activity than the corresponding 6-membered tetrahydropyridine derivative (**22**), however, extension of this argument to the 7-membered tetrahydroazepine (**23**) cannot be made due to the variability in the pretreatment averages.

Experimental Section

All melting points were determined on a Thomas-Hoover capillary melting point apparatus and are cor. Where analyses are indicated only by symbols of the elements, anal. results obtained for those elements were within ±0.4% of the theor values. Nmr and ir spectra were recorded for all the compds and are consistent with assigned structures.

2-(3,4-Dimethylphenyl)amino-1-pyrroline·HCl (16).—A soln of $POCl_3$ (31.0 g, 0.2 mole) in 20 ml of PhMe was added in dropwise amts to a stirred, cooled (10°) soln of 2-pyrrolidinone (**4**) (34.0 g, 0.4 mole) in 20 ml of PhMe. The temp during the addn (20 min) was maintained at 10–15°, then allowed to return to room temp for 3 hr. A soln of 3,4-xylidene (24.2 g, 0.2 mole) in 20 ml of PhMe was added, and the mixt was heated to reflux overnight. It was cooled to room temp, and the PhMe layer was decanted. The residue was dissolved in 150 ml of H_2O and extd with 150 ml of C_6H_6. NaOH (100 ml, 6 *N*) was then added to the aq layer. The resultant alkaline mixt was cooled and 27.65 g (73%) of a light tan solid collected, mp 150.5–152.5°. Recrystn from MeCN yielded light tan crystals, mp 151–153°. *Anal.* ($C_{12}H_{16}N_2$) C, H, N.

The HCl salt was prepd in Et_2O by addn of Et_2O satd with dry HCl. Recrystn from EtOH–Et_2O gave a colorless powder, mp 222–223°. *Anal.* ($C_{12}H_{16}N_2 \cdot HCl$) C, H, N, Cl.

2-(2,6-Dichlorophenyl)amino-3,4,5,6-tetrahydropyridine·HCl (22).—A cold (−10°), stirred soln of cyclopentanone oxime (9.9 g, 0.1 mole), 2.5 *N* KOH (50 ml), and Me_2CO (10 ml) was treated dropwise with $PhSO_2Cl$ (18 g, 0.1 mole). The temp of the resultant mixt was maintained at −10° for 1 hr. The reaction mixt was then extd with 100 ml of C_6H_6, and the C_6H_6 ext was washed with 50 ml of H_2O and dried ($MgSO_4$). 2,6-Dichloroaniline (16.2 g, 0.1 mole) was then added to the dried C_6H_6 ext, and the mixt was heated to reflux overnight. The reaction mixt was cooled to room temp and extd with H_2O (2 × 75 ml). The aq ext was made alk by adding 30 ml of 2.5 *N* NaOH. The alk mixt was cooled in ice water, and 1.6 g (7%) of a brown solid, mp 136–141°, was collected. Recrystn (EtOH–H_2O) provided a light tan solid, mp 143–145°, HCl salt, mp 283–284°. *Anal.* ($C_{11}H_{12}Cl_2N_2 \cdot HCl$) C, H, N, Cl.

2-(2,6-Dichlorobenzyl)amino-1-pyrroline·HCl (25).—A soln of 2,6-dichlorobenzylamine·HCl[10] (4.25 g, 0.02 mole) and 2-methoxy-1-pyrroline[11] (3.95 g, 0.04 mole) in 75 ml of $CHCl_2$ was heated to reflux for 48 hr. The reaction mixt was cooled and evapd to dryness *in vacuo*. Trituration of the residue with Et_2O provided 5.05 g (90%) of a colorless solid, which did not melt <280°. *Anal.* ($C_{11}H_{12}Cl_2N_2 \cdot HCl$) C, H, N, Cl.

2-(2,6-Dichlorophenyl)ethylamine Acetate.—A soln of 2,6-dichlorophenylacetonitrile (22.3 g, 0.12 mole) in AcOH (200 ml) was hydrogenated at room temp (4 atm) using Raney Ni catalyst. After consumption of the theor quantity of H_2, the catalyst was filtered, and the filtrate was evapd to dryness *in vacuo*. Recrystn of the residue from EtOAc furnished 18.9 g (63%) of colorless needles, mp 166.5–167.5°. *Anal.* ($C_{14}H_{13}Cl_2NO_2$) C, H.

