Pyridoxal Model Compounds. I. The Regioselective Formylation of Methoxy-substituted Aromatic Compounds[1]

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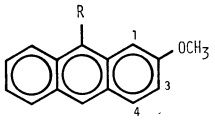
9-Substituted 2-methoxyanthracenes (IVa—d) and -triptycenes (Va, b), and 3-substituted anisoles (VIa, b) were formylated by the use of the Vilsmeier-Haack method (Method A) and the metallation method using *n*-butyllithium (Method B). By the Method A, IVa—c, Vs', and VIs' were regioselectively formylated at C-1, C-3, and C-6 respectively, without exception, while by the Method B IVa—c, Va, VIa, and VIb were regioselectively formylated at C-3, C-3, C-2, and C-6 respectively, and Vb gave C-1 and C-3 formylated derivatives in the ratio of 10 to 1 respectively. Possible transition states concerning the occurrence of the regioselectivity were proposed and discussed.

Pyridoxal catalyzes many reactions of amino acids,[2] and the study of the reaction mechanism has shown that the *ortho*-positioning of the formyl and the hydroxy groups on the pyridine ring is essential to the activity.[3] In practice, it has been demonstrated that salicylaldehyde derivatives with a similar interrelation of these two functional groups to pyridoxal indicate a pyridoxal-like activity for amino acids.[4] On the basis of this advanced knowledge, we designed synthetic schemes to obtain new model compounds of pyridoxal functioning, as expected, as an "asymmetric inversion catalyst".[5] In the present paper we wish to report the first example of the regioselective formylation at *ortho*-positions of these methoxy-substituted aromatic compounds: 9-substituted 2-methoxyanthracenes (IVa—c), 9-substituted 2-methoxytriptycenes (Va, b), and 3-substituted anisoles (VIa, b).

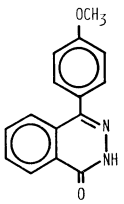
Since, to our knowledge, there is a dearth of systematical investigations concerning the regioselective introduction of a formyl group into methoxy-substituted aromatic compounds, our interest was focused on the elucidation of the reactivity of these compounds for Vilsmeier-Haack reagents and *n*-butyllithium.

Results and Discussion

Synthesis of Starting Materials. The 2-methoxyanthracenes (IVa—d) were prepared in four steps from the reaction of phthalic anhydride with anisole. The reduction of *o*-(*p*-methoxybenzoyl)benzoic acid (I) with zinc–ammonia gave *o*-(*p*-methoxybenzyl)benzoic acid (II) quantitatively. In this step, the Clemmensen reduction (zinc–hydrochloric acid) of (I) yielded II and 3-(*p*-methoxyphenyl)phthalide (IIa) in a ratio of about 2 to 1 respectively.[6] The Wolff-Kishner reduction (hydrazine–*n*-butanol–potassium hydroxide) of (I) afforded only 3-(*p*-methoxyphenyl)-6-oxo-1H-phthalazine (IIb). The dehydrative cyclization of II with concd. sulfuric acid gave 2-methoxy-9-anthrone (III) in a good yield; it was then treated with the corresponding Grignard reagents to give IVa—c. To exemplify and compare the results with those of the literature,[7] 2-methoxyanthracene (IVd) was prepared by the reduction of III with sodium borohydride. 2-Methoxytriptycenes (Va, b) were synthesized by the addition of IVa and IVd respectively to benzyne.

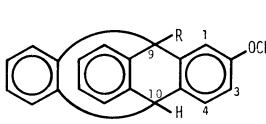


IIa

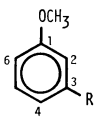


IIb

IVa R=2-*p*-cymenyl
IVb R=$-C_6H_5$
IVc R=$-CH_3$
IVd R=$-H$



Va R=2-*p*-cymenyl
Vb R=$-H$



VIa R=$-OCH_3$
VIb R=*tert*-C_4H_9

Regioselective Formylation. Formylation was carried out by the use of two methods: the Vilsmeier-Haack method (Method A)[8] and the metallation method using *n*-butyllithium–*N*-methylformanilide (Method B).[9] The results obtained are shown in Table 1.

