: Reference 1, pp 85-105.

(5) (a) Iten, P. X.; Hofmann, A. A.; Eugster, C. H. *Helv. Chim. Acta* **1978**, *61*, 430. (b) Koreeda, M.; Jung, K.-Y.; Ichita, J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2129, and references cited therein.

(6) Singleton, D. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1967**, *89*, 6547; **1968**, *90*, 1582.

(7) (a) Yagi, H.; Hernandez, O.; Jerina, D. M. *J. Am. Chem. Soc.* **1975**, *97*, 6881. (b) Yagi, H.; Thakker, D. R.; Hernandez, O.; Koreeda, M.; Jerina, D. M. *Ibid.* **1977**, *99*, 1604.

(8) Both naphthalene *syn*- and *anti*-diol epoxide derivatives have also been synthesized in a similar manner from 1-(tosyloxy)-2-bromobenzene in comparable yields.

0002-7863/90/1512-7413$02.50/0