

concentrated and acidified to give crystalline products. The crude acids were esterified with MeOH (150 mL) containing concentrated  $\text{H}_2\text{SO}_4$  (2 mL) under reflux for 3 h. The reaction mixture was concentrated into dryness, diluted with water, made alkaline with  $\text{Na}_2\text{CO}_3$ , and extracted with EtOAc. The crystalline residue after evaporation of the solvent was recrystallized from EtOAc-*n*-hexane to give **35** (2.2 g, 34.4%), mp 104–106 °C. Anal. ( $\text{C}_8\text{H}_5\text{N}_3\text{O}_4$ ) C, H, N.

**6-Chloro-5-methylnicotinamide (33).** (A) Treatment of **31** (0.5 g, 2.7 mmol) with 28%  $\text{NH}_4\text{OH}$  at room temperature for 16 h gave **33** (0.28 g, 60.9%), mp 211–212 °C. Anal. ( $\text{C}_7\text{H}_7\text{ClN}_2\text{O}$ ) C, H, Cl, N.

(B) Nitronicotinamide **36** (0.2 g, 1.0 mmol) was refluxed in  $\text{SOCl}_2$  (10 mL) for 3 h. The IR and NMR spectra of the compound (0.07 g, 37.2%), mp 211–212 °C, were identical with that of **33** obtained above.

**2-Chloro-5-methylnicotinamide (34).** This compound was prepared in 48.8% yield from the ester **32** using the procedure described above: mp 141–143 °C. Anal. ( $\text{C}_7\text{H}_7\text{ClN}_2\text{O}$ ) C, H, Cl, N.

**5-Methyl-6-nitronicotinamide (36).** By a similar method described above, **36** was prepared from **35** in 74% yield, mp 196–198 °C. Anal. ( $\text{C}_7\text{H}_7\text{N}_3\text{O}_3$ ) C, H, N.

**2-Chloro-6-methylnicotinamide (49).** This compound was prepared from **48** in 64.5% yield by method F: mp 176–178 °C. Anal. ( $\text{C}_7\text{H}_7\text{ClN}_2\text{O}$ ) C, H, Cl, N.

**6-Methyl-2-nitronicotinamide (46).** By methods G and A **46** was prepared from **49** in 11% yield, mp 225–227 °C. Anal. ( $\text{C}_7\text{H}_7\text{N}_3\text{O}_3$ ) C, H, N. The IR was superimposable with that of **46** obtained from **44**.

**2-Methyl-3-nitropyridine-6-carboxamide (54).** To a solution of  $\text{NH}_2\text{OH}$  in 90% EtOH (40 mL), prepared from  $\text{NH}_2\text{OH}\cdot\text{HCl}$  (0.6 g, 8.5 mmol) and NaOAc (0.7 g, 8.5 mmol), was added portionwise a solution of the aldehyde **56**<sup>12</sup> (1.8 g, 10 mmol). The mixture was stirred at 80 °C for 30 min and cooled to give a crystalline product **57** (1.3 g, 66.4%), mp 217–219 °C. Anal. ( $\text{C}_7\text{H}_7\text{N}_3\text{O}_3$ ) C, H, N.

A mixture of **57** (1.3 g, 7 mmol) and  $\text{Ac}_2\text{O}$  (10 mL) was refluxed for 12 h, cooled and poured into ice-water, made alkaline with  $\text{Na}_2\text{CO}_3$ , and extracted with  $\text{CHCl}_3$ . The brown oily residue after removal of the solvent was purified by silica gel chromatography to give a pale yellow oil, **58** (1.0 g, 85.5%). Anal. ( $\text{C}_7\text{H}_5\text{N}_3\text{O}_2$ ) C, H, N.

Compound **58** (1.0 g, 6 mmol) was hydrolyzed with concentrated  $\text{H}_2\text{SO}_4$  as described in method F and the product was recrystallized from EtOAc to give **54** (0.9 g, 81.1%), mp 170–171 °C. Anal. ( $\text{C}_7\text{H}_7\text{N}_3\text{O}_3$ ) C, H, N. The IR spectrum of the compound was identical with that of **54** obtained from dimethylnitropyridine **52** by method B.

