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SYNTHESIS OF RATIONALLY DESIGNED ORGANIC COMPOUNDS FOR MALARIA --ETC(U)

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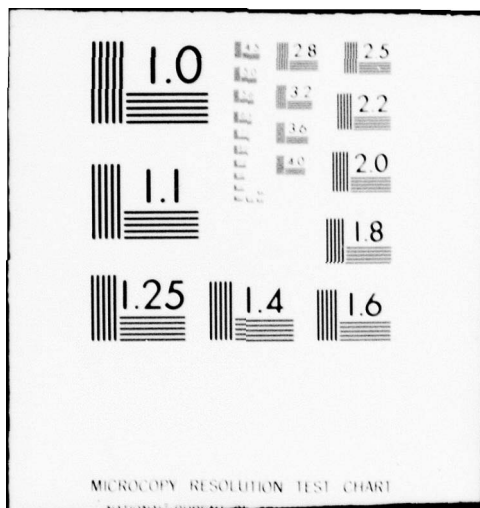
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SYNTHESIS OF RATIONALLY DESIGNED ORGANIC COMPOUNDS  
FOR MALARIA CHEMOTHERAPY STUDIES

FINAL REPORT

(1 August 1975 to 31 March 1978)

LEVEL #

by

C. C. Cheng, Ph.D.

May 1978

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Kansas City, Missouri 64110

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) During the past 12 years, 561 compounds of 15 categories were synthesized, characterized, and submitted for antimalarial evaluation. Three working hypotheses were developed for rational design of antimalarial agents. A total of 20 publications resulted from our study.		

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### SUMMARY

The purpose of the work performed is to rationally design and synthesize selected novel organic compounds for malaria chemotherapy studies. Compounds prepared and studied include derivatives of monocyclic and polycyclic aromatic (benzene, naphthalene, and phenanthrene) and heterocyclic compounds (benzimidazole, 2,9-diazaanthracene, imidazole, imidazoline, isoxazole, phenothiazine, pyrazole, pyrazolo[3,4-d]-v-triazine, pyrimidine, quinazoline, quinoline, quinoxaline, sydnone and related mesoionic compounds, tetrahydrofuran, thiadiazole, thiazole and thiazolidine. This report was prepared at Midwest Research Institute under Contract No. DAMD-17-76-C-6015.

More than 500 compounds were synthesized, characterized and submitted to WRAIR for biological testing. The structures of all the compounds synthesized are enclosed in this report. Among these compounds submitted, many were found to possess antimalarial activity against Plasmodium berghei in mice, against P. gallinaceum in chicks, as well as prophylactic activity in sporozoite-induced mouse and chick tests.

A total of 20 publications resulting from our work done in connection with the malaria study appeared in the following journals: Journal of Heterocyclic Chemistry, Journal of Medicinal Chemistry, Journal of Pharmaceutical Sciences, Journal of Theoretical Biology, and Mikrochimica Acta.

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FOREWARD

This report was prepared at Midwest Research Institute under Contract No. DAMD-17-76-C-6015 with the U.S. Army Medical Research and Development Command. The work was carried out under the direction of Dr. C. C. Cheng, Principal Investigator. The synthetic work was performed by Dr. C. C. Cheng, Dr. Ping-Lu Chien, Dr. Shou-Jen Yan, and Mr. William H. Burton.

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## I. INTRODUCTION

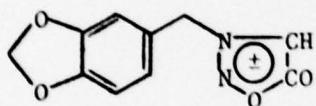
This is the Final Report from Midwest Research Institute (MRI) under Contract No. DAMD-17-76-C-6015 with the U.S. Army Medical Research and Development Command on synthesis of rationally designed organic compounds for malaria chemotherapy studies. The present contract, which covered the period from 1 June 1975 through 30 September 1977, is a continuation of the Contract No. DA(DA)-49-193-MD-2749 which covered the period from 1 June 1965 through 31 May 1975.

A total of 40 compounds have been synthesized, characterized, and submitted for antimalarial evaluation. These compounds, together with 521 compounds prepared during the aforementioned earlier contract, comprised a total of 561 compounds synthesized by the Medicinal Chemistry Section of Midwest Research Institute for the Walter Reed Army Institute of Research of the U.S. Army Medical Research and Development Command.

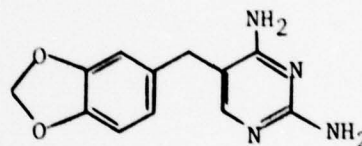
## II. RESULTS AND DISCUSSION

### A. 3-Piperonylsydnone and Related Compounds

The unique antimalarial activity exhibited by 3-piperonylsydnone prompted us to search for its mode of action and better analogs by synthesizing its possible precursors and metabolites as well as structural modifications of the parent compound. This included the preparation of other piperonyl-substituted sydnone and related mesoionic compounds (anhydro-1,2,4-triazolium hydroxides, anhydro-1,3,5-oxadiazolium hydroxides, anhydro-1,2,3,4-oxatriazolium hydroxides) as well as piperonyl-substituted pyrazoles, isoxazoles, thiazoles, 1,3,4-oxadiazoles, 1,3,4-thiadiazoles, 1,2,4-triazoles, imidazoles, tetrazoles, pyrimidines, and 1,2,4-triazines. All WR designation numbers are provided together with structures and names of compounds in Section III to assist in retrieval of data.



A-1 (WR-4033)



A-2 (WR-40070)

Among these compounds, 3-piperonylsydnone (A-1, WR-4033) was shown to be active against *P. berghei*. 2,4-Diamino-5-piperonylpyrimidine (A-2, WR-40070) was found also to be active against *P. berghei* in mice, against *P. gallinaceum* in chicks, and inhibited the growth of *Streptococcus faecalis*, *Lactobacillus casei* and *Pediococcus cerevisiae*. Its pattern of action was found to be different from that of a closely related compound, trimethoprim [2,4-diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine].

#### Antimalarial activity against *Plasmodium berghei*:

Compound	Dosage (mg/kg)				
	80	160	320	640	1,280
WR-4033	+5.6	+8.2	+11.4	+15.8	5T
WR-40010	+1.2	+4.8	+5.6	2C	

Detailed discussion and experimental procedures have been reported in our Annual Progress Reports Nos. 1 through 5 as well as in the following publications:

W. H. Nyberg and C. C. Cheng, "3-Piperonylsydnone. A New Type of Antimalarial Agent," *J. Med. Chem.*, **8**, 531 (1965).

