# SYNTHESIS OF BENZO[b]PHENANTHRIDINES BY THE PICTET–SPENGLER AND BISCHLER–NAPIERALSKI REACTIONS

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UDC 615.277.3:547.836.3].012.1

Previous reports have been made on a AD → C → B pattern synthesis of benzo[b]phenanthridine with alkoxyl substituents in rings A and D as well as with oxygen functions in ring C [2]. The amides of 1,4-diacetoxy-3-(3,4-dimethoxyphenyl)-6,7-dimethoxynaphthaline have been shown to be easily cyclicized by the Bischler–Napieralski reaction. The present work is concerned with a further study of the above-indicated pattern as well as with the employment of the Pictet–Spengler reaction to obtain quinoid benzo[b]phenanthridines in order to examine their antitumor activity.

The starting compound for the synthesis of benzo[b]phenanthridines was 2,6,7-trimethoxy-3-(3,4-dimethoxyphenyl)-1,4-naphthoxynone (I) (diagram I) which, when boiled with $NH_3$ or $MeNH_2$ in ethanol formed quantitative yields of the corresponding aminoquinones (II, III) [2]. When boiled with AcOCHO, amine III forms 6,7-dimethoxy-3-(3,4-dimethoxyphenyl)-2-(N-methyl-N-formyl)amino-1,4-naphthoxynone (V). Amine II under the same conditions is converted to the mono- and diformyl derivatives of naphthoxynones (IV and VI) with yields of 83.1 and 2.6% respectively.

Our attempt to cyclicize the amides IV, V, and VI by the Bischler–Napieralski reaction was not successful. What we obtained was a multi-component mixture of products that was difficult to separate. We were also unsuccessful in our attempt to reduce these quinones with $NaBH_4$ or $Na_2S_2O_4$ in ethanol inasmuch as the resultant biphenols were unstable and quickly reoxidized to the original quinones.

By the reductive acylation of amide V we obtained a 55% yield of 1,4-diacetoxy-3-(3,4-dimethoxyphenyl)-6,7-dimethoxy-2-(N-methyl-N-formyl)aminonaphthaline (VII) whose cyclization by the Bischler–Napieralski reaction resulted in the formation of 7,12-diacetoxy-6-methyl-2,3,9,10-tetramethoxybenzo[b]phenanthridinium chloride (VIII). A similar attempt at a reductive methylation of the amide V by diemthylsulfate was unsuccessful. Only the original compound was obtained.

Naphthoquinone II in $Ac_2O$ is cyclicized with conc. $H_2SO_4$ into 7,12-dioxy-5-methyl-2,3,9,10-tetramethoxybenzo[b]phenanthridine (IX) (diagram 2). The same aminolquinone in the Pictet–Spengler reaction yields a complex mixture of products from which we obtained a 44.5% yield of 7,12-dioxo-2,3,9,10-tetramethoxybenzo[b]phenanthridine (X) which was formed upon the spontaneous dehydrogenation of the immediate reaction product. A seven-ringed product (XI) at a very low yield (0.93%) was also obtained from this reaction mixture.

*Deceased.

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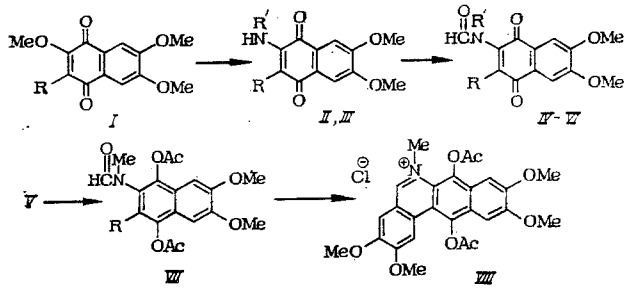
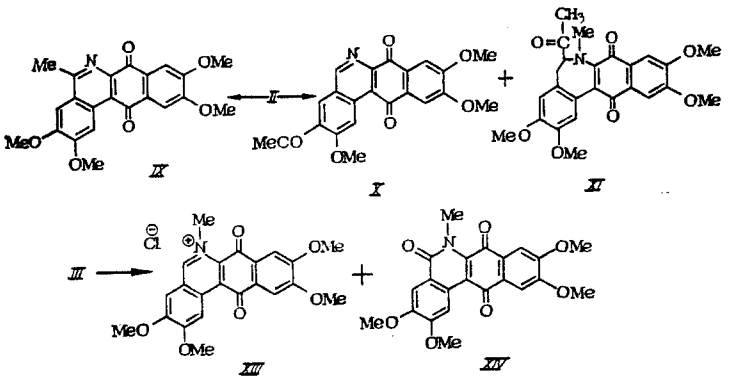
0091-150X/89/2312-0955$12.50 