2-(2,6-Dichlorophenethyl)amino-1-pyrroline·HCl (26).—A soln of 2-(2,6-dichlorophenyl)ethylamine in $CHCl_3$ was prepd by treating the acetate salt (5.0 g, 0.02 mole) with 100 ml of 2.5 *N* NaOH, and then extg the alk mixt with 100 ml of $CHCl_3$. The $CHCl_3$ layer was then added to a soln of 2-methoxy-1-pyrroline (3.95 g, 0.04 mole) in 50 ml of $CHCl_3$. The $CHCl_3$ mixt was heated to reflux for 48 hr and then evapd to dryness *in vacuo*. Recrystn of the residue from petr ether (40–60°) yielded 3.6 g (94%) of brown needles, mp 123.5–125°; HCl salt, mp 238.5–240.5°. *Anal.* ($C_{12}H_{14}Cl_2N_2 \cdot HCl$) C, H, N, Cl.

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(11) S. Petersen and E. Tietze, *Chem. Ber.*, **90**, 909 (1957).

Antihypertensive and Monoamine Oxidase Inhibitory Activity of Some Azacycloalkyl-Substituted Benzaldehyde Hydrazone Derivatives

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The hydrazones derived by condensation of certain azacycloalkyl-substituted benzaldehydes with 3-amino-2-oxazolidinone were evaluated for their antihypertensive and MAO-inhibitory activity. Some of these compds were more potent than pargyline in their antihypertensive response. However, they were less active than pargyline as regards MAO inhibition. The most potent compd of the series was *N*-[2-*N*-methylpiperazino-5-nitrobenzylidene]-3-amino-2-oxazolidinone. There was no direct correlation between the antihypertensive effect and MAO inhibition in this series.

Furazolidone, *N*-[5-nitro-2-furfurylidene]-3-amino-2-oxazolidinone, has been reported to produce slow, gradual reduction of arterial blood pressure in patients with primary hypertension when administered orally.[1] Confirmation of the significant hypotensive effect of furazolidone at high doses in hypertensive patients has been provided by other workers.[2] This substance is also reported to produce irreversible inhibition of monoamine and diamine oxidase in the rat liver and brain.[3] *N*-[1-(5-Nitro-2-furyl)ethylidene]-3-amino-2-oxazolidinone, a compd closely related to furazolidone, is reported to produce a slight hypotensive effect in anesthetized dogs.[4] The present report deals with the evaluation of the antihypertensive and MAO-inhibitory activities of certain hydrazones derived by condensation of certain azacycloalkyl-substituted benzaldehydes with 3-amino-2-oxazolidinone.

Chemistry.—Starting from 2-chloro-5-nitrobenzaldehyde[5] the 3-amino-2-oxazolidinone derivative Ic was prepared by treatment of the β-hydroxyethyl hydrazone derivative Ib with $COCl_2$. By treatment of 2-chloro-5-nitrobenzaldehyde, 3-nitro-4-chlorobenzaldehyde,[6] and 3-chloro-4-nitrobenzophenone[7] with cyclic secondary amines, the corresponding substituted

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(2) V. C. Desiderio and J. R. Beem, *Proc. Soc. Exp. Biol. Med.*, **100**, 343 (1959).
(3) D. Palm, U. Magnus, H. Grobecker, and J. Jonsson, *Arch. Exp. Pathol. Pharmakol.*, **256**, 281 (1967).
(4) A. I. Eldin, J. P. Buckley, W. J. Kinnard, and M. D. Aceto, *Arch. Int. Pharmacodyn.*, **149**, 434 (1964).
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(6) H. H. Hodgson and H. G. Beard, *J. Chem. Soc.*, 20 (1927).
(7) R. B. Davis and L. C. Pizzini, *J. Org. Chem.*, **27**, 1605 (1962).

nitrobenzaldehydes and nitrobenzophenones were obtained. Condensation with 3-amino-2-oxazolidinone, methylhydrazine, and β-hydroxyethylhydrazine gave the corresponding hydrazones. Guanyl hydrazones were obtained in an analogous way. Hydrogenation of the nitrobenzylidene derivatives using Pd/C gave the corresponding amino compds. In the case of IIa hydrogenation as above gave the bimolecular condensation product IIa.

