Para Products from *m*-Arylcadmium Reagents: A Cine Substitution

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The apparent rearrangement of *m*-anisylcadmium reagent (**1a**) has been studied for the purpose of elucidating the scope and mechanism of this unusual behavior. Trapping experiments have been carried out with acetyl chloride, acetyl bromide, acetic anhydride, diacetyl sulfide, phenyl cyanate, and bromine, the products being analyzed by GLC and confirmed by IR and NMR spectroscopy. The extent of formation of the para isomer is the same for the two acid halides and bromine and considerably less for acetic anhydride and phenyl cyanate. With diacetyl sulfide there is no para isomer observed. Experiments with other substituted arylcadmium reagents support the view that this behavior depends on the electron-donor capability of the substituent. Thus, reagents substituted at the meta position with CH_3, CF_3, and F afforded only meta products with acetyl chloride, while the CH_3S substituent afforded some para isomer. Deuterium labeling and trapping experiments have been used to gain information about intermediates in this cine substitution.

A rearrangement in the aryl moiety of an in situ arylcadmium compound was first reported by Klemm, Mann, and Lind in 1958.[2] They found that the anisylcadmium reagent, prepared from *m*-bromo- or *m*-iodoanisole, reacted with *m*-methoxybenzoyl chloride to afford, in low yield, a mixture of the "normal" 3,3′-dimethoxybenzophenone and the unexpected 3,4′ isomer (eq 1).

$$m\text{-}CH_3OC_6H_4Br(I) \xrightarrow[(2)\ CdCl_2]{(1)\ Mg} (m\text{-}CH_3OC_6H_4)_2Cd$$

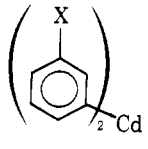
$$\xrightarrow{m\text{-}CH_3OC_6H_4COCl} (m\text{-}CH_3OC_6H_4)_2CO + \begin{matrix}(m\text{-}CH_3OC_6H_4)\\(p\text{-}CH_3OC_6H_4)\end{matrix}\!\!>\!CO \quad (1)$$

Dauben and Collette[3] observed the same peculiar behavior when "*m*-anisyl" cadmium reagent was allowed to react with 1-cyclohexenecarbonyl chloride, acetyl chloride, β-(carbomethoxy)propionyl chloride, and acetic and succinic anhydrides, but only the "normal" product could be found in the reaction with biacetyl. A third research group[4] observed rearrangement accompanying the reaction of the *m*-anisylcadmium reagent with 2-bromo-3-nitrobenzoyl chloride but not with 3-nitrophthalic anhydride.

In view of the widely recognized utility of organocadmium reagents in synthesis,[5,6] it is important to determine whether other arylcadmium compounds may lead to rearranged products whose structures might have been misassigned. We thus undertook a study of trapping experiments with several in situ meta-substituted arylcadmium reagents to determine the generality of the cine substitution and any factors which may be involved in its occurrence.

Results and Discussion

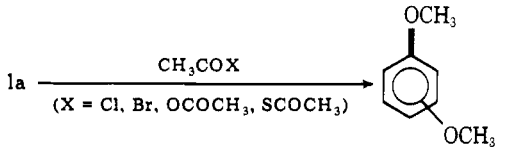
We prepared in situ arylcadmium reagents in ether where the meta substituent was methoxy (**1a**), methylthio (**1b**), methyl (**1c**), fluoro (**1d**), and trifluoromethyl (**1e**) from the corresponding aryl bromides.



1a, X = CH_3O
b, X = CH_3S
c, X = CH_3
d, X = F
e, X = CF_3

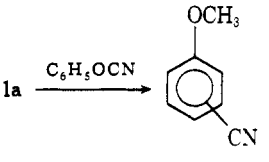
The *m*-anisyl reagent **1a** was examined in greatest detail because, as was subsequently shown,[7] it was most prone to lead to para products. As trapping agents for **1a** we chose acetyl chloride, acetyl bromide, acetic anhydride, diacetyl sulfide, phenyl cyanate,[8] and bromine. With bromine, appropriate control experiments were carried out to correct for any *m*-bromoanisole from unchanged starting material and for any *p*-bromoanisole arising from direct bromination of anisole.

