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Synthesis and Acylation of *peri*-Amino Derivatives of Anthra[1,9-*cd*]pyrazol-6-one

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Abstract—Heating of 5- and 7-chloro-6*H*-anthra[1,9-*cd*]pyrazol-6-ones in butylamine and aniline gives the corresponding *peri*-amino-substituted anthrapyrazole derivatives. Acylation of the latter occurs at the N^1 atom of the heterocyclic fragment to afford monoacyl derivatives having an *ana*-quinonimine structure.

One of the methods for synthesizing *peri*-amino derivatives of anthrapyrazolone is based on nucleophilic substitution of halogen by amines. However, only a few relevant published data are available. Bradley and Geddes [1] reported on the replacement of chlorine in position *5* of anthrapyrazolone by aniline and piperidine and in position *7* by piperidine.

In the present communication we describe the synthesis of a series of *peri*-amino derivatives of anthrapyrazolone and their reactions with acylating agents. Nucleophilic substitution of the chlorine atom in compounds **I**–**IV** by butylamine and aniline gave the corresponding *peri*-amino derivatives **VII**–**XIII** (Scheme 1). The ease of the process depends on the position of halogen and amine basicity. For example, 5-chloroanthrapyrazole **I** readily reacts with strongly basic butylamine, while its reaction with less basic aniline is more difficult. Likewise, chloro derivative **III** containing a butyl group in the heterocyclic fragment is converted into amines **X** and **XI**. 7-Chloroanthrapyrazole **II** failed to react with aniline, whereas its reaction with butylamine gave butylamino derivative **IX** in a poor yield. The presence of a butyl group in the pyrazole moiety favors replacement of chlorine in position *7*. Compound **IV** is capable of reacting with aniline, as was reported in [2] for 7-chloro-2-methylanthra[1,9-*cd*]pyrazolone. Reactions of amines with *N*-acetyl derivatives of 5- and 7-chloroanthrapyrazoles **V** and **VI** result in elimination of the acetyl group and formation of compounds **I** and **II** containing small amounts of amines **VII**–**IX**.

Our attempts to synthesize 5-aminoanthrapyrazole **XIV** by the procedure reported in [3], i.e., by heating 1-chloro- and 1-phenoxy-5-aminoanthraquinones with hydrazine hydrate in pyridine, were unsuccessful, and the initial compounds were recovered from the reaction mixture. 5-Amino derivative **XIV** was obtained by hydrolysis of 5-benzoylaminoanthrapyrazole which was synthesized in a satisfactory yield from 1-benzoylamino-4-chloroanthraquinone (**XV**) and hydrazine hydrate by the procedure described in [4]. It should be noted that, unlike compound **XV**, 1-acetylamino-4-chloroanthraquinone almost did not react with hydrazine hydrate.

The structure of products **VII**–**XIV** follows from the synthetic procedure and is supported by the data of elemental analysis and IR and electron spectroscopy (Tables 1, 2).

It is known [3, 5, 6] that acylation of anthrapyrazolones having no electron-donor substituents in the *peri*-position relative to the carbonyl group occurs at the N^2 atom to give monoacyl derivatives with a *para*-quinonimine [7] bond distribution. By heating compounds **VII**–**IX** in acetic anhydride we obtained previously unknown derivatives **XVI**–**XVIII** in quantitative yield. According to the data of elemental analysis and mass spectra (Table 2), products **XVI**–**XVIII** are monoacetyl derivatives of *peri*-aminoanthrapyrazolones **VII**–**IX**. The IR spectra of **XVI**–**XVIII** lack absorption due to stretching vibrations of pyrazole NH group, indicating that the acylation occurred at the pyrazole fragment. The longwave