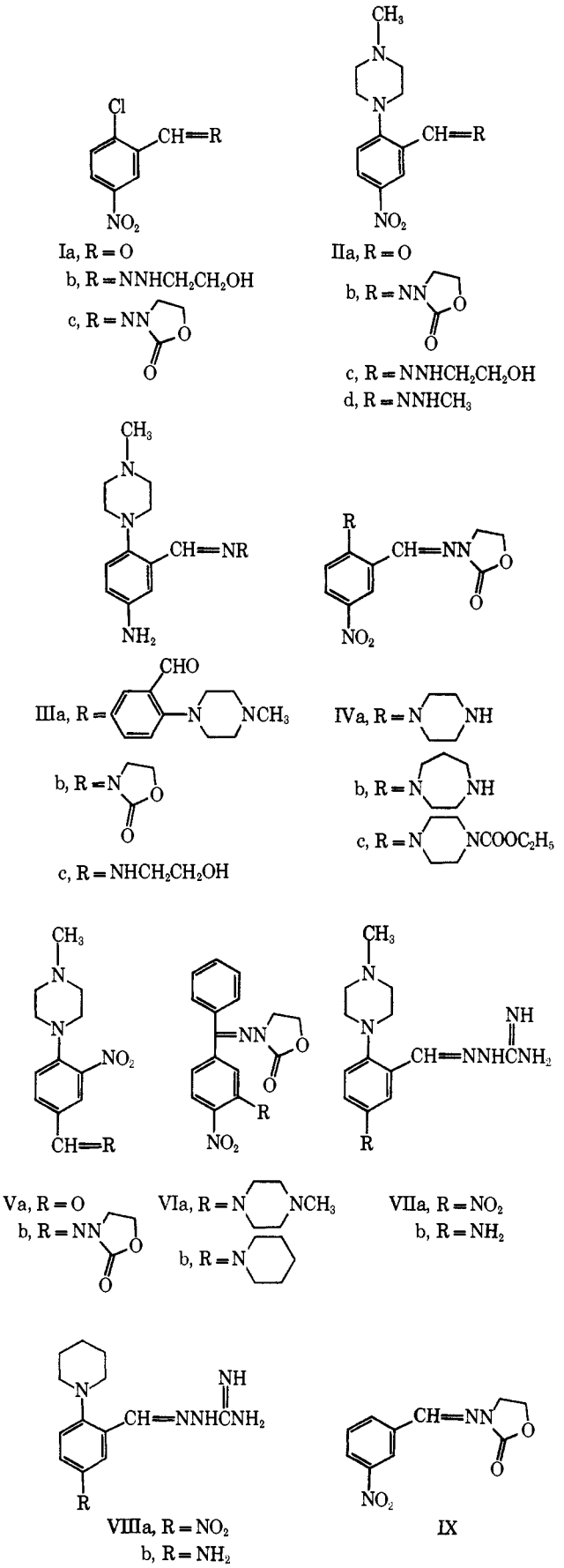
Results and Discussion

Most of the compds including pargyline did not show any marked hypotensive activity in normotensive anesthetized animals except IIb and VIIb (Table I). Although these compds were not active in acute experiments, most of them showed good antihypertensive response in renal hypertensive rats. The antihypertensive activity of many of the compds was comparable to that of pargyline which was used as a standard drug. Like pargyline, most of the compds did inhibit MAO from rat brain homogenates *in vivo*. The degree of inhibition was slightly less than that of pargyline. Out of the 2 compds which showed good hypotensive response, we selected IIb for detailed study because VIIb did not show any antihypertensive effect.

Compd IIb produced a prolonged fall of blood pressure of about 40 to 60 mm at 1 mg/kg iv in anesthetized dogs and cats. The substance was orally absorbed in both the species. It lowered the blood pressure of renal hypertensive rats by −42 and −100 mm at 30 and 100 mg/kg po, resp, given for 10 days. Pargyline at similar doses was approximately half as active (Table I). Like many other MAO inhibitors, this compd showed weak and transient ganglion-blocking activity as measured by preganglion inhibition (62% inhibition of preganglionic and 15% inhibition of postganglionic fibers at 9 mg/kg iv). No significant effect on the inotropic and chronotropic effect of the isolated cat heart was observed up to 1 mg. The coronary flow was, however, increased by about 25%. The toxicity of this compd was low as compared to pargyline (LD_{50} in mice; 678 ± 64 mg/kg iv).