Diagram 1



R = 3,4-dimethoxyphenyl; R'=H (II, IV); Me (III, V); CHO (VI)

Diagram 2



Phenanthridine X does not form a hydrochloride but does yield a perchlorate (XII) which was poorly soluble in all of the solvents we used. In that connection the NMR-spectrum of this salt was not recorded.

When naphthaquinone III was treated by the Pictet–Spengler reaction it formed 7,12-dioxo-2,3,9,10-tetramethoxy-6-methylbenzo[b]phenanthridinium chloride (XIII) along with 5,7,12-trioxo-6-methyl-2,3,9,10-tetramethoxybenzo[b]phenanthridone (XIV) at a 1:1 ratio.

The structural changes of the compounds in the chain of the indicated conversions agree well with the electron spectra of the systems. The electron spectra of the quinoid compounds IV, V, and VI exhibit 2 bands that characterize the 1,4-naphthoquinone system [6, 7], $\lambda_{max}$, nm (log $\varepsilon$):215-216 (4,7) 285-287 (4, 5). The UV-spectrum of formylaminophenol diacetate has 2 absorption bands: $\lambda_{max}$ 256, 353 nm with log $\varepsilon$ 4.21 and 3.1 respectively. The UV-spectra of compounds VIII-X, XII-XIV are distinct by the presence of a series of absorption bands that are characteristic of the tetracylic nitrogen-containing system of benzo[b]phenanthridine [3, 5], $\lambda_{max}$, nm (log $\varepsilon$): 206-218 (4, 3), 231-233 (4, 4), 244-250 (4, 3), 275-285 (4, 0), 312-318 (4, 4), $390_{pl}$ (3, 4), 416 (3, 6) (Table 1).

The IR-spectra of 1,4-naphthoquinones II, IV, V, and VI have one absorption band 1650-1655 $cm^{-1}$ that corresponds to the quinoid carbonyl groups. The $\nu$ (CO) value is lower than that of the unsubstituted 1,4-naphthoquinone [$\nu$ (CO) 1675 $cm^{-1}$] which is in accord with the values and the shift direction of the carbonyl absorption bands exposed to substituents in positions 2 and 3 of 1,4-naphthoquinone [4, 8].

The PMR-spectra of the compounds are given in Table 2.

## EXPERIMENTAL (CHEMICAL)

IR spectra were recorded on a UR-20 instrument in petroleum jelly, in $CHCl_3$, and in KBr pellets. UV-spectra were recorded on a Specord UV-Vis spectrophotometer in alcohol. The NMR $^1H$ and $^{13}C$ spectra were recorded on a Bruker WP-200 instrument (200 MHz). Shifts were measured relative to the tetramethylsilane signal. Mass spectra were obtained on a MAT-112 chromatomass spectrometer, ionizing electron energy 70 eV. Temperature of the ionization chamber was 180°C. Specimen directly fed into source.

TABLE 1. Physicochemical Characteristics and Spectral Data for Compounds II, IV-XIV