The products, which, in principle, could be mixtures of meta and para isomers in each case, are outlined in eq 2–4.



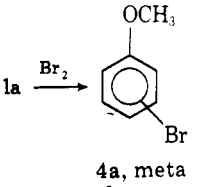
(2)

2a, meta
b, para



(3)

3a, meta
b, para



(4)

4a, meta
b, para

Crude products were worked up in a standard way and analyzed by GLC, with biphenyl as an internal standard. Besides the trapping products, reaction mixtures contained anisole (major) and *m*-bianisyl (minor). All components were identified by peak enhancement and/or collection and analysis by IR or NMR spectroscopy. Yields of the trapping products ranged from 20 to 40% in duplicate runs; no effort was made to optimize conditions. The relative amounts of meta and para products for the series are summarized in Table I.

It is most likely that rearrangement does not occur during formation of the organocadmium reagent but rather in the trapping step, in view of the observation[2] that the *m*-anisyl Grignard reagent leads exclusively to meta products. From the results in Table I it is clear that the nature of the trapping agent plays a role in the distribution of meta and para prod-

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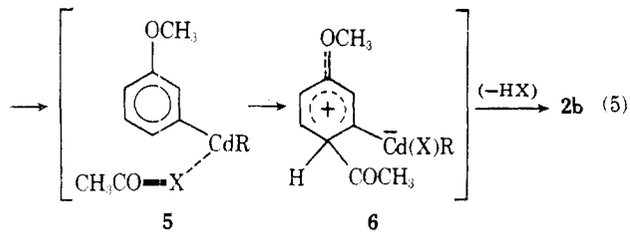
Table I. Trapping Experiments with In Situ *m*-Anisylcadmium Reagent

reagent	registry no.	% meta	registry no.	% para	registry no.
CH_3COCl	750-36-5	25 (35)[a]	586-37-8	75 (65)[a]	100-06-1
CH_3COBr	506-96-7	25		75	
$(CH_3CO)_2O$	108-24-7	75		25	
$(CH_3CO)_2S$	3232-39-1	100		0	
C_6H_5OCN	103-71-9	91	1527-89-5	9	874-90-8
Br_2	7726-95-6	25	2398-37-0	75	104-92-7

[a]Values reported by Dauben and Collette from UV analysis.[3]

ucts. The explanation for para acetylation from **1a**, advanced earlier,[2,3] is a process in which the acylating agent attacks the position para to the methoxyl, in a Friedel–Crafts-like reaction, the cadmium function serving as an internal Lewis acid (eq 5). This would be consistent with our observation that the

1a + CH_3COX



5 **6**

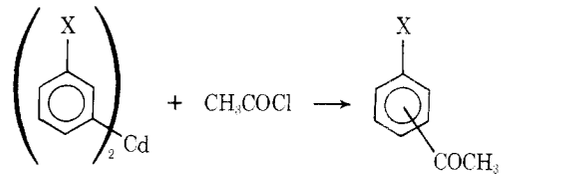
R = *m*-anisyl

o-anisylcadmium reagent shows no tendency for cine substitution. The nature of X in structure **5** can cause several effects. It will affect the electrophilicity of the carbonyl group; in this case, acetyl chloride would be the most electrophilic and therefore lead to the most extensive rearrangement. As X becomes larger (X = Br or S), the ring size in the five-membered transition state leading to **6** will increase. A third effect would be the basic character of X. Because cadmium is relatively soft,[9] one might predict that the softest base (S) would coordinate most effectively. Either this is not the case or, if coordination with S is strong, other factors (electrophilicity, ring size) impede attack at the para position. It should be noted that the formation of para isomers in eq 3 and 4 likewise involves cases where the coordinating moiety is Br and O.