In vivo, IIb produced a marked inhibition of MAO of rat brain homogenates when given orally or ip. Unlike pargyline which is more active when given ip, IIb was equiactive by either route. The approximate ED_{50} values in mg/kg are for pargyline 45 and 27 and for IIb 71 and 75 po and ip, resp (Figure 1). Although the onset of activity of IIb was rather slow as compared to pargyline, the duration of action was fairly long (Figure 2); 72 hr after single dose administration 50% of the enzyme activity was still inhibited (Figure 2).

Despite the fact that this substance exhibited fairly good *in vivo* MAO inhibitory activity, the substance was not very active *in vitro*. Even a dose of 1×10^{-3} *M* produced only 50% inhibition of the MAO. Dosage beyond this was not tried as there was precipitation of the compd on incubation. The failure of IIb to produce any marked inhibition of MAO *in vitro* at low doses was rather surprising in view of the fact that this substance was quite active *in vivo*. It is possible that this substance gets metabolized *in vivo* to some other compds which produces the marked effect observed *in vivo*. Similar observations have been reported by Everett, *et al.*,[8] with a compd which was a potent MAO inhibitor *in vivo* but not *in vitro*.



(8) G. M. Everett, R. G. Wiegand, and F. U. Rinaldi, *Ann. N. Y. Acad. Sci.*, **107**, 1068 (1963).

TABLE I

ANTIHYPERTENSIVE AND MAO-INHIBITORY ACTIVITY OF SOME AZACYCLOALKYL-SUBSTITUTED BENZALDEHYDE HYDRAZONE DERIVATIVES

Compd	Hypotensive act[a] Cat	Hypotensive act[a] Dog	Antihypertensive effect[b]	MAO inhibition, %[c] Kynuramine	MAO inhibition, %[c] 5-HT	Remarks
IIa	−	0	0 (30)	0		
IIb	++	+++	−42 (30)	69	72	Orally absorbed
			−100 (100)	32	46	Orally absorbed
IIc	−	+	−85 (100)	40	30	Orally absorbed, liver toxicity
IId	+	+	0 (30)	43		
IIIa	−	−		0		
IIIb	++	++	−34 (100)	46	31	Orally absorbed
IIIc	++	++	−60 (100)	31	46	Orally absorbed
IVa	−	−		0	0	
IVb	+	++	−32 (100)	55		Orally inactive
IVc	−	0		0	0	
Vb	−	0	−32 (100)	0	20	
VIa	−	0	−43 (30)	84	60	
VIb	0	0		0	0	
VIIa	++	++	0	0	0	Orally inactive
VIIb	−	+++	0	0	0	
VIIIb	−	0		0	0	
IX	0	−	−15 (30)	0		
Pargyline	⊕	−	−25 (30)	73	57	
			−47 (100)	53	39	

[a] By hypotensive activity is meant that the fall of blood pressure was more than 15 mm and lasted for more than 15 min. (+) Activity at 9 mg/kg iv; (++) activity at 3 mg/kg iv; (+++) activity at 1 mg/kg iv; (0) no activity; (⊕) no activity up to 15 mg/kg iv. [b] Numbers in parentheses are dosages in mg/kg po. [c] For MAO inhibition studies the compds were given at 100 mg/kg po and animals killed 16 hr later. Wherever there are 2 inhibitions reported in the Table, the second one refers to 50 mg/kg po.

TABLE II[a]

Treatment	Tissue	% Increase NE	% Increase Dopamine	% Increase 5-HT
Pargyline	Brain	59 ($P < 0.01$)	22	138 ($P < 0.001$)
Pargyline	Heart	16		
IIb	Brain	39 ($P < 0.01$)	24	32 ($P < 0.05$)
IIb	Heart	19		

[a] *In vivo* effect of pargyline and IIb (100 mg/kg po) on norepinephrine, dopamine, and 5-hydroxytryptamine content of rat tissues. All animals were killed 16 hr after treatment. Control levels of norephinephrine (NE), dopamine, and 5-hydroxytryptamine (5-HT) were 0.32 ± 0.02 (brain), 0.75 ± 0.02 (heart), 0.50 ± 0.02, 0.33 ± 0.01, resp.

