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A NEW METHOD FOR THE PREPARATION OF SUBSTITUTED PYRROLOANTHRONE

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1-Benzylaminoanthraquinone reacted with benzyl chloride in the presence of powdered KOH in DMSO to give spiro[1-dibenzylamino-10-anthrone-9,3'-[2]phenyloxirane](1) quantitatively under a nitrogen atmosphere. The oxirane(1) was converted into 1-phenyl-2-benzylpyrrolo[4,3,2-mn]anthracene-6-one(2)(substituted pyrroloanthrone) having strong fluorescence in ethanol by treatment with hydrochloric acid.

In the course of investigation on the behavior of aminoanthraquinones(NH_2AQ) in KOH-DMSO system, we found that the amide ion, formed by the deprotonation of the amino group of NH_2AQ in the presence of powdered KOH in DMSO, reacted with alkyl halides to yield the alkylaminoanthraquinones. Thus, the amide ion of 1-NH_2AQ reacted with butyl iodide or hexadecyl bromide for 1 h at 30°C to yield 1-monoalkylaminoAQ in 52 or 51% yields, respectively. On the other hand, the reaction of the amide ion of 2-NH_2AQ with these alkyl halides to yield 2-dialkylaminoAQ in 93 or 70% yields, respectively.

In the reaction of 2-NH_2AQ with benzyl chloride, 2-dibenzylaminoAQ was obtained in a 93% yield, while the reaction of 1-NH_2AQ didn't produce a 1-benzylaminoAQ but an oxirane(1) together with a trace amount of substituted pyrroloanthrone(2). The resulted oxirane(1) was converted into 2 by treatment with hydrochloric acid. Pyrroloanthrones have been known to be good fluorophores.1) In this paper we will report a new method for the preparation of substituted pyrroloanthrone having strong fluorescence, and the anomalous behavior of benzyl chloride for the amide ions.

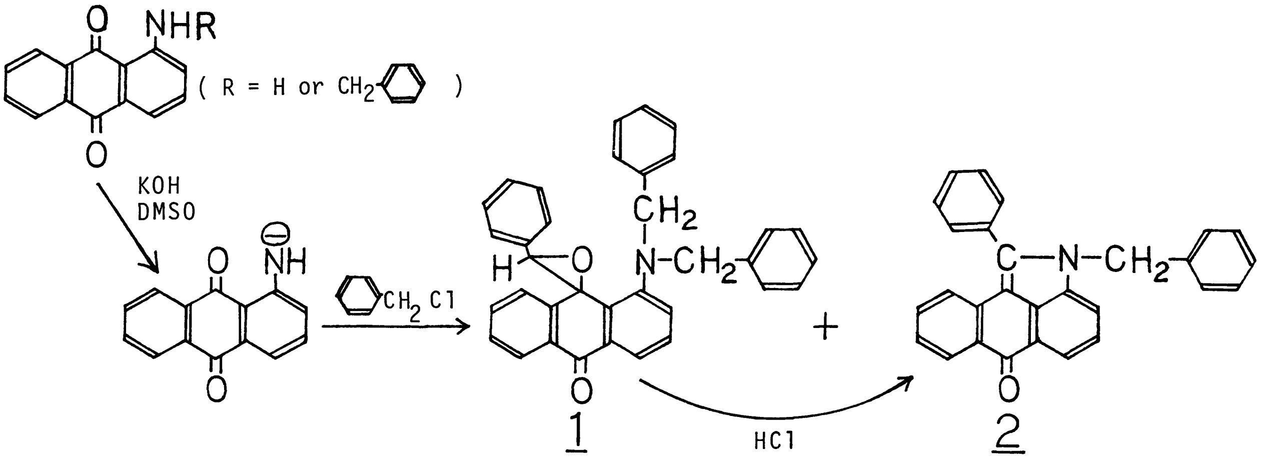


Table 1. Spectroscopic and Elemental Analyses of New Compounds(1 and 2)

	1	2
mp	Yellow crystals from C_2H_5OH 202.0-202.8°C	Orange crystals from C_2H_5OH 228.5-230.0°C
$UV_{max}(C_2H_5OH)$ nm(log ε)	394(3.17), 275^{sh}(4.28), 259(4.32).	426(4.16), 356(3.61),306(4.09), 276(4.23), 245(4.42).
IR(KBr)cm^{-1}	1670(C=O), 1245, 1150, 830, 820.	1630, 1610, 1595, 1550, 1180, 970.
MS(m/e)	493.2054. Calcd for $C_{35}H_{27}NO_2$: M, 493.2042.	385. Calcd for $C_{28}H_{19}NO$: 385.
^1H-NMR($CDCl_3$)	3.46(ABq,J=12Hz,2H,CH_2), 4.32(ABq, J=16Hz,2H,CH_2), 6.28(s,1H,CH), 5.9-6.2(m,2H,arom), 6.7-8.0(m, 20H, arom).	5.20(s,2H,CH_2), 6.8-8.6(m,17H, arom).
EA Found(%)	C, 85.13; H, 5.42; N, 2.85.	C, 87.24; H, 4.69; N, 3.41.
EA Calcd(%)	C, 85.16; H, 5.51; N, 2.83.	C, 87.25; H, 4.97; N, 3.63.