Table 1. The regioselective formylation of methoxy-substituted aromatic compounds. Yields and the formylated positions

Compound	Method A		Method B	
	Formylated position	Yield(%)	Formylated position	Yield(%)
IVa	1	98	3	71
IVb	1	50	3	64
IVc	1	48	3	63
IVd[a]	1, 3	40, 23[b]	—	—
Va	3	79	3	58
Vb	3	82	1, 3	41, 4[c]
VIa	6[d]	62[d]	2[e]	75[e]
VIb	6	95	6	17

a) In the lit.[7] 1 and 3 formylated products have been obtained in almost equal amounts in about 70% total yield. b) 40% for 1 and 23% for 3. c) 41% for 1 and 4% for 3. d) By use of dimethylformamide and phosphorus oxychloride,[10] the same C-6 formylated product has been regioselectively obtained in 85% yield. e) By metallation with phenyllithium and subsequent formylation with *N*-methylformanilide in abs. ether at r.t.,[11] the same C-2 formylated product has been regioselectively obtained in 55% yield.

The data listed in Table 1 indicate (a) that the formylation according to Method A is strictly regioselective for all types of compounds and that the formylated position is independent of the substituent group in each case and (b) that the formylation according to Method B is less selective and that the regioselectivity is dependent on the substituent group except for the case of anthracenes.

The Determination of the Structures of Formylated Compounds. The structures of the formylated compounds were determined by the use of IR, UV, NMR, and elemental analyses. The lanthanide-induced NMR spectra were especially effective for the determination of the introduced position of the formyl group.

The NMR Spectral Data. The lanthanide-induced spectra with the aid of tris(dipivalomethanato)europium(III), $Eu(DPM)_3$, were measured for all the formylated anthracenes and triptycenes. From the spectra, the following findings were obtained: (a) the metal ion of the shift reagent associated more tightly with the aldehyde oxygen atom than with the methoxy group: (b) the formyl proton of the C-3 position experiences greater shift than that of the C-1 position by about 10 factors, and (c) the effect of the interaction between the shift reagent and the neighboring protons of the formyl group is transferred more effectively through the bond than the space. Detailed analyses of the induced spectra are in progress; the results will be published in the forthcoming paper.

On the basis of these findings the chemical shifts and the coupling constants of the main protons of the formylated compounds in the original NMR spectra were assigned as is shown in Tables 2 and 3. In the C-1 formylated 9-arylanthracenes, the aldehydic protons appears in a higher field than that of the other aldehydic protons by *ca.* 1.3 ppm (Table 2). The shift may be due to the anisotropic effect of the ring current of the peri-aryl substituent and to the steric effect of the peri-substituent affecting the non-coplanarity of the formyl group and the aromatic ring. The C-1 aromatic proton of the C-3 formylated anthracenes may experience a similar ring current anisotropy of the 9-aryl group and reveals a chemical shift at a higher field. In the NMR data of triptycenes (Table 3), the formyl protons showed the normal chemical shifts. However, in the C-1 formylated triptycene the C-9 methine proton was deshielded by the anisotropic effect of the adjacent formyl group and showed a chemical shift at a field lower by 1.97 ppm than that of the C-3 formylated triptycene. In Table 4, the chemical shifts and the coupling constants of the formylated anisoles are collected. One of the aromatic protons at the *meta*-position of the formyl group showed spin-spin coupling with the formyl proton when one of the *ortho*-positions of the formyl group was not substituted.[12]

The UV Spectral Data. The structural features of the formylated compounds were well reflected on the UV spectra. The UV spectral data of some of the anthracene derivatives are summarized in Table 5. In the table the original ^1B_b band, the longitudinally-polarized transition, at 255—259 nm splits into two electronic transitions of nearly equal intensities when the C-3 position is formylated. One appears on the shorter-wavelength side, and the other, on the side longer than the original band. The spacings of these bands are almost constant; in the C-3 formylated compound of IVd, 266.5−244.2=22.3 nm, and in that of IVa, 277−256=21 nm. Therefore, it is apparent that these two ^1B_b bands are due to the longitudinal polarization in the directions of both the methoxy and the formyl groups. The vibrational structures of the transversely-polarized ^1L_a bands on the side with wave-

Table 2. NMR data of formylated compounds of 2-methoxyanthracenes

δ ppm (J in Hz)