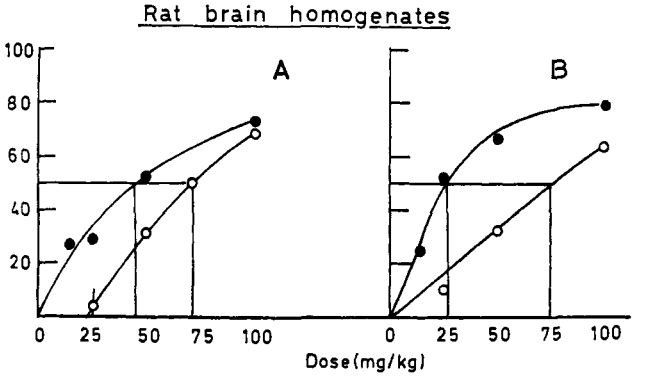


Figure 1.—*In vivo* effect of different doses of IIb (open circles) and pargyline (closed circles) on MAO-inhibitory activity of rat brain homogenates, (A) po, (B) ip, using kynuramine as a substrate. All inhibitions were calcd for an incubation period of 0.5 hr. Each value is the mean of at least 2 observations. Note that pargyline is more active when given ip than po but IIb is equiactive when given po and ip. Values on the ordinate are per cent inhibition.

Substance IIb depicts typical effects of MAO inhibitors in experimental animals. It potentiates the effect of epinephrine and norepinephrine on the blood pressure, antagonizes reserpine-induced hypothermia (60% at 25 mg/kg po), and gives a positive "dopa test."[9] Like many other MAO inhibitors, IIb increased the levels of biogenic amines, namely norepinephrine, dopamine, and 5-hydroxytryptamine. Significant increase in the brain norepinephrine and 5-hydroxytryptamine was observed with both pargyline and IIb. However, the effect on the heart norepinephrine and brain dopamine was less marked (Table III).

Although the hydroxyethylhydrazone derivative IIc showed good antihypertensive and MAO-inhibiting properties, it was associated with liver toxicity. The methylhydrazone analog IId did not show any antihypertensive activity. The amino compds IIIb and IIIc obtained by catalytic reduction of IIb and IIc showed activity of a much lesser order. Compds obtained by replacement of *N*-methylpiperazino by piperazino, homopiperazino, or *N*-carbethoxypiperazino groups (IVa–c) showed reduced activity. Vb, in which the relative positions of the nitro- and the aminooxazolidinone residue with respect to the *N*-methylpiperazino group are interchanged, was devoid of any MAO-inhibiting activity, although retaining a low degree of antihypertensive activity. Guanyl hydrazone VIIb showed marked hypotensive properties in anesthetized animals but had no antihypertensive or MAO-inhibiting activity. The condensation product of *m*-nitrobenzaldehyde with 3-amino-2-oxazolidinone showed neither MAO inhibition nor antihypertensive activity.

Generally speaking in this series all the compds which showed MAO inhibition *in vivo* did exhibit antihypertensive response. However, the relationship between the MAO inhibition and antihypertensive response was not very good, *e.g.*, maximum inhibition of MAO

(9) G. M. Everett, *Antidepressant Drugs, Proc. Int. Symp., 1st*, **1966**, 164 (1967).