Reaction mixtures from the other arylcadmium reagents **1b–e** with acetyl chloride were analyzed in the same way for the presence of para products. As is evident from the results in Table II, **1b** is the only reagent besides **1a** that affords cine substitution. This is convincing support for the view that the directing effect of the substituent (meta to the original cadmium) is a major factor, in line with electrophilic substitutions. In fact, among the substituents included in this study, only the two (CH_3O, CH_3S) with the most negative σ^+ values[10] give rise to para substitution.

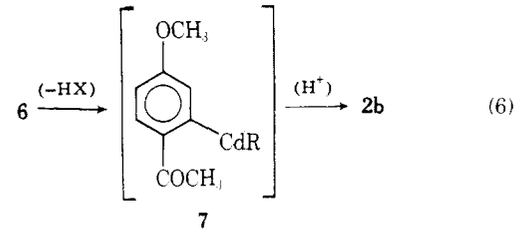
The pathway outlined in eq 5 does not include information on the nature of the transformation of **6** to the final product **2b.** We were interested in experiments which might serve to distinguish between at least two possibilities: namely, the loss of HX from **6** to afford the transient cadmium compound **7,** which would then undergo protonolysis to **2b;** or the protonolysis of **6** to afford the same σ complex **8** which would arise from Friedel–Crafts acetylation of anisole. Dauben and Collette assumed that the former (eq 6) was the case because of formation of a tetrahydrofluorenone with cyclohexene-1-carbonyl chloride. According to eq 6 and 7, decomposition of the reaction mixture with DCl/D_2O should lead to deuteration

Table II. Reaction of Various Meta-Substituted Arylcadmium Reagents with Acetyl Chloride



1a–e (meta and para)

cadmium reagent	% meta	registry no.	% para	registry no.
1a	25		75	
1b	84	1441-99-2	16	1778-09-2
1c	100	585-74-0	0	
1d	100	455-36-7	0	
1e	100	349-76-8	0	



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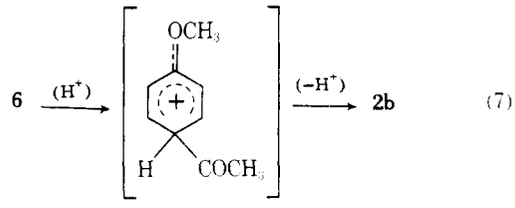

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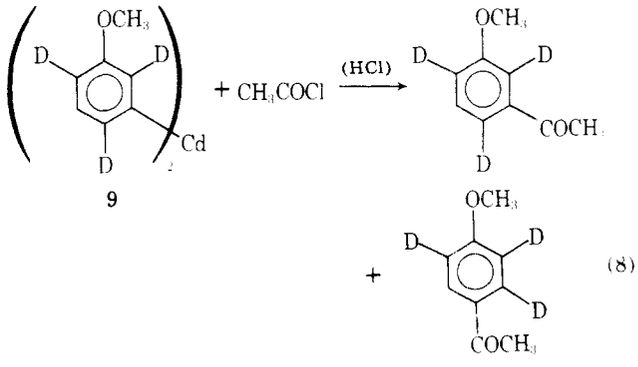
at the Cd-bearing carbon, but, on the contrary, the *p*-methoxyacetophenone, collected by preparative GC, contained less than half of the expected deuterium at that position, as estimated by NMR integration.[11]

We then carried out a similar experiment with the trideuterio compound **9,** by decomposing the mixture with HCl, in



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order to trace the fate of the ring deuteriums. In both the meta and para products substantial amounts of trideuterio compounds were present, as deduced from NMR and mass spectra. Mono- and dideuterio products, also present in the reaction mixture, are assumed to arise at least partially by H/D exchange during treatment with excess HCl. The fact that the para product contains the dideuterio compound in greater abundance than does the meta product is consistent with this supposition, inasmuch as the para isomer would be more susceptible to electrophilic exchange.