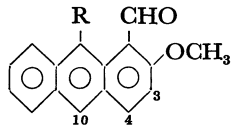
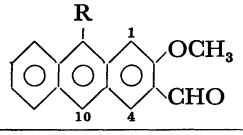
Compounds		Solv.	C_1–H	C_3–H	C_4–H	C_{10}–H	$-OCH_3$	–CHO
	R=2-*p*-cymenyl	CCl_4	—		8.01 J=9.5	8.33	3.82	9.41
	R=$-C_6H_5$	CCl_4	—	7.03 J=9.2	7.71 J=9.2	8.14	3.76	9.41
	R=$-CH_3$	$CDCl_3$	—	7.23 J=9.5	8.06 J=9.5	8.21	4.03	10.85
	R=–H	$CDCl_3$	—	7.45 J=9.0	8.07 J=9.0	8.31	4.06	10.94
	R=2-*p*-cymenyl	$CDCl_3$	6.76	—	8.54	8.60	3.74	10.56
	R=$-C_6H_5$	CCl_4	6.76	—	8.46	8.46	3.73	10.47
	R=$-CH_3$	$CDCl_3$	7.34	—	8.35	8.47	4.07	10.52
	R=–H	$CDCl_3$	7.23	—	8.46	8.46	3.97	11.36

Table 3. NMR data of formylated compounds of 2-methoxytriptycenes

δ ppm (J in Hz)

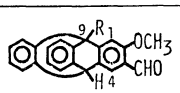
Compounds		Solv.	C_1–H	C_3–H	C_4–H	C_9–H	C_{10}–H	$-OCH_3$	–CHO
1-Formyl-2-methoxytriptycene		$CDCl_3$	—	6.44 J=8.0	7.37 J=8.0	7.33	5.29	3.74	10.55
	R=2-*p*-cymenyl	$CDCl_3$	6.92	—	7.75	—	5.34	3.76	10.24
	R=–H	CCl_4	7.02	—	7.76	5.36	5.36	3.85	10.25

Table 4. NMR data of formylated compounds of anisoles

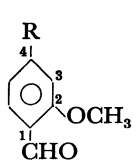
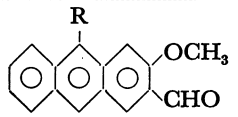
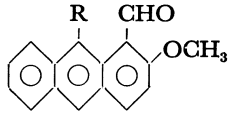
Compounds	Solv.	C_2–OCH_3	C_4–OCH_3	C_6–OCH_3	C_3–H	C_4–H	C_5–H	C_6–H	–CHO
					δ ppm (J in Hz)				
2,6-Dimethoxybenzaldehyde	CCl_4	3.86	—	3.86	6.51 J=8.5	7.35 J=8.5	6.51 J=8.5	—	10.39
 R=–OCH_3	CCl_4	3.88	3.84	—	6.34 J=2.2	—	6.47 J=8.5 2.2 0.75	7.71 J=8.5	10.20 J=0.75
R=*tert*-C_4H_9	CCl_4	3.93	—	—	6.92 J=1.8	—	6.98 J=8.0 1.8 0.8	7.68 J=8.0	10.33 J=0.8

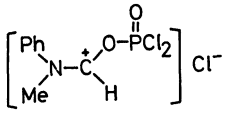
Table 5. The UV spectral data of the anthracene derivatives (in Ethanol)

IVa	λ_{max}	259	318	333.5	351	376	396.5		
	log ε	5.07	3.41	3.69	3.79	3.79	3.79		
IVd	λ_{max}	255	314	329	346.5	368.5	388.5		
	log ε	5.15	3.38	3.61	3.67	3.60	3.59		
 R=–H	λ_{max}	244.2	266.5	354[s]	371	419			
	log ε	4.68	4.76	3.64	3.91	3.80			
R=2-*p*-cymenyl	λ_{max}	256	277	330	347	365	399	432	451[s]
	log ε	4.67	4.70	3.70	3.83	3.72	3.35	3.39	3.33
 R=–H	λ_{max}	251	263.5[s]	281[s]	295[s]	314[s]	346	364	416.5
	log ε	4.84	4.50	4.25	4.01	3.63	3.64	3.83	3.65
R=2-*p*-cymenyl	λ_{max}	261	324.5	343	361	394	415.5[s]		
	log ε	4.94	3.50	3.62	3.74	3.80	3.72		

s: shoulder band

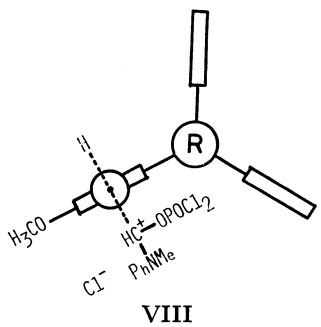
lengths longer than 314 nm disappeared when the C-1 or C-3 positions of IVd and the C-3 position of IVa were formylated. However, in the C-1 formylated derivative of IVa the vibrational characteristics remained considerably clear, although the bands showed slightly bathochromic shifts. This may be assumed to be due to the non-coplanarity of the formyl group and the anthracene ring affected by the steric overlap of the formyl group with the aryl group at the peri-position and the methoxy group at C-2; this reliable assumption coincides with the results of the analysis of the NMR spectral data.