| Compound | Yield, % | mp, °C (crystallization solvent) | UV-spectrum $\lambda_{max}$, nm (log ε) (in ethanol) | IR spectrum, $cm^{-1}$ | Empirical formula | M | |
|---|---|---|---|---|---|---|---|
| | | | | | | found | calculated |
| II | 83,0 | 273 (diethyl ether) | 254 (4,57); 314 (3,91); 343 (4,10); 445 (2,80) | 3430 ($NH_2$); 3340 ($NH_2$); 1675 (C=O); 1620 (C=C) | $C_{20}H_{19}NO_6$ | 369 | 369,40 |
| IV | 83,1 | 220 (toluene) | 215,1 (4,76), 287,3 (4,72) | 3308 (NH); 1730 (C=O) 1670 (C=O); 1620 (C=C) | $C_{21}H_{19}NO_7$ | 397 | 397,41 |
| V | 90,0 | 232 (benzene) | 215,1 (4,66); 285,7 (4,52) | 1705 (C=O); 1670 (C=O); 1620 (C=C) | $C_{22}H_{21}NO_7$ | 411 | 411,39 |
| VI | 2,6 | 240 (toluene) | 215,1 (4,48); 285,7 (4,33) | 1730 (C=O); 1690 (C=O); 1670 (C=O); 1650 (C=O); 1620 (C=C) | $C_{22}H_{19}NO_8$ | 425 | 425,41 |
| VII | 55,0 | 255 (acetone) | 256 (4,21); 353 (3,1) | 1775 (C=O); 1685 (C=O); 1620 (C=C) | $C_{26}H_{27}NO_9$ | 497 | 497,51 |
| VIII | 96,0 | 205 (MeOH) | 232,5 (5,21); 278 (5,42); 322,5 (5,40); 390 (4,58); 416,6 (4,75); 440 (4,32) | 1775 (C=O); 1620 (C=C) | $C_{26}H_{27}NO_8Cl$ | 379 (—$CH_3Cl$, 2$COCH_3$) | 515,95 |
| IX | 47,17 | 247 (ethyl acetate) | 231 (4,38); 275,5 (4,51); 284,9 (4,59); 333 (4,36) | 1640 (C=O); 1620 (C=C) | $C_{22}H_{19}NO_6$ | 393 | 393,40 |
| X | 44,5 | 323 ($CHCl_3$) | 212,7 (4,33); 244 (4,39); 277,7 (4,29); 315 (4,45) | 1680 (C=O); 1625 (C=C) | $C_{21}H_{17}NO_6$ | 379 | 379,37 |
| XI | 0,93 | 209 (toluene) | 213 (4,26); 274 (3,86); 317 (4,15) | 1720 (C=O); 1670 (C=O); 1625 (C=C) | $C_{25}H_{25}NO_7$ | 451 | 451,48 |
| XII | 70,8 | 311 (ethanol) | 212,7 (4,20); 245 (4,17); 277,7 (4,06); 314 (4,26) | 1685 (C=O); 1620 (C=C) | $C_{21}H_{18}NO_{10}Cl$ | 379 (—$HClO_4$) | 479,83 |
| XIII | 27,8 | 172 (ethanol) | 218 (4,41); 250 (4,31); 274 (4,13); 318 (4,40) | 1690 (C=O); 1620 (C=C) | $C_{22}H_{20}NO_6Cl$ | 379 (—$CH_3Cl$) | 429,86 |
| XIV | 26,9 | 250 (ethanol) | 206,2 (3,69); 256,4 (3,69); 285,7 (3,79); 312,5 (3,73) | 1670 (C=O); 1620 (C=C) | $C_{22}H_{19}NO_7$ | 409 | 409,40 |