**6-Bromo-5-methyl-3-nitropyridine (68).** Method J. A mixture of 6-hydroxy-5-methyl-3-nitropyridine<sup>15</sup> (9.0 g, 58 mmol) and  $\text{PBr}_3$  (45 mL) was heated at 130 °C for 2 h, cooled and poured

into ice-water, made neutral with  $\text{NaHCO}_3$ , and extracted with EtOAc. The extract was dried and the solvent was removed to give a crystalline residue. Recrystallization from EtOAc-*n*-hexane gave **68** (4.8 g, 37.9%), mp 57–58 °C. Anal. ( $\text{C}_8\text{H}_5\text{BrN}_3\text{O}_2$ ) C, H, Br, N. From the mother liquor, the starting material (2.5 g, 27.8%) was recovered.

**6-Cyano-5-methyl-3-nitropyridine (69).** Method K. A mixture of **68** (2.0 g, 9 mmol) and  $\text{CuCN}$  (1.8 g, 20 mmol) was heated at 160–165 °C for 3 h, cooled, and extracted with EtOAc. The extract was decolorized with carbon and concentrated into a small volume, and addition of *n*-hexane gave **69** (0.8 g, 53.3%), mp 75–76 °C. Anal. ( $\text{C}_7\text{H}_5\text{N}_3\text{O}_2$ ) C, H, N.

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## References and Notes

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## Antileukemic Activity of Ungeremine and Related Compounds. Preparation of Analogues of Ungeremine by a Practical Photochemical Reaction<sup>1</sup>

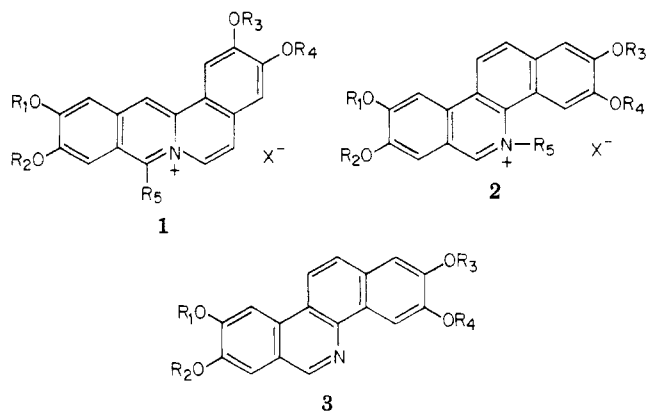
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A number of alkoxypyrrrolophenanthridinium salts and their analogues related to the antileukemic alkaloid ungeremine were prepared by a practical photochemical cyclization. The importance of the quaternary nitrogen atom and of alkoxy groups, the planarity of a molecule, and steric considerations relative to antileukemic activity are discussed.

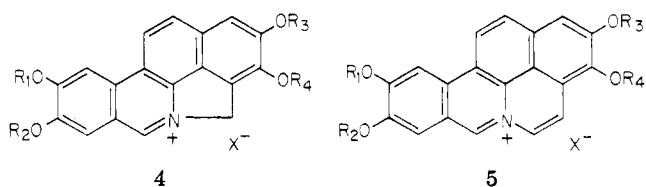
Although both the tetraalkoxydibenzo[*a,g*]quinolizinium salts **1**, such as coralyne,<sup>2–7</sup> and the tetraalkoxybenzo[*c*]phenanthridinium salts **2**, such as nitidine,<sup>8–10</sup> are alkoxyisoquinoline derivatives which possess activity against leukemias L1210 and P388, one structural difference is worthy of notice: the dibenzoquinolizinium salts **1** contain

a relatively stabilized, "locked-in" quaternary nitrogen, wherein the N atom is at a bridgehead position of the ring structure. On the other hand, in the benzophenanthridinium salt series **2**, the quaternary nitrogen is created by alkylation after the ring system is formed. In aqueous solution the alkyl group on the quaternary nitrogen species