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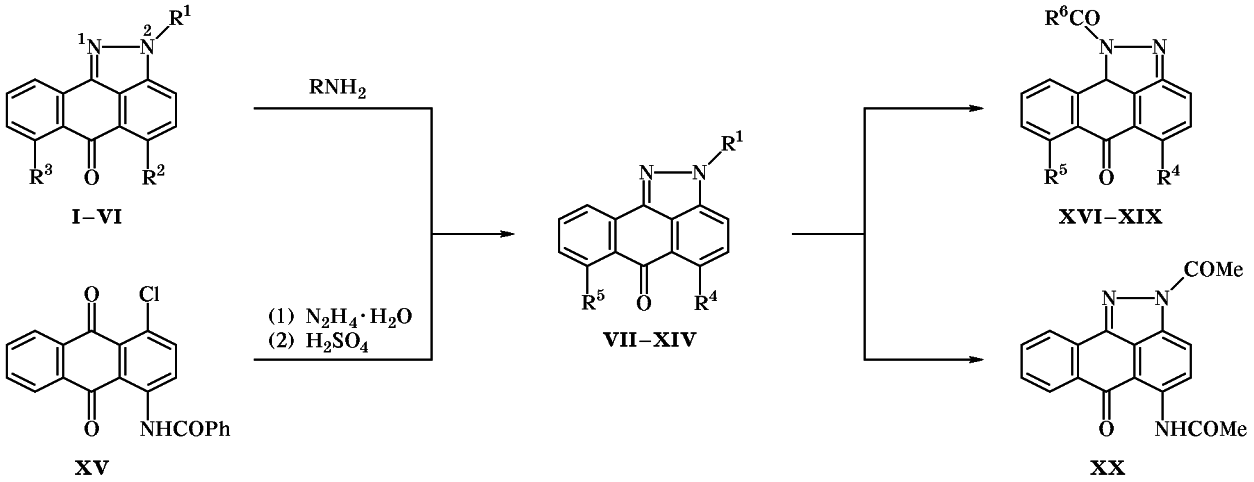
Scheme 1.



I, $R^1 = R^3 = H$, $R^2 = Cl$; **II**, $R^1 = R^2 = H$, $R^3 = Cl$; **III**, $R^1 = Bu$, $R^2 = Cl$, $R^3 = H$; **IV**, $R^1 = Bu$, $R^2 = H$, $R^3 = Cl$; **V**, $R^1 = COMe$, $R^2 = Cl$, $R^3 = H$; **VI**, $R^1 = COMe$, $R^2 = H$, $R^3 = Cl$; **VII**, $R^1 = R^5 = H$, $R^4 = NHBu$; **VIII**, $R^1 = R^5 = H$, $R^4 = NHPh$; **IX**, $R^1 = = R^4 = H$, $R^5 = NHBu$; **X**, $R^1 = Bu$, $R^4 = NHBu$, $R^5 = H$; **XI**, $R^1 = Bu$, $R^4 = NHPh$, $R^5 = H$; **XII**, $R^1 = Bu$, $R^4 = H$, $R^5 = NHBu$; **XIII**, $R^1 = Bu$, $R^4 = H$, $R^5 = NHPh$; **XIV**, $R^1 = R^5 = H$, $R^4 = NH_2$; **XVI**, $R^4 = NHBu$, $R^5 = H$, $R^6 = Me$; **XVII**, $R^4 = NHPh$, $R^5 = H$, $R^6 = Me$; **XVIII**, $R^4 = H$, $R^5 = NHBu$, $R^6 = Me$; **XIX**, $R^4 = NHBu$, $R^5 = H$, $R^6 = Ph$.

absorption band in the electron spectra of **XVI**–**XVIII** is displaced to the red region relative to the corresponding band of initial *peri*-amino derivatives **VII**–**IX**. These data suggest a more extended conjugated bond system in molecules **XVI**–**XVIII** and lead us to conclude that the acetyl group is attached to the N^1 atom. This means that acetyl derivatives **XVI**–**XVIII** have *ana*-quinonimine structure. The fact that the longwave absorption bands of N^2-acetylanthrapyrazolones are located at shorter wavelength, as compared to parent nonacylated compounds **I** and **II** [3, 6], can be regarded as an additional proof for the assumed structure of products **XVI**–**XVIII**.

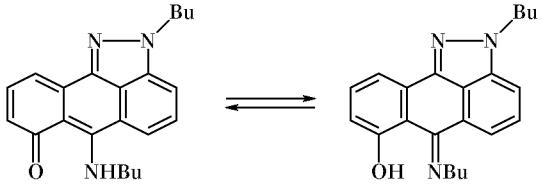
The acylation of anthrapyrazolones **VII**–**IX** with other acylating agents and under different conditions follows a similar pattern. For example, benzoylation of compound **VII** both in the neutral and in the anionic form occurs at the N^1 atom, yielding *ana*-benzoyl derivative **XIX**.

Thus introduction of an electron-donor amino group into the *peri*-position with respect to the carbonyl group of anthra[1,9-*cd*]pyrazol-6-one having no substituent in the pyrazole fragment leads to strong electron density redistribution in the molecule, so that the acylation occurs at the N^1 atom with formation of products possessing an *ana*-quinonimine structure.

