Synthesis of 2,6-Dihydronaphth[1,2,3-*cd*]indol-6-ones[1)]

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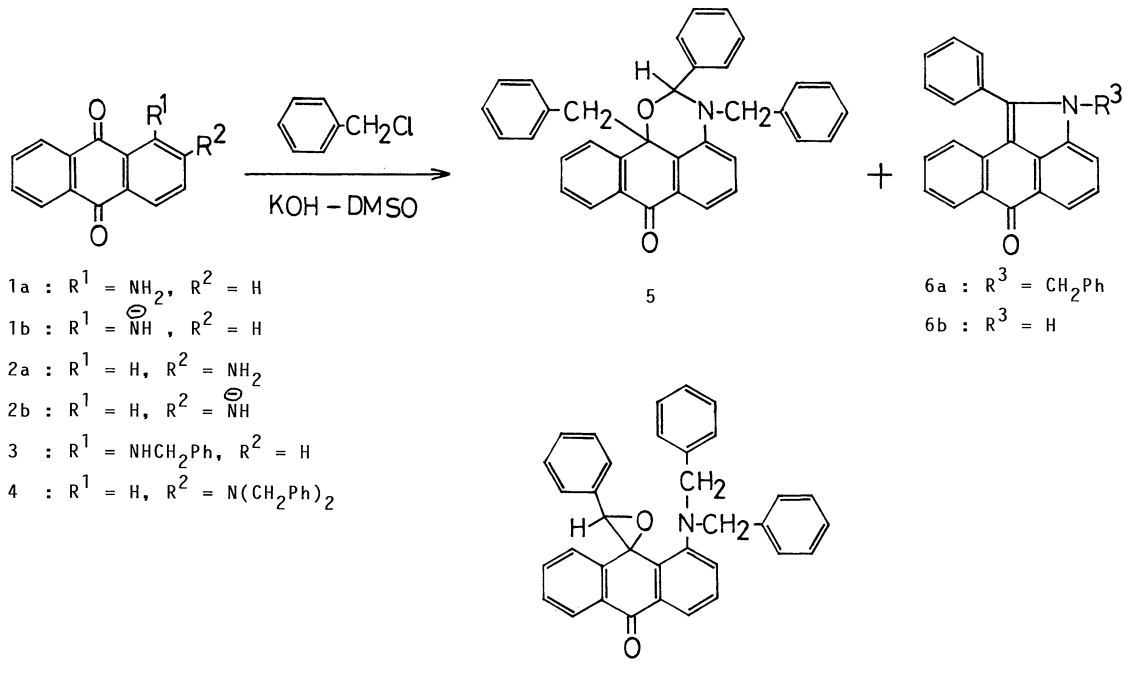
Synopsis. The reaction of 1-aminoanthraquinone with benzyl chloride in KOH–DMSO system afforded 3,11b-dibenzyl-2-phenyl-2,3,7,11b-tetrahydroanthra[1,9-*de*][1,3]-oxazin-7-one (**5**; 78% yield), whose structure was determined by single-crystal X-ray diffraction. The reaction of compound **5** with aluminium chloride gave 1-phenyl-2,6-dihydronaphth[1,2,3-*cd*]indol-6-one (52% yield) having strong fluorescence.

In our previous paper we reported that amide ions were formed by the loss of a proton from the amino group of aminoanthraquinones in the presence of powdered potassium hydroxide (KOH) in dimethyl sulfoxide (DMSO).[1,2)] The amide ion of 1-aminoanthraquinone (**1a**) reacted with excess alkyl halides such as 1-iodobutane and 1-bromohexadecane to yield red 1-alkylaminoanthraquinones, while the *N*-alkylation of 2-aminoanthraquinone (**2a**) afforded 2-dialkylaminoanthraquinones in good yields.[2)] The reaction of **1a** with benzyl chloride, however, produced not a predicted red 1-benzylaminoanthraquinone (**3**) but yellow product together with a trace amount of highly fluorescent compound. These unexpected results prompted us to examine the reaction of aminoanthraquinones with benzyl chloride in KOH–DMSO system. In this paper we will report a new method for the preparation of 2,6-dihydronaphth[1,2,3-*cd*]indol-6-ones having strong fluorescence.

Results and Discussion

Reaction of Aminoanthraquinone (1a or 2a) with Benzyl Chloride in KOH–DMSO System. The compound **1a** or **2a** was first converted to its amide ion by treating it with powdered KOH in DMSO. Then excess benzyl chloride was added to the green amide ion solution (**1b** or **2b**). In the reaction of **2a**, 2-dibenzylaminoanthraquinone (**4**) was obtained in 93% yield. The reaction of **1a**, however, unexpectedly afforded a yellow product with a trace amount of strongly fluorescing compound.