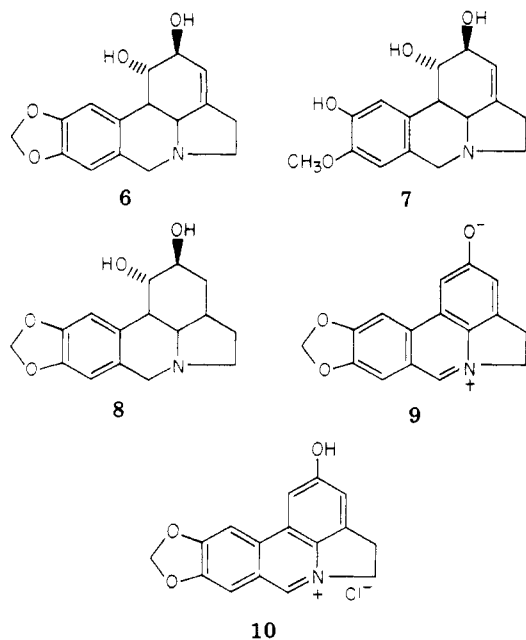
of **2** is not very stable and the less soluble, uncharged ring compounds gradually precipitate from solution on standing.<sup>9</sup> These uncharged molecules (**3**) did not show inhibitory activity against the leukemia L1210 and P388 systems.

In order to circumvent this problem and to design structures with increased stability, it was thought to link the C-4 and N-5 of **2** with either a one-carbon or a two-carbon bridge. The resulting quaternary salts (**4** and **5**)



would be more stable and their antileukemic activity, hopefully, would be retained. Those compounds with an unsaturated two-carbon link, as in **5**, are of particular interest since they contain ring features of both the nitidine and coralyne series.

Although compounds of types **4** and **5** have not as yet been prepared, a search of the literature revealed that certain alkaloids of the family *Amaryllidaceae* contain similar structural features closely related to those considered in the present study. In fact, many of these alkaloids have shown interesting biological activity: lycorine<sup>11</sup> (**6**) and hemanthamine<sup>12</sup> possess confirmed KB



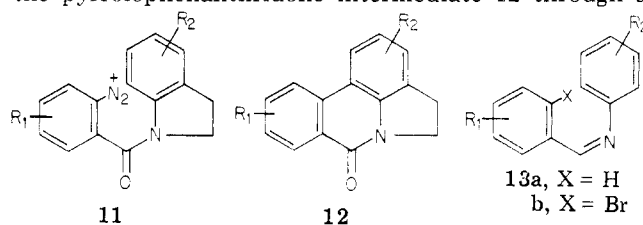
tissue culture inhibitory activity.<sup>13</sup> The former alkaloid is also active against sarcoma 37.<sup>14</sup> Pretazettine is active

against advanced Rauscher leukemia in mice.<sup>15-18</sup> This compound and pseudolycorine (**7**) inhibit protein synthesis in tumor cells.<sup>19</sup> Pseudolycorine also possesses antiviral activity against leukemia virus and neurotropic RNA virus.<sup>16,19-21</sup> Narciclasine, isolated from species of *Narcissus*, has been known to have antitumor effect and possesses marked antimitotic activity.<sup>22</sup> These compounds and dihydrolycorine (**8**) halt HeLa cell growth and block protein synthesis in Krebs II ascites cells, essentially by inhibiting peptide bond formation.<sup>23,24</sup>

Ungeremine (originally isolated from *Ungernia minor*),<sup>25,26</sup> a betaine having a positive quaternary nitrogen atom adjacent to a double bond, has a clear structural relationship with **4**. This alkaloid has recently been reported to possess inhibitory activity against the following experimental tumor systems: Ehrlich ascites, Yoshida sarcoma, and sarcoma-180.<sup>27</sup> Since this alkaloid has not previously been evaluated for antileukemic activity, both ungeremine (**9**, mp 245–250 °C) and its hydrochloride salt **10** (mp >300 °C) were prepared by oxidation of lycorine<sup>26,28</sup> (**6**) and screened. Preliminary test results indicated that both **9** and **10** were active against leukemia P388 in mice.

Attention was thus directed to determining the minimum structural requirement for antileukemic activity in compounds of this type and probing the previously proposed N–O–O antileukemic triangulation hypothesis.<sup>29</sup> Consequently, a search for practical preparative methods of alkoxyphenanthridinium, alkoxyrpyrrolophenanthridinium, and alkoxyrpyridinophenanthridinium salts was initiated.

