^{13}C NMR parameters of 1,4-lactones and imido-1,4-lactones are similar.

(k) The following 2-epimeric intermediates and products are observed by ^{13}C NMR using $K^{13}CN$ in reaction with D-erythrose: nitriles, imido-1,4-lactones, amidines, amides, aldono-1,4-lactones, and aldonates. A dimer(s) formed by reaction between imido-1,4-lactone and nitrile is proposed.

Registry No. 7, 73713-14-1; D-glyceraldehyde, 453-17-8; D-threose, 95-43-2; D-erythrose, 583-50-6; D-arabinose, 10323-20-3; D-lyxose, 1114-34-7; D-ribose, 50-69-1; D-xylose, 58-86-6; [*R*-(*R**,*S**)]-2,3,4-trihydroxybutanoic acid, 7306-96-9; D-lyxonic acid, 526-92-1; D-arabinonic acid, 488-30-2; D-gluonic acid, 526-95-4; D-mannonic acid, 642-99-9; D-galactonic acid, 576-36-3; D-allonic acid, 21675-42-3; D-gulonic acid, 20246-33-7; D-gluconate pertrimethylsilylated, 38165-89-8; glycolaldehyde trimethylsilylated, 18147-36-9; D-glyceraldehyde pertrimethylsilylated, 73712-76-2; 2,4-*O*-ethylidene-D-erythrose trimethylsilylated, 73712-77-3; D-erythrose pertrimethylsilylated, 73745-84-3; D-threose pertrimethylsilylated, 73788-50-8; D-arabinose pertrimethylsilylated, 18622-97-4; D-lyxose pertrimethylsilylated, 73745-85-4; D-ribose pertrimethylsilylated, 33648-69-0; D-xylose pertrimethylsilylated, 18623-22-8; D-glycerate pertrimethylsilylated, 73712-78-4; D-erythronate pertrimethylsilylated, 73745-86-5; D-threonate pertrimethylsilylated, 73745-87-6; D-arabinonate pertrimethylsilylated, 73745-88-7; D-ribonate pertrimethylsilylated, 65167-67-1; D-lyxonate pertrimethylsilylated, 73745-89-8; D-xylonate pertrimethylsilylated, 73745-90-1; D-allonate pertrimethylsilylated, 73745-91-2; D-altronate pertrimethylsilylated, 73745-92-3; D-gulonate pertrimethylsilylated, 73745-93-4; D-idonate pertrimethylsilylated, 73745-94-5; D-mannonate pertrimethylsilylated, 73745-95-6; D-galactonate pertrimethylsilylated, 73745-96-7; D-talonate pertrimethylsilylated, 73745-97-8; D-glyceronitrile pertrimethylsilylated, 73712-79-5; D-erythrononitrile pertrimethylsilylated, 73712-80-8; D-threononitrile pertrimethylsilylated, 73712-81-9; 3,5-*O*-ethylidene-D-arabinonitrile pertrimethylsilylated, 73712-82-0; 3,5-*O*-ethylidene-D-ribononitrile pertrimethylsilylated, 73712-83-1; D-arabinononitrile pertrimethylsilylated, 73712-84-2; D-ribononitrile pertrimethylsilylated, 73712-85-3; D-lyxononitrile pertrimethylsilylated, 73712-86-4; D-xylononitrile pertrimethylsilylated, 73712-87-5; D-gluconontrile pertrimethylsilylated, 73712-88-6; D-mannononitrile pertrimethylsilylated, 73712-89-7; D-galactononitrile pertrimethylsilylated, 73712-90-0; D-allononitrile pertrimethylsilylated, 73712-91-1; D-gulononitrile pertrimethylsilylated, 73712-92-2; D-idononitrile pertrimethylsilylated, 73712-93-3; D-arabinono-1,4-lactone pertrimethylsilylated, 32384-55-7; D-ribono-1,4-lactone pertrimethylsilylated, 10589-34-1; D-arabinonamide pertrimethylsilylated, 73712-94-4; D-ribonamide pertrimethylsilylated, 73712-95-5; D-lactaldehyde hydrate, 73712-96-6; D-*threo*-2,3-dihydroxybutanal hydrate, 73712-97-7; D-*erythro*-2,3-dihydroxybutanal hydrate, 73728-17-3; DL-glyceronitrile, 70849-07-9; DL-2-hydroxybutyronitrile, 73683-30-4; D-*threo*-2,3-dihydroxybutyronitrile, 73712-98-8; D-*erythro*-2,3-dihydroxybutyronitrile, 73712-99-9; D-threononitrile, 70849-39-7; D-erythrononitrile, 73713-00-5; D-lyxononitrile, 70878-63-6; D-xylononitrile, 52387-25-4; DL-2-hydroxybutyrate, 600-15-7; D-lyxono-1,4-lactone, 15384-34-6; D-xylono-1,4-lactone, 15384-37-9; D-threonoamidine, 73713-01-6; D-erythronoamidine, 73713-02-7; D-arabinonitrile, 70878-64-7; D-arabinoimido-1,4-lactone, 73713-03-8; D-arabinonamide, 15909-88-3; D-arabinono-1,4-lactone, 2782-09-4; D-arabinono-1,5-lactone, 73745-98-9; D-arabinonoamidine, 73713-04-9; D-ribononitrile, 52387-24-3; D-ribonoimido-1,4-lactone, 73713-05-0; D-ribonamide, 73713-06-1; D-ribono-1,4-lactone, 5336-08-3; D-ribono-1,5-lactone, 6866-49-5; D-ribonic acid, 642-98-8; D-ribonoamidine, 73713-07-2; D-5-deoxyarabinonoimido-1,4-lactone, 73713-08-3; D-5-deoxyribonoimido-1,4-lactone, 73713-09-4; D-5-deoxylyxonoimido-1,4-lactone, 73713-10-7; D-5-deoxyxylonoimido-1,4-lactone, 73713-11-8; D-5-deoxyarabinonamide, 73745-99-0; D-5-deoxyribonamide, 73746-00-6; D-erythronoimido-1,4-lactone, 73713-12-9; D-erythroamide, 73713-13-0; D-erythro-1,4-lactone, 23732-41-4; D-talononitrile, 70849-36-4; D-altrononitrile, 70849-34-2.

