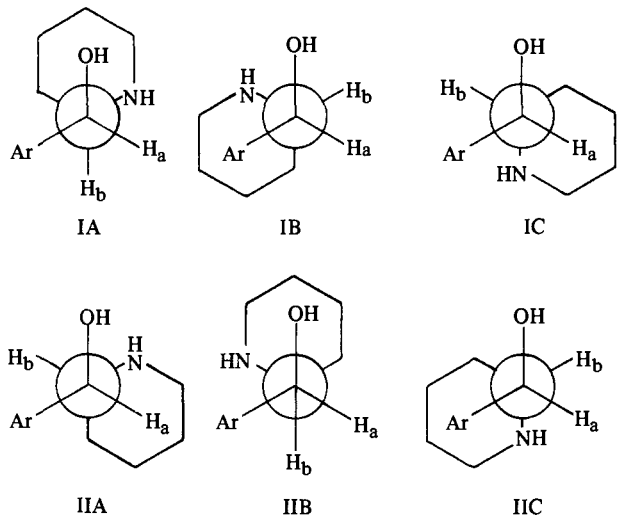

Ar = 3,6-Bis(trifluoromethyl)-9-phenanthryl

coupling constants observed in DMSO for the free bases and their protonated forms. Evidently, on protonation, the bulk of the solvated quaternary N in I · HCl is significantly increased by H bonding with DMSO. This would enhance the population of IA at the expense of IB and IC. Similarly, protonation of II should increase the population of IIA with a concomitant decrease in IIB, due to the increased steric requirements of the solvated ammonium group.

Biological Data. The *dl*-erythro and *dl*-threo isomers of α-(2-piperidyl)-3,6-bis(trifluoromethyl)-9-phenanthrenemethanol were tested[12] for antimalarial activity as their HCl and TsOH salts and as their oxazolopyridine derivatives against *Plasmodium berghei* in mice and *P. gallinaceum* in chicks by Dr. Leo Rane at the University of Miami. The test results, furnished to us through the Walter Reed Army Institute of Research, show these materials to be highly active against *P. berghei*, giving 5 cures out of 5 infected mice at dosages of 40 mg/kg for the threo epimers and 5 cures at 80 mg/kg for the erythro compds.§ No toxic deaths were reported up to dosages of 640 mg/kg. Against *P. gallinaceum*, the minimum dosage showing activity was 20 and 160 mg/kg for the threo and erythro compds, respectively.

To attempt a general correlation of epimer conformation with antimalarial activity on the above limited data is premature.

Experimental Section#

dl-erythro-α-(2-Piperidyl)-3,6-bis(trifluoromethyl)-9-phenanthrenemethanol Hydrochloride (I · HCl). H_2 was passed through a mixt of 115 g (0.275 mole) of 2-pyridyl 3,6-bis(trifluoromethyl)-9-phenanthryl ketone, 5.0 g of PtO_2 (Engelhard 85%), 4.2 l. of MeOH, and 40 ml of concd HCl for 16 hr. Darco was added and, after filtration, the filtrate was evapd *in vacuo* to 10% the original vol, pptg a mass of white crystals. The solids were dissolved in MeOH (Darco) and again concd to 10% the original vol to give 96.0 g (82.3%) of I · HCl, mp 331–332° dec. *Anal.* ($C_{22}H_{19}NOF_6$ · HCl) C, H, Cl, N.

dl-threo-α-(2-Piperidyl)-3,6-bis(trifluoromethyl)-9-phenanthrenemethanol Hydrochloride (II · HCl). The mother liquors from the above recryst were concd to dryness, treated with dil K_2CO_3 soln, and dried. The mixt of I and II (15.0 g, 35 mmoles) in 200 ml of MeOH was treated with 4.9 g (25 mmoles) of TsOH · H_2O, refluxed for 5 min, and cooled to ppt II · TsOH. Recrystn (2x, MeOH, Darco) gave an analytical material, mp 269–270°. *Anal.* ($C_{29}H_{27}NO_4F_6S$) C, H, N, F.