**Chemistry.** For the synthesis of compounds related to ungeremine, the existing preparative method leading to the pyrrolophenanthridone intermediate **12** through a



diazonium salt **11** by the Pschorr reaction gives only a low yield of the cyclized product.<sup>30</sup> A study of ring cyclization by means of the photochemical process was therefore conducted.

Even though the photochemical cyclization reaction of a Schiff base **13a** in Et<sub>2</sub>O in the presence of dissolved air has recently been reported to form the phenanthridine derivatives,<sup>31</sup> in our hands, the reported reaction conditions were rather unsatisfactory and, in most cases, starting material was recovered. Attempted photochemical cyclization of bromoanils **13b** in C<sub>6</sub>H<sub>6</sub>–MeOH or C<sub>6</sub>H<sub>6</sub>–*t*-BuOH also did not give the expected cyclized product in isolable yield (product was detected by TLC and UV). These experiments indicated that the rate of photochemical cyclization of these Schiff bases in these solvents was rather slow; therefore, a practical synthesis of phenanthridines by this route probably cannot be realized.

Effort was then directed to the study of photochemical cyclization<sup>32,33</sup> of the bromoanilide **14** to **15**. After ex-

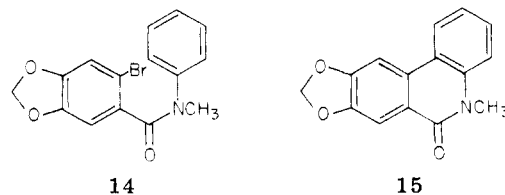


Table I. Analogues of Ungeremine and Related Compounds

Compd (n)	Mol formula	Precursors <sup>a-c</sup> (n)	Mp, °C	Yield, %	Analyses
20a (2)	C <sub>16</sub> H <sub>12</sub> BrNO <sub>3</sub>	18a + a	166-168	93	C, H, N
20b (2)	C <sub>17</sub> H <sub>6</sub> BrNO <sub>3</sub>	18b + a	234-236	95	C, H, N
20a (3)	C <sub>17</sub> H <sub>14</sub> BrNO <sub>3</sub>	18a + b	172-174	88	C, H, N
20b (3)	C <sub>18</sub> H <sub>8</sub> BrNO <sub>3</sub>	18b + b	188-190	92	C, H, N
21a (2)	C <sub>16</sub> H <sub>11</sub> NO <sub>3</sub>	20a (2)	231-233	60	C, H, N
21b (2)	C <sub>17</sub> H <sub>5</sub> NO <sub>3</sub>	20b (2)	271-273	75	C, H, N
21a (3)	C <sub>17</sub> H <sub>13</sub> NO <sub>3</sub> ·0.5H <sub>2</sub> O	20a (3)	178-180	62	C, H, N
21b (3)	C <sub>18</sub> H <sub>7</sub> NO <sub>3</sub>	20b (3)	241-243	81	C, H, N
23b (2)	C <sub>17</sub> H <sub>16</sub> ClNO <sub>2</sub> ·3H <sub>2</sub> O	21b (2)	228-230	82	C, H, N
23a (3)	C <sub>17</sub> H <sub>14</sub> ClNO <sub>2</sub> ·H <sub>2</sub> O	21a (3)	318-320	71	C, H, N
23b (3)	C <sub>18</sub> H <sub>18</sub> ClNO <sub>2</sub> ·EtOH·H <sub>2</sub> O	21b (3)	222-224	77	C, H, N
24a	C <sub>15</sub> H <sub>12</sub> BrNO <sub>3</sub>	18a + c	136-138	90	C, H, N
24b	C <sub>16</sub> H <sub>16</sub> BrNO <sub>3</sub>	18b + c	130-131	95	C, H, N
25a	C <sub>15</sub> H <sub>11</sub> NO <sub>3</sub>	24a	244-246	45	C, H, N
25b	C <sub>16</sub> H <sub>15</sub> NO <sub>3</sub>	24b	220-222	50	C, H, N
27a	C <sub>15</sub> H <sub>12</sub> ClNO <sub>2</sub> ·2H <sub>2</sub> O	25a	280-282	80	C, H, N
27b	C <sub>16</sub> H <sub>16</sub> ClNO <sub>2</sub> ·2 <sup>2</sup> / <sub>3</sub> H <sub>2</sub> O	25b	218-220	85	C, H, N