TABLE III

Compd	Method	Mp, °C	Solvent of recrystn	Yield, %	Formula	Analysis
Ib	B	85	MeOH	76	$C_9H_{10}ClN_3O_3$	C, H, Cl
Ic	B	218	$CHCl_3$–MeOH	32	$C_{10}H_8ClN_3O_4$	C, H, N
IIa	A	159	CH_2Cl_2–hexane	61	$C_{12}H_{15}N_3O_3$	C, H, N
IIb	B	243–244	$CHCl_3$	71	$C_{15}H_{19}N_5O_4 \cdot HCl \cdot 0.5H_2O$	C, N, N
IIc	B	188	$CHCl_3$	66	$C_{14}H_{21}N_5O_3 \cdot 2HCl$	C, H, N
IId	B	200	CH_2Cl_2–MeOH	63	$C_{13}H_{19}N_5O_2 \cdot 2HCl$	C, H, Cl
IIIa	C	310	MeOH–dioxane	68	$C_{24}H_{32}N_6O$	C, H, N
IIIb	C	287	$CHCl_3$–EtOH	64	$C_{15}H_{21}N_5O_2 \cdot 2HCl \cdot H_2O$	C, H, Cl
IIIc	C	152	$CHCl_3$–MeOH	57	$C_{14}H_{23}N_5O$	C, H, N
IVa	A	190	MeOH	31	$C_{14}H_{17}N_5O_4$	C, H, N
IVb	A	160	MeOH–CH_2Cl_2	61	$C_{15}H_{19}N_5O_4 \cdot 2HCl$	C, H, N
IVc	A	237	MeOH–CH_2Cl_2	57	$C_{12}H_{15}N_3O_3$	C, H, N
Va	A	81	CH_2Cl_2–hexane	60	$C_{12}H_{15}N_3O_3$	C, H, N
Vb	B	183	MeOH	62	$C_{15}H_{19}N_5O_4 \cdot HCl \cdot H_2O$	C, H, Cl
VIa	A, B	235	C_2H_5OH	63	$C_{21}H_{23}N_5O_4 \cdot HCl$	C, H
VIb	A, B	208	C_2H_5OH	58	$C_{21}H_{22}N_4O_4$	C, H, N
VIIa	B	295	MeOH	54	$C_{13}H_{19}N_7O_2 \cdot 2HCl \cdot 0.5H_2O$	C, H, N
VIIb	C	283	MeOH	57	$C_{13}H_{21}N_7 \cdot 3HCl$	C, H, N
VIIIa	B	236	C_2H_5OH	47	$C_{13}H_{18}N_6O_2$	C, H, N
VIIIb	C	244	C_2H_5OH	59	$C_{13}H_{20}N_6$	C, H, N
IX	B	193	C_2H_5OH	69	$C_{10}H_9N_3O_4$	C, H, N

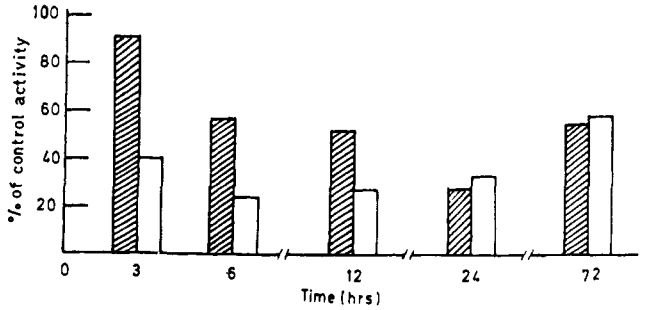


Figure 2.—*In vivo* effect of IIb (100 mg/kg po, crossed columns) and pargyline (100 mg/kg po, open columns) on the MAO-inhibitory activity of rat brain homogenates (using kynuramine as a substrate). All inhibitions were calcd for an incubation period of 0.5 hr. Each value is the mean of at least 2 observations. Note the delay in the onset of action of IIb as compared to pargyline but the duration of action is similar to pargyline (at least up to 72 hr).

was seen 16 hr after treatment with these compds but the antihypertensive effect was not seen up to 2–3 days. It has been suggested that the hypotensive action of MAO inhibitors is not related to MAO inhibition.[8,10]

Despite the fact that this series of compds showed good antihypertensive activity along with low toxicity, they were not studied further because of the side effects (hypertensive crisis, etc.) associated with MAO inhibitors in the clinic.

Experimental Section

Melting points were taken in glass capillary tubes and are uncorrected.

N-(**2-Chloro-5-nitrobenzylidene**)-**3-amino-2-oxazolidinone** (**Ic**).—A mixt of 2-chloro-5-nitrobenzaldehyde (Ia, 7.44 g) and β-hydroxyethylhydrazine (3.34 g) in EtOH (100 ml) contg concd HCl (2 drops) was heated under reflux for 4 hr. The solid obtd on evapn of the solvent was treated with dil $NaHCO_3$, filtered, and recrystd from MeOH to give the hydrazone Ib, mp 85°. A suspension of Ib (12 g) in a satd soln of $COCl_2$ in PhMe was stirred while bringing the soln to reflux. Refluxing was contd and the prod was filtered and worked-up in the usual way to give 4.1 g of Ic, mp 218°, from $CHCl_3$–MeOH.