Some conclusions about the fate of **6** in eq 5 can be made from the labeling experiments. The source of the proton which

eventually becomes attached to the Cd-bearing carbon is not primarily external HCl or solvent. It might be transferred from the para position in a concerted process, or it might arise from loss of HCl followed by rapid protonolysis of the carbon–cadmium bond. Available experimental information does not allow a distinction between these two alternatives.

Experimental Section

Infrared spectra were recorded as films on a Perkin-Elmer Model 337 grating spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Jeol JMN-MH-100 spectrometer in deuteriochloroform. Chemical shifts are reported in parts per million downfield from tetramethylsilane as an internal standard. All spectra were compared to those reproduced by Sadtler Laboratories[12] where appropriate.

Gas–liquid partition chromatographic analyses and separations were performed with a Varian Model 90-P gas chromatograph equipped with a 10 ft × 0.25 in. copper column packed with 10% Carbowax 2M on Chromosorb W. Peaks were identified, where possible, by peak enhancement, and samples were collected from the GC for IR and NMR analyses. Peak areas were determined as the product of the height and the half-height peak width. Yields of the methoxyacetophenones were determined by adding biphenyl as an internal standard; ratios of the other acetophenones and other trapping products (**3, 4**) were normalized.

Melting points were determined on a Hoover capillary melting point apparatus and are uncorrected. All temperatures are reported in degrees Centigrade. Elemental analyses were performed either by Galbraith Laboratories, Knoxville, Tenn., or by Mrs. Judy Daigle, Department of Chemistry, University of New Hampshire. Mass spectra were determined by Dr. C. E. Costello, Department of Chemistry, Massachusetts Institute of Technology.

General Procedure for Organocadmium Reactions. All operations were carried out under a stream of nitrogen. A three-neck, round-bottom flask, fitted with a mechanical stirrer, addition funnel, and reflux condenser, containing magnesium (either turnings from J. T. Baker or triply sublimed magnesium from Dow Chemical Co.; both seemed to exhibit similar reactivity) was flame-dried. The Grignard reaction was started by the addition, with stirring, of one-half of the bromo compound in ether; after the remainder of the bromo compound had been introduced, the mixture was held at reflux for 0.5 h. The cadmium chloride (dried at 125 °C for 48 h) was added in one portion; the mixture was stirred until the Gilman test[13] was negative and then was heated at reflux for 0.5 h. After the cadmium reagent had been cooled, the next reactant, dissolved in ether, was added dropwise as rapidly as possible and then the mixture was stirred for 1 h. Workup consisted of hydrolysis with 10% HCl, stirring for 30 min or longer, separating the ether layer, washing the aqueous layer once with ether, washing the combined ether portions with 5% $NaHCO_3$ and saturated brine, drying over $MgSO_4$ or Na_2SO_4, and rotary evaporating the solution to give crude products.

Reactions of *m*-Dianisylcadmium. A. Acetyl Chloride. The reaction, carried out with 0.06 g (0.025 mol) of magnesium, 4.68 g (0.025) of *m*-bromoanisole, 2.30 g (0.031 mol) of cadmium chloride, and 1.96 g (0.025 mol) of acetyl chloride, afforded 2.90 g of crude oil. The yield of the mixture of *m*- and *p*-methoxyacetophenones (**2a, 2b**) was 37%. In a second run the yield was 41%. **2a:** IR 1690 (C=O) and 1035 (C–O) cm^{-1}; NMR δ 2.44 (s, 3, CH_3CO), 3.64 (s, 3, CH_3O), and 6.80–7.30 (m, 4, ArH). **2b:** IR 1675 (C=O) and 1028 (C–O) cm^{-1}; NMR δ 2.44 (s, 3, CH_3CO), 3.70 (s, 3, CH_3O), and 7.15 (midpoint) (AB quart, 4, J = 8 Hz, ArH).