<sup>a</sup> Indoline. <sup>b</sup> 1,2,3,4-Tetrahydroquinoline. <sup>c</sup> N-Methylaniline.

perimenting with a variety of solvents and reaction conditions, it was found that when a mixture of C<sub>6</sub>H<sub>6</sub> and Et<sub>3</sub>N was used as the reaction solvent, several grams of the cyclized compound 15 could be obtained in 40-60% yield in one operation and the product isolated was of high purity. During the course of the reaction, the resulting Et<sub>3</sub>N·HBr salt separated from the reaction mixture and, together with a small amount of cyclized product, deposited on the wall of the immersed UV light tube. Although from time to time (every 4-5 h) the reaction had to be stopped and the deposits removed, the formation of an insoluble salt actually favorably shifted the equilibrium of the reaction and minimized the possibility of side-product formation due to cleavage of reaction product. In addition, the observed quantity of salt formation on the glass wall could also be used to estimate the extent of the reaction.

The aforementioned successful photochemical cyclization technique was applied to the synthesis of other phenanthridones 21 and 25 to give comparable yields. The bromoanilides 20 and 24 were prepared by the conventional method as shown in Scheme I (see Table I).

Diborane treatment of the cyclized amides 21 and 25 in THF reduced these compounds to the unstable tertiary amines 22 and 26, respectively, which were readily oxidized to the desired phenanthridinium chlorides 23 and 27, respectively, with air in the presence of ethanolic HCl. Overall yields of these salts from 18 were 35-55%.

The unoxxygenated methylphenanthridinium methosulfate 28 was prepared by methylation of phenanthridine with (CH<sub>3</sub>)<sub>2</sub>SO<sub>4</sub>.

**Biological Activity and Discussion.** Antileukemic screening data of ungeremine and related compounds against leukemia P388 in mice are given in Table II. Both the betaine form 9 and the chloride salt 10 are active. Among the analogues of ungeremine screened, the deoxy compound 23a (n = 2) is also active but the activity is somewhat lower. The N-methylated compounds 27a and 27b, which are also active, may satisfy the minimum structural requirements in this series. Compound 27b, in fact, contains part of the structure of nitidine. The alkoxyphenanthridinium salts 23a and 23b (n = 3), on the other hand, possess either very low or no activity. All the intermediates leading to these phenanthridinium salts are inactive and the unoxxygenated phenanthridinium salt 28 has only a marginal activity.

A comparison of the structures of the ungeremine series with those of the coralyne and nitidine series leads to the following observations.

(1) The cationic character of the quaternary N atom in heteroaromatic systems is important to antineoplastic activity. The presence of a C=C-C=N<sup>+</sup>- linkage may facilitate in vivo attack by cellular nucleophiles<sup>34</sup> such as sulfhydryl groups.

(2) The planarity of a molecule, which facilitates in vivo interaction or intercalation with pertinent macromolecules such as DNA,<sup>2b,6</sup> may be a prerequisite for desired biological activity of compounds studied.

(3) The environment around the carbon atoms next to the quaternized nitrogen atom is rather critical. Excessive steric hindrance may have a deleterious effect on biological activity.

(4) Alkoxy groups at the proper positions of the molecule may either serve as additional binding sites or may activate desired metabolic processes.<sup>35,36</sup> They may also prevent certain undesired metabolic processes from taking place at or near such position(s).<sup>37</sup>

