Bromination of 4*H*-Cyclopenta[*def*]phenanthrenamines

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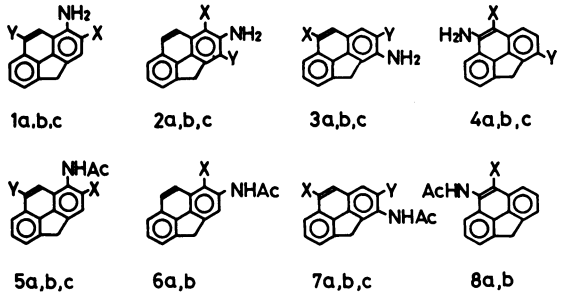
Synopsis. Bromination of 4*H*-cyclopenta[*def*]phenanthren-1-amine, -2-amine, -3-amine, or -8-amine with bromine in chloroform took place at the 2-, 1-, 8-, or 9-position, respectively. The second bromine was introduced at the 8-, 3-, 2-, or 3-position. Similar regioselectivity was observed in the system of bromine in acetic acid–48% hydrobromic acid and of hydrobromic acid in dimethyl sulfoxide. The corresponding acetylamino compound was brominated at the same position as that of the parent amine.

The electrophilic bromination of 4*H*-cyclopenta[*def*]-phenanthrene has been reported to give 1-bromide accompanied by 3- and 8-bromo isomers.[1] When the 1-, 2-, or 3-position of 4*H*-cyclopenta[*def*]phenanthrene was already occupied by an electron-withdrawing group such as a nitro, bromo, or acetyl substituent, the second substituent entered the 5- or 7-position upon nitration or acetylation.[2]

The present paper deals with the bromination of 4*H*-cyclopenta[*def*]phenanthrene having an electron-donating amino group.



(a: X=Y=H, b: X=Br, Y=H, c: X=Y=Br)
Scheme 1.

Table 1. Bromination of 4*H*-cyclopenta[*def*]-phenanthrenamines

Reactant	Procedure[a]	Bromide (%) Mono-	Bromide (%) Di-	Recovered reactant %
1a	I	89(**1b**)	trace(**1c**)	trace
1a	II	31(**1b**)		65
5a	III	15(**5b**)		85
2a	I	80(**2b**)	12(**2c**)	trace
2a	II	16(**2b**)		71
6a	III	99(**6b**)		
3a	I	20(**3b**)	34(**3c**)	26
3a	II	15(**3b**)		29
7a	III	61(**7b**)		33
4a	I	45(**4b**)	31(**4c**)	13
4a	II	52(**4b**)		47
8a	III	84(**8b**)		trace

a) See Experimental.

Brominations of 4*H*-cyclopenta[*def*]phenanthren-1-amine (**1a**),[3] -2-amine (**2a**), -3-amine (**3a**), and -8-amine (**4a**) were carried out to afford the monobromides (**1b**, **2b**, **3b**, **4b**) and dibromides (**1c**, **2c**, **3c**, **4c**). The substitution with bromine in the acetamides (**5a**, **6a**, **7a**, **8a**) took place at the same position as that of the parent amines to give the monobromides (**5b**, **6b**, **7b**, and **8b**) (Scheme 1). Table 1 shows the results obtained by gas-chromatographic analyses.

The structural proof of these monobromo amines was established by deamination which gave the known bromo-4*H*-cyclopenta[*def*]phenanthrenes.[1] The configuration of the dibromo amines was estimated by the IR, NMR, and UV spectral data. These physical properties are summarized in Table 2.

In each bromination, no other monobromo isomers were detected by methods of NMR, gas chromatography (Silicone DC-QF 1 or Dexsil 300 GC), and high performance liquid chromatography. The reaction of the amines with bromine in carbon tetrachloride or carbon disulfide gave results similar to those in chloroform. The same regioselectivity was observed in the bromination using a solvent system of acetic acid–48% hydrobromic acid (4 : 1 by volume) in which it had been expected the amines would convert easily to the corresponding conjugated acids.[4] No dibromo amine could be detected by the reaction with hydrobromic acid (48%) in dimethyl sulfoxide, which is similar to the reaction of fluorenamine.[5]

The reaction of **4a** proceeds with regioselectivity analogous to that of 9-phenanthrenamine.[6] The 9-position of **4a** corresponds to the highly reactive 1-position of 2-methoxynaphthalene.[7] A second bromine may be introduced at the 3-position of **4b**, and reactions of **2a** and **3a** can be explained by similar considerations. The bromination of **1a** took place at the 2-position, which corresponds to the reactive 2-position of 1-methoxynaphthalene.[7]

In the acetamide series, the yield of **5b** was only 50% after 60 min of reaction; on the other hand, 98% of **6b** was obtained after 1 min. The low reactivity of **5a** may be interpreted by the fact that the 2-position of the parent hydrocarbon is less reactive than the other positions. The 1-acetylamino group is less electron-donating than the 1-amino group and controls the regioselectivity to be effective at the 2-position, but does not enhance the reactivity significantly.