B. Acetyl Bromide. From the cadmium reagent prepared as above and 2.00 g (0.016 mol) of acetyl bromide there was obtained 2.9 g of oil. The yield of the mixture of **2a** and **2b** was 29%.

C. Acetic Anhydride. From the cadmium reagent prepared as above and 3.00 g (0.025 mol) of acetic anhydride there was obtained 2.7 g of oil. The yield of **2a** and **2b** was 24%.

D. Diacetyl Sulfide. From the cadmium reagent prepared as above and 1.18 g (0.010 mol) of diacetyl sulfide[14] the yield of **2a** was 17.5%.

E. Phenyl Cyanate. To the ethereal cadmium reagent, prepared from 5.61 g (0.03 mol) of *m*-bromoanisole, 0.72 g (0.03 mol) of magnesium, and 2.75 g (0.015 mol) of cadmium chloride, was added 3.54 g (0.03 mol) of phenyl cyanate[15] in benzene. After being heated at reflux for 4 h, the mixture was hydrolyzed with 10% HCl. A white precipitate, collected and recrystallized from $CHCl_3$/hexane, mp 230–231 °C, was shown by IR and NMR comparisons to be phenyl cyanurate (lit.[16] mp 224–225 °C), yield 15%.

The ether layer was separated and washed twice with 15% NaOH, dried ($MgSO_4$), and concentrated in vacuo. An infrared spectrum of the residue showed the presence of nitrile (ν(C≡N) 2220 cm^{-1}). GC analysis showed one strong peak (I) at a retention time of 33.0 min and one weaker peak (II) with a retention time of 39.5 min, in addition to several peaks with low retention times. By collection of peaks I and II and spectrophotometric analyses, it could be shown that II is *p*-methoxybenzonitrile (**3b**) (compared with the IR spectrum published by Sadtler[12]). Peak I is assigned as *m*-methoxybenzonitrile (**3a**): IR 2222 (CN) and 690 and 750 (meta ArH) cm^{-1}; NMR δ 3.72 (s, 3, CH_3O) and 6.82–7.34 (m, 4, ArH).

F. Bromine. The cadmium reagent was prepared from 0.24 g (0.10 mol) of magnesium, 1.87 g (0.010 mol) of *m*-bromoanisole, and 0.92 g (0.005 mol) of cadmium chloride in ether. After a reflux period of 1.5 h, 3 mL of the mixture was withdrawn and worked up in the usual manner. GC analysis showed the absence of bromoanisole. To the remainder of the cooled mixture was added rapidly 1.60 g (0.010 mol) of bromine. After the mixture had been stirred for 5 s, it was decomposed by the rapid addition of 25 mL of saturated $NaHSO_3$ and then worked up in the usual way. GC analysis of the oil (1.75 g) showed the presence of both **4a** and **4b.**

Reactions of Acetyl Chloride with Other Arylcadmium Reagents. A. Bis[*m*-(methylthio)phenyl]cadmium (1b). The cadmium reagent was prepared in ether from 0.25 g (0.010 mol) of magnesium, 2.03 g (0.010 mol) of *m*-bromothioanisole,[17] and 0.92 g (0.005 mol) of cadmium chloride. Reaction with 0.78 g (0.010 mol) of acetyl chloride and the usual workup afforded 1.65 g of oil, whose GC analysis showed the presence of a mixture of *m*- and *p*-(methylthio)acetophenone in 30% yield.

Meta isomer: IR 1690 cm^{-1} (C=O); NMR δ 2.45 (s, 3, CH_3S), 2.52 (s, 3, CH_3CO), and 7.12–7.82 (m, 4, ArH). Semicarbazone: mp 183.5–184 °C (EtOH/H_2O). Anal. Calcd for $C_{10}H_{13}N_3OS$: C, 53.81; H, 5.87; N, 18.82. Found: C, 54.07; H, 5.87; N, 18.66.