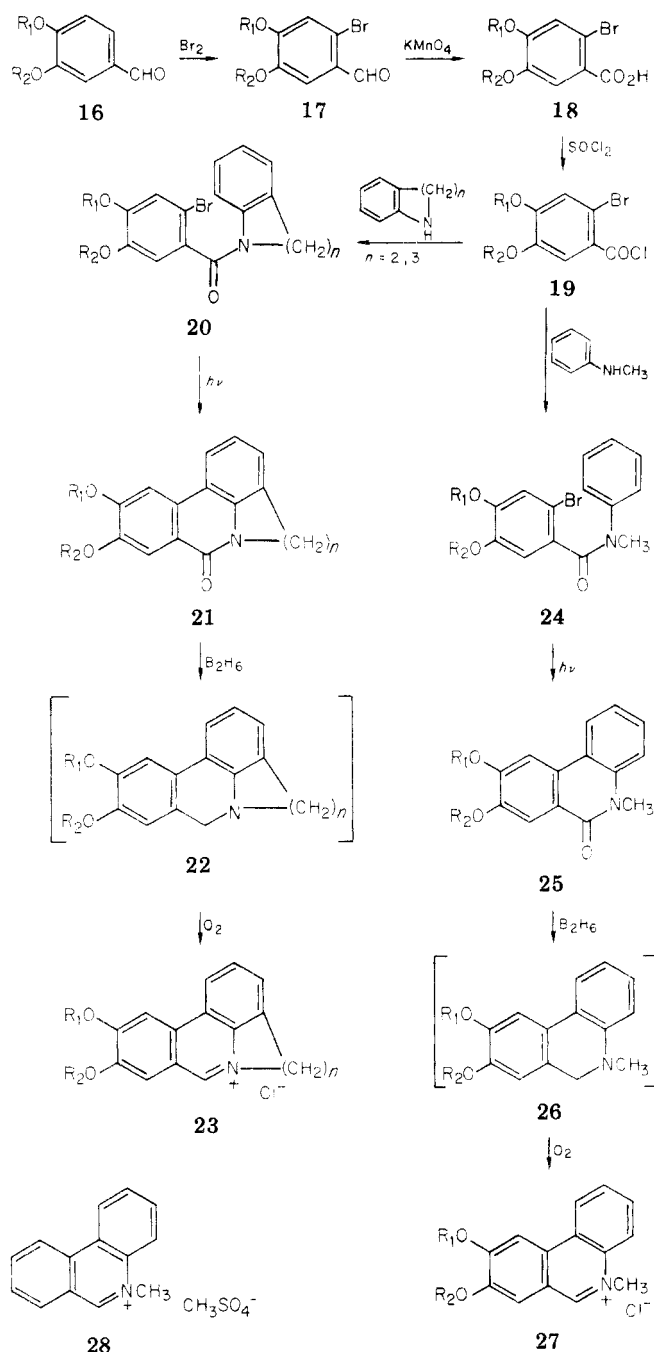
## Experimental Section

Melting points were taken with a Thomas-Hoover melting point apparatus. The mass spectral data were obtained with a Varian Mat CH-4B mass spectrometer. The infrared spectra were taken on a Perkin-Elmer Infracord, and the ultraviolet absorption spectra were measured with a Beckman DK-2 spectrophotometer. Where analyses are indicated only by symbols of the elements, analytical results obtained for these elements were within ±0.4% of the theoretical values.

**1-[(6-Bromo-1,3-benzodioxol-5-yl)carbonyl]-2,3-dihydro-1H-indole (20a, n = 2).** To 30 g (0.122 mol) of azeotropically dried 2-bromo-4,5-methylenedioxybenzoic acid (18a) in 300 mL of dry benzene was added dropwise 50 g (0.42 mol) of SOCl<sub>2</sub> followed by 1.5 mL of HCONMe<sub>2</sub>. The mixture was heated slowly to a gentle reflux and maintained at reflux for 7 h with stirring. The solvent was removed by evaporation under reduced pressure and the residue (19a) was dissolved in 750 mL of CH<sub>2</sub>Cl<sub>2</sub>. The solution was added dropwise (15 min) into an ice-cooled solution of 21 g (0.18 mol) of indoline in 300 mL of 8% aqueous NaOH and 50 mL of CH<sub>2</sub>Cl<sub>2</sub>. The resulting mixture was stirred in an ice bath for 3 h. The layers were separated and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 300 mL). The combined organic layer was washed successively with H<sub>2</sub>O (2 × 150 mL), 3% HCl (2 × 150 mL), and water (2 × 150 mL) and dried (Na<sub>2</sub>SO<sub>4</sub>). On evaporation, a residue was obtained, which was triturated with 50 mL of petroleum ether (bp 30-60 °C), filtered, and dried to give 39.5 g (93% yield) of the product, mp 161-163 °C. An analytical sample was obtained by recrystallization from C<sub>6</sub>H<sub>6</sub>-petroleum ether: mp 166-168 °C; λ<sub>max</sub><sup>EtOH</sup> 255 nm (log ε 4.39), 293 (4.28). Anal. (C<sub>16</sub>H<sub>12</sub>BrNO<sub>3</sub>) C, H, N. Compounds 20b (n = 2), 20a (n = 3), 20b (n = 3), 24a, and 24b were prepared in a manner similar to that described above (see Table I).