Possible Transition States of Formylation. By many authors[13] since Vilsmeier,[8] several reaction mechanisms have been proposed for the Vilsmeier-Haack reaction. Of these proposals, it seems most reasonable to adopt the mechanism suggested by Bosshard and Zollinger,[14] where the following reactive intermediate (VII) of the formylating reagents attacks the most electron-rich



VII

position of the substrate molecule. However, it should be noted that VII is bulky around the positive charge and that, thus, VII would select the reaction point of the substrate with respect not only to the electronic density but also to the steric environment if there is not much difference in electronic density. Practically, from the results shown in Table 1, it seems clear that, in methoxyanthracenes (IVa—d), the regioselectivity of formylation by Method A is due only to the difference in electronic density,[15] and that in methoxytriptycenes (Va, b) and methoxybenzenes (VIa, b) the steric factors govern the reaction predominantly. Typically, for example, in methoxytriptycenes involving a C_s point group the transition state of formylation attacking the C-1 position could be shown by a tetrahedral intermediate like VIII. In this model it is apparent that the attack of the formylating active species (VII) on the C-1 position may be prevented because of the steric interaction of VII with the bridged benzene rings and the C-9 substituent. Therefore, the C-3 position will be regioselectively formylated in methoxytriptycenes. In a similar manner, it may be



VIII

Fig. 1. A transition state model of formylation of methoxytriptycenes. VIII is projected from the front side of the R-axis and C-9 carbon is on the plane. The rectangle shows the hydrogen-abbreviated benzene ring.

suggested that the results of formylation in anisoles can be explained by the steric interaction of VII and the substituent, and that the C-6 position is regioselectively formylated.

In formylation by the metallation method (Method B), it was empirically observed that no types of aromatic compounds were formylated by the addition of *N*-methylformanilide without the formation of the dark green or blue colored complex of the substrate with *n*-butyllithium. Thus, the driving force of formylation by Method B seems to be the formation of the lithium complex, doubtless a radical anion. Although, unfortunately, the reactivity of the radical anions is not yet known in detail,[16] the results found by Method B may be explained on the basis of the following assumptions: (a) the electronic distribution of the substrate is quite different from that of the substrate-lithium complex, and (b) the unstable lithium complex and the transition state of formylation have nearly the same energy content, and thus their interconversion will involve only a small reorganization of the molecular structure, in agreement with the Hammond's postulation.[17] In methoxyanthracenes the fact that the C-3 position is regioselectively formylated without exception may be understood on the basis of the (a) assumption; that is, the C-3 position may be nucleophilically more active than the C-1 position in the complex state. The experimental results that the dependency of formylation on the substituents was shown in triptycenes and anisoles seem to give evidence of the least gap of the energy content being between two reactive positions in the complex, as is indicated in the cases of Vb and VIa. Also, the results in Va and VIb seem alternatively to demonstrate that the substituent effects on formylation may be due to mainly the steric effect. Therefore, it could be concluded that, in the case of Method A, the reaction selectivity may be determined by the steric interaction of the formylating reagents with the substrate in the transition state and the electronic density, while in Method B the perturbation of the electronic distribution of the substrate in the complex state may cause the regioselectivity of the formylated positions.