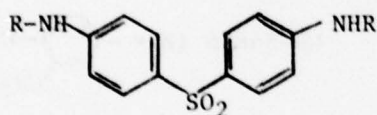
S. G. Boots and C. C. Cheng, "Structural Modification Studies of 3-Piperonylsydnone. I. Synthesis of Piperonyl-Substituted Pyrazoles, Isoxazoles, Triazoles, Oxadiazoles and Thiadiazoles," *J. Heterocycl. Chem.*, **4**, 272 (1967).

W. H. Burton, W. L. Budde, and C. C. Cheng, "Structural Modification Studies of 3-Piperonylsydnone. II. Synthesis of Piperonyl-Substituted Hydantoin, Thiohydantoin, Thiazolidinedione, Rhodanine, Imidazolinone, and Related Compounds," *J. Med. Chem.*, **13**, 1009 (1970).

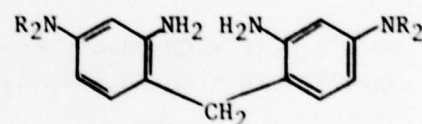
D. J. McCaustland, W. H. Burton, and C. C. Cheng, "Structural Modification of 3-Piperonylsydnone. III. Some Analogs of 3-Piperonylsydnone and 2,4-Diamino-5-piperonylpyrimidine," *J. Heterocycl. Chem.*, **8**, 89 (1971).

#### B. Phenothiazine Dioxides

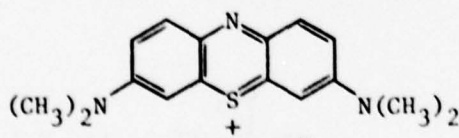
A combination of the essential structural features of the anti-malarials 4,4'-diaminodiphenyl sulfone (DDS, B-1a), its acetylated derivative B-1b (DADDS), 2,4-bis(substituted amino)diphenylmethanes (B-2), and Methylene Blue (B-3) has resulted in the synthesis of five 2,7-bis(substituted amino)phenothiazine 5,5-dioxides (B-4).



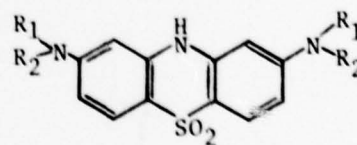
B-1a. R = H  
b. R = COCH<sub>3</sub>



B-2



B-3



B-4

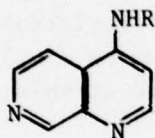
WR-28450 (R<sub>1</sub> = H, R<sub>2</sub> = COCH<sub>3</sub>)  
WR-28776 (R<sub>1</sub>, R<sub>2</sub> = H)  
WR-30210 (R<sub>1</sub> = H, R<sub>2</sub> = C<sub>2</sub>H<sub>5</sub>)  
WR-30211 (R<sub>1</sub> = H, R<sub>2</sub> = CH<sub>3</sub>)  
WR-31872 (R<sub>1</sub>, R<sub>2</sub> = CH<sub>3</sub>)

Antimalarial evaluation results revealed that compounds of this type did not show activity against *P. berghei* in mice. Apparently the rigid phenothiazine dioxide ring system failed to retain the original antimalarial activity of B-1, B-2 and B-3.

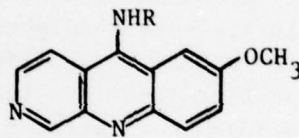
For detailed discussion and experimental procedures, see our Annual Progress Report No. 1 and the following publication: P.-L. Chien and C. C. Cheng, "2,8-Bis(substituted amino)phenothiazine 5,5-Dioxides," *J. Med. Chem.*, **9**, 960 (1966).

### C. 1,7-Naphthyridines and Related Derivatives

A number of 4-(substituted amino)-1,7-naphthyridines (C-1) and 6-methoxy-10-(substituted amino)-2,9-diazaanthracenes (C-2) were synthesized as the appropriate aza analogs of antimalarial 4-aminoquinolines such as chloroquine (C-3), and 9-aminoacridines such as quinacrine (C-4), respectively.

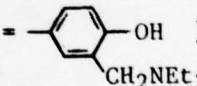


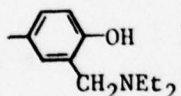
C-1

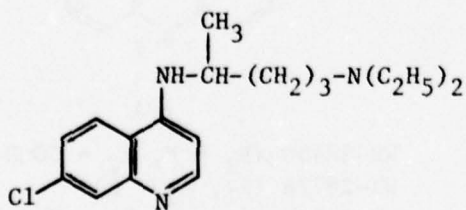


C-2

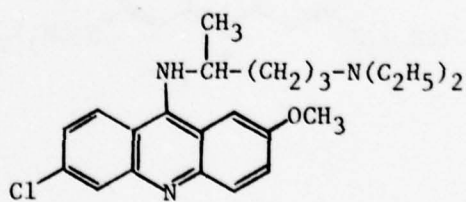
WR-47710 (R = CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NEt<sub>2</sub>)  
 WR-47714 (R = CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NEt<sub>2</sub>)

WR-56636 (R = )

WR-8715 (R = )



C-3



C-4

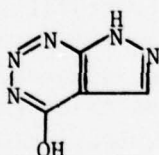
Antimalarial activity against Plasmodium berghei:

<u>Compound</u>	<u>Dosage (mg/kg)</u>					
	<u>20</u>	<u>40</u>	<u>80</u>	<u>160</u>	<u>320</u>	<u>640</u>
WR-8715		+0.7		+2.7		+4.7
WR-47710	+0.5		+0.5		+0.7	
WR-47714		+0.7		+1.3		+4.1
WR-56636	+0.2	+0.2	+1.4	+3.2	+4.8	+6.0

Detailed discussion and experimental procedures of these compounds were given in our Annual Progress Reports Nos. 1 and 2 as well as in the following publication: P.-L. Chien and C. C. Cheng, "Synthesis and Antimalarial Evaluation of Some 1,7-Naphthyridines and 2,9-Diazaanthracenes," J. Med. Chem., 11, 164 (1968).

D. Pyrazolo[3,4-d]-v-triazine and Related Compounds

In connection with our previous work on pyrazolo[3,4-d]pyrimidines, 4-hydroxypyrazolo[3,4-d]-v-triazine (D-1, WR-51898A) and related compounds (WR-10412, WR-10461, WR-10485, WR-45684, WR-51897, WR-81791, WR-90210, WR-92104, WR-92443, WR-94409, WR-95564, AC-16712, AT-70202, and AT-70211) were synthesized. Compounds of this type, which are structural analogs of hypoxanthine, could well be inhibitors of xanthine oxidase and thereby are potential antagonists of purine metabolism. However, antimalarial activity of compounds of this type versus P. berghei was not significant for additional study.



D-1 (WR-51898)

During our synthetic study of the pyrazolo[3,4-d]-v-triazine ring system, a method of introducing a nitro group at position 5 in the pyrazole ring was also uncovered.