Notes

Conversion of Alcohols to Methylene Acetals by Reaction with Dimethyl Sulfoxide-Bromine

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Dimethyl sulfoxide (Me_2SO) oxidizes alcohols to carbonyl compounds in the presence of electrophilic reagents[1] such as chlorine,[2] dicyclohexylcarbodiimide,[3] acetic anhydride,[4] and trifluoroacetic anhydride[5] at low temperatures. These oxidations are, however, found to be inefficient above room temperature due to competing Pummerer rearrangements which give rise to dimethylthio ethers. In the presence of *N*-bromosuccinimide (NBS) at 50 °C, Me_2SO transforms alcohols to the corresponding methylene acetals.[6] Acetal formation has been suggested to arise from the Pummerer rearrangement of an initially formed bromosulfoxonium ion to give an α-alkoxy sulfoxide intermediate.

In this paper, we wish to report that alcohols also react with Me_2SO in the presence of bromine above room temperature to give the corresponding dialkyl methylene acetals (1) in the yields indicated in Table I. We also

$$Me_2SO + Br_2 \xrightarrow[CCl_4]{ROH} \underset{1}{ROCH_2OR} \qquad (1)$$

suggest that the methylene group originates from a "dimethyl sulfide–bromine" adduct (Me_2S–Br_2) and not from the expected Me_2SO–Br_2 adduct.[7]

The sequence of mixing the reagents has a profound effect on the course of the reaction and the yields of the acetals. Thus, addition of 1-butanol to a preformed Me_2SO–Br_2 mixture (procedure A) gave 78% of di-*n*-butyl methylene acetal; while this product was isolated in only 45% yield when a solution of bromine in CCl_4 was added to a mixture of 1-butanol and Me_2SO in CCl_4 (procedure B).

In the case of secondary alcohols, procedure B also leads to oxidation products. Thus, for example, 3-pentanol gives 2-bromo-3-pentanone (2) and 2,4-dibromo-3-pentanone (3),

(1) K. Omura and D. Swern, *Tetrahedron*, **34**, 1651 (1978).
(2) E. J. Corey and C. U. Kim, *Tetrahedron Lett.*, 919 (1973).
(3) K. E. Pfitzner and J. G. Moffat, *J. Am. Chem. Soc.*, **85**, 3027 (1963).
(4) J. D. Albright and L. Goldman, *J. Am. Chem. Soc.*, **87**, 4214 (1965).
(5) K. Omura, A. K. Sharma, and D. Swern, *J. Org. Chem.*, **41**, 957 (1976).
(6) S. Hanessian, G. Yang-Chung, P. Lavalee, and A. G. Pernet, *J. Am. Chem. Soc.*, **94**, 8929 (1972); S. Hanessian and A. G. Pernet, *Carbohydr. Res.*, **26**, 258 (1973).