**4,5-Dihydro-7H-[1,3]dioxolo[4,5-f]pyrrolo[3,2,1-de]-**

## Scheme I



**phenanthridin-7-one (21a,  $n = 2$ ).** A stirred solution of 6 g (0.017 mol) of 20a ( $n = 2$ ) in 380 mL of dry  $\text{C}_6\text{H}_6$  and 30 mL of  $\text{Et}_3\text{N}$  was irradiated in a 500-mL quartz photochemical immersion well with a 450-W medium-pressure Hg lamp for 18 h. Every 4–5 h, the photochemical reaction was temporarily interrupted, the solid, which deposited on the immersion well, was removed, and the photochemical reaction was resumed. The combined solid was added to 50 mL of  $\text{H}_2\text{O}$ , with stirring. Filtration of the insoluble solid gave 0.6 g of the cyclized product, mp 229–231 °C. The reaction solution after irradiation was evaporated to dryness under reduced pressure; the solid residue was triturated with 18 mL of  $\text{EtOH}$  and filtered to give 2.8 g of the cyclized product. The combined solids (3.4 g) were purified by dissolving in  $\text{CHCl}_3$  and washing the solution successively with dilute  $\text{HCl}$ , dilute  $\text{Na}_2\text{CO}_3$ , and water to give 2.76 g (60% yield) of pure product, mp 231–233 °C. The product could also be purified by column chromatography using  $\text{CHCl}_3$  as eluent. An analytical sample was prepared by recrystallization from  $\text{EtOH}-\text{CHCl}_3$ : mp 231–233 °C (lit.<sup>30,32</sup> mp

Table II. Antileukemic Activity of Ungeremine and Related Compounds

Compd (n)	Dose, mg/kg	Antileukemic act. (P388) <sup>a</sup>		
		Survival	Wt diff	T/C (%) <sup>b</sup>
9	50	6/6	−3.9	152
	25	6/6	−2.1	148
	12.5	6/6	−1.9	148
	6.25	6/6	−0.7	136
	3.13	6/6	−0.7	133
10	50	2/6		
	25	5/6	−3.9	164
	12.5	6/6	−2.4	155
	6.25	6/6	−1.7	151
	3.13	6/6	−0.7	133
23a (2)	50	2/6		
	25	6/6	−2.9	153
	12.5	6/6	−2.1	142
	6.25	6/6	−1.5	127
	3.13	6/6		
23a (3)	50	0/6		
	25	11/12	−3.3	120
	18.8	6/6	−2.4	132
	12.5	12/12	−1.9	129
	6.25	6/6	−1.7	126
27a	3.13	6/6	−0.2	110
	25	6/6	−2.5	151
	18.8	6/6	−1.3	144
	12.5	6/6	−1.0	135
	6.25	6/6	−0.9	129
23b (2)	3.13	6/6	−0.3	126
	100	5/6	−5.1	114
	50	6/6	−1.7	118
	25	6/6	−0.9	108
	12.5	6/6	−0.1	108
23b (3)	50	6/6	−3.2	110
	25	6/6	−0.1	108
	12.5	6/6	−1.4	109
	100	17/18	−3.8	123
	50	18/18	−1.6	130
27b	25	18/18	−1.0	121
	12.5	18/18	−1.1	113
	50	6/6	−6.4	113
	25	12/12	−3.2	125
	12.5	6/6	−2.2	120
28	6.25	6/6	−1.0	117
	3.13	6/6	−0.8	108

<sup>a</sup> For the general screening procedure and data interpretation, cf. R. I. Geran, N. H. Greenberg, M. M. MacDonald, A. M. Schumacher, and B. J. Abbott, *Cancer Chemother. Rep.*, 3 (2), 1 (1972); instruction booklet 14, "Screening Data Summary Interpretation and Outline of Current Screen", Drug Evaluation Branch, Division of Cancer Treatment, National Cancer Institute, Bethesda, Md., 1977. <sup>b</sup> Against leukemia P388, the minimum requirement for activity should have a test/control (T/C) of 125. A standard dosing schedule of one single dose daily was employed among all compounds tested.