Para isomer: IR 1670 cm^{-1} (C=O); NMR δ 2.52 (s, 6, CH_3) and 7.10–7.83 (AB quart, 4, J = 9 Hz, ArH).

B. Di-*m*-tolylcadmium (1c). Reaction of the cadmium reagent, prepared in ether from 0.06 g (0.025 mol) of magnesium, 4.28 g (0.025 mol) of *m*-bromotoluene, and 2.20 g (0.013 mol) of cadmium chloride, with 1.96 g (0.025 mol) of acetyl chloride afforded 2.5 g of oil, whose GC showed the presence of only *m*-methylacetophenone in 52% yield: IR 1675 cm^{-1} (C=O); NMR δ 2.36 (s, 3, CH_3Ar), 2.53 (s, 3, CH_3CO), and 7.10–7.72 (m, 4, ArH). 2,4-Dinitrophenylhydrazone: mp 201–202 °C (EtOH/H_2O) (lit.[18] mp 207°C).

C. Bis(*m*-fluorophenyl)cadmium (1d). The cadmium reagent, prepared from 0.48 g (0.020 mol) of magnesium, 3.50 g (0.020 mol) of *m*-bromofluorobenzene,[19] and 1.83 g (0.010 mol) of cadmium chloride, was allowed to react as above with 1.56 g (0.020 mol) of acetyl chloride. After the usual workup, there was obtained 2.5 g of oil, whose GC showed the presence of only *m*-fluoroacetophenone in 82% yield: IR 1695 cm^{-1} (C=O); NMR δ 2.50 (s, 3, CH_3CO) and 6.88–7.60 (m, 4, ArH). 2,4-Dinitrophenylhydrazone: mp 220 °C (EtOH/H_2O) (lit.[20] mp 210 °C).

D. Bis[*m*-(trifluoromethylphenyl]cadmium (1e). The cadmium reagent was prepared in ether from 0.25 g (0.010 mol) of magnesium, 2.25 g (0.010 mol) of *m*-bromotrifluoromethylbenzene,[21] and 0.93 g (0.005 mol) of cadmium chloride. Reaction with 0.79 g (0.010 mol) of acetyl chloride in ether afforded 3.2 g of oil, whose GC showed the presence of only *m*-(trifluoromethyl)acetophenone in 84% yield: IR 1685 cm^{-1} (C=O); NMR δ 2.59 (s, 3, CH_3CO) and 7.30–8.10 (m, 4, ArH). Semicarbazone: mp 207–208 °C (H_2O) (lit.[22] mp 206–208 °C).

E. Di-*o*-anisylcadmium. The cadmium reagent was prepared in ether from 1.20 g (0.050 mol) of magnesium, 8.55 g (0.050 mol) of *o*-bromoanisole, and 4.60 g (0.025 mol) of cadmium chloride. Because the Gilman test[13] was still positive for Grignard reagent after a reflux period of 1 h, refluxing was continued for an additional 10 h, when the test was negative. Then 3.93 g (0.05 mol) of acetyl chloride was added, and the mixture was heated at reflux for 30 min and worked up in the usual manner. GC analysis of the crude product (5.40 g) indicated the presence of *o*-methoxyacetophenone uncontaminated by isomers. The IR of a sample collected by preparative GC was identical with that of an authentic specimen.[12]

Deuterium Exchange in *m*-Bromoanisole. Preparation of 2,4,6-Trideuterio-3-bromoanisole. A flame-dried, three-neck, 50-mL round-bottom flask, fitted with a condenser topped with a $CaCl_2$ drying tube and a septum, was charged with 3.74 g (0.020 mol) of *m*-bromoanisole and 7 mL (0.025 mL) of 20% DCl in D_2O, introduced via a syringe, that was filled under nitrogen. After a reflux period of 19 h, the solution was extracted into ether; the ether layer was separated, washed with 5% $NaHCO_3$, dried (Na_2SO_4), and concentrated in vacuo to give 3.70 g of oil: NMR δ 3.60 (s, 3, CH_3O) and 6.85

(s, 1.09, ArH).