II · TsOH (50 g, 0.1 mole) was neutralized by stirring overnight with dil aq NaOH soln. II was dissolved in anhyd Et_2O and satd with HCl gas to ppt II · HCl. Refluxing with CCl_4 removed a yellow impurity to leave II · HCl as a white powder, mp 284–285° (44.2 g, 95%). *Anal.* ($C_{22}H_{21}NOF_6$ · HCl) C, H, N, Cl.

1-[3,6-Bis(trifluoromethyl)-9-phenanthryl]hexahydro-3*H*-oxazolo[3,4-*a*]pyridine. III. A mixt of 4.9 g (11 mmoles) of I, 2 ml of $(CH_2O)_3$ soln, and 50 ml of MeOH was refluxed 8 hr. Addl $(CH_2O)_3$ soln (2 ml) was added, the reflux was contd overnight. The mixt was cooled and filtered, and the product was recrystd (EtOH, Darco) to give 3.0 g (63%) of III as white flakes, mp 167–168°. *Anal.* ($C_{23}H_{19}NOF_6$) C, H, N.

IV. A similar reaction of II gave 4.5 g of crude product. The solid was dissolved in $CHCl_3$, poured onto a silica gel H column (75 g), and eluted with $CHCl_3$. Recrystn (MeOH–H_2O) gave 4.0 g (84%) of IV as a white powder, mp 181–182°. *Anal.* ($C_{23}H_{19}NOF_6$) C, H, N.

Acknowledgment. The author wishes to thank Roy Putnam for the nmr spectra.

References

(1) D. W. Boykin, A. R. Patel, R. E. Lutz, and A. Burger, *J. Heterocycl. Chem.*, 4, 459 (1967).
(2) A. D. Ainley and H. King, *Proc. Roy. Soc., Ser. B*, 125, 60 (1938); R. F. Brown, *et al.*, *J. Amer. Chem. Soc.*, 68, 2705 (1946); E. R. Buchman and D. R. Howton, *ibid.*, 68, 2718 (1946); E. R. Buchman, H. Sargent, T. C. Meyers, and D. R. Howton, *ibid.*, 68, 2710 (1946); E. R. Buchman, H. Sargent, T. C. Meyers, and J. A. Seneker, *ibid.*, 68, 2697 (1946); J. B. Koepfli, M. M. Rapport, A. E. Senear, and J. F. Mead, *ibid.*, 68, 2697 (1946); R. E. Lutz, *et al.*, *ibid.*, 68, 1813 (1946); J. F. Mead, A. E. Senear, and J. B. Koepfli, *ibid.*, 68, 2708 (1946); R. A. Seibert, T. R. Norton, A. A. Benson, and F. W. Bergstrom, *ibid.*, 68, 2721 (1946); A. E. Senear, H. Sargent, J. F. Mead, and J. B. Koepfli, *ibid.*, 68, 2605 (1946); S. Winstein, T. L. Jacobs, E. F. Levy, D. Seymour, G. B. Linden, and R. B. Henderson, *ibid.*, 68, 2714 (1946).
(3) H. Sargent, *ibid.*, 68, 2688 (1946).
(4) F. Y. Wiselogle, "A Survey of Antimalarial Drugs, 1941–1945," J. W. Edwards, Ann Arbor, Mich., 1946.
(5) E. A. Nodiff, K. Tanabe, C. Seyfried, S. Matsuura, Y. Kondo, E. H. Chen, and M. P. Tyagi, *J. Med. Chem.*, 14, 921 (1971).
(6) T. A. Crabb and R. F. Newton, *J. Heterocycl. Chem.*, 3, 418 (1966).
(7) A. Dudas and I. Weisz, *Chem. Ber.*, 94, 412 (1960).
(8) J. Kovar, J. Jary, and K. Blaha, *Collect. Czech. Chem. Commun.*, 28, 2199 (1963).
(9) P. S. Portoghese, *J. Med. Chem.*, 10, 1057 (1967).
(10) M. E. Munk, M. K. Meilahn, and P. Franklin, *J. Org. Chem.*, 33, 3480 (1968).
(11) O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, 86, 1256 (1964).
(12) T. S. Osdene, P. B. Russell, and L. Rane, *J. Med. Chem.*, 10, 431 (1967).