Experimental

All the melting points are uncorrected. The IR and UV data were recorded with IR-G spectrophotometer (JASCO) as KBr pellets, and using model UV-180 apparatus (Shimadzu) as cyclohexane solutions, respectively. The ^{1}H NMR spectra were obtained with JNM-C-60HL instrument (JEOL) using

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Table 2. Physical properties of bromo-4*H*-cyclopenta[*def*]phenanthrenamines

Compd	Mp(decomp) θ_m/°C	IR $\tilde{\nu}$/cm^{-1}	NMR δ	UV λ_{max}/nm (log ε)	Retention time/s
1b	169.0—169.5	3320, 3420	4.17 (2H, s), 4.61 (2H, s, NH_2), 7.50—7.74(6H, m)	236 (4.62), 282 (4.45), 310 (3.93), 356 (3.68), 373 (3.74)	330
2b	170.5—171.0	3280, 3400	4.16 (2H, s), 4.37 (2H, s, NH_2), 7.11 (1H, s, H-3), 7.39—7.83 (5H, m)	243 (4.38), 268 (4.84), 289 (4.24), 309 (3.98), 364 (3.49), 373 (3.49), 380 (3.51)	380
3b	123.5—124.5	3310, 3400	4.03 (2H, s, NH_2), 4.09 (2H, s), 6.94 (1H, d, J=8.4 Hz, H-2), 7.48—7.95 (5H, m)	252 (4.64), 290 (4.01), 329 (4.12), 363 (3.67)	460
4b	153.0—154.0	3340, 3440	4.26 (2H, s), 4.76 (2H, s, NH_2), 7.47—7.85 (6H, m)	229 (4.49), 254 (4.66), 323 (4.05), 364 (3.45)	360
1c	164.0—165.0	3360, 3470	4.19 (2H, s), 4.53(2H, s, NH_2), 7.51—7.91 (5H, m)	238 (4.60), 254 (4.40), 290 (4.53), 319 (3.93), 366 (3.70), 383 (3.72)	830
2c	215.0—215.5	3300, 3460	4.20 (2H, s), 4.76(2H, s, NH_2), 7.44—7.86 (5H, m)	269 (4.86), 291 (4.27), 313 (4.14), 363 (3.65), 380 (3.70)	810
3c	175.0—175.5	3370, 3460	4.03 (2H, s), 4.40(2H, s, NH_2), 7.54—7.83 (5H, m)	228 (4.49), 257 (4.70), 292 (4.05), 330 (4.13), 348 (3.95), 365 (3.89)	980
4c	162.0—163.0	3360, 3460	4.13 (2H, s), 4.80(2H, s, NH_2), 7.55—7.69 (5H, m)	231 (4.52), 257 (4.65), 325 (4.12), 370 (3.49)	810
5b	236.0—237.0	1658, 3240	2.21 (3H, s), 4.33(2H, s), 7.44—7.91 (6H, m), 9.79 (1H, s, NH)	218 (4.44), 262 (4.71), 297 (4.08), 308 (4.10), 337 (3.16), 354 (3.07)	870
6b	220.0—220.5	1652, 3260	2.15 (3H, s), 4.35(2H, s), 7.72—8.20 (6H, m), 9.63 (1H, s, NH)	241 (4.17), 273 (4.80), 309 (3.95), 330 (3.05), 346 (3.24), 364 (3.33)	810
7b	251.5—252.0	1660, 3250	2.16 (3H, s), 4.35(2H, s), 7.71—7.80 (5H, m), 8.10 (1H, s, H-9), 9.98 (1H, s, NH)	222 (4.26), 259 (4.56), 311 (4.16), 355 (3.10)	1390
8b	227.0—228.0	1654, 3240	2.24 (3H, s), 4.41(2H, s), 7.64—7.98(6H, m), 10.02 (1H, s, NH)	238 (4.48), 257 (4.69), 302 (4.09), 313 (4.09), 335 (3.23), 353 (3.15)	820
5c	255.0—257.0	1658, 3240	2.23 (3H, s), 4.39(2H, s), 7.70—8.04 (5H, m), 9.96 (1H, s, NH)	235 (4.36), 263 (4.75), 301 (4.12), 313 (4.13), 341 (3.50), 358 (3.50)	
7c	314.0—315.0	1662, 3250	2.18 (3H, s), 4.30(2H, s), 7.77—7.87 (3H, m), 8.16—8.21 (2H, m), 9.87 (1H, s, NH)	230 (4.42), 264 (4.80), 311 (4.15), 339 (3.37), 357 (3.37)	