Reaction of (1-Methoxy-2,4,6-trideuterio-3-phenyl)cadmium Reagent with Acetyl Chloride. To the Grignard reagent, prepared from 0.24 g (0.10 mol) of magnesium and 1.90 g of 2,4,6-trideuterio-3-bromoanisole in a total of 25 mL of dry ether, which had been heated at reflux for 60 min and stirred at room temperature for 30 min, was added 0.91 g (0.005 mol) of cadmium chloride. Stirring at room temperature was continued for 90 min; then 0.78 g (0.010 mol) of acetyl chloride in 25 mL of dry ether was added, and the mixture was stirred for 60 min. The usual workup with 10% HCl gave 1.5 g of crude oil. GC separation yielded pure *m*- (**2a**) and *p*-methoxyacetophenones (**2b**). **2a:** NMR δ 2.56 (s, 3, CH_3CO), 3.81 (s, 3, CH_3O), and 7.26 (s, 1.19, ArH); the MS indicated 66.1% d_3, 28.2% d_2, and 4.2% d_1. **2b:** NMR δ 2.43 (s, 3, CH_3CO), 3.77 (s, 3, CH_3O), and 7.77 (s, 1.0, ArH); the MS indicated 39.2% d_3, 46.7% d_2, and 11.0% d_1.

DCl/D_2O Quenching of the Reaction Mixture from *m*-Dianisylcadmium and Acetyl Chloride. The reaction mixture, prepared exactly as above except from unlabeled *m*-bromoanisole, was decomposed with 2.0 g (0.020 mol, 2.0 mL) of 20% DCl in D_2O (Aldrich), which was added via a drybag-filled syringe. After the mixture had been stirred for 90 min, it was worked up in the usual way, as described earlier, to afford 2.1 g of oil, which was separated by GC. **2a:** NMR δ 2.43 (s, 0.6, CH_3CO), 3.76 (s, 3, CH_3O), and 6.70–7.40 (m, 4, ArH). **2b:** NMR δ 2.43 (s, 0.5, CH_3CO), 3.80 (s, 3, CH_3O), and 7.25 (midpoint) (AB quartet, lower doublet at δ 7.8, 1.6; upper doublet at δ 6.8, 2.0; ArH, J = 9 Hz). Some starting *m*-bromoanisole recovered by GC showed no evidence of ring deuteration: NMR δ 3.58 (s, 3, CH_3O) and 6.45–6.91 (m, 4, ArH).

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Registry No.—**1a,** 68758-02-1; **1b,** 68758-03-2; **1c,** 55142-69-3; **1d,** 68758-04-3; **1e,** 68758-05-4; **9,** 68758-06-5; cadmium chloride, 10108-64-2; *m*-bromothioanisole, 33733-73-2; *m*-bromotoluene, 591-17-3; *m*-bromofluorobenzene, 1073-06-9; *m*-bromotrifluoromethylbenzene, 401-78-5; di-*o*-anisylcadmium, 68758-07-6; *o*-bromoanisole, 578-57-4; *o*-methoxyacetophenone, 579-74-8; 2,4,6-trideuterio-3-bromoanisole, 68758-08-7; *m*-bromoanisole, 2398-37-0; phenyl cyanurate, 1919-48-8.