Experimental

The instruments for spectral measurements were a Shimadzu IR-27 (IR) apparatus, a Hitachi 124 spectrophotometer (UV), and a Varian HA-100D (NMR) apparatus. Merck Art. 7734 was used for the preparative separation of products on a silica gel column by elution chromatography, and Wakogel B-5 UA, for thin-layer chromatography. The *m*-methoxyanisole (VIa) was commercially available, and the *m-tert*-butylanisole (VIb) was obtained by the methylation of the corresponding phenol (commercially available) with dimethyl sulfate in a good yield. The melting points are uncorrected.

o-(p-*Methoxybenzoyl*)*benzoic Acid (I).* To a mixture of phthalic anhydride (148 g, 1 mol) and anisole (250 ml) in 250 ml of carbon disulfide we added 140 g of aluminium chloride under vigorous stirring at room temperature. After all the anhydride disappeared to form a viscous dark red solution, the solution was hydrolyzed with ice water, and the solvents were removed by steam distillation. From the cooled residual solution, a grey solid was precipitated. After most of the supernatant solution had been decanted, *ca.* 1000 ml of chloroform was poured into the flask to dissolve the solid and the organic layer was separated. The solvent was then evaporated to give almost pure (I) (204—250 g; 80—97%). For analytical use, a part of the solid was recrystallized from acetic acid; colorless plates; mp 122—123.5 °C. Found: C, 70.30; H, 4.65%. Calcd for $C_{15}H_{12}O_4$: C, 70.30; H, 4.72%. IR (KBr disk): ν_{max} 1664 (–CO–) and 1689 (–COOH) cm^{-1}.

o-(p-*Methoxybenzyl*)*benzoic Acid (II).* In a three-necked flask, 64 g (0.25 mol) of (I), 600 ml of 20% ammonia, and 60 ml of 20% ammonia containing 5 g of cupric sulfate were successively added, after which the mixture was heated until gentle reflux. Then 150 g of zinc powder was added in limited amounts. After having been stirred at 95—100 °C for 24 hr, the mixture was cooled and filtered to give a transparent solution which was acidified by the addition of *ca.* 1500 ml of 10% hydrochloric acid. The white precipitate was collected and dried to give II (50.6—57.6 g; 84—95%). For analytical use, a part of the solid was recrystallized from 50% aqueous ethanol; colorless fine crystals; mp 117—118 °C. Found: C, 74.29; H, 5.75%. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.83%. IR (KBr disk): ν_{max} 1680 (–COOH) and 1250 (=C–O–C) cm^{-1}.

2-Methoxy-9-anthrone (III). Fine powdered II (57.6 g, 0.238 mol) was dissolved in 250 ml of ice-cold concd. sulfuric acid, after which the mixture was stirred at 0—5 °C for 2 hr. Then the solution was poured into *ca.* 2000 ml of ice water to give III (35.8 g; 67%) as a yellow solid. The solid was purified by elution chromatography with THF; fine yellow needles; mp 96—97.5 °C. IR (KBr disk): ν_{max} 1648 (–CO–) and 1296 (=C–O–C) cm^{-1}. The purified III was used for the subsequent reactions.

Synthesis of 9-Substituted 2-Methoxyanthracenes by the Grignard Reaction. General Procedure. The compounds from IVa—IVc were synthesized by the following procedure. Into 0.02 mol of turnings-magnesium in 30 ml of dry THF, 0.02 mol of the corresponding aryl or alkyl bromide was vigorously stirred under a nitrogen atmosphere at room temperature. To the resulting Grignard reagent 0.01 mol of III in 20 ml of THF was added drop by drop at the temperature of ice water. After the completion of the reaction, followed by tlc, the reaction mixture was hydrolyzed with ice water containing ammonium chloride, acidified with *ca.* 6M HCl, and stirred until all the corresponding 9-substituted 2-methoxy-9-anthranol had been dehydrated to the corresponding 9-substituted 2-methoxyanthracene. The mixture was extracted with ethyl acetate, and the organic layer was separated and dried with anhydrous Na_2SO_4. After the removal of the solvents under reduced pressure, the residue was chromatographed on a silica gel column with benzene to give the corresponding pure 9-substituted 2-methoxyanthracenes.

*9-(2-*p*-Cymenyl)-2-methoxyanthracene (IVa).* Obtained in a 76% yield; a yellow green viscous liquid. Found: C, 88.09; H, 7.10%. Calcd for $C_{25}H_{24}O$: C, 88.19; H, 7.11%. NMR (CCl_4): δ 1.27 (6H, d, J=7.0 Hz, $-CH(C\underline{H}_3)_2$), 1.83 (3H, s, $Ar-C\underline{H}_3$), 3.86 (1H, qui, J=7.0 Hz, $-C\underline{H}(CH_3)_2$), 7.03 (1H, quar, J=2.7, 9.0 Hz, C_3–H), and 7.82 (1H, d, J=9.0 Hz, C_4–H) ppm. IR (neat): ν_{max} 1632, 1468, 1268, 1230, and 1210 cm^{-1}. UV data are shown in Table 5.