(7) A Me_2SO–Br_2 adduct has been postulated as the brominating species in the conversion of aniline hydrobromide to *p*-bromoaniline in Me_2SO: P. A. Zoretic, *J. Org. Chem.*, **40**, 1867 (1975). Its structure would be expected to be similar to that of the Me_2SO–Cl_2 adduct suggested by Corey:[2] $(Me_2S^+(Cl)=O)Cl^-$.

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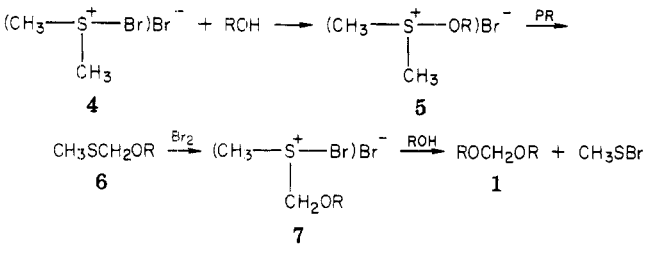
Table I. Conversion of Alcohols to Methylene Acetals by Treatment with Me_2SO-Br_2[a]

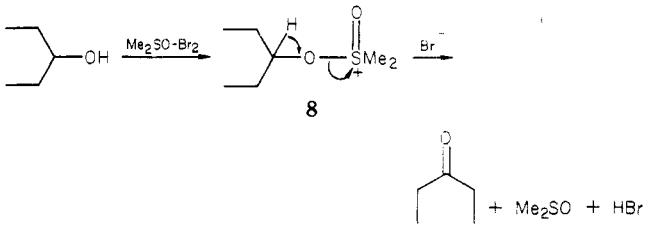
alcohol[b]	product[c]	bp, °C (torr)	% yield[d]
1-propanol	$(CH_3CH_2CH_2O)_2CH_2$	27 (2.5)[e]	84
1-butanol	$(CH_3CH_2CH_2CH_2O)_2CH_2$	173-175[e]	78
2-methylpropanol	$[(CH_3)_2CHCH_2O]_2CH_2$	50-51 (5)	88
1-octanol	$[CH_3(CH_2)_6CH_2O]_2CH_2$	154-155 (4)	75
3-pentanol	$[(CH_3CH_2)_2CHO]_2$	70-72 (6)	69
cyclopentanol	$(c\text{-}C_5H_9O)_2CH_2$	86-88 (4)	64
cyclohexanol	$(c\text{-}C_6H_{11}O)_2CH_2$	105-110 (5)	60

[a] Procedure A. [b] Reagent grade alcohols were used without further purification. [c] Compounds were identified by NMR and IR spectral data. [d] Yields of pure distilled acetals. [e] Also prepared by treatment of the alcohol with formalin in the presence of anhydrous calcium chloride and hydrochloric acid.[12]

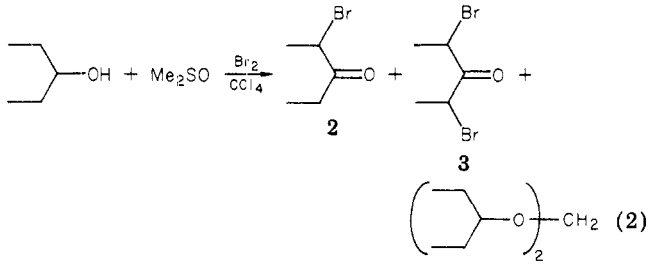
Scheme I



Scheme II



in addition to the expected acetal (eq 2). Oxidation products were not detected when primary alcohols were treated according to procedure B.



The fact that reaction of secondary alcohols with the preformed Me_2SO-Br_2 mixture (procedure A) leads to acetals which are uncontaminated with ketone byproducts, in contrast to procedure B, suggests that two different intermediates are involved in both procedures. We have recently[8] shown that Me_2SO reacts with Br_2 (eq 3) in di-

$$Me_2SO + Br_2 \xrightarrow[CH_2Cl_2]{<\text{room temp}} \underset{4}{(Me_2S^+\text{-}Br)Br^-} \qquad (3)$$

chloromethane or CCl_4 to give dimethylsulfonium dibromide (4). Compound 4 arises from the initial reduction of Me_2SO to dimethyl sulfide (Me_2S),[9] which then complexes with molecular bromine to give 4. We believe that in the case of acetal formation (procedure A) the alcohol initially reacts with 4 to give a dimethylalkoxysulfonium bromide (5). The bromide 5 then undergoes a Pummerer rearrangement[10] to give an α-alkoxy sulfide (6) which reacts with more bromine to give 7. Another alcohol molecule reacts with 7 to give the acetal and methylsulfenyl bromide (Scheme I) which can interact with excess Me_2SO and bromine to yield 4.[11]