References and Notes

(1) Taken in part from the Ph.D. Dissertation of James G. Shelnut, 1978.
(2) L. H. Klemm, R. Mann, and C. D. Lind, *J. Org. Chem.*, **23,** 349 (1958).
(3) W. G. Dauben and J. W. Collette, *J. Am. Chem. Soc.*, **81,** 967 (1959).
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(5) J. Cason, *Chem. Rev.*, **40,** 15 (1947).
(6) D. A. Shirley, *Org. React.*, **8,** 28 (1954).
(7) It had already been shown that the *m*-tolylcadmium reagent afforded only meta product with acetyl chloride: W. G. Dauben and K. A. Seagebarth, *J. Am. Chem. Soc.*, **73,** 1853 (1951).
(8) To our knowledge, this is the first instance of a reaction of an organic cyanate with a cadmium reagent.
(9) T.-L. Ho, *Chem. Rev.*, **75,** 1 (1975).
(10) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80,** 4979 (1958).
(11) The CH_3CO hydrogens did exchange with deuterium during this experiment, as was the case in control reactions with *m*- and *p*-methoxyacetophenones.
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Preparation of Derivatives of 8-, 9-, 10-, and 11-Hydroxybenz[*a*]anthracene-7,12-diones, Benz[*a*]anthracenes, and 7,12-Dimethylbenz[*a*]anthracenes[1]

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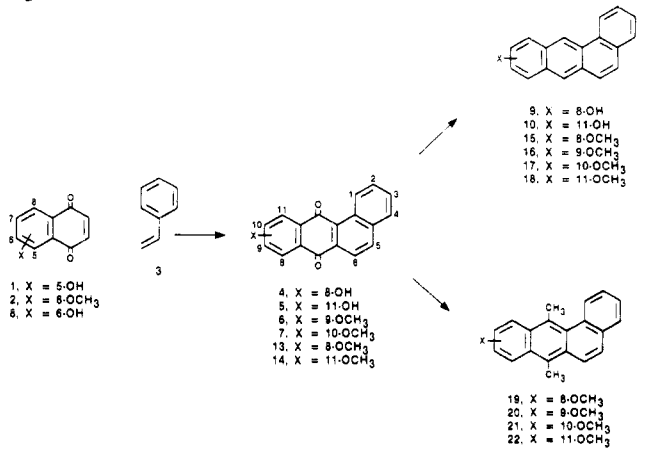
Methoxy- and hydroxybenz[*a*]anthracene-7,12-diones substituted at the 8, 9, 10, and 11 positions have been prepared by reaction of 5- and 6-substituted-1,4-naphthoquinones with styrene (**3**). The methoxy diones were reduced to the corresponding benz[*a*]anthracenes by either a zinc/pyridine/acetic acid reagent or aluminum tricyclohexaoxide in refluxing cyclohexanol. These diones also were converted to the respective 7,12-dimethylbenz[*a*]anthracenes by the classical Grignard method. Spectral data and certain limitations of the method are discussed.

Current investigations concerning the carcinogenicity of 7,12-dimethylbenz[*a*]anthracene (DMBA) have led to postulations that oxidative metabolism of the angular benzene ring[2] and/or the 8-, 9-, 10-, and 11-ring[3] convert DMBA to its ultimate carcinogenic form. To test aspects of the latter hypothesis by using possible metabolic products, a facile synthesis of the 8-, 9-, 10-, and 11-hydroxy derivatives of DMBA was desirable.

Morreal and Alks[4] prepared the 8-, 10-, and 11-methoxy derivatives of DMBA via a multi-step synthesis involving initial reaction of naphthylmagnesium bromide with the appropriate methoxyphthalic anhydrides. Pataki and Ballick[5] prepared the 9- and 10-hydroxy DMBA's via a similar sequence of reactions. In both instances Friedel-Crafts reactions were used to construct the carboskeleton from substituted naphthalenes and benzenes. More recently, Newman and Kumar[6] and Newman et al.[7] prepared methoxy and hydroxy DMBA's substituted in the 1, 2, 3, 4, 6, 9, and 10 positions. These synthetic pathways consisted of reactions of various organometallics with assorted carbonyl compounds followed



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