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SELECTIVE FORMYLATION OF 9-SUBSTITUTED 2-METHOXYANTHRACENES

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Formylation of 9-substituted 2-methoxyanthracenes with N-methylformanilide and phosphorus oxychloride gave its 1-formyl derivatives, while with N-methylformanilide and n-butyllithium it afforded the corresponding 3-formyl derivatives.

Hunsberger and co-worker[1] reported that the Vilsmeier formylation of 2-methoxyanthracene (Id) gave a mixture of the corresponding 1- and 3-formyl derivatives in approximately equal amounts. However, there has been no study on formylation of 9-substituted 2-methoxyanthracenes with regard to selectivity.

In the course of the present studies concerning the synthesis of an enantioselective catalyst[2] as a co-enzyme model of pyridoxal, we found the first example of conspicuously selective formylation of 9-alkyl or aryl-substituted 2-methoxyanthracenes either at 1- or 3-position of the anthracene using N-methylformanilide (MFA) - phosphorus oxychloride (Method A) or n-butyllithium (n-BuLi) - MFA (Method B), respectively.

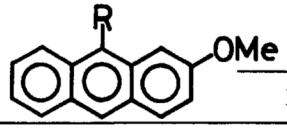
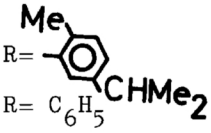
The starting materials, 9-p-cymenyl(Ia: yellow-green viscous liquid)-, 9-phenyl (Ib: mp 100-102°C)-, and 9-methyl(Ic: mp 147-149°C)-2-methoxyanthracenes, were prepared from the corresponding Grignard reagents and 2-methoxy-9-anthrone(mp 96-97.5°C), which was synthesized by three step reactions from anisole and phthalic anhydride.

Method A. To a solution of I (1 mol) in MFA (2.6 mol) was added dropwise phosphorus oxychloride (3.7 mol), and the mixture was heated at 70-80°C for 2 hr. After the mixture had been treated with sodium acetate-iced water, it was extracted with benzene or chloroform. After 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 I (1 mol) in tetrahydrofuran was added to a solution of n-BuLi (1.5-2.5 mol) in hexane (ca. 20%) under nitrogen atmosphere, followed by addition of MFA (1.5-2.5 mol). The mixture was stirred at room temperature or in an ice-bath for 1.5-2 hr. After the usual workup, the products were isolated by silica gel column chromatography with benzene or chloroform.

The results are summarized in the Table 1. On the basis of these results it is reasonably assumed that the methods A and B are very effective for selective formylation of 9-substituted 2-methoxyanthracenes.

Table 1. Yield and melting points of the prepared compounds.

	Yield (%)				mp (°C) (uncorrected)	
	Method A		Method B			
	1-CHO	3-CHO	1-CHO	3-CHO	1-CHO	3-CHO
Ia R= 	98	0	0	71	110-112	118-119
Ib R= C_6H_5	50	0	0	64	131.5-132.5	160.4-162.6
Ic R= CH_3	48	trace	0	63	177.5-179	150.4-152.4
Id R= H	40	23	trace	0	185-186	113-114
(ref. 1, R= H	ca. 35	ca. 35	———	———	192-194.5	116-117)

These selectivities may be rationalized by postulating that the variations in the attacked position of the anthracene ring are due to the differences in the activated species in the formylating step of the reaction. In the case of the method A, it is proposed that the interaction of MFA and phosphorus oxychloride is the driving force of formylation.[3] Hence the most electron rich position of the anthracene ring may be, in principle, formylated despite of the steric interaction of the reagents with the peri-substituent. On the other hand, in the case of the method B, formation of the π-complex of an anthracene derivative with n-BuLi is the key step of the reaction[4] and the complex may have different reactivity from that of the metal ion-free state. Thus such electronical perturbation of the molecule may be related to the reaction selectivity. Detail discussion will be given in the forthcoming paper.

The structures of all the newly synthesized compounds were well supported on the basis of spectral data and elemental analyses, especially of NMR shift reagent studies.

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References

1) J. L. Ferrari and I. M. Hunsberger, J. Org. Chem., 25, 485 (1960); J. L. Ferrari, I. M. Hunsberger, and H. S. Gutowsky, J. Amer. Chem. Soc., 87, 1247 (1965).
2) Y. Izumi, Angew. Chem. Int. Ed., 10, 871 (1971).
3) M.-R. de Maheas, Bull. Soc. Chim. Fr., 1989 (1962).
4) See, for example; "Radical Ions", ed. by E. T. Kaiser and L. Kevan, John Wiley and Sons, Inc. (1968), p. 245.

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