The yellow product shows an M^+ ion at *m/z* 493. Its IR spectrum shows the presence of carbonyl group but no N–H group. The ^1H NMR shows two remarkable features: AB quartet at around 3.46 and 4.32 ppm, and a singlet at 6.28 ppm. The quartets wre assigned to two sets of benzylic protons caused by restricted rotation. From these results and analytical data we have given this yellow product an oxirane structure (**7**), 1-dibenzylamino-3′-phenylspiro[anthracene-9(10*H*), 2′-oxiran]-10-one in our previous communication.[1)] However, after further examination, we came to a view that 1,3-dihydrooxazine structure (**5**) was more plausible than the previously-proposed **7**. The ^{13}C NMR spectrum displays two benzyl methylene carbons at 49.3 and 51.6 ppm, a CH carbon at 87.5 ppm, and



Scheme 1.

carbonyl carbon at 184.0 ppm. These results indicate that two benzyl groups are placed at different positions. Since spiro[anthracene-9(10*H*), 2′-oxiran]-10-one was reported to easily react with boron trifluoride to yield 10-formyl-10-phenylanthrone,[3] oxirane **7** would be expected to afford a formyl compound. In the reaction of the yellow product with excess boron trifluoride in diethyl ether, however, the starting compound was recovered and no formyl compound was observed. These results suggest that the yellow product would not be oxirane **7**. The molecular structure was finally established by X-ray crystal analysis, and the Oak Ridge Thermal Ellipsoid Program (ORTEP) drawing is illustrated in Fig. 1. Figure 1 unequivocally shows that the yellow product is not oxirane **7** but 3,11b-dibenzyl-2-phenyl-2,3,7,11b-tetrahydroanthra[1,9-*de*][1,3]oxazin-7-one (**5**). Figure 1 also suggests that the rotation of the benzyl group is restricted mainly by the steric hindrance in the structure.

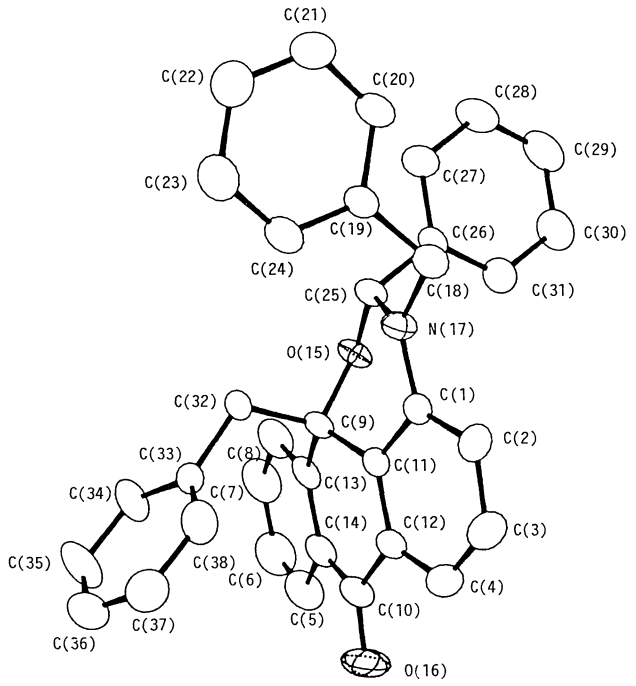


Fig. 1. ORTEP drawing of **5** showing 50% probability ellipsoids for all nonhydrogen atoms.

The structure of the strongly fluorescing compound was determined from both spectroscopic and analytical data to be 2-benzyl-1-phenyl-2, 6-dihydronaphth[1,2,3-*cd*]indol-6-one (**6a**).

Synthesis of 2,6-Dihydronaphth[1,2,3-*cd*]indol-6-ones. The compound **6a** was formed in a trace amount by the reaction of **1a** with benzyl chloride in KOH–DMSO system as described above. In fact the treatment of **5** with KOH in DMSO gave **6a** in very low yield (3%) and **5** was recovered in 85% yield. It was found that **5** was transformed more easily into **6** under acidic conditions. Table 1 shows that both Brønsted and Lewis acids were effective for the transformation. It is interesting to note that in the reaction of **5** with aluminium chloride compound **6b** was obtained together with **6a** and the total yield of **6** was increased, while other Lewis acids ($ZnCl_2$, $FeCl_3$, and $TiCl_4$) did not afford **6b**. The compound **6b** would be obtained by debenzylation of **6a**, because **6b** was obtained in 84% yield by the treatment of **6a** with $AlCl_3$ (see Table 2). The ratio of $AlCl_3$ to **5** was found to be important for the conversion of **5** to **6b**. In the case of 1:1 ratio, **6a** was obtained in 44% yield and **6b** was not formed. The best result (**6b**; 73% and **6a**; 11%) was obtained by the successive addition of $AlCl_3$: the reaction mixture was refluxed at 4:1 ratio for 1 h, then at 6:1 ratio for 2 h. The dealkylation was examined for **6a** and alkylaminoanthraquinones. Table 2 demonstrats that $AlCl_3$ was effective for the debenzylation, though **1a** was obtained in 14% yield in the case of 1-cyclohexyl-