9-Phenyl-2-methoxyanthracene (IVb). Yield, 96%; pale yellow plates; mp 100—102 °C. Found: C, 88.71; H, 5.62%. Calcd for $C_{21}H_{16}O$: C, 88.70; H, 5.67%. NMR (CCl_4): δ 3.63 (3H, s, $-OCH_3$), 6.71 (1H, d, J=2.7 Hz, C_1–H), 7.04 (1H, quar, J=2.7, 9.0 Hz, C_3–H), 7.80 (1H, d, J=9.0 Hz, C_4–H), and 8.27 (1H, s, C_{10}–H) ppm. UV (ethanol): λ_{max} (log ε) 258.2 (5.10), 318 (3.41), 333.8 (3.67), 351.5 (3.78), 376.5 (3.76), and 396 (3.76) nm. IR (KBr disk): ν_{max} 1628 and 1225 cm^{-1}.

9-Methyl-2-methoxyanthracene (IVc). Yield, in 64%; light yellow needles; mp 147—149 °C. Found: C, 86.25; H, 6.18%. Calcd for $C_{16}H_{14}O$: C, 86.45; H, 6.35%. NMR (CCl_4): δ 2.97 (3H, s, Ar–CH_3), 3.95 (3H, s, –OCH_3), 7.70 (1H, quar, J=2.7, 9.0 Hz, C_3–H), 7.79 (1H, d, J=9.0 Hz, C_4–H), 7.26 (1H, d, J=2.7 Hz, C_1–H), and 8.13 (1H, s, C_{10}–H) ppm. UV (ethanol): λ_{max} (log ε) 259 (5.16), 319 (3.36), 334 (3.61), 352 (3.71), 377 (3.72), and 397 (3.71) nm. IR (KBr disk): ν_{max} 1630, 1469, 1213, and 735 cm^{-1}.

2-Methoxyanthracene (IVd). III (1.5 g, 0.067 mol) was reduced with 0.265 g (0.07 mol) of sodium borohydride in ethanol and hydrolyzed with ice water containing methanol and *ca.* 6M HCl. The precipitate was collected by filtration, and the solid was dehydrated in benzene by then addition of concd. sulfuric acid with vigorous stirring overnight. The supernatant solution was then separated, and the solvent was removed under reduced pressure. The residue was chromatographed on a silica gel column with benzene to give IVd (1.20 g, 86%) as a pale yellow solid; mp 163—165 °C. Found: C, 86.66; H, 5.85%. Calcd for $C_{15}H_{12}O$: C, 86.51; H, 5.81%. NMR ($CDCl_3$): δ 3.76 (3H, s, –OCH_3), 7.04 (1H, quar, J=2.4, 9.0 Hz, C_3–H), 7.85 (1H, d, J=9.0 Hz, C_4–H), 8.21 (1H, s, C_9–H), and 8.29 (1H, s, C_{10}–H) ppm. IR (KBr disk): ν_{max} 1640, 1465, 1214 (=C–O–C), and 875 $cm.^{-1}$ The UV data are shown in Table 5.

Synthesis of 9-(2-p-Cymenyl)-2-methoxytriptycene (Va) and 2-Methoxytriptycene (Vb). The preparation of benzyne and its addition to anthracenes were carried out by the same method as has been described previously.[18] Then the products were isolated by elution-column chromatography with cyclohexane–benzene (1: 9 v/v). Va was obtained in a 27% yield as a yellow viscous liquid. Found: C, 89.39; H, 7.04%. Calcd for $C_{31}H_{28}O$: C, 89.38; H, 6.78%. UV (cyclohexane): λ_{max} (log ε): 226 (4.42), 244 (s) (4.01), 255 (s) (3.74), 261 (3.60), 269.5 (3.57), 277 (3.60) and 289.5 (3.49) nm. IR (neat): ν_{max} 1460, 1280, and 1230 $cm.^{-1}$ NMR (CCl_4): δ 1.39 (6H, d, J=7.5 Hz, –$CH(CH_3)_2$), 1.77 (3H, s, Ar–CH_3), 3.59 (3H, s, –OCH_3), 5.19 (1H, s, C_{10}–H), 6.36 (1H, quar, J=2.5, 8.0 Hz, C_3–H), and 7.17 (1H, d, J=8.0 Hz, C_4–H) ppm. Vb was obtained in a 33% yield as pale yellow crystals from petroleum ether; mp 173—174 °C. Found: C, 88.75; H, 5.50%. Calcd for $C_{21}H_{16}O$: C, 88.70; H, 5.67%. UV (cyclohexane): λ_{max} (log ε) 224.5 (4.19), 273 (3.62), 280 (3.75), and 291 (3.62) nm. NMR (CCl_4): δ 3.65 (3H, s, –OCH_3), 5.23 (2H, s, C_9–H and C_{10}–H), 7.12 (1H, d, J=2.0 Hz, C_1–H), 6.37 (1H, quar, J=2.0, 8.0 Hz, C_3–H) ppm.