General Methods. A. Prepn of Substituted Nitrobenzaldehydes and Nitrobenzophenones.—Chloronitro compd (1 mole) and the amine (1.1 moles) were refluxed together in dioxane for 4 hr. The prod was collected by filtration or by evapn of the solvent, treated with dil $NaHCO_3$, filtered, and recrystd from the appropriate solvent.

B. Condensn of Nitrobenzaldehydes and Nitrobenzophenones with 3-Amino-2-oxazolidinone and Other Substituted Hydrazines.—The aldehyde (1 ml) was refluxed with the appropriate hydrazine (1.1 ml) in EtOH contg concd HCl (2 drops), and the reaction prod was worked up as described for Ib.

C. Hydrogenation of the Nitrobenzaldehydes to Aminobenzaldehydes.—A mixt of the nitrobenzaldehyde (5 g) and Pd/C (10%, 1 g) was shaken in a hydrogenation apparatus at normal temp and pressure until 3 moles of H_2 were absorbed. The suspension was filtered, and the filtrate was evapd. The residue was recrystd from the appropriate solvent.

Pharmacological Experiments. (a) Effect on Blood Pressure.—Dogs and cats of either sex were anesthetized with pentobarbital, 35 mg/kg iv and 45 mg/kg ip, resp. The blood pressure was recorded from a carotid artery. The effect of various compds was investigated by iv and intraintestinal routes.

(b) Renal Hypertensive Rats.—Renal rats were prepared according to the method of Goldblatt, *et al.*,[11] They were given 30 and 100 mg/kg po of the compd once a day for 10 days. The blood pressure was measured by a plethysmographic method from the tail of a rat under light ether anesthesia.[12]

(c) Isolated Perfused Heart.—Lagendorff's method was used. The effect on the inotropic, chronotropic, and coronary flow was observed after treatment with the compd.

(d) Effect on the Nictitating Membrane of the Cat.—The contractions of the nictitating membrane were elicited by stimulations of the pre- and postganglionic fibers of the cervical sympathetic chain (3.2 V, 32 cps, 0.42 duration for 10 sec) in pentobarbital-anesthetized cats.

(e) **Catecholamine Estimation.**—The tissues were extd with 2% PCA, adsorbed on acid-washed alumina at pH 8.4, and eluted with 0.2 *N* AcOH as described by Crout, *et al.*[13] Dopamine was estimated as described by Carlsson and Waldeck[14] with some modifications.[15]

(f) Monoamine Oxidase Inhibition.—MAO inhibition in the rat brain homogenate was measured using 2 different substrates,

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(14) A. Carlsson and B. Waldeck, *Acta Physiol. Scand.*, **44**, 293 (1958).

(15) A. Carlsson and M. Lindquist, *ibid.*, **54**, 87 (1962).

kynuramine[16,17] and 5-hydroxytryptamine.[18] In the case of kynuramine, the appearance of 4-hydroxyquinoline was measured, and in the case of 5-hydroxytryptamine, its disappearance. The endogenous 5-HT content of the brain was also measured, according to the method of Anden and Magnusson.[18]

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(17) M. Krajl, *Biochem. Pharmacol.*, **14**, 1684 (1965).
(18) W. E. Anden and T. Magnusson, *Acta Physiol. Scand.*, **69**, 87 (1967).

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Antihypertensive and Monoamine Oxidase Inhibitory Activity of Some Derivatives of 3-Formyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine

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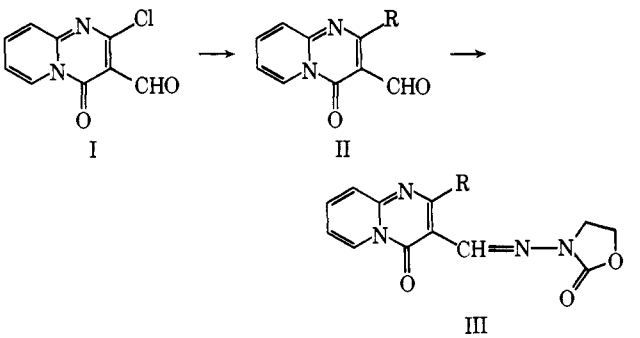
The antihypertensive and MAO-inhibitory activity of a variety of compounds derived from 2-chloro-3-formyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine are described. The most potent among these compds were the 3-amino-2-oxazolidinone derivatives of 2-piperidino-3-formyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine and its tetrahydro and hexahydro derivatives. The correlation between the MAO inhibition and antihypertensive response was not very good. The toxicity of the compds was very low as compared to other MAO inhibitors.