§The synthesis and activity of I · HCl has been previously reported by Nodiff, *et al.*[5]

#All melting point (uncorr) were taken on a Büchi apparatus. Instruments employed were: Beckman IR-9 infrared spectrophotometer, Varian Model DP-60 high-resolution nmr spectrophotometer and Beckman DK-2 uv spectrophotometer. Elemental anal. were correct (±0.3%) and were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

N-Demethylation of Morphine and Structurally Related Compounds with Chloroformate Esters†

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Hundreds of modifications of morphine and structurally related compounds have been performed and the compounds tested in an effort to analyze the relationship between structure and analgetic activity.[1,2] The most common of these modifications is replacement of the Me group attached to the basic N with some other substituent. Thus,

†This investigation was supported by NIH Grant NS 08738.

the secondary amine serves as an important intermediate in the synthesis of such compounds. Although there are several methods reported[3-7] for the demethylation of tertiary amines, they suffer from the disadvantage of the toxicity of reagents employed and/or the low yields of demethylated product.

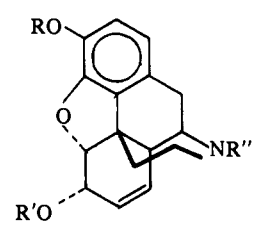
One approach to this problem which seemed worthwhile exploring involved demethylation of analgetics with a chloroformate ester[8] followed by hydrolysis of the resulting carbamate to the secondary amine as outlined below.

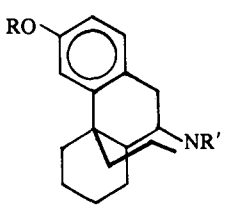
$$R^1R^2NME \xrightarrow{ClCO_2R} R^1R^2NCO_2R \xrightarrow{HOH} R^1R^2NH$$

Cleavage of tertiary amines with chloroformate esters was first reported in 1911.[8] Gadamer and Knoch[9] studied the effect of ethyl chloroformate on a variety of cyclic tertiary amines and observed that bulbocapnine, corydine, and laudanosine were converted to the corresponding ethyl carbamates, whereas compounds such as morphine, codeine, heroin, and tropine were not cleaved. Several examples of this reaction have been published since,[10-13] and in this regard, phenyl chloroformate was found to be superior to both benzyl and ethyl chloroformate in the cleavage of tertiary amines.[14] We wish to describe the utilization of this reaction as a means of conveniently demethylating, in high yield, structures related to morphine.

Treatment of morphine (1) with phenyl chloroformate in the presence of $KHCO_3$ in boiling $CHCl_3$ and subsequent treatment of the product with a mild base afforded, after purification, a nonbasic crystalline material which was assigned structure 2, based on its spectral properties. This assignment was confirmed further by LAH reduction of 2 to morphine and by its hydrolytic conversion to normorphine (3) with KOH. It is noteworthy that the reaction of morphine with phenyl chloroformate was unsuccessful in the absence of base, possibly because esterification of the 3- or 6-OH generates HCl which may protonate the basic N and hence diminish its reactivity.

Codeine (4) was demethylated with ethyl chloroformate in a two-phase system containing aq KOH and $CHCl_3$. The spectral characteristics of the neutral intermediate appear to be in harmony with 5. The ethyl carbonate group of 5 could be hydrolyzed selectively to 6 which then was cleaved to norcodeine (7) under more vigorous conditions.