232–234 °C). In subsequent experiments, the residue obtained after evaporation was simply triturated with  $\text{MeOH}$  and treated with diluted acid and base as mentioned above to yield a product of practically the same purity. Anal. ( $\text{C}_{16}\text{H}_{11}\text{NO}_3$ ) C, H, N. Compounds 21b ( $n = 2$ ), 21a ( $n = 3$ ), 21b ( $n = 3$ ), 25a, and 25b were prepared in a manner similar to that described above (see Table I).

**4,5-Dihydro[1,3]dioxolo[1,5-*j*]pyrrolo[3,2,1-*de*]phenanthridinium Chloride (23a,  $n = 2$ ).** To a stirred solution of 4.2 g (0.016 mol) of 21a ( $n = 2$ ) in 150 mL of dry tetrahydrofuran was slowly added, at 0 °C, 100 mL of 1 M  $\text{B}_2\text{H}_6$  in tetrahydrofuran. The resulting mixture was stirred at room temperature for 5 h and then refluxed for 20 h. It was cooled to room temperature and the upper clear solution was carefully decanted from the precipitated residue into another flask. To the clear solution cooled in an ice bath was added dropwise 15 mL of 40% ethanolic  $\text{HCl}$  to decompose excess  $\text{B}_2\text{H}_6$ . The resulting precipitate was collected by filtration to give 3.9 g (85% yield) of the  $\text{HCl}$  salt of 4,5-dihydro-7H-[1,3]dioxolo[4,5-*j*]pyrrolo[3,2,1-*de*]phenanthridine (22a,  $n = 2$ ) as a white solid, mp 232 °C dec. Its IR

spectrum had no carbonyl absorption at  $1640\text{ cm}^{-1}$ . Basification of 10 mg of this intermediate in 0.3 mL of  $\text{H}_2\text{O}$  with 0.3 mL of 5%  $\text{NaHCO}_3$  yielded the free base **22a** ( $n = 2$ ).

The HCl salt of **22a** ( $n = 2$ ) was suspended in 300 mL of 95% EtOH and 1 mL of concentrated HCl. A stream of dry air was bubbled through this mixture for 5 h. The resulting precipitate was collected by filtration to give 3.6 g (86% yield) of the desired product as a pale yellow solid. The overall yield from **21a** ( $n = 2$ ) was 73%. An analytical sample was prepared by recrystallization from EtOH: mp  $282\text{--}284^\circ\text{C}$  dec (lit.<sup>30</sup> mp  $280\text{--}285^\circ\text{C}$  dec). Compounds **23b** ( $n = 2$ ), **23a** ( $n = 3$ ), **23b** ( $n = 3$ ), **27a**, and **27b** were prepared in a manner similar to that described above (see Table I).

**5-Methylphenanthridinium Methyl Sulfate (28).** To a warm ( $60^\circ\text{C}$ ) solution of 1.8 g (0.01 mol) of phenanthridine in 20 mL of xylene was added dropwise 3.6 mL (0.028 mol) of methyl sulfate. A solid separated immediately. The mixture was heated at reflux for 20 min and then cooled. It was diluted with 30 mL of  $\text{Et}_2\text{O}$ . The solid was collected by filtration and washed with  $\text{Et}_2\text{O}$  to give 3.1 g (quantitative yield) of **28**, mp  $186\text{--}188^\circ\text{C}$ . An analytical sample was prepared by recrystallization from  $\text{MeOH-Et}_2\text{O}$ : mp  $188\text{--}190^\circ\text{C}$ ;  $\lambda_{\text{max}}^{\text{EtOH}}$  246 nm ( $\log \epsilon$  4.64), 320 (3.89), and 360 (3.52). Anal. ( $\text{C}_{15}\text{H}_{15}\text{NO}_4\text{S}$ ) C, H, N.

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