General Procedure of Formylation. The formylation of the compounds from IV to VI was carried out by two kinds of procedure. One was the Vilsmeier-Haack method using *N*-methylformanilide (MFA) and phosphorus oxychloride (Method A); the other was the metallation method using *n*-butyllithium and MFA (Method B).

Method. A. To a solution of a methoxyaromatic compound (1 mmol) in MFA (2.6 mmol), we added phosphorus oxychloride (3.7 mmol) drop by drop after which the mixture was heated at 70—80 °C for 2 hr. After the mixture had been treated with sodium acetate–ice water, it was extracted with benzene or chloroform. After the removal of the solvents, the residue was chromatographed on a silica gel column with benzene–ethyl acetate to give the products.

Method B. A solution of a methoxyaromatic compound (1 mmol) in THF was added to a solution of *n*-butyllithium (1.5—2.5 mmol) in hexane (*ca.* 20%) under a nitrogen atmosphere, and then MFA (1.5—2.5 mmol) was added. The mixture was stirred at room temperature or in an ice-bath for 1.5—2 hr. After the usual work-up, the products were isolated by silica-gel column chromatography with benzene or chloroform.

Formylation of IVa by Method A. Yield of 9-(2-*p*-cymenyl)-1-formyl-2-methoxyanthracene, 98%; dark brown shell ligaments; mp 110—112 °C. Found: C, 84.73; H, 6.61%. Calcd for $C_{29}H_{24}O_2$: C, 84.75; H, 6.57%. The NMR and UV data are shown in Tables 2 and 5 respectively. IR (KBr disk): ν_{max} 1690 (–CO–) and 1250 (=C–O–C) cm^{-1}.

Formylation of IVb by Method A. Yield of 1-formyl-2-methoxy-9-phenylanthracene, 50%; mp 131.5—132.5 °C. The NMR data are shown in Table 2.

Formylation of IVc by Method A. Yield of 1-formyl-2-methoxy-9-methylanthracene, 48%; yellow crystals; mp 177.5—179 °C. Found: C, 81.55; H, 5.58%. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64%. UV (cyclohexane): λ_{max} (log ε) 256 (4.67), 319 (s) (3.56), 350 (3.45), 368 (3.59), and 421 (3.52) nm. IR (KBr disk): ν_{max} 1650 (–CO–) and 1250 (=C–O–C) cm^{-1}.

Formylation of IVd by Method A. Yield of 1-formyl- and 3-formyl-2-methoxyanthracenes, 40 and 23% respectively.

The 1-formyl derivative; pale yellow needles; mp 185—186 °C (lit.[7] 192—194.5 °C). Found: C, 81.62; H, 5.18%. Calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12%. IR (KBr disk); ν_{max} 1650 (–CO–) and 1250 (=C–O–C) cm^{-1}. The NMR and UV data are shown in Tables 2 and 5 respectively.

The 3-formyl derivative; pale yellow needles; mp 113—114 °C (lit.[7] 116—117 °C). Found: C, 81.41; H, 5.00%. IR (KBr disk): ν_{max} 1668 (–CO–), 1265, and 1215 (=C–O–C) cm^{-1}. The NMR and UV data are shown in Tables 2 and 5 respectively.

Formylation of Va by Method A. Yield of 9-(2-*p*-cymenyl)-3-formyl-2-methoxytriptycene, 79%; yellow red crystals; mp 93.2—94.5 °C. Found: C, 86.65; H, 6.39%. Calcd for $C_{32}H_{28}O_3$: C, 86.45; H, 6.35%. UV (cyclohexane): λ_{max} (log ε) 226 (4.51), 248.5 (s) (4.20), 254 (4.05), 261 (4.00), 266 (3.78), 278 (3.96), 278 (s) (3.94), and 333 (3.81) nm. IR (KBr disk): ν_{max} 1680 (–CO–), 1260, and 1230 (=C–O–C) cm^{-1}. The NMR data are shown in Table 3.