In order to test the above suggestion, we stirred a mixture of 1 molar equiv of freshly prepared 4 and 2 molar equiv of the alcohol in CH_2Cl_2 at room temperature for 16 h. Workup gave the expected acetal in good yield. Although a mechanism similar to that postulated by Hanessian[6] in the case of NBS cannot be ruled out in our case, *initial* conversion of Me_2SO to 4 appears to us to be more attractive, whether bromine or NBS is used.

The ketone byproducts in procedure B are thought to arise from the fast reaction of the excess alcohol with a "Me_2SO-Br_2" adduct resembling Corey's "Me_2SO-Cl_2" adduct.[7] In this case, bromide ion acts as base in the conversion of intermediate 8 to ketone (Scheme II). The initially generated ketone is then α-brominated via HBr-catalyzed enolization to give the isolated bromo ketones.

Experimental Section

NMR spectra were obtained on a Perkin-Elmer R-12 spectrometer with Me_4Si as the internal standard. Infrared spectra were recorded neat on a Pye Unicam SP 200G spectrophotometer. Reagent grade chemicals supplied by British Drug House (BDH) were used without further purification.

Reaction of Alcohols with Me_2SO-Br_2. Procedure A. A solution of Me_2SO (15.6 g, 0.20 mol) in CCl_4 (100 mL) was placed into a three-necked, 250-mL, round-bottomed flask fitted with two addition funnels, a reflux condenser, and a magnetic stirrer. To the stirred solution was added a solution of bromine (5.1 mL, 0.10 mol) in CCl_4 (15 mL) over a period of 20 min. The temperature rose to ca. 50 °C during the addition of the bromine. A solution of *n*-butyl alcohol (7.4 g, 0.10 mol) in CCl_4 (15 mL) was finally added to the Me_2SO-Br_2 solution, and the whole mixture was stirred for 4 h at room temperature. After this time, the CCl_4 solution was extracted with 10% bicarbonate solution, washed with water, dried ($MgSO_4$), and evaporated under vacuum to leave a light yellow oil which was passed through a short column of alumina (low boiling point petroleum ether) to give 6.3 g (78%) of di-*n*-butyl methylene acetal: bp 173-175 °C; NMR ($CDCl_3$) δ 0.80-1.10 (m, 6 H, 2 CH_3), 1.20-1.70 (m, 8 H, 2 CH_2CH_2), 3.45 (t, 4 H, J = 5.0 Hz, 2 OCH_2), 4.55 (s, 2 H, OCH_2O); IR (neat) 2950, 1490, 1415, 1180 cm^{-1}.[12]

Reaction of Alcohols with Me_2SO-Br_2. Procedure B. A solution of 3-pentanol (8.8 g, 0.10 mol) and Me_2SO (15.6 g, 0.20 mol) in CCl_4 (100 mL) was placed into a three-necked, 250 mL, round-bottomed flask fitted with an addition funnel, a reflux condenser, and a magnetic stirrer. To the stirred solution was slowly added a solution of bromine (5.1 mL, 0.10 mol) in CCl_4 (15 mL). The mixture was stirred at ambient temperature for 5 h, extracted with 10% aqueous bicarbonate, washed with water, dried ($MgSO_4$), and evaporated under vacuum to leave 12 g of a clear yellow liquid which was shown by NMR to consist of the

(8) R. M. Munavu and J. A. Ogur, *J. Sci. Technol. (Kenya)*, in press.
(9) D. Martin, A. Berger, and R. Peschel, *J. Prakt. Chem.*, 312, 683 (1970).
(10) C. R. Johnson and W. G. Phillips, *J. Am. Chem. Soc.*, 91, 682 (1969).
(11) H. H. Szmant in "Dimethyl Sulfoxide", S. W. Jacob, E. E. Rosenbaum, and D. C. Wood, Eds., Vol. 1, Marcel Dekker, New York, 1971, p 68.
(12) R. F. Webb, A. J. Duke, and L. S. A. Smith, *J. Chem. Soc.*, 4307 (1962).