Table 1. The Conversion of **5** into **6**

Reagent	Solvent	Temp/°C	Time/h	Yield/% **6a**	**6b**
KOH[a]	DMSO	30	3	3	0
concd HCl	EtOH	Reflux	3	51	0
concd HCl	PhH	Reflux	3	8	0
CH_3CO_2H	—	Reflux	1	20	0
H_3BO_3[b]	EtOH	Reflux	3	0	0
$ZnCl_2$[b]	PhH–EtOH	Reflux	23	14	0
$FeCl_3$[b]	PhH	RT	10	53	0
$FeCl_3$[b]	PhH	Reflux	1	60	0
$AlCl_3$[b]	PhH	Reflux	1	21	52
$TiCl_4$[b]	PhH	RT	3	45	0

a) Molar ratio. 5: KOH=1: 10. b) Molar ratio. 5: acid= 1: 5.

Table 2. Dealkylation of **6a** and Alkylaminoanthraquinones[a]

Substrate	Acid	Solvent	Time/h	Product	Yield/%
6a	concd HCl	EtOH	7	**6b**	8
6a	$AlCl_3$	PhH	3	**6b**	84
1-$PhCH_2NHAQ$	concd HCl	EtOH	3	—	0
1-$PhCH_2NHAQ$	$AlCl_3$	PhH	0.5	**1a**	94
1-CH_3NHAQ	$AlCl_3$	PhH	2.5	—	0
1-*n*-C_4H_9NHAQ	$AlCl_3$	PhH	3	—	0
1-⟨H⟩-NHAQ	$AlCl_3$	PhH	5	**1a**	14
2-$(PhCH_2)_2NAQ$	$AlCl_3$	PhH	3	**2a**	88

a) The reactions were run at reflux temperature. Molar ratio. Substrate: acid=1: 5.

aminoathraquinone.

Dihydronaphthindolones have been known to be good fluorophores[4] and our procedure is a facial and useful one for the preparation of 2,6-dihydronaphth-[1,2,3-*cd*]indol-6-ones, though some synthetic methods have been reported.[5]

Experimental

Materials. All commercial compounds were reagent grade and used without further purification. Dimethyl sulfoxide was distilled twice under reduced pressure and stored under a nitrogen atmosphere. Benzyl chloride was distilled under a nitrogen atmosphere. Aminoanthraquinones were purified as described previously.[2]

Instruments. Melting points were obtained on a Yamato melting point apparatus MP-21 and are uncorrected. UV and visible spectra were recorded with a Hitachi 220A spectrometer. ^{1}H and ^{13}C NMR data were recorded on a Hitachi R-24 (60 MHz) or JEOL FX90Q (90 MHz) spectrometers using Me_4Si as internal standard. IR spectra were measured on a JASCO IRA-1 spectrometer. Mass spectra were recorded with a JEOL JMS-DX 300 spectrometer by the electron impact (EI) ionizing technique at 70 eV. Elemental analyses were performed on a Yanaco MT2 CHN corder.

Reaction of Aminoanthraquinone with Benzyl Chloride in KOH-DMSO System. A typical procedure is described for the reaction with 1-aminoanthraquinone (**1a**). The compound **1a** (446 mg, 2 mmol) was treated with powdered KOH (1.12 g, 20 mmol) in DMSO (60 cm^3) for 30 min at 30°C and the mixture rapidly turned from red to green. Then, benzyl chloride (2.53 g, 20 mmol) was added and the solution was stirred for 1 h at 30°C. The resulting brown solution was poured into water (1000 cm^3) and then extracted with benzene. After evaporation of the extract, the residue was chromatographed on a silica-gel column with benzene eluent. The yellow fractions (R_f=0.49 by SiO_2 TLC, benzene as eluent) together with a trace amount of orange fractions (R_f=0.23) fluorescing in intense yellowish green were isolated. The yellow fractions were concentrated, and recrystallized from ethanol to afford 3,11b-dibenzyl-2-phenyl-2,3,7,11b-tetrahydroanthra[1,9-*de*][1,3]oxazin-7-one (**5**) (769 mg, 78%) as yellow crystals: Mp 202.0—202.8°C; UV (C_2H_5OH) 259 (log ε 4.32), 275 (sh), and 394 nm (3.17); IR (KBr) 1670 (C=O), 1245, 1150, 830, and 820 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.46 (2H, ABq, J=12 Hz, CH_2), 4.32 (2H, ABq, J=16 Hz, CH_2), 5.9—6.2 (2H, m, ArH), 6.28 (1H, s, CH), and 6.7—8.0 (20H, m, ArH); ^{13}C NMR ($CDCl_3$) δ=49.3, 51.6, 87.5, 115.5, 116.5, 126.4—144.6, and 184.0.