1, R = R' = H; R'' = Me
2, R = R' = H; R'' = COOPh
3, R = R' = R'' = H
4, R = Me; R' = H; R'' = Me
5, R = Me; R' = R'' = COOEt
6, R = Me; R' = H; R'' = COOEt
7, R = Me; R' = R'' = H

8, R = R' = Me
9, R = Me; R' = COOPh
10, R = Me; R' = H
11, R = Me; R' = COOEt
12, R = R' = H

Reaction of 3-methoxy-*N*-methylmorphinan (8) with phenyl chloroformate at room temp afforded carbamate ester 9. The carbamate was obtained in crystalline form by selectively hydrolyzing the phenyl chloroformate contaminant with aq K_2CO_3. Structure 9 was corroborated by its reconversion to 8 with LAH. Hydrolysis of 9 with KOH gave the desired secondary amine (10). Demethylation of 8 also was carried out with ethyl chloroformate. Hydrolysis of this product (11) with HBr-HOAc afforded 3-hydroxymorphinan (12).

It is noteworthy that the present procedure also can be employed as a convenient and relatively inexpensive method for introducing radioactivity into a *N*-Me group. Thus, [^{3}H]LAH reduction of the carbamate intermediate obtained from the demethylation step would afford a ^{3}H-labeled Me group.‡ A ^{14}C label may be incorporated by demethylating with [^{14}C]ClCOOR followed by reduction.[15]

Experimental Section§

N-Carbophenoxynormorphine (2). A stirred suspension of 2.5 g (0.0088 mole) of morphine (1) and 15 g (0.15 mole) of $KHCO_3$ in $CHCl_3$ (250 ml) was treated with 11.5 g (0.077 mole) of phenyl chloroformate and refluxed for 60 hr. The mixt was treated with H_2O (100 ml) and the $CHCl_3$ phase was sepd and concd *in vacuo*. The residue was dissolved in MeOH (150 ml), treated with an aq soln (100 ml) contg 5.6 g of KOH and 10.0 g of $KHCO_3$, and stirred under N_2 for 24 hr. After the mixt was acidified with concd HCl, the MeOH was removed and the residue was dild with H_2O and extd (Et_2O). The Et_2O was removed and the oily residue was chromatogd on a column of 45 g of silica gel (E. Merck AG, 70–325 mesh) and eluted with Et_2O. Fractions 6–12 (50 ml each) were pooled, and the solvent was removed *in vacuo* to afford 3.12 g of 2: mp 127–130° (yield 91%); mass spec (70 eV) *m/e* 391. *Anal.* ($C_{23}H_{21}NO_5$) C, H, N.

LAH Reduction of Carbophenoxynormorphine (2). A THF soln (50 ml) contg 0.8 g (0.002 mole) of 2 was added slowly to a cooled, stirred suspension of LAH (0.2 g) in THF (150 ml). The mixt was refluxed under N_2 for 20 hr, cooled, treated with EtOAc (15 ml), and refluxed for 30 min. The mixt was treated with 2 *N* HCl (50 ml) and sodium potassium tartrate (6 g) and refluxed for 4 hr. This was concd *in vacuo* to remove THF and extd with Et_2O. The acid phase was adjusted to pH 8.5 and extd with a mixt of $CHCl_3$–*i*-PrOH (3:1). The exts were concd *in vacuo*, and the residue was crystd from 50 ml of MeOH–H_2O (1:4) to afford 0.45 g of morphine: mp 252–254° (reported 254–256°)[16] (yield 76%).

Normorphine (3). A soln of 0.4 g (0.001 mole) of 2 in a mixt of EtOH (80 ml) and 50% KOH (20 ml) was refluxed under N_2 for 24 hr. The soln was treated with concd HCl (20 ml), the EtOH was removed *in vacuo*, and the residue was extd with Et_2O. The Et_2O ext contd some unreacted 2 as shown by tlc. The acid phase was filtered, adjusted to pH 8.5, and extd with $CHCl_3$–*i*-PrOH (3:1). The solvent was removed *in vacuo* to afford 0.12 g of 3: mp 277° dec (reported 276–277°);[17] 3 · HCl, mp 307°dec (reported 305° dec);[17] yield, 43.5%.