expected acetal and 2,4-dibromo-3-pentanone in about a 1:1 ratio, with a trace of unreacted alcohol. A 3-g portion of the product was separated by using an alumina column and low-boiling petroleum ether to give 1.2 g (40%) of the pure acetal: bp 70–72 °C (6.5 torr); NMR ($CDCl_3$) δ 0.7–1.1 (t, 12 H, J = 5.0 Hz, 4 CH_3), 1.2–1.7 (p, 8 H, J = 5.0 Hz, 4 CH_2), 3.2–3.6 (p, 2 H, J = 5.0 Hz, 2 OCH), 4.65 (s, 2 H, OCH_2O). There was also obtained 1.4 g (47%) of the pure 2,4-dibromo-3-pentanone: bp 54–55 °C (2 torr); NMR ($CDCl_3$) δ 1.7–1.9 (d, 6 H, J = 5.0 Hz, 2 CH_3), 4.8–5.15 (q, 2 H, J = 5.0 Hz, 2 CHBr); IR (neat), 1720 cm^{-1} (C=O).[13]

Reaction of Alcohols with Me_2S–Br_2. The dimethylsulfonium dibromide was prepared by slow addition of a solution of molecular bromine (51 mL, 1.0 mol) in dichloromethane (50 mL) to a magnetically stirred solution of Me_2SO (200 mL, 3.80 mol) in dichloromethane (80 mL) at 0 °C. The yellow solid which had formed 1 h after complete addition of the bromine solution was quickly filtered and washed with dichloromethane (200 mL). The yellow solid liberated bromine on contact with a metal spatula or on prolonged exposure to air. A 25-g sample (~0.1 mol) of the slightly wet compound was added to a magnetically stirred solution of 2-methylpropanol (14.8 g, 0.20 mol) in dichloromethane (150 mL) in an open round-bottomed flask, and stirring was continued for 16 h at room temperature. The reaction mixture was poured into 200 mL of aqueous bicarbonate, and the organic layer was separated, washed with water, dried (Na_2SO_4), and evaporated to leave 10.4 g of a light yellow oil (65% crude yield). Distillation at 50–51 °C under vacuum (5 torr) gave a clear product (9.8 g, 61%) whose NMR and IR spectra were identical with those of the product obtained when 2-methylpropanol was treated according to procedure A: NMR ($CDCl_3$) δ 0.90 (d, 12 H, J = 5.0 Hz, 4 CH_3), 1.40–2.15 (m, 2 H, 2 CH), 3.21 (d, 4 H, J = 5.0 Hz, 2 CH_2), 4.55 (s, 2 H, OCH_2O); IR (neat) 2900–2960, 1450, 1370, 1350 cm^{-1}. This procedure gave a lower yield of the acetal than via procedure A. This is attributed to the fact that the complex which forms between Me_2S–Br_2 and the alcohol is not very soluble in CH_2Cl_2.

Acknowledgment. Financial support from the Research Fund, University of Nairobi, is gratefully acknowledged.

Registry No. 1 (R = Pr), 505-84-0; 1 (R = Bu), 2568-90-3; 1 (R = *i*-Bu), 2568-91-4; 1 (R = $CH_3(CH_2)_7$), 16849-79-9; 1 (R = $(CH_3CH_2)_2CH$), 73728-32-2; 1 (R = cyclopentyl), 73728-33-3; 1 (R = cyclohexyl), 1453-21-0; **3**, 815-60-1; **4**, 50450-21-0; 1-propanol, 71-23-8; 1-butanol, 71-36-3; 2-methylpropanol, 78-83-1; 1-octanol, 111-87-5; 3-pentanol, 584-02-1; cyclopentanol, 96-41-3; cyclohexanol, 108-93-0; Me_2SO, 67-68-5; Br_2, 7726-95-6.

(13) An identical sample of the dibromo ketone was prepared by brominating 3-pentanone with 2 equiv of bromine in acetic acid. D. P. Evans and J. R. Young, *J. Chem. Soc.*, 1310 (1954).