The acylation of 5-aminoanthrapyrazolone **XIV** with excess acetic anhydride involves both the amino group and the pyrazole N^2 atom, yielding diacetyl derivative **XX**. Its *para*-quinonimine structure follows from the IR and electron absorption spectra. The electron absorption spectrum of **XX** resembles those of the acetyl derivatives of unsubstituted anthra[1,9-*cd*]-pyrazol-6-one [5] and its 5-chloro analog **V** [3]. It should be noted that 7-aminoanthra[1,9-*cd*]pyrazol-6-one, which is isomeric to **XIV**, also reacts with excess β-chloropropionyl chloride to give the corresponding diacyl derivative [8].

We previously showed [3] that 2-butyl-6-butylamino-7*H*-anthra[1,9-*cd*]pyrazol-7-one (**XXI**) gives rise to O,N-prototropy involving hydrogen transfer between the *peri*-arranged carbonyl oxygen atom and nitrogen atom of the butylamino group. As a result, more energetically favorable isomer **XXIa** is formed (Scheme 2).

Scheme 2.



XXI **XXIa**

ana-Anthrapyrazolone derivatives **XVI**–**XIX** turned out to be incapable for such tautomeric transformations: the spectral curves of **XVI**–**XIX** did not change on variation of solvent polarity.

Table 1. Yields, melting points, and electron absorption and IR spectra of aminoanthra[1,9-*cd*]pyrazol-6-ones **VII**–**XIV** and *N*-acyl derivatives **XVI**–**XX**

Comp. no.	Yield, %	mp, °C (solvent)	Electron absorption spectrum ($CHCl_3$), λ_{max}, nm (log ε)	IR spectrum (KBr), ν, cm^{-1}
VII	87	226–227 ($CHCl_3$–hexane)	346 (3.79), 364 (3.84), 408 (3.76), 456 (3.95), 480 (4.03)	3160 (N^2–H); 2936 (CH_{aliph}); 1652, 1612 (C=O, C=N)
VIII	40	276–278 ($CHCl_3$–hexane) 282–283 (chlorobenzene) [1]	365.5 (3.94), 475 (4.19)	3168 (N^2–H); 1656, 1616 (C=O, (C=N)
IX	14	119–120 (benzene–hexane)	375 (3.58), 496 (3.99)	3272 (N^2–H); 2928, 2856, 2336 (CH_{aliph}); 1615, 1600 (C=O, C=N)
X	82	83.5–84 (hexane)	364 (3.93), 377 (3.97), 461 (4.06), 487 (4.18)	2928, 2860 (CH_{aliph}); 1656, 1606 (C=O, C=N)
XI	55	141–142 (benzene–hexane)	377 (4.02), 483 (4.21)	2928, 2856 (CH_{aliph}); 1648, 1608 (C=O, C=N)
XII	35	116–117 (hexane)	337 (3.54), 388 (3.57), 407 (3.63), 503 (4.03)	2928, 2848 (CH_{aliph}); 1616 (C=O, C=N)
XIII	16	152–153 (hexane)	337 (3.76), 391 (3.53), 408 (3.61), 503 (4.09)	2956, 2940, 2880 (CH_{aliph}); 1618 (C=O, C=N)
XIV	79	341–342 (decomp., AcOH)	354 (3.61), 431 sh (3.72), 449 (3.76)	3412, 3280 (NH_2); 3172 (N^2–H); 1654, 1616 (C=O, C=N)
XVI	96	165–166 (benzene–hexane)	344 sh (4.00), 354 (4.01), 380 sh (3.73), 463 (3.92), 485 (3.94) 336 (4.03), 352 (4.07), 379 (3.88), 451 (3.92), 474 (3.97)[a]	2957, 2932, 2864 (CH_{aliph}); 1720, 1660, 1608 (C=O, C=N)
XVII	98	216–217 ($CHCl_3$–hexane)	340 (4.19), 476 (4.16)	1718, 1658, 1608 (C=O, C=N)
XVIII	88	154–155 (hexane)	355 (3.84), 365 (3.83), 502 (4.00) 350 (3.85), 366 (3.88), 488 (4.00)[a]	2960, 2940, 2860 (CH_{aliph}); 1712, 1620 (C=O, C=N)
XIX	94[b], 90[c]	153–154 ($CHCl_3$–hexane)	347 sh (4.12), 385 sh (4.12), 382 sh (3.78), 470 sh (3.83), 485 (3.84)	2952, 2872 (CH_{aliph}); 1690, 1656, 1620 (C=O, C=N)
XX	83	264–265 ($CHCl_3$–hexane)	357 (4.00), 409 (4.10)	1720, 1688, 1654, 1628 (C=O, C=N)