(+)-3-Methoxy-17-carbophenoxymorphinan (9). A soln of 3.0 g (0.011 mole) of 8 and 2.0 g (0.013 mole) of phenyl chloroformate in CH_2Cl_2 (30 ml) was maintd at 25° for 24 hr. The CH_2Cl_2 was removed *in vacuo*, and the residue was suspended in 1 *N* HCl (50 ml) and extd with Et_2O. Basification of the aq soln afforded 0.86 g of unreacted 8. The Et_2O soln was concd under reduced pressure and the oily residue was dissolved in MeOH (60 ml) and treated with 2% aq K_2CO_3 (40 ml). The mixt was maintd at room temp for 24 hr and the MeOH removed *in vacuo*. Crystn (MeOH–H_2O) afforded 2.7 g (yield, 65%) of 9, mp 100–102°. *Anal.* ($C_{24}H_{27}NO_3$) C, H, N.

(+)-3-Methoxymorphinan Hydrochloride (10 · HCl). An EtOH soln (80 ml) contg 2.5 g (0.007 mole) of 9 was treated with 50% aq KOH (20 ml) and the reaction mixt was refluxed under N_2 for 24 hr. The soln was dild with H_2O (20 ml) and the EtOH was partially removed under reduced pressure. The aq suspension was extd with Et_2O and the Et_2O layer was extd with 1 *N* HCl. Removal of Et_2O afforded 0.8 g of 9. The aq acid soln was filtered, basified, and extd with Et_2O. The Et_2O was dried ($MgSO_4$) and treated with ethanolic HCl to give 1.45 g of crude 10 · HCl: yield, 74.5%; recrystd 10 · HCl (MeOH–EtOAc), mp 253.5–255°. *Anal.* ($C_{17}H_{24}NO$ · HCl) C, H, N.

LAH Reduction of 9. A THF soln (100 ml) contg 0.8 g (0.002 mole) of 9 was added slowly to a cooled, stirred suspension of 0.2 g of LAH in THF (100 ml). The mixt was refluxed under N_2 for 4 hr,

‡A. E. Takemori and J. Wang, Dept. of Pharmacology, University of Minnesota, have successfully prepared ^{3}H-labeled morphine by employing a modification of our procedure.

§Melting points were detd in open capillary tubes using a Thomas-Hoover melting point apparatus and are uncorrected. Microanalyses were performed by M-H-W Laboratories, Garden City, Mich. The ir spectra were obtd with a Perkin-Elmer 237B spectrophotometer in $CHCl_3$ solution or KBr disk. The nmr spectra were obtd with a Varian A-60D spectrometer ($CDCl_3$, TMS). Mass spectra were obtd with a Hitachi Perkin-Elmer RMU-6D mass spectrometer.

cooled, treated with EtOAc (10 ml), and refluxed for 30 min. After addn of H_2O and 1 *N* NaOH alternately, the mixt was filtered and concd *in vacuo* to remove THF. The residue was acidified with 6 *N* HCl and extd with Et_2O. The aq acid soln was basified and extd with Et_2O, and the dried Et_2O ext was treated with ethanolic HCl to afford 0.51 g (yield, 78%) of **8** · HCl.

(+)-3-Hydroxymorphinan (12). A $CHCl_3$ soln (25 ml) contg 4.0 g (0.0015 mole) of **7** was treated with ethyl chloroformate (20 ml) and anhyd K_2CO_3 (2 g). The reaction mixt was stirred for 24 hr and the $CHCl_3$ then removed *in vacuo*. The residue was suspended in 1 *N* HCl (50 ml) and extd with Et_2O. Removal of Et_2O afforded an oil (2.5 g) which was dissolved in a mixt of glacial AcOH (10 ml) and 48% HBr (10 ml). After refluxing under N_2 for 6 hr, the reaction mixt was poured in ice water (300 ml), extd with Et_2O, and basified to afford 1.1 g (31%) of **12**, mp 260–263° [reported for (–)-3-hydroxymorphinan, mp 260–262°].[18]