Preparation of Site Specifically Deuterated 7,12-Dimethylbenz[*a*]anthracene Derivatives: Mechanism of Hydrogenolysis of Aryl Halides with Lithium Aluminum Hydride

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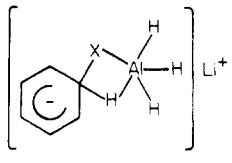
Hydrogenolysis of aromatic halides by LAH is known to proceed in excellent yield.[1] In general, the reactivity of aryl halides is in the order I > Br > Cl > F. Electron-donating groups in the para position decrease the rate of reaction whereas electron-withdrawing groups increase the rate of reaction.[1,2] Additionally, steric compression owing to bulky substituents in the ortho position is known to increase the rate of hydrogenolysis.[1,2] As expected, rates of hydrogenolysis are dependent upon the nature of the solvent and the reaction temperature.[1,2] A minimum of 2 mol of LAH per mole of aryl halide is required for an optimum reaction rate. In light of these observations, hydrogenolysis of aryl halides is thought to proceed either by direct hydride displacement of the halogen[2,3] or by four-membered transition state **1**.[2] It was concluded that bond breaking must be involved in the rate-determining step.[1,2]

Table I. Hydrogenolysis of Aryl Bromides

compd	reagent	% ^2H	% H
2	$LiAl^2H_4/^2H_2O$	100[a]	
	$LiAl^2H_4/H_2O$	23 ± 1[a]	77 ± 1
	$LiAlH_4/^2H_2O$	58 ± 1[a]	42 ± 1
5	$LiAl^2H_4/^2H_2O$	100[b]	
	$LiAl^2H_4/H_2O$	23 ± 1[b]	77 ± 1
	$LiAlH_4/^2H_2O$	58 ± 1[b]	42 ± 1

[a] Site-specific labeling at the 5 position. [b] Site-specific labeling at the 9 position.



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In connection with our program on chemical carcinogenesis, we required a number of site specifically deuterated and tritiated 7,12-dimethylbenz[*a*]anthracene (DMBA) derivatives.[4] Hydrogenolysis of 5-bromo-7,12-dimethylbenz[*a*]anthracene (**2**) in refluxing THF for 24 h resulted in site-specific labeling and furnished [5-^2H]-7,12-dimethylbenz[*a*]anthracene (**3b**). However, the extent of ^2H incorporation was dependent upon the method of reaction workup (Table I). Only when LA^2H followed by ^2H_2O workup was employed was 100% deuterium incorporated. Similar results were obtained by hydrogenolysis of 9-bromoanthracene (**5**) (Table I).

Differences in ^2H-incorporation upon hydrogenolysis of **2** with LA^2H/H_2O (**3b**, 23%) vs. $LAH/^2H_2O$ (**3b**, 58%) suggest that the major portion of the reaction proceeds via the intermediates **4a–d** and **6a–c**. Solvolysis of presumed intermediate **4a**, **4b**, or **4c** would be expected to yield **6a**, **6b**, or **6c**, respectively. In **6a–c**, hydride or deuteride transfer could result either from the HO (or ^2HO) function bonded directly to Al. Furthermore, the reaction likely is complicated by isotope effects.

In contrast to the hydrogenolysis of aryl halides **2** and **5**, LA^2H reduction of 7-(chloromethyl)-12-methylbenz-

(1) G. J. Karabatsos, R. L. Shone, and S. E. Scheppele, *Tetrahedron Lett.*, 2113 (1964); G. J. Karabatsos and R. L. Shone, *J. Org. Chem.*, 33, 619 (1968).

(2) H. C. Brown and S. Krishnamurthy, *J. Org. Chem.*, 34, 3918 (1969).

(3) Aromatic halides have been shown to incorporate deuterium at the site of halogen substitution (see ref 1); site-specific deuteration to furnish **3b** on hydrogenolysis with $LiAl^2H_4$ of **2** was established by detailed 90-MHz NMR analysis; site-specific incorporation of deuterium at C-5 upon hydrogenolysis of **2** was indicated by NMR analysis [DMBA (**3a**), δ 8.0 (d, C-6, 1 H, J = 9.6 Hz, 8.4 (m, aromatic, 3 H) vs. [5-^2H]-DMBA (**3b**), δ 8.0 (s, C-6, 1 H), 8.4 (m, aromatic, 3 H)]. For preliminary results on deuteration of DMBA also see M. Muschik and J. E. Tomaszewski, Abstract No. ORGN 109, National American Chemical Society Meeting, Miami, FL, September 1978.

(4) 7-(Chloromethyl)-DMBA derivatives **7a-d** were prepared by the reaction of anhydrous HCl in ethyl acetate with the corresponding 7,12-dihydro-7,12-dimethyl-7,12-dihydroxybenz[*a*]anthracenes synthesized in these laboratories. M. S. Newman, J. M. Khanna, K. Kanakarajan, and S. Kumar, *J. Org. Chem.*, 43, 2553 (1978).

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