Formylation of Vb by Method A. Yield of 3-formyl-2-methoxytriptycene, 82%; pale yellow crystals from cyclohexane-ethanol; mp 242.5—243 °C. Found: C, 84.58; H, 4.87%. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16%. UV (cyclohexane): λ_{max} (log ε) 234 (4.60), 256 (3.91), 263.5 (3.97), 272.5 (4.02), 275 (s) (4.00), 323 (3.85), and 331 (3.85) nm. IR (KBr disk): ν_{max} 1670 (–CO–) and 1250 (=C–O–C) cm^{-1}. The NMR data are shown in Table 3.

Formylation of VIa by Method A. Yield of 4-methoxy-*o*-anisaldehyde, 62%; pale yellow crystals; mp 70.5—71.5 °C. Found: C, 65.27; H, 5.77%. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07%. IR (KBr disk): ν_{max} 1674 (–CO–), 1265, and 1220 (=C–O–C) cm^{-1}. The NMR data are shown in Table 4.

Formylation of VIb by Method A. Yield of 4-*tert*-butyl-*o*-anisaldehyde, 95%; colorless liquid. Found: C, 74.83; H, 8.38%. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39%. IR (neat): ν_{max} 1684 (–CO–) and 1230 (=C–O–C) cm^{-1}. The NMR data are shown in Table 4.

Formylation of IVa by Method B. Yield of 9-(2-*p*-cymenyl)-3-formyl-2-methoxyanthracene, 71%; brown red needles; mp 118—119 °C. Found: C, 84.64; H, 6.26%. Calcd for $C_{29}H_{24}O_2$: C, 84.75; H, 6.57%, IR (KBr disk): ν_{max} 1695 (–CO–), 1231, and 1210 (=C–O–C) cm^{-1}. The NMR and UV data are shown in Tables 2 and 5 respectively.

Formylation of IVb by Method B. Yield of 3-formyl-2-methoxy-9-phenylanthracene, 64%; yellow needles; mp 160.4—162.6 °C. IR (KBr disk): ν_{max} 1680 (–CO–), 1225, and 1215 (=C–O–C) cm^{-1}. The NMR data are shown in Table 2.

Formylation of IVc by Method B. Yield of 3-formyl-2-methoxy-9-methylanthracene, 63%; yellow needles; mp 150.4

—152.4 °C. The NMR data are shown in Table 2.

Formylation of IVd by Method B. A trace of 1-formyl-2-methoxyanthracene was detected on tlc. However, its isolation was not attempted.

Formylation of Va by Method B. This yielded the same product as was detected by Method A in a 58% yield. Its behavior on tlc, EA, NMR, UV, and IR data were consistent with 9-(2-*p*-cymenyl)-3-formyl-2-methoxytriptycene.

Formylation of Vb by Method B. Yields of 1-formyl and 3-formyl-2-methoxytriptycenes, 41 and 4% respectively.

The 1-formyl isomer; fine crystals from cyclohexane; mp 210.5—212 °C. Found: C, 84.68; H, 5.07%. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16%. UV (cyclohexane): λ_{max} (log ε) 223 (4.24), 236.7 (4.16), 257 (s) (3.97), 269.7 (3.82), 277.5 (3.86), and 333.5 (3.68) nm. IR (KBr disk): ν_{max} 1675 (–CO–), 1266, and 1237 (=C–O–C) cm^{-1}. The NMR data are shown in Table 3.

Formylation of VIa by Method B. Yield of 6-methoxy-*o*-anisaldehyde, 75%; needles; mp 98—99 °C (lit.[11] mp 98—99 °C). Found: C, 65.04; H, 5.99%. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07%. IR (KBr disk): ν_{max} 1675 (–CO–) and 1250 (=C–O–C) cm^{-1}. The NMR data are shown in Table 4.

Formylation of VIb by Method B. This yielded the same product as was isolated by formylation with Method A in a 17% yield. Its behavior on tlc, IR, and NMR were coincident with 4-*tert*-butyl-*o*-anisaldehyde.

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