Norcodeine (7). A soln of 3.8 g (0.012 mole) of codeine (**4**) in $CHCl_3$ (50 ml) was treated with ethyl chloroformate (5 ml) and 15% aq KOH (50 ml). The 2-phase reaction mixt was shaken for 24 hr. Five successive 1-ml portions of ethyl chloroformate were added to the reaction mixt at 1-hr intervals, and KOH soln was added when necessary to maintain a pH > 10. At the end of 24 hr, the $CHCl_3$ layer was sepd and extd with 1 *N* HCl. The $CHCl_3$ was removed *in vacuo* to afford an oil (3.2 g) whose ir spectrum included characteristic absorptions at 1690 cm^{-1} (C=O of N-CO_2Et) and 1740 cm^{-1} (C=O of O^6–CO_2Et). This was treated with a mixt of MeOH (90 ml) and 10% aq K_2CO_3 (10 ml) for 2 hr, concd *in vacuo* to remove MeOH, extd with Et_2O, and the Et_2O was extd with 1 *N* HCl. Removal of Et_2O afforded 2.5 g of an oily uncrystallizable material. A soln of 2.0 g of the oil in 95% EtOH (80 ml) was treated with 50% aq KOH (20 ml) and refluxed under N_2 for 24 hr. The soln was dild with H_2O (20 ml) and the EtOH was removed under reduced pressure. The aq acid soln was basified and extd with Et_2O. The Et_2O was removed under reduced pressure to give 0.7 g (yield, 43%) of **7**: mp 183–185° (reported mp 185°);[19] **7** · HCl, mp 309–311° dec (reported mp 309° dec).[19]

References

(1) P. S. Portoghese, *J. Pharm. Sci.*, **55**, 865 (1966).
(2) "Analgetics," G. deStevens, Ed., Academic Press, New York, N. Y., 1965.
(3) H. A. Hageman, *Org. React.*, **7**, Chapter 4 (1953).
(4) O. Diels and E. Fischer, *Ber.*, **47**, 2043 (1914).
(5) A. Pohland and H. R. Sullivan, Jr., U. S. Patent 3,342,824 (1967).
(6) E. Speyer and L. Walther, *Ber.*, **69B**, 852 (1930).
(7) E. Späth, L. Marion, and E. Zajic, *ibid.*, **69B**, 251 (1936).
(8) F. Bayer and Co., German Patent 255,942 (1911).
(9) J. Gadamer and F. Knoch, *Arch. Pharm. (Weinheim)*, **259**, 135 (1921).
(10) E. H. Flynn, H. W. Murphy, and R. D. McMahon, *J. Amer. Chem. Soc.*, **77**, 3104 (1955).
(11) J. A. Campbell, *J. Org. Chem.*, **22**, 1259 (1957).
(12) M. M. Abdel-Monem and T. O. Soine, *J. Pharm. Sci.*, **56**, 976 (1967).
(13) G. Kraiso and L. Nador, *Tetrahedron Lett.*, **57** (1971).
(14) J. D. Hobson and J. B. McCluskey, *J. Chem. Soc.*, 15 (1967).
(15) R. E. McMahon in "Advances in Tracer Methodology," Vol. 4, S. Rothchild, Ed., Plenum Press, New York, N. Y., 1968, p 29.
(16) Merck Index, 8th Ed., D. G. Stecher, Ed., Merck and Co., Inc., Rahway, N. J., 1968, p 702.
(17) Reference 16, p 749.
(18) O. Schnider and A. Grussner, *Helv. Chim. Acta*, **34**, 2211 (1951).
(19) Reference 16, p 747.