Found: C, 85.13; H, 5.42; N, 2.85%; *m/z* 493.2054. Calcd for $C_{35}H_{27}NO_2$: C, 85.16; H, 5.51; N, 2.83%; M, 493.2042.

The fluorescing fractions were concentrated and recrystallized from ethanol to give 2-benzyl-1-phenyl-2,6-dihydronaphth[1,2,3-*cd*]indol-6-one (**6a**) (23 mg, 3%) as orange crystals: Mp 228.5—230.0°C; UV (C_2H_5OH) 245 (log ε 4.42), 276 (4.23), 306 (4.09), 356 (3.61), and 426 nm (4.16); IR (KBr) 1630, 1610, 1595, 1550, 1180, and 970 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=5.20 (2H, s, CH_2) and 6.8—8.6 (17H, m, ArH); ^{13}C NMR ($CDCl_3$) δ=47.8, 107.9, 115.4—141.8, 184.0.

MS *m/z* 358 (M^+); Found: C, 87.25; H, 4.69; N, 3.41%. Calcd for $C_{28}H_{19}NO$: C, 87.25; H, 4.97; N, 3.63%.

2-(Dibenzylamino)anthraquinone (4): Mp 144.5—145.5°C; IR (KBr) 3075, 3040, 1670, 1590, 1405, 1300, 943, and 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.82 (4H, s, CH_2) and 6.9—8.4 (17H, m, ArH).

MS *m/z* 403 (M^+); Found: C, 83.57; H, 5.18; N, 3.37%. Calcd for $C_{28}H_{21}NO_2$: C, 83.35; H, 5.25; N, 3.47%.

The Conversion of 5 into 6. A typical procedure is described for the reaction of **5** with concd HCl. A mixture of **5** (200 mg, 0.4 mmol) and concd HCl (5 cm^3) in ethanol (35 cm^3) was refluxed for 3 h. The mixture was concentrated and chromatographed on silica gel column with benzene as eluent to afford **6a** (81 mg, 51%).

Dealkylation. A typical procedure is described for the debenzylation of compound **6a.** A mixture of compound **6a** (62 mg, 0.16 mmol) and $AlCl_3$ (106 mg, 0.80 mmol) in benzene was refluxed for 3 h. The mixture was poured into ice-water. The benzene extract was evaporated and chromatographed on a silica-gel column with benzene as eluent to afford 1-phenyl-2,6-dihydronaphth[1,2,3-*cd*]indol-6-one (**6b**) (40 mg, 84%): Mp 321—322°C; UV (C_2H_5OH) 248 (log ε 4.45), 277 (4.12), 305 (4.03), 359 (3.63), and 430 nm (4.08); IR (KBr) 3260, 3050, and 1630 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ=7.3—8.5 (12H, m, ArH) and 12.3 (1H, s, NH); ^{13}C NMR (DMSO-d_6) δ=105—141 and 182.4 (C=O).

MS *m/z* 295 (M^+); Found: C, 85.51; H, 4.32; N, 4.67%. Calcd for $C_{21}H_{13}NO$, C, 85.40; H, 4.44; N, 4.74%.

X-Ray Crystallographic Analysis of 5. A large, well-shaped triclinic crystal of **5** was obtained by slow evaporation of an ethanol solution: $C_{35}H_{27}NO_2$=493.2; space group $P\bar{1}$; a=10.043(5), b=15.665(9), c=8.454(4) Å; β=83.02(4)°; V=1270.1 Å^3; Z=2. Lattice constants and intensity data of **5** were measured by using graphite-monochromated Cu$K\alpha$ radiation on a Rigaku AFC-5 diffractometer. A total of 4202 unique reflections with $F_o > 4\sigma$ (F_o) were obtained by using the ω–2θ scanning method with a 2θ scan speed of 4° min^{-1} to 2θ=145°. The structure was solved by the RASA-II system (Rigaku Corp.) on the basis of the direct method and refined to a final R value of 0.073. Further crystallographic details were deposited as Document No. 9094 at the Office of the Editor of Bull. Chem. Soc. Jpn.

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