Detailed discussion and experimental procedures of these compounds were given in our Annual Progress Reports Nos. 2 and 3 as well as in the following publications:

C. C. Cheng, R. K. Robins, K. C. Cheng, and D. C. Lin, "Pyrazoles. I. Synthesis of 4-Hydroxypyrazolo[3,4-d]-*v*-triazine. A New Analog of Hypoxanthine," *J. Pharm. Sci.*, **57**, 1044 (1968).

C. C. Cheng, "Pyrazoles. II. Reactions of 1-Methyl-5-amino-4-pyrazolecarboxamide and Nitrous Acid. Introduction of a Nitro Group at Position 5 in the Pyrazole Ring," *J. Heterocycl. Chem.*, **5**, 195 (1968).

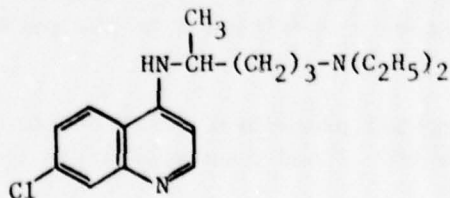
#### E. Pyrimidines, Furoxans, and Furazans

As a means of ensuring the binding of a drug to the erythrocytes, where it may exert its maximum effect on the schizontal form of the malaria parasite, some selected ring systems of biological interest were selected. Some 2,4,5-trisubstituted pyrimidines (AD-488, AD-497, AF-11794, AF-55643, AF-59374, AF-59383, AF-59392, AF-93009, AF-93018, AF-93027, AF-93036, AF-93072, AS-37024, AS-37042, AS-39920, AS-39930, AS-39948, AS-59468, AS-59486, AS-59495, AT-15961, AT-15943, AT-17714, AT-17698, AT-70195, AT-88259, AT-88268, AT-88277, AT-90697, AT90704, and AT-90713), furoxans (AF-12648, AF-12657, AF-16020, AF-55652, AF-55670, AF-55698, AF-93054, AF-93063, AS-37051, AS-37060, AS-39957, AS-39966, AS-59459, AS-59477, AT-17643, and AT-17661) and furazans (AF-16011, AF-55661, AF-55689, AF-59409, AF-59445, AF-93045, AS-37015, AS-37033, AS-37097, and AT-17670) were therefore synthesized.

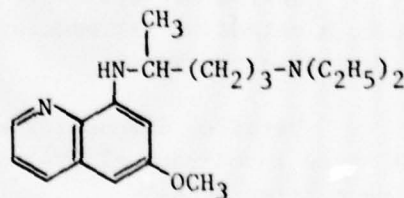
Detailed discussion and experimental procedures were given in our Annual Progress Reports Nos. 3 and 4.

#### F. 1,5-Naphthyridines

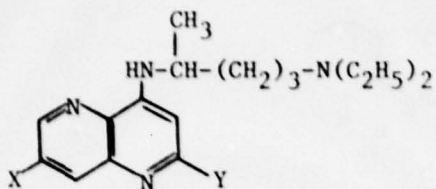
Incorporation of the structural features of chloroquine (F-1, a 4-aminoquinoline derivative and a schizontocidal drug) and pamaquine (F-2, an 8-aminoquinoline derivative and a gametocytocidal drug) resulted in the design and synthesis of 7-chloro-4-(4-diethylamino-1-methylbutylamino)-2-methoxy-1,5-naphthyridine (F-3a), 5-azachloroquine (F-3b), and 5-azapamaquine (F-3c). Further structural modification of 1,5-naphthyridines, wherein a 2-oxo group is incorporated into the naphthyridine ring system (such as F-4a and F-4b), was also studied.



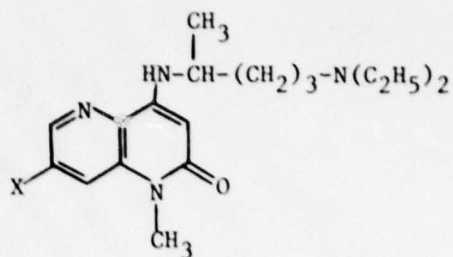
F-1



F-2



- F-3a. X = Cl, Y = OCH<sub>3</sub> (AT-70239)  
 b. X = Cl, Y = H (AU-93237)  
 c. X = H, Y = OCH<sub>3</sub> (WR-90010)



- F-4a. X = H (BG-89344)  
 b. X = Cl (BH-03027)

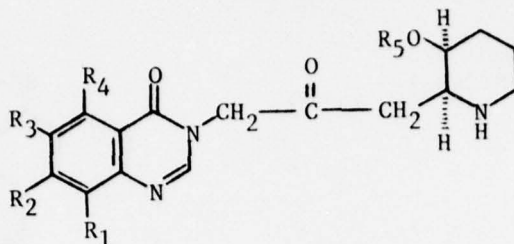
Antimalarial activity against P. berghei:

Compound	Dosage (mg/kg)					
	20	40	80	160	320	640
AU-93237	+0.3	+2.9	+8.5	+8.9	+10.5	+14.2 (1C)
Chloroquine diphosphate	+6.6	+7.4	+8.0	+8.5	10T	10T

Preceding data indicated that 5-azachloroquine (AU-93237) possessed antimalarial activity against P. berghei comparable to that of chloroquine but was less toxic. For detailed discussion and experimental procedures, see our Annual Progress Reports Nos. 2, 3, 4, and 12 as well as the following publication: D. J. McCaustland and C. C. Cheng, "1,5-Naphthyridines. Synthesis of 7-Chloro-4-(4-diethylamino-1-methylbutylamino)-2-methoxy-1,5-naphthyridine and Related Compounds," J. Heterocycl. Chem., 7, 467 (1970).

G. Analogs of Febrifugine

In connection with a structural modification study of the antimalarial alkaloid febrifugine, for which resistance by plasmodia strains has not yet been reported, the following methylenedioxy analogs of febrifugine and related methyl ethers were synthesized.