A typical procedure for the preparation of oxirane(1) is as follows. 1-NH_2AQ (1 mmol) was treated with powdered KOH(10 mmol) in DMSO(30 ml) for 30 min at 30°C. The color of the mixture rapidly turned from red to green. Then, benzyl chloride (10 mmol) was added and the solution stirred for 1 h at 30°C. The resulting brown solution was poured into water(700 ml) and then extracted with benzene. After removal of the solvent, the residue was chromatographed on silica gel with a benzene eluent. The orange fractions(1) together with a trace amount of yellow fractions fluorescing intense yellowish green(2) were isolated.

The structures of new compounds(spiro[1-dibenzylamino-10-anthrone-9,3'-[2] phenyloxirane(1) and 1-phenyl-2-benzylpyrrolo[4,3,2-mn]anthracene-6-one(2)) were substantiated by both spectroscopic and elemental analyses as summerized in Table 1. The conversion of the cabonyl groups of AQ into the oxirane was reported to be accomplished by the use of sulfur ylides$^{2)}$ or by the reaction of benzylidenanthrone with hydrogen peroxide under a basic condition$^{3)}$, but, no synthesis by the use of benzyl halides has been published. Since 1 affords 2 in a 3% yield by treatment with KOH in DMSO at 30°C for 3 h, 2 may be formed by the reaction of 1. This fact also supports the idea that the isomeric structure, a C=O function is present at C-9, is excluded. The 1-NH_2AQ reacted with alkyl halides to give the monoalkylaminoAQ, while in the reaction of 2-NH_2AQ the dialkylaminoAQ were obtained. Therefore, it is worthwhile to point out that the amino group of 1-NH_2AQ was dialkylated in the oxirane formation.

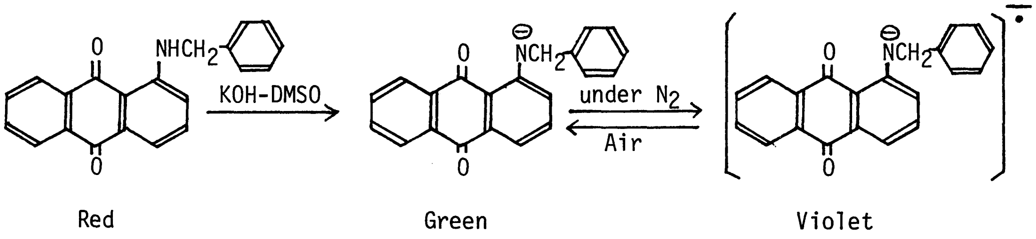
Table 2. The Reaction of Aminoanthraquinones with Benzyl Chloride in the Presence of KOH

Entry	AQ	Solvent	Atmosphere	Time(h)	Yield(%) of 1
1	1-NH_2AQ	DMSO	Air(sealed)	3	65
2	〃	DMF	Air(sealed)	3	55
3	〃	DMSO	Air(sealed)	1	48
4	〃	DMSO	Air(open)	1	13
5	〃	DMSO	N_2	1	78
6	1-$NHCH_2Ph$AQ	DMSO	Air(sealed)	1	13
7	〃	DMSO	Air(open)	1	2[a)]
8	〃	DMSO	N_2	1	97

a) 1-NH_2AQ was obtained in a 61% yield.

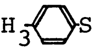
The yields of 1 under various reaction conditions are summerized in Table 2. The oxirane(1) was also obtained in DMF. It may be considered that 1-NH_2AQ was first converted to 1-benzylaminoAQ and then 1 was formed. In the reaction of 1-benzylaminoAQ, however, the yield was very low and dealkylation occurred predominantly: 1-NH_2AQ was obtained in a 61% yield(Entry 7). Strikingly, a quantitative yield was obtained under a N_2 atmosphere(Entry 8).

It was found that the green color(λ_{max} 695nm) of the amide ion of 1-benzylaminoAQ was rapidly changed to violet(λ_{max} 566, 500nm) under a N_2 atmosphere. ESR measurement of the violet solution showed the presence of a radical species(g= 2.003). When air was bubbled into the violet solution, the color returned to green and no radical species was detected. These results reveal that the violet species is not a radical anion of 1-benzylaminoAQ, but that of the amide ion:



These observations seem to indicate the reaction mechanism alternative to that of the Darzens condensation[4)], and may suggest that the radical anion of the amide ion plays an important role on the formation of 1. However 2-NH_2AQ, which genarated the radical species, didn't give the oxirane under a N_2 atmosphere. The detail mechanism of this reaction is ambiguous.

Table 3. The Conversion of Oxirane(1) into Substituted Pyrroloanthrone(2)

Entry	Condition	Temp(°C)	Time(h)	Yield(%) of 2	Recovered 1(%)
1[a]	KOH — DMSO	30	3	3	85
2	conc. HCl — C_2H_5OH	reflux	3	51	43
3[b]	CH_3SO_3H — benzene	reflux	1	36	0

a) 1-NH_2AQ was obtained in a 12% yield.

b) The unidentified product having yellowish green fluorescence was obtained.

The substituted pyrroloanthrone(2) having strong fluorescence in ethanol was obtained in a very low yield by treatment of 1 with KOH, but 1 could be transformed more easily into 2 by treatment with hydrochloric acid in ethanol(Table 3).

Some routes of the syntheses of pyrroloanthrones have been reported: The reaction of unstable 1-amino-10-anthrone with carboxylic acid in the presence of an acid anhydride[5)] or the reaction of aminoanthraquinone, derived from 1-chloroAQ and N-phenylglycine, with acetic anhydride[1)]. Although recently Russian chemists also reported the syntheses of pyrroloanthrones[6)], our two step procedure is a useful one for the preparation of substituted pyrroloanthrones.

In order to demonstrate generality of this new method, further studies are now in progress.

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