Synthesis of 4(3*H*)-Pteridinones

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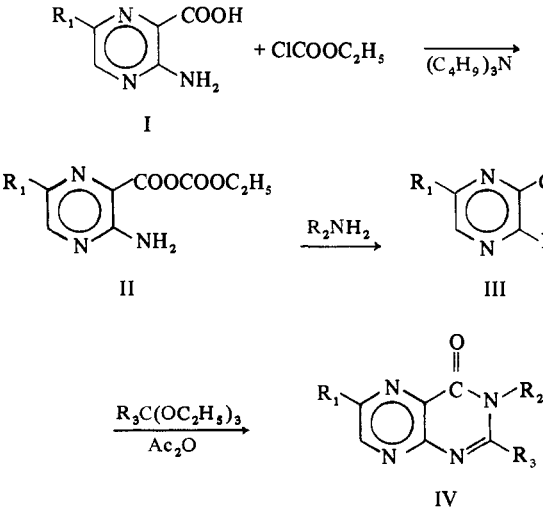
The sedative-hypnotic activity of some 4(3*H*)-quinazolones[1] prompted us to synthesize a number of the isosteric 4(3*H*)-pteridinones and to investigate their hypnotic and sedative activities. The existing literature gives only a few examples of preparation of 3-alkyl or 3-aryl substituted 4(3*H*)-pteridinones[2-4] and no data at all on their pharmacology. The synthesis of the title compounds involved the intermediate 3-aminopyrazinecarboxamides, described in Table I, which were obtained, in good yield, from 3-aminopyrazinoic acid (I),[5] *via* the mixed anhydride (II)[6] and reaction of the latter with appropriate amines (R_2NH_2).



The 3-aminopyrazinecarboxamides (III) could be cyclized to the desired 4(3*H*)-pteridinones (IV) by condensation with an ortho ester $R_3C(OC_2H_5)_3$ in Ac_2O solution. The amides (III), in contrast to the 4(3*H*)-pteridinones (IV), reveal a characteristic fluorescence under uv light, which is helpful for their identification by chromatography.

In preliminary CNS screening the majority of the compounds were found to be without hypnotic or sedative activity. Compds **23**, **30**, and **31** showed a slight sedative activity at 300 mg/kg (mouse) and with **30**, **31**, and **38** some analgetic activity was observed at 150–250 mg/kg (mouse; phenylbenzoquinone test) and 150–500 mg/kg (mouse; hot-plate test), but all the compounds showed too low a therapeutic index, the LD_{50} (mg/kg; mouse; Litchfield and Wilcoxon) being 1250 (1042–1500), 575 (483–684), 1220 (1070–1391), and 1750 (1400–2187) for **23**, **30**, **31**, and **38**, respectively.

Experimental Section

The melting points of all but four compds **21–47** were taken with a Mettler FP-1 apparatus, all the others with a Büchi apparatus, and are uncorrected. Uv and ir spectra were measured for some typical compds and were as expected. Where analyses are indicated only by symbols of the elements, analytical results obtained for those elements were within ±0.4% of the theoretical value.

3-Aminopyrazinecarboxamides (1–20). A mixt of 5.56 g (0.04 mole) of 3-aminopyrazinoic acid, 7.4 g (0.04 mole) of Bu_3N, and 50 ml of dioxane was stirred at room temp until a clear soln resulted. This soln was cooled to 7–8° and 4 ml (0.04 mole) of EtOCOCl was added dropwise, keeping the temp at 11–12°. After cooling again to 7–8°, 0.04 mole of the appropriate amine hydrochloride was added, and the reaction was allowed to proceed at room temp for 3 hr. The solvent was removed on a rotatory evaporator under reduced pressure and the residue was triturated for 30 min with 50 ml of H_2O, filtered, dried, and recrystd. Recrystn solvents and physical data are given in Table I.

4(3*H*)-Pteridinones (21–47). A mixt of 0.01 mole of III, 25 ml of ortho ester, and 20–30 ml of Ac_2O was refluxed for 5 hr and then concd on a rotatory evaporator at room temp *in vacuo*. The residue was triturated with 20 ml of EtOH, and, after evapn of the solvent, washed with Et_2O, filtered, dried, and recrystd. Recrystn solvents and physical data are given in Table II. For **23** the reaction was carried out in anhyd HCO_2H, and for 24 in 1:1 anhyd HCO_2H-Ac_2O