- G-1a. R<sub>1</sub> + R<sub>2</sub> = OCH<sub>2</sub>O; R<sub>3</sub>, R<sub>4</sub> = H; R<sub>5</sub> = CH<sub>3</sub> (AU-93246)  
 b. R<sub>2</sub> + R<sub>3</sub> = OCH<sub>2</sub>O; R<sub>1</sub>, R<sub>4</sub> = H; R<sub>5</sub> = CH<sub>3</sub> (WR-90212)  
 c. R<sub>2</sub> + R<sub>3</sub> = OCH<sub>2</sub>O; R<sub>1</sub>, R<sub>4</sub>, R<sub>5</sub> = H (WR-92103)  
 d. R<sub>3</sub> + R<sub>4</sub> = OCH<sub>2</sub>O; R<sub>1</sub>, R<sub>2</sub> = H; R<sub>5</sub> = CH<sub>3</sub> (AU-13211)

Antimalarial activity against *P. berghei*:

Compound	Dosage (mg/kg)							
	2.5	5	10	20	40	80	160	320
AU-13211			+1.4	+1.7	+4.9	+5.8	+7.8	5T
AU-93246			+0.3	+0.4	+0.5	+3.4	+4.8	+5.9
WR-90212			+0.6	+1.4	+1.6	+2.8	+4.4	+7.4
WR-92103		+1.3	+1.3	+4.5	+4.9	5T	5T	5T
Febrifugine	+2.1	+4.3	+6.1	+8.8				

Detailed discussion and experimental procedures were reported in our Annual Progress Reports Nos. 2 through 5 and in the following publication: P.-L. Chien and C. C. Cheng, "Structural Modification of Febrifugine. Some Methylenedioxy Analogs," *J. Med. Chem.*, **13**, 867 (1970).

#### H. Phenanthrene Aminoalcohols

A systematic structure-activity relationship study on antimalarial phenanthrene aminoalcohols was conducted, with particular emphasis on the side chain modification. In addition to uncovering many compounds with excellent antimalarial activity (several compounds, such as AX-27845, AX-29812, AX-29821, AY-64567, and AY-65779, possessed activity at 10 mg/kg and are curative at 20 mg/kg against *P. berghei* with no toxicity to the host), the following observations were also made:

1. The antimalarial activity of compounds of type Ar-CHOH-CH<sub>2</sub>-NHR is of slightly higher order than that of type Ar-CHOH-CH<sub>2</sub>-NR<sub>2</sub> (R ≠ H).

2. Alkyl N-substitution in the α-piperidyl function on the side chain yields compounds of activity comparable to those of the corresponding

N-unsubstituted derivatives. In some cases, introduction of an alkyl group facilitates separation of diastereomers.

3. Diastereomers prepared by us possess different antimalarial activity and toxicity.

4. The basicity of the N atom (the "basic center") on the side chain plays an important role in antimalarial activity. For example, substitution on N with an ethoxycarbonyl or an alkyl carbonyl group, which reduces the basicity of the N atom, nullifies the original activity.

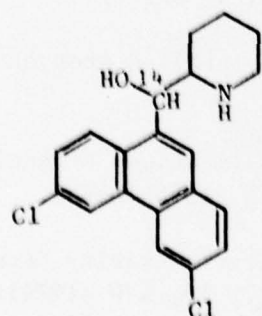
5. The importance of the basic center on the side chain can be further demonstrated by the fact that the activity of several phenanthrene aminoalcohols having bulky groups substituted at the N atom ("concealed" basic centers) on the side chain is reduced or abolished.

6. On the other hand, the presence of more than one basic N on the side chain not only nullifies the antimalarial activity, but sometimes increases toxicity to the host.

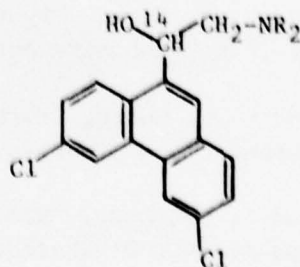
7. The order of activity of three substituted phenanthrene rings studied (with identical aminoalcohol side chains) is: 3,6-bis(trifluoromethyl)- > 3,6-dichloro- > 6-bromophenanthrene.

8. Insertion of a  $-\text{CH}_2-$  linkage between the carbinol carbon and the N atom does not appreciably alter the original activity.

Three  $^{14}\text{C}$ -labeled phenanthrene aminoalcohols (H-1, H-2a and H-2b) were synthesized (WR designation not given).



H-1



H-2a. R =  $(\text{CH}_2)_3-\text{CH}_3$   
b. R =  $(\text{CH}_2)_6-\text{CH}_3$

Antimalarial activity against *P. berghei*:

Compound	Dosage (mg/kg)						
	10	20	40	80	160	320	640
AW-20958 (MO-362)	+0.3	+0.3	+0.5	+7.3	3C	4C	5C
AW-45026 (MO-364)	+0.3	+0.5	+0.7	+7.1	+14.3	3C	5C
AX-20828 (MO-368)	+0.5	+1.1	+15.1	3C	5C	5C	
AX-20837 (MO-367)	+0.7	+0.7	+0.9	+5.9	+14.4	5T	
AX-25476 (MO-371)		+0.3	+0.3	+0.5	+3.7	+5.1	3C
AX-25485 (MO-372)	+3.3	+8.6	+13.9	3C	5C	5C	5C
AX-25903 (MO-373)	+0.5	+0.7	+11.5	3C	5C	5C	5C
AX-27836 (MO-378)	+10.3	+12.7	+16.1	3C	5C	5C	
AX-27845 (MO-379)	+7.9	1C	3C	5C	5C	5C	
AX-28691 (MO-381)	+13.7	+16.3	5C	5C	5C	5C	5C
AX-29812 (MO-383)	+11.1	2C	5C	5C	5C	5C	5C
AX-29821 (MO-384)	+11.3	2C	5C				
AX-58797 (MO-377)	+3.1	+10.1	1C	2C	5C	5C	5C
AX-66628 (MO-388)	+0.3	+0.4	+6.3	+12.8	+2C	5C	5C
AX-68033 (MO-389)	+15.1	4C	5C	5C	5C	5C	5C
AY-61388 (MO-391)	+0.5	+1.1	+5.3	+10.4	2C	4C	5C
AY-62367 (MO-394)	+0.8	+10.4	3C	5C	5C		
AY-64567 (MO-398)	+9.9	3C	5C	5C	5C	5C	5C
AY-65779 (MO-400)	+6.9	2C	4C	5C	5C	5C	5C
AY-99935 (MO-411)	+0.5	+0.5	+0.5	+5.5	1C	2C	5C

Detailed discussion and experimental procedures were given in our Annual Progress Reports Nos. 5 through 9 and in the following publications:

P.-L. Chien, D. J. McCaustland, W. H. Burton, and C. C. Cheng, "Structure-Activity Relationship Studies on Antimalarial Phenanthrene Amine Alcohols. Modification of the Side Chain," *J. Med. Chem.*, 15, 28 (1972).

P.-L. Chien and C. C. Cheng, "Synthesis of Three <sup>14</sup>C-Labelled Phenanthrene Aminoalcohols," *Mikrochimica Acta*, 401 (1973).