It has been previously reported[1] that 3-amino-2-oxazolidinone derivatives of some azacycloalkyl-substituted nitrobenzaldehydes showed marked antihypertensive and MAO-inhibitory activity. Compds wherein the NO_2 was replaced by NH_2 failed to show activity. Furazolidinone which is also known to produce slow and gradual reduction in arterial blood pressure, is also derived from a nitroheterocyclic aldehyde, namely, 5-nitrofurfural.[2]

We were interested in preparing a few derivatives of 2-chloro-3-formyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine[3] for biological evaluation. Treatment of this compd with secondary amines gave the corresponding ortho-substituted amino compds which on condensation with 3-amino-2-oxazolidinone showed pronounced antihypertensive and MAO-inhibitory activity. The structural pattern required for eliciting optimum antihypertensive and MAO-inhibiting properties in pyrido[1,2-*a*]pyrimidine series was found to be different from the one found in the series described earlier.[1] The toxicity of these compds was also found to be very low.

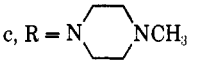
Chemistry.—2-Chloro-3-formyl-4-oxo-4*H*-pyrido-[1,2-*a*]pyrimidine (I)[3] was treated with an excess of primary and secondary amines to give the corresponding secondary and tertiary amino substituted aldehydes IIa–IIg which on condensation with 3-amino-2-oxazolidinone gave compds IIIa–IIIg. Direct condensation of I with the above reagent gave IIIh. Controlled catalytic hydrogenation of IIIa and IIIb with Pd/C until 2 moles of H_2 was absorbed, gave IVa and IVb, resp. Hydrogenation of IIIa using 10% Pd/C until 3 moles of H_2 was absorbed gave Va. Treatment of the latter with ethyl isocyanate gave Vb. Reaction of IIa and IIc with amioguanidine hydrogen carbonate in EtOH containing AcOH gave VIa and VIb, resp. Condensation of IIa with *N*-aminopiperidine and 4-amino-1,2,4-triazole gave VIIa and VIIb, resp.



I, II, III

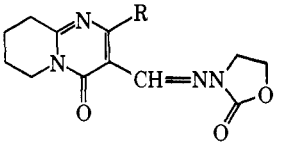
a, R = N⟨ ⟩

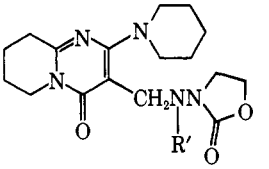
b, R = N⟨ ⟩



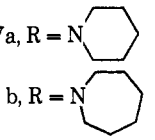
c, R = N⟨ ⟩NCH$_3$

d, R = NEt_2
e, R = $N(CH_2CH{=}CH_2)_2$
f, R = $NHCH_2CH_2N(CH_3)_2$
g, R = $NHCH_3$
h, R = Cl



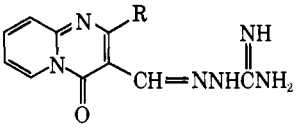


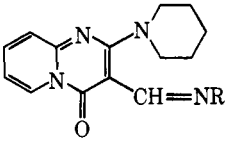
IVa, R = N⟨ ⟩



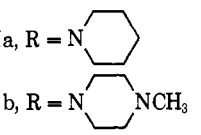
b, R = N⟨ ⟩

Va, R′ = H
b, R = $CONHC_2H_5$



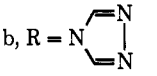


VIa, R = N⟨ ⟩



b, R = N⟨ ⟩NCH$_3$

VIIa, R = N⟨ ⟩



b, R = N⟨ ⟩

(1) T. George, C. L. Kaul, R. S. Grewal, and D. V. Mehta, *J. Med. Chem.*, **14**, 909 (1971).
(2) B. Calesnick, *Amer. J. Med. Sci.*, **236**, 736 (1958).
(3) E. A. Ingalls and F. D. Popp, *J. Heterocycl. Chem.*, **4**, 523 (1967).