[a] In hexane.
[b] In nitrobenzene.
[c] In aqueous dioxane.

peri-Amino derivatives **VII**–**XIV** and **XVI**–**XX** are characterized by positive solvatochromism, i.e., their longwave absorption maximum shifts red as the solvent polarity increases. The Δλ values for amines **VII** and **VIII** are about 5 nm in going from carbon tetrachloride to propanol and 10–14 nm for *N*-acylanthrapyrazoles **XVI**–**XIX** in going from hexane to chloroform. This means that the excited state of molecules **VII**–**XIV** and **XVI**–**XX** is more polar than the ground state, so that in polar solvents the energy of electron transition decreases [9] due to more effective solvation of the excited state.

EXPERIMENTAL

The electron absorption spectra were measured on a Specord M-40 spectrophotometer. The IR spectra were recorded on a Specord M-80 instrument in KBr. The mass spectra (70 eV) were obtained on a Varian Match-6 mass spectrometer with direct sample admission into the ion source. The melting points were determined on a PTP device according to TU (technical specification) 25-11-1144-76. The products were purified by column chromatography using silica gel (40/100 μm) and aluminum oxide (Brockman activity

Table 2. Elemental analyses of aminoanthra[1,9-*cd*]pyrazol-6-ones **VII**, **IX**–**XIV** and *N*-acyl derivatives **XVI**–**XIX**

Comp. no.	Found, %			Formula	Calculated, %		
	C	H	N		C	H	N
VII	74.71	5.38	13.68	$C_{18}H_{17}N_3O$	74.20	5.88	14.42
IX	74.38	5.81	13.70	$C_{18}H_{17}N_3O$	74.20	5.88	14.42
X	76.65	7.05	10.80	$C_{22}H_{25}N_3O$	76.05	7.25	12.09
XI	79.00	6.20	12.02	$C_{24}H_{21}N_3O$	78.45	5.76	11.44
XII	75.75	7.55	11.43	$C_{22}H_{25}N_3O$	76.05	7.25	12.09
XIII	78.63	5.54	11.70	$C_{24}H_{21}N_3O$	78.45	5.76	11.44
XIV			17.30	$C_{14}H_9N_3O$			17.86
XVI	72.57	5.22	12.04	$C_{20}H_{19}N_3O_2$[a]	72.05	5.74	12.60
XVII	74.60	4.20	11.70	$C_{22}H_{15}N_3O_2$[a]	74.77	4.28	11.89
XVIII	72.15	5.60	12.50	$C_{20}H_{19}N_3O_2$[a]	72.05	5.74	12.60
XIX	68.15	3.82	13.01	$C_{18}H_{13}N_3O_3$	67.70	4.10	13.16

[a] Found *M* (by mass spectrometry): **XVI**, 333; **XVII**, 353; **XVIII**, 333. Calculated *M*: **XVI**, 333.37; **XVII**, 353.36; **XVIII**, 333.37.

grade II). The yields, melting points, spectra data, and elemental analyses of the products are given in Tables 1 and 2.

***peri*-Amino-substituted anthra[1,9-*cd*]pyrazol-6-ones VII–XIII (*general procedure*).** 5- or 7-Chloroanthrapyrazolone **I**–**IV** [3] was heated in butylamine or aniline under reflux. The reaction time was 5–7 h in the synthesis of 5-isomers **VII**, **VIII**, **X**, and **XI** or 10–15 h in the synthesis of 7-isomers **IX**, **XII**, and **XIII**. The progress of the reaction was monitored by TLC, following the disappearance of initial compound **I**–**IV**. The mixture was poured into 10% hydrochloric acid, and the precipitate was filtered off, washed with water, and dried. *peri*-Amino derivatives **VII**–**XIII** were isolated by column chromatography. 5-Butylaminoanthrapyrazolone **VII** was purified on aluminum oxide using chloroform as eluent; the eluate was evaporated, and the residue was subjected to chromatography on silica gel (eluent chloroform). Products **VIII** and **IX** were purified by chromatography on silica gel using chloroform–ethyl acetate (5:1) for primary and chloroform for secondary purification of compound **IX**. Compound **VIII** was purified using diethyl ether as eluent. Butylamino derivatives **X**–**XIII** were purified by chromatography on silica gel with benzene as eluent. Products **VII**–**XIII** were additionally purified by recrystallization from appropriate solvent (Table 1).