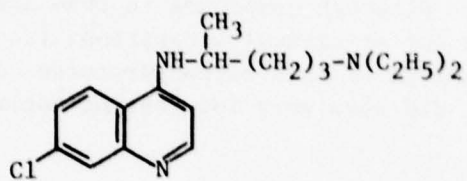
P.-L. Chien and C. C. Cheng, "Further Side Chain Modifications of Antimalarial Phenanthrene Amino Alcohols," *J. Med. Chem.*, 16, 1093 (1973).

P.-L. Chien and C. C. Cheng, "Difference in Antimalarial Activity Between Certain Amino Alcohol Diastereomers," *J. Med. Chem.*, 19, 170 (1976).

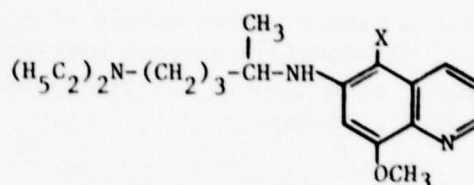
I. Naphthylamines

Several deaza analogs of 4-aminoquinolines (e.g., chloroquine, I-1), 6-aminoquinolines (I-2) and 8-aminoquinolines (e.g., pamaquine, I-3)

were synthesized to study the importance of these ring nitrogen atoms to antimalarial activity. A total of four target compounds [I-4 (WR-94797), I-5a (AY-96121), I-5b (AY-64576) and I-6 (AY-95580)] were prepared for this investigation.

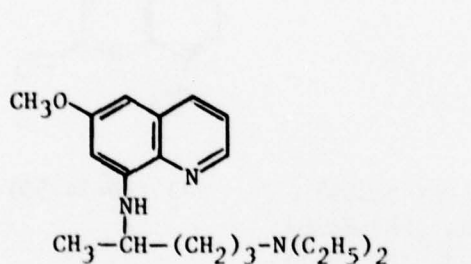


I-1

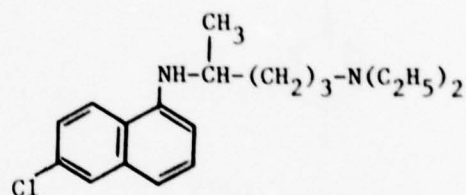


I-2

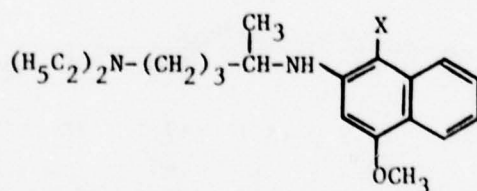
(X = H, OCH<sub>3</sub>)



I-3

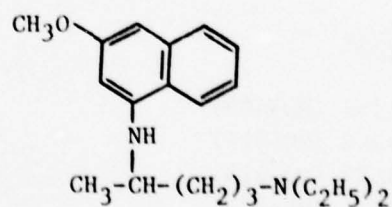


I-4 (WR-94797)



I-5a. X = H (AY-96121)

b. X = OCH<sub>3</sub> (AY-64576)

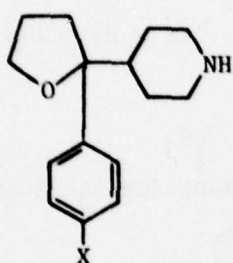


I-6 (AY-95580)

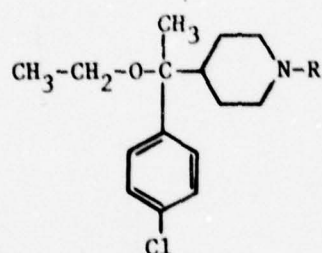
Compounds I-4, I-5a and I-6 failed to show any antimalarial activity but compound I-5b had a quinine equivalent of 14 for SD<sub>90</sub> (daily dose required for 90% suppression of the parasitemia) and Q = 20 for SD<sub>70</sub>. For detailed discussion and experimental procedures, see our Annual Progress Report No. 7 and the following publication: D. J. McCaustland, P.-L. Chien, C. C. Cheng, J. Novotny, W. L. Schreiner, and F. W. Starks, "Deaza Analogs of Some 4-, 6-, and 8-Aminoquinolines," *J. Med. Chem.*, **16**, 1311 (1973).

J. Analogs of 2-(p-Chlorophenyl)-2-(4-piperidyl)tetrahydrofuran

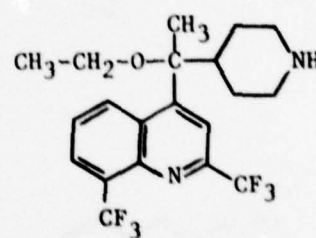
Structural modification study of the antimalarial compound 2-(p-chlorophenyl)-2-(4-piperidyl)tetrahydrofuran (J-1a) was carried out in a systematic and comprehensive manner. This included modifications of the tetrahydrofuran portion, the p-chlorophenyl portion, and the piperidyl portion as well as combined modifications. Although compounds in this series have a rather narrow margin of activity for structural alterations [see J-1b (BB-44064)], several open-chain analogs of this tetrahydrofuran compound, such as J-2a (AY-91395) and J-3, did show very interesting antimalarial activity.



J-1a. X = Cl  
b. X = F (BB-44064)



J-2a. R = H (AY-91395)  
b. R = CH<sub>3</sub> (BB-48428)  
c. R = C<sub>2</sub>H<sub>5</sub> (BC-59211)



J-3 (BD-54453)

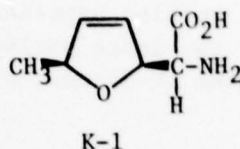
Antimalarial activity against *P. berhei*:

Compound	Dosage (mg/kg)						
	10	20	40	80	160	320	640
AY-91395 (MO-403)	+0.3	+0.5	+0.9	+3.1	+7.1	2C	5T
BB-44064 (MO-419)			+0.5		4T		5T
BB-48428 (MO-423)		+0.3	+0.5	+1.1	+4.4	+5.1	2C
BC-59211 (MO-436)		+0.3	+1.2	+3.9	+6.2	+7.7	+9.9
BD-54453 (MO-456)		+0.1	+0.3	+0.5	+1.1	2C	3C

Detailed discussion and experimental procedures were given in our Annual Progress Reports Nos. 7 through 9 and in the following publication: D. J. McCaustland, P.-L. Chien, W. H. Burton, and C. C. Cheng, "A Structural Modification Study of the Antimalarial 2-(p-Chlorophenyl)-2-(4-piperidyl)-tetrahydrofuran," *J. Med. Chem.*, **17**, 993 (1974).

### K. Analogs of Furanomycin

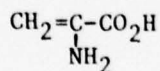
Structural modification of the antibiotic furanomycin (K-1), a heterocyclic amino acid which displayed activity against P. berghei, was conducted. However, none of the analogs synthesized were found to be active against P. berghei.