$CDCl_3$ (**1**—**4**) or DMSO-d_6 (**5**—**8**) as the solvent. The agreement between the calculated and found values in the elemental analysis of the new compounds is within ±0.3% of variation.

The yield of each bromination is estimated from the average value of three or more runs. The components of the reaction mixtures were separated by gas chromatography (Shimadzu GC-6AM) using a column (1 m) containing 3% Dexsil 300 GC on Chromosorb WAW at 250 °C using FID detector. The amount of each peak was calculated by comparison with octacosane or dotriacontane which has been added as the internal reference to the substrate before the reaction. Retention time of each product is tabulated in Table 2.

The reactants were synthesized by the method similar to that described elsewhere.[3] Chloroform was percolated through an alumina column before use and the other solvents were distilled.

Bromination of 4H-Cyclopenta[def]*phenanthren-1-amine (**1a**).* *Typical Procedure I*: Amine **1a** (103.2 mg, 0.5035 mmol) and dotriacontane (21.10 mg) were dissolved in $CHCl_3$ (50 ml), and cooled at 0 °C in the dark. A solution of Br_2 (1.2 mol equivalent to **1a**) in $CHCl_3$ (*ca.* 10 ml) was added all at once to the mixture, and the resulting mixture was stirred for 1 min. Aqueous $NaHSO_3$ (1%, 50 ml) was added to quench the reaction; the organic layer was neutralized by aqueous ammonia (28%) and dried over anhydrous Na_2SO_4, and the solution was submitted to gas chromatography.

Upon evaporation of the solvent, the residue was chromatographed on a silica-gel column (1.8 cm ϕ, 60 cm) with benzene. The lower band of the column was extracted with benzene to give a trace amount of **1c**, mp 164.0—165.0 °C (decomp). The middle band yielded 82 mg (58%) of **1b**, mp 169.0—169.5 °C (decomp) by recrystallization from a mixture of benzene–hexane (*ca.* 1 : 1). The upper band of the column gave a trace amount of **1a**, mp 128—129 °C.

Procedure II: The amine (0.5 mmol) was treated with HBr (48%, 0.6 mmol) in DMSO (60 ml) at 80 °C for 60 min. After addition of aqueous $NaHSO_3$ and neutralization by aqueous ammonia, the mixture was extracted with benzene (50 ml) and analyzed by means of gas chromatography.

The reaction of **3a** gave, in addition to **3b**, a significant amount of dark tar materials from a silica-gel column; these were not studied further.

Procedure III: The acetamide (0.5 mmol) was allowed to react with Br_2 (0.6 mmol) in $CHCl_3$ (85 ml) at 0 °C for 5 min. The resulting solution was treated by a method similar to that described above.

*Deamination of **1b**.* Bromo amine **1b** (134.6 mg, 0.47 mmol) was dissolved in a mixture of THF (2 ml), concd HCl (5 ml), and H_2O (5 ml) and the resulting amine hydrochloride was diazotized with aqueous $NaNO_2$ (5%, 1 ml) at 0—5 °C according to the literature.[8] The reaction mixture was stirred with H_3PO_2 (*ca.* 50%, 3.5 ml) for 17 h at room temperature. The precipitate was extracted with benzene and the benzene solution was chromatographed on a silica gel to yield 2-bromo-4*H*-cyclopenta[*def*]phenanthrene (30.4 mg, 24%), mp 91—92 °C, identical in all respects with an authentic sample.[1]

Also, **2b** afforded the 1-bromide (50% yield, mp 85—86 °C), **3b** gave 8-bromide (42%, mp 94.5—95.5 °C), and **4b** yielded 8-bromide (66%), respectively, by a treatment similar to those described above.

*Acetylation of **1b**.* Bromo amine **1b** (142 mg, 0.50 mmol) was treated with Ac_2O (10 ml) in dry benzene (50 ml) at reflux for 30 min to give **5b** (160 mg, 98%), mp 236—237 °C (decomp), which was identical in all respects with the product obtained by bromination of **5a**.

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