5-Amino-6*H*-anthra[1,9-*cd*]pyrazol-6-one (XIV). 5-Benzoylaminoanthra[1,9-*cd*]pyrazol-6-one [4], 0.5 g, was mixed with 10 ml of sulfuric acid (cp), and the mixture was heated to 90–100°C over a period of 10–15 min, stirred for 5 min at that temperature, cooled, and poured onto ice. The precipitate was filtered off, washed with water, dried, and recrystallized from acetic acid. Yield 0.28 g (79%), Dark yellow crystals.

Acetyl derivatives XVI–XVIII and XX (*general procedure*). A mixture of 30–50 mg of compound **VII**–**IX** or **XIV** in 3–5 ml of acetic anhydride was heated for 15–20 min under reflux. It was then cooled and poured into water, and the precipitate was filtered off, dried, and recrystallized from appropriate solvent.

Benzoylation of 5-butylaminoanthra[1,9-*cd*]-pyrazol-6-one (VII). *a. In the neutral form.* A mixture of 0.03 g (1.02×10^{-4} mol) of compound **VII**, 2 ml of nitrobenzene, and 0.015 g (1.09×10^{-4} mol) of potassium carbonate was heated while stirring to 100–115°C, 0.03 g (2.16×10^{-4} mol) of benzoyl chloride was added, and the mixture was refluxed for 5 min and cooled to 100°C. Nitrobenzene was removed by steam distillation, the still residue was cooled, and the precipitate was filtered off, washed with water, and dried. The product was subjected to chromatography on silica gel using chloroform as eluent, an orange–yellow fraction was collected, the solvent was distilled off, and the residue was recrystallized from hexane–chloroform. We isolated 0.04 g (94%) of 1-benzoyl-5-butylaminoanthra[1,9-*cd*]pyrazol-6-one (**XIX**) as dark yellow voluminous crystals.

b. In the anionic form. Compound **VII**, 0.024 g (8.16×10^{-5} mol), was dissolved in a mixture of 3 ml of dioxane and 6 ml of water, containing 0.34 g (6.07×10^{-3} mol) of potassium hydroxide. The mixture

was cooled to 0–5°C, 0.16 g (1.38×10^{-3} mol) of benzoyl chloride was added, and the mixture was stirred for 10–15 min at that temperature and diluted with water. The precipitate was filtered off, washed with a 5% solution of sodium carbonate and water, and dried. The product was purified as described above in *a*. Yield 0.029 g (90%), dark yellow crystals. The products was identical in the R_f value, melting point, and electron absorption spectrum to that synthesized as described in *a*.

REFERENCES

1. Bradley, W. and Geddes, K.W., *J. Chem. Soc.*, 1952, pp. 1630–1635.
2. Bradley, W. and Bruce, C.S., *J. Chem. Soc.*, 1954, pp. 1894–1902.
3. Sokolyuk, N.T., Pisulina, L.P., and Kozhevnikova, E.I., *Zh. Org. Khim.*, 1992, vol. 28, no. 10, pp. 2193–2200.
4. Singh, M.R. and Shah, K.H., *Indian J. Chem., Sec. B*, 1978, vol. 16, no. 2, pp. 100–102.
5. Urseanu, F. and Draghici, C., *Rev. Chim.*, 1973, vol. 24, no. 9, pp. 683–685.
6. Sokolyuk, N.T. and Pisulina, L.P., *Izv. Vyssh. Uchebn. Zaved., Ser. Khim. Khim. Tekhnol.*, 1993, vol. 36, no. 12, pp. 12–15.
7. Sokolyuk, N.T. and Pisulina, L.P., *Zh. Org. Khim.*, 1994, vol. 30, no. 3, pp. 447–452.
8. Belgium Patent no. 638211, 1964; *Chem. Abstr.*, 1965, vol. 62, p. 9275b.
9. Sverdlova, O.V., *Elektronnye spektry v organicheskoi khimii* (Electron Spectra in Organic Chemistry), Leningrad: Khimiya, 1985, p. 179.