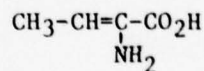
Detailed discussion and experimental procedures were given in our Annual Progress Reports Nos. 9 and 10.

### L. $\alpha,\beta$ -Unsaturated Amino Acids and Related Compounds

The fact that nisin, a peptide antibiotic, contains  $\alpha,\beta$ -unsaturated amino acids dehydroalanine (L-1) and  $\beta$ -methyldehydroalanine (L-2) possessed antimalarial activity against P. berghei prompted us to synthesize some amino acids containing the  $\alpha,\beta$ -unsaturated linkage.



L-1



L-2

In addition, other amino acid derivatives designed as L-isoleucine antagonists were also synthesized since L-isoleucine is virtually absent from most hemoglobins. L-Isoleucine antagonists therefore may interfere with the protein synthesis of malaria plasmodia.

Detailed discussion and experimental procedures are described in our proposal B-1579 (1974) and in our Annual Progress Report No. 10.

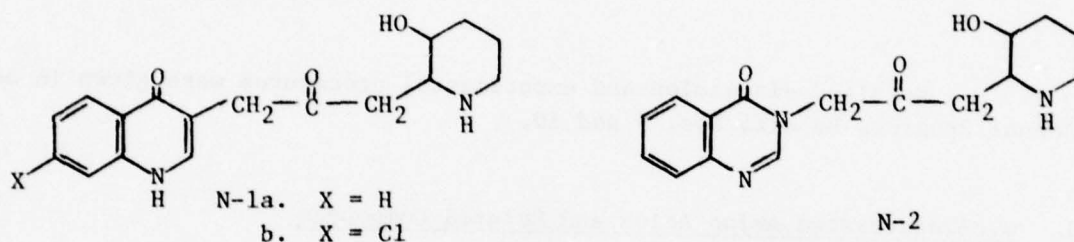
### M. Potential Prophylactic Antimalarial Agents

Based on a working hypothesis developed in this laboratory (vide infra), a variety of compounds containing a specific triangular structural feature were synthesized. For detailed discussion and experimental procedures, see our Annual Progress Reports Nos. 10 and 11 as well as the following publication: S. J. Yan, W. H. Burton, P.-L. Chien, and C. C. Cheng,

"Potential Causal Prophylactic Antimalarial Agents. Synthesis of Quinoxaline, Benzimidazole, and Alkoxybenzene Derivatives Containing a Novoldiamine Moiety," *J. Med. Chem.*, **15**, 297 (1978).

#### N. Deazafebrifugines

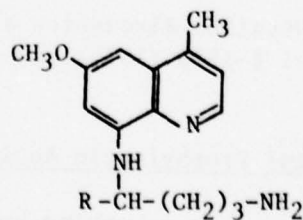
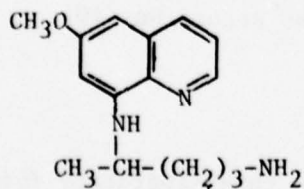
Based on another working hypothesis developed in this laboratory (*vide infra*), syntheses of two deaza analogs (N-1a and N-1b) of the antimalarial alkaloid febrifugine (N-2) were studied.



Detailed discussion and experimental procedures of this study can be found in our Annual Progress Reports Nos. 10 through 12.

#### O. 8-Aminoquinolines

In connection with a search of analogs of primaquine (O-1) with higher antimalarial activity and lower toxicity, several compounds were synthesized. All of these compounds were found to be less toxic than the parent primaquine and one of these, 8-(6-amino-3-hexylamino)-6-methoxy-4-methylquinoline (O-2a, WR-215761), displayed outstanding activity against *P. berghei* as well as exhibiting excellent prophylactic antimalarial activity in Schmidt's rhesus (SR) monkey tests against *P. cynomolgi*.



Antimalarial activity against P. berghei:

<u>Compound</u>	<u>ΔMST (days) after a single sc dose (mg/kg)</u>					
	<u>20</u>	<u>40</u>	<u>80</u>	<u>160</u>	<u>320</u>	<u>640</u>
Primaquine	+4.0	+5.0	+9.4	+10.8	5T	5T
				(2T)		
WR-215761	+7.3	+7.9	+9.7	+11.5	5C	5C
WR-226573	+3.1	+4.1	+5.7	+6.3	+9.1	+12.3
WR-235202	+3.4	+5.2	+6.8	+7.8	+7.2	1C
				(1C)		

Prophylactic antimalarial activity against P. cynomolgi:

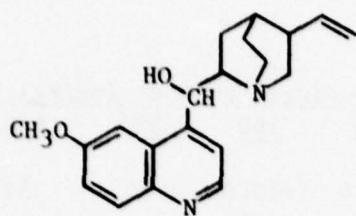
<u>Compound</u>	<u>Dosage (mg/kg)</u>				
	<u>0.0625</u>	<u>0.125</u>	<u>0.25</u>	<u>0.5</u>	<u>1.0</u>
WR-216571	0/2 C	6/7 C	4/4 C	1/1 C	1/1 C

A manuscript entitled "Synthesis and Antimalarial Activity of 8-(1-Alkyl-4-aminobutylamino)-6-methoxy-4-methylquinolines" by S.-J. Yan, P.-L. Chien and C. C. Cheng was submitted to WRAIR on 28 February 1978 for approval. For a detailed discussion and experimental procedures of compounds in this series, see our Annual Progress Reports Nos. 9, 11 and 12.

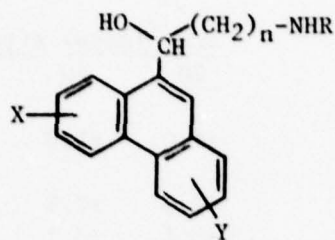
P. Three Working Hypotheses for the Rational Design of Antimalarial Agents

During the past 12 years of our investigation, we uncovered the existence of three common structural features among different groups of antimalarials. These structural features should assist in the rational development of novel antimalarial agents.

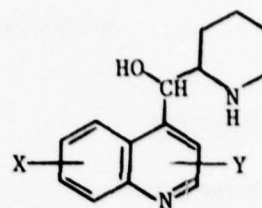
I. First hypothesis: Antimalarials acting mainly as blood schizontocides, such as quinine (P-1), aminoalcohols illustrated by general structures (P-2 through P-4), tetrahydrofuran derivatives, such as P-5, and the related open-chain compound P-6.