TABLE 2. NMR $^1H$ Spectra for Compounds II, IV-XI, XIII, and XIV

| Compound | Chemical shifts, δ, ppm, in $CDCl_3$ (200 MHz) |
|---|---|
| II | 7,60 s (1H, $C^5$—H), 7,52 s (1H, $C^8$—H), 6,98 d ($I_{5'6'}$, 8,05 Hz, 1H, $C^{5'}$—H), 6,90 dd ($I_{2'6'}$, 1,92 Hz, 1H, $C^{6'}$—H), 6,87 dd (1H, $C^{2'}$—H), 5,20 br.s (2H, $NH_2$), 4,03 s (6H, $2OCH_3$), 3,93 s (3H, $OCH_3$), 3,89 s (3H, $OCH_3$) |
| IV | 8,32 d ($I_{CH.NH}$ 9,86 Hz, 1H, COH), 7,90 br.d. (1H, NH), 7,56 s (2H, $C^8$—H, $C^5$—H), 6,99 d ($I_{5'6'}$, 8,04 Hz, 1H, $C^{5'}$—H), 6,89 dd ($I_{2'6'}$, 1,83 Hz, 1H, $C^{6'}$—H), 6,82 dd (1H, $C^{2'}$—H), 4,05 s (3H, $OCH_3$), 4,04 s (3H, $OCH_3$), 3,94 s (3H, $OCH_3$), 3,89 s (3H, $OCH_3$) |
| V | 8,08 s (1H, COH), 7,58 s (1H, $C^5$—H), 7,56 s (1H, $C^8$—H), 6,90 d ($I_{5'6'}$, 8,06 Hz, 1H, $C^{5'}$—H), 6,86 dd ($I_{2'6'}$, 1,71Hz, 1H, $C^{6'}$—H), 6,79 dd (1H, $C^2$—H), 4,06 s (3H, $OCH_3$), 4,05 s (3H, $OCH_3$), 3,93 s (3H, $OCH_3$), 3,88 s (3H, $OCH_3$), 2,89 s (3H, $NCH_3$) |
| VI | 8,85 br.s *. (2H, 2COH), 7,58 s (1H, $C^8$—H), 7,57 s (1H, $C^5$—H), 6,91 d ($I_{5'6'}$, 8,24 Hz, 1H, $C^{5'}$—H), 6,83 dd ($I_{2'6'}$, 1,83 Hz, 1H, $C^{6'}$—H), 6,76 dd (1H, $C^{2'}$—H), 4,05 s (6H, $2OCH_3$), 3,92 s (3H, $OCH_3$), 3,84 s (3H, $OCH_3$) |
| VII | 8,11 br.s* (1H, COH), 7,06 s (1H, $C^8$—H), 7,03 s (1H, $C^5$—H), 6,92 d ($I_{5'6'}$, 8,30 Hz, 1H, $C^{5'}$—H), 6,8 br.m * (2H, $C^{6'}$—H, $C^2$—H), 4,03 s (3H, $OCH_3$), 4,01 s (3H, $OCH_3$), 3,92 s (3H, $OCH_3$), 3,84 br.s * (3H, $OCH_3$), 2,77 s (3H, N—$CH_3$), 2,43 s (3H, $OCOCH_3$), 2,09 s (3H, $OCOCH_3$) |
| VIII** | 9,91 s (1H, $C^5$—H), 8.63 s (1H, $C^1$—H), 7,98 s (1H, $C^8$—H), 7,29 s (1H, $C^{11}$—H), 7,23 s (1H, $C^4$—H), 4,66 s (3H, $+N{\cdot}CH_3$), 4,22 s (3H, $OCH_3$), 4,06 s (3H, $OCH_3$), 4,05 s (3H, $OCH_3$), 4,03 s (3H, $OCH_3$), 2,81 s (3H, $OCOCH_3$), 2,76 s (3H, $OCOCH_3$) |
| IX | 7,73 s (1H, $C^1$—H), 7,72 s (1H, $C^{11}$—H), 7,54 s (1H, $C^8$—H), 7,27 s (1H, $C^4$—H), 4,13 s (3H, $OCH_3$), 4,11 s (3H, $OCH_3$), 4,09 s (3H, $OCH_3$), 4,02 s (3H, $OCH_3$), 2,84 s (3H, C—$CH_3$) |
| X | 9,36 s (1H, $C^5$—H), 9,32 s (1H. $C^1$—H), 7,78 s (1H, $C^4$—H), 7,72 s (1H, $C^8$—H), 7,32 s (1H, $C^{11}$—H), 4,18 s (3H, $OCH_3$), 4,11 s (6H, $2OCH_3$), 4,10 s (3H, $OCH_3$) |
| XI | 8,12 s (1H, $C^1$—H), 7,63 s (1H, $C^{12}$—H). 7,45 s (1H, $C^9$—H), 6,63 s (1H, $C^4$—H), 4,83 t ($I_{5,6}$ 6,41 Hz, 1H, $C^6$—H), 4,06 s (3H, $OCH_3$), 4,00 s (3H, $OCH_3$), 3,97 s (3H, $OCH_3$), 3,90 s (3H, $OCH_3$), 3,57 s (3H, $N{\cdot}CH_3$), 2,85 dd ($I_{5H^1H^2}$ 16.48 Hz, IH, $C^5$—$H^1$) 2,67 dd (1H, $C^5$—$H^2$), 2,03 s (3H, $COCH_3$) |
| XIII** | 9,95 s (1H, $C^5$—H), 9,17 s (1H, $C^1$—H), 7,95 s (1H, $C^4$—H), 7,66 s (1H, $C^8$—H), 7,61 s (1H, $C^{11}$—H), 4,69 s (3H, $^+NCH_3$), 4,18 s (3H, $OCH_3$), 4,09 s (3H, $OCH_3$), 4,03 s (6H, $2OCH_3$) |
| XIV | 9,01 s (1H, $C^1$—H), 7,88 s (1H, $C^4$—H), 7,58 s (1H, $C^8$—H), 7,48 s (1H, $C^{11}$—H), 4,11 s (3H, $OCH_3$), 4,07 s (3H, $OCH_3$), 4,06 s (3H, $OCH_3$), 4,05 s (3H, $OCH_3$), 3,99 s (3H, $NCH_3$) |