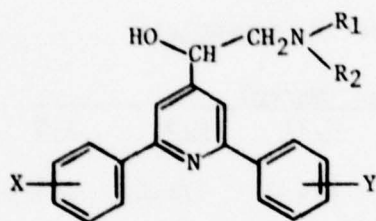
P-1



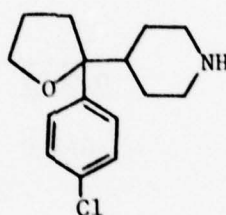
P-2



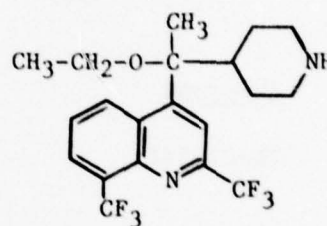
P-3



P-4

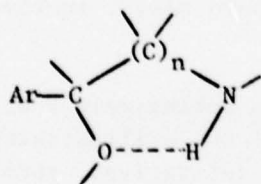


P-5

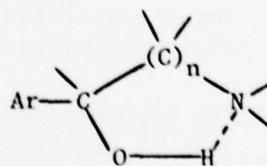


P-6

Each compound is composed of three parts: a planar (aromatic or heteroaromatic) ring, an oxygen-containing portion, and a nonplanar nitrogen-containing portion. Examination and comparison of Dreiding and Briegleb-Stuart molecular models revealed that the oxygen and the nitrogen atoms are in close proximity to each other in these molecules and they are linked by hydrogen bonding (the H-atom can be contributed by either O or N) to form a five- or six-membered ring, as shown in P-7 and P-8 ( $n = 1$  or  $2$ ).



P-7



P-8

The interatomic distance between the oxygen atom and the nitrogen atom and the distance of each of the aforementioned atoms to the center of the aromatic (or heteroaromatic, as the case may be) ring, to which the side chain is attached, were measured and are presented in Figure 1.

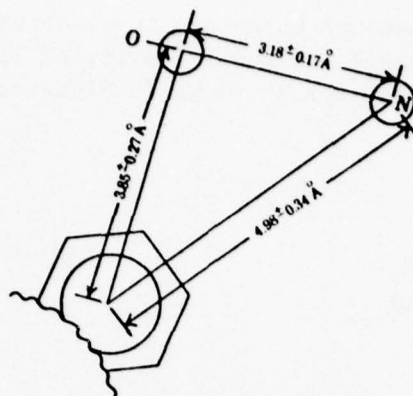


Figure 1

It is possible that these compounds may bind to pertinent receptor sites of certain biopolymers of malarial parasites. The  $\pi$ -deficient planar ring systems may act as charge-transfer acceptors in the formation of complexes with biopolymers.

This observation was reported in 1971 [*J. Pharm. Sci.*, 60, 1590 (1971)]. Interestingly, a proposed triangulation feature for  $\alpha$ -adrenergic receptors (Figure 2) among a number of phenethylamines (epinephrine, norepinephrine, etc.) containing a similar aminoalcohol side chain [B. Pullman et al., *J. Med. Chem.*, 15, 17 (1972)] bears a marked resemblance to our proposed feature. The distance between the N and the O atoms has also been confirmed by Professor W. Peters' group in England [D. C. Warhurst and S. C. Thomas, *Trans. Royal Soc. Trop. Med. Hyg.*, 67, 15 (1973)] in their antimalarial schizontocides study.

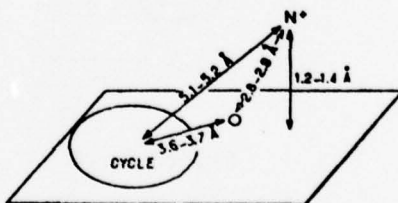


Figure 2

2. Second hypothesis: Antimalarials acting mainly as causal prophylactic agents, such as 8-aminoquinolines (P-9), 6-aminoquinolines (P-10, P-11), naphthoquinones (e.g., P-12), and others, have a common

structural feature composed of three electronegative atoms (N, O, etc.) substituted around a benzene nucleus at positions 1, 2, and 4, with minimum distances between each atom as shown in Figure 3 [J. Med. Chem., 63, 307 (1974)].

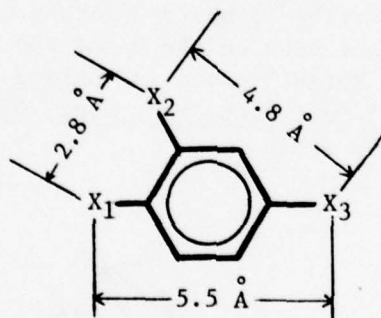
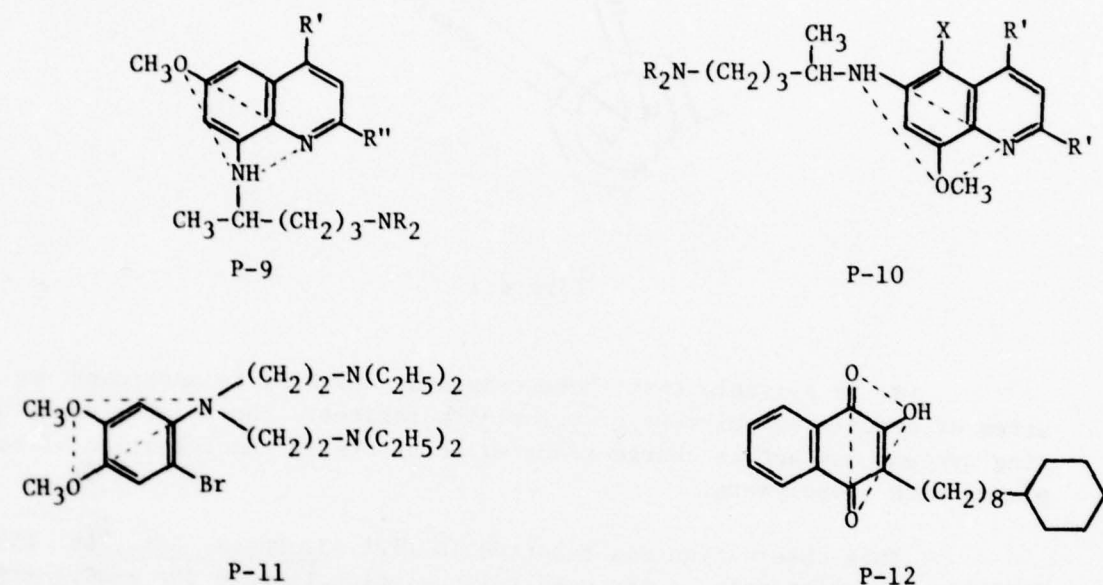
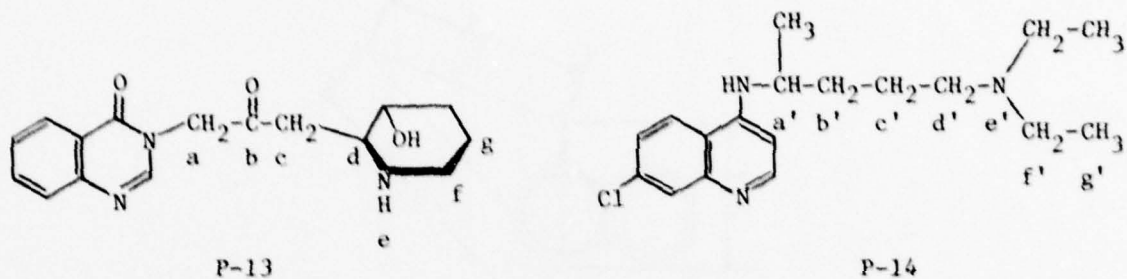