*Broadened through the retarded rotation around the amide bond.

**Compound's spectrum recorded in DMSO.

Reaction progress and purity of reaction products was controlled by TLC on Silufol UV-254 plates (Kavalier, Czechoslovakia) in a 12:5 toluene—acetone system. Silica gel 100/160 and 100/250 (Czechoslovakia) was used for column chromatography. Spot detection in UV-light. The found values of element analyses corresponded to the calculated ones.

**2-Amino-6,7-dimethoxy-3-(3,4-dimethoxyphenyl)-1,4-naphthoxyquinone (II).** A suspension of 0.75 g of 3-(3,4-dimethoxyphenyl)-2,6,7-trimethoxy-1,4-naphthoxyquinone I in 150 ml of ethanol saturated with $NH_3$ was placed into a 450 cc ampule which was then heated at 100° for 8 h. Upon cooling the product was filtered, washed with ethanol and dried. Yield was 0.59 g of substance II.

**6,7-Dimethoxy-3-(3,4-dimethoxyphenyl)-2-formylamino-1,4-naphthoquinone (IV).** A mixture of 1 g of the amine II and 17 ml of AcOCHO (obtained from 7.6 ml of formic acid and 10.5 ml of $Ac_2O$ at 50-60° for 2 h) was boiled for 20 min. At 20° the mixture was decanted into 100 ml of cold water. The crystals were filtered, washed with water, and dried at 20°C. A yield of 0.89 g of compound IV was obtained by column chromatography in a 12:5 toluene—acetone system.

**6,7-Dimethoxy-3-(3,4-dimethoxyphenyl)-2-diformylamino-1,4-naphthoquinone (VI).** A yield of 0.03 g of the imide VI was obtained by from appropriate portions of the eluate by chromatographing the products of the previous reaction.

**6,7-Dimethoxy-3-(3,4-dimethoxyphenyl)-2-(N-methyl-N-formylamino)-1,4-naphthoquinone (V).** A mixture of 10 g of the amine III and 167 ml of AcOCHO (obtained from 76 ml of formic acid and 105 ml of $Ac_2O$ at 50-60°C for 2 h) was boiled for 1.5 h. At 20°C the reaction mixture was decanted into 1 liter of cold water. The precipitate was filtered off to yield 9.66 g of the aminoquinone V.

**1,4-Diacetoxy-3-(3,4-dimethoxyphenyl)-6,7-dimethoxy-2-(N-methyl-N-formylamino)naphthalene (VII).** A 0.2 g portion of $NaBH_4$ was added to a suspension of 0.3 g of compound V in 25 ml of MeOH. The mixture was boiled until the solution lost its color after which 2 ml of $Ac_2O$ was added. At 20°C the mixture was decanted into 200 ml of cold water. The precipitate was filtered, washed with water until pH 7, and dried. The yield of substance VII was 0.37 g.

**7,12-Diacetoxy-6-methyl 2,3,9,10-tetramethoxybenzo[b]phenanthridinium chloride (VIII).** A 0.08 g portion of amide VII was dissolved in 5 ml of boiling anhydrous MeCN to which 0.1 ml of freshly distilled $POCl_3$ was added. The mixture was then boiled for 30 min. The reaction mixture was then cooled to 20°C and decanted into 50 ml of diethyl ether. The precipitate was filtered and washed with ether to yield 0.08 g of the VIII salt. NMR $^{13}C$ spectrum (50 MHz, DMSO), $\delta$, ppm: 2CO — 169.28, 168.65; $C^5$ — 156.84; $C^2$, $C^3$, $C^9$, $C^{10}$ — 157.89, 152.87, 152.66 150.12; $C^7$, $C^{12}$ — 139.86, 133.55; $C^{4a}$, $C^{6a}$, $C^{7a}$, $C^{11a}$, $C^{12a}$, $C^{12b}$ — 128.67, 123.82, 123.50, 123.06, 118.13, 114.68; $C^1$, $C^4$, $C^8$, $C^{11}$ — 112.26, 106.46, 99, 62, 99.21; 4 $OCH_3$ — 56.79, 56.20, 56.20, 50.62; $^+NCH_3$ — 37.29; 20 $COCH_3$ — 21.23, 21.08.

**7,12-Dioxo-5-methyl-2,3,9,10-tetramethoxybenzo[b]phenanthridine (IX).** A mixture of 0.1 g of amine II, 5 ml of $Ac_2O$, and 3 drops of conc. $H_2SO_4$ was left standing at 20°C for 24 h. The reaction mixture was then decanted into 50 ml of cold water. After 30 min the precipitate was filtered off, washed with water to pH 7, and dried. Column chromatography separation in a 12:5 toluene—acetone system yielded 0.05 g of compound IX. NMR $^{13}C$ spectrum (50 MHz, $CDCl_3$), $\delta$, ppm: 2CO — 179.77, 162.35; $C^5$ — 146.58; $C^2$, $C^3$, $C^9$, $C^{10}$ — 150.51, 149.52, 149.07, 148.89; $C^{4a}$, $C^{6a}$, $C^{7a}$, $C^{11a}$, $C^{12a}$, $C^{12b}$ — 142.83, 130.58, 115.68, 113.78, 112.91, 110.83; $C^1$, $C^4$, $C^8$, $C^{11}$, — 103.21, 100.26, 95.47; 4 $OCH_3$ — 56.60, 56.19, 55.91, 55.91; $CH_3$ — 14.61.

**7,12-Dioxo-2,3,9,10-tetramethoxybenzo[b]phenanthridine (X).** A mixture of 0.9 g of amine II, 45 ml of formalin, 90 ml of ethanol, and 2 ml of conc. HCl was boiled for 2 h, then cooled to 20°C. The solvent was vacuum-evaporated and the residue was extracted with $CHCl_3$ after which the residue was washed with water and dried with $Na_2SO_4$. The solvent was vacuum evaporated to yield 0.41 g of compound X.

**6-Acetyl-5,6-dihydro-7-methyl-7H,2,3,10,11-tetramethoxynaphthoquinone[2,3b]benzapine (XI)** was obtained from the mother liquor upon recrystallizing the products of the previous reaction, followed by column chromatography to yield 0.02 g of compound XI.

**7,12-Dioxo-2,3,9,10-tetramethoxybenzo[b]phenanthridinium perchlorate (XII).** A mixture of 0.08 g of phenanthridine X, 20 ml of ethanol, and 5 ml of 33% $HClO_4$ was boiled for 30 min. At 20°C the precipitate was filtered, washed with ethanol to pH 7, and dried to yield 0.07 g of the perchlorate XII.

**7,12-dioxo-2,3,9,10-tetramethoxy-6-methylbenzo[b]phenantthridinium chloride (XIII).** A mixture of 0.25 g of amine III, 13 ml of formalin, 25 ml of ethanol, and 0.2 ml of conc. HCl was boiled for 2 h. ASt 20°C the mixture was filtered and the filtrate was vacuum-evaporated. The residue was recrystallized three times from a 3:1 mixture of $CHCl_3$—ethanol to yield 0.08 g of compound XIII.

**5,7,12-Trioxo-6-methyl-2,3,9,10-tetramethoxybenzo[b]phenanthridine (XIV).** A yield of 0.07 g of compound XIV was obtained from appropriate portions of the filtrate after recrystallizing the products of the previous reaction.

## EXPERIMENTAL (BIOLOGICAL)

The antitumor activity of compounds VIII, X, and XIII was tested on non-line white male rats with Jensen's sarcoma. The preparations were administered daily ip 3-4 days after the tumor transplants in a 10% solution of polyvinylpyrrolidine with 0.8% Tween for a period of 8 days. The antiblastic effect was evaluated by the degree to which tumor growth was inhibited ($I_T$).

The greatest activity among the tested substances was exhibited by the quaternary salt VIII [1] which at doses of 15-30 mg/kg inhibited Jensen's sarcoma by 35-74%. Compound X at a dose of 25 mg/kg inhibited tumor growth by 32%. Quaternarized quinone XIII exhibited a poor antitumor action. At a dose of 10 mg/kg it suppressed Jensen's sarcoma by 30%. However, when the dose was increased to 15 mg/kg animal death resulted.

Thus, the replacement of a hydroquinone C ring in the benzo[b]phenanthridines by a quinoid ring resulted in lowered antitumor activity. An analogous phenomenon was observed in the case of mytomycin C where the *in vivo* reduction of the quinone ring was essential to the manifestation of this activity.

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# SYNTHESIS AND BIOLOGICAL ACTIVITY OF 9-[(N,N-DIALKYLAMINOACETYL)AMINO]-1,2,3,4-TETRAHYDROACRIDINES


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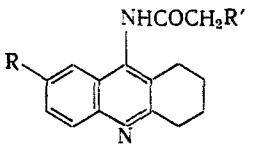
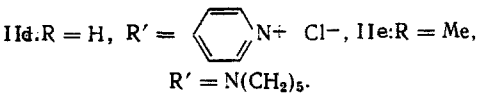
UDC 547.835.615.21


9-Amino-1,2,3,4-tetrahydroacridine (tacrine) is a drug which is effective for the treatment of mental disturbances caused by esters of substituted glycol acids [4]. 9-[(N,N-diethylaminoacetyl)amino]-1,2,3,4-tetrahydroacridine has a strong local anesthetic action at comparatively low toxicity [5]. The present work was under taken as part of a search for new 9-[(N,N-dialkylaminoacetyl)amino]-1,2,3,4-tetrahydroacridines (IIa-e) with antidepressant properties (see Table 1).



Ia-c, IIa-e

Ia: R = H, Ib: R = Me, Ic: R = Br; Ia-c: $R^1$ = Cl;
IIa: R = H, R′ = $N(CH_2CH_2)_2O$, IIb: R = Br,
R′ = $N(CH_2)_5$, IIc: R = Me, R′ = $NEt_2$,



IId: R = H, R′ = N+ Cl−, IIe: R = Me,
R′ = $N(CH_2)_5$.

9-Chloroacetylamino-1,2,3,4-tetrahydroacridines (Ia-c) were obtained by heating a mixture of the corresponding 9-amino-1,2,3,4-tetrahydroacridine with chloracetyl chloride.

Experiments showed that compounds Ia-c reacted with dialkylamines when a mixture of the starting compounds in alcohol was heated under reflux. The desired products IIa-e were obtained in yields of 52-71%, as colorless crystalline substances which absorbed in the IR at 3246-60 $cm^{-1}$ (NH) and at 1660-1680 $cm^{-1}$ (CO). The compounds were basic and formed hydrochlorides with HCl. Refluxing a mixture of the amide Ia and pyridine in ethanol gave the chloride of 9-(pyridinoacetyl)amino-1,2,3,4-tetrahydroacridine (IId).


Perm Pharmaceutical Institute. Translated from Khimiya-farmatsevticheskii Zhurnal, Vol. 23, No. 12, pp. 1441-1442, December, 1989. Original article submitted April 12, 1989.





0091-150X/89/2312-0960$12.50