Figure 3

The second structural feature probably encompasses most agents that participate in biological redox reactions. While the proposed structural feature serves only as a working hypothesis for a search of new types of antimalarials, it nevertheless differentiates some classes of compounds containing similar functional groups. For example, the 4-aminoquinolines (such as chloroquine) and 9-aminoacridines (such as mepacrine), although containing the same dialkylaminoalkylamino side chain, differ in their mode

of action from the 6- and the 8-aminoquinolines since both of the former compounds lack the proposed common structural feature.

3. Third hypothesis: A common structural feature between the synthetic antimalarial chloroquine and the antimalarial alkaloid febrifugine was noted [*J. Theoretical Biol.*, 59, 497 (1976)].



When the quinoline ring of chloroquine (P-14) is placed directly over the quinazolinone ring of febrifugine (P-13) such that both nitrogens at the 1-position overlap, not only is the quinazolinone oxygen of P-13 in the vicinity of the 4-amino nitrogen atom of P-14, but the side chains of both compounds can be turned along their axes in such a way that the piperidyl nitrogen of P-13 and the tertiary nitrogen of P-14, along with their nearby carbon chains (carbon atoms b, c, d of P-13 versus b', c', d' of P-14, respectively, and carbon atoms f and g of P-13 versus f' and g' of P-14, respectively, are superimposable (see Figure 4).

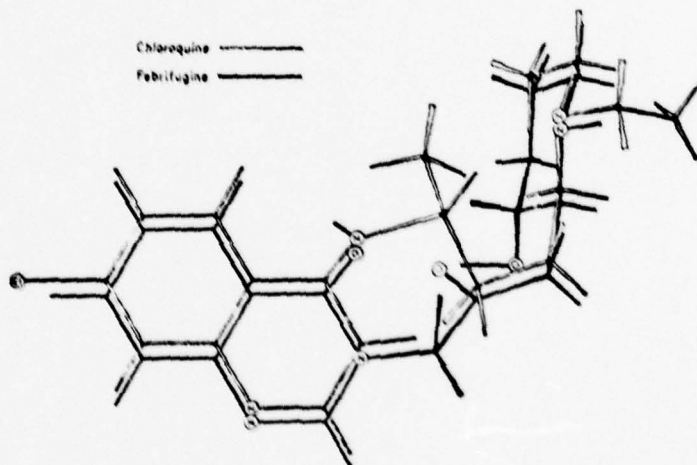


Figure 4

Similar relationships can also be found between compound P-13 and other 4-aminoquinolines (such as amodiaquine) as well as 9-aminoacridines (such as quinacrine). Thus a common triangular feature can be proposed for these antimalarials (see Figure 5, X = O or N). Minimum optimum distances between each of the aforementioned atoms were obtained through measurements of Dreiding molecular models.

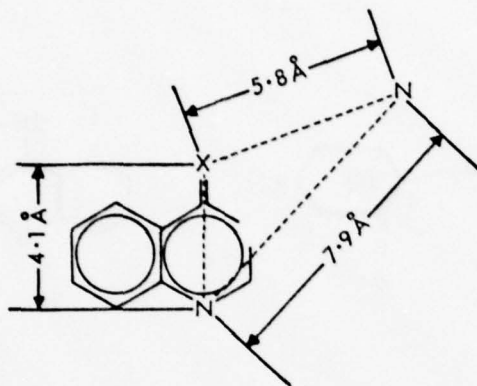


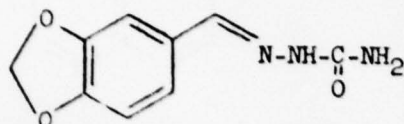
Figure 5

It therefore appears that the alkaloid febrifugine and the potent antimalarial 4-aminoquinolines (and 9-aminoacridines) may share similar sites in the in vivo binding to certain biopolymers which are pertinent to their antimalarial action.

III. COMPOUNDS SUBMITTED FOR ANTIMALARIAL SCREENING

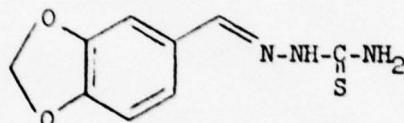
MO-1 (SB-I-11-12, WR-6116-A):

Piperonal semicarbazone



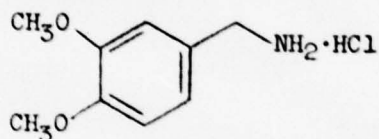
MO-2 (SB-I-16-12, WR-6117-A):

Piperonal thiosemicarbazone



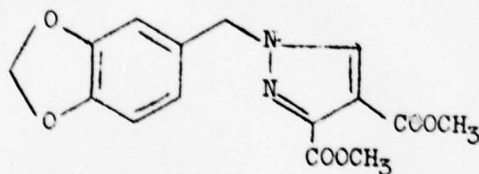
MO-3 (RB-I-20-12, WR-16910-B):

3,4-Dimethoxybenzylamine hydrochloride



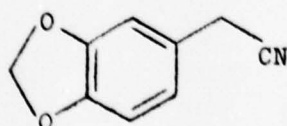
MO-4 (RB-I-47-11, WR-6464-A):

Dimethyl piperonylpyrazole-3,4-dicarboxylate



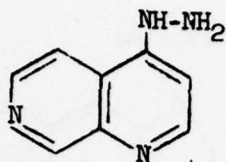
MO-5 (SB-I-29-11, WR-6465-A):

Homopiperonylnitrile



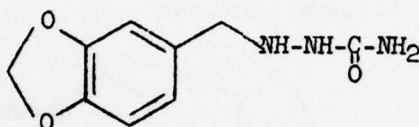
MO-6 (PC-I-17, WR-6466-A):

4-Hydrazino-1,7-naphthyridine



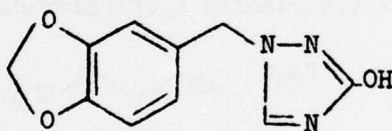
MO-7 (SB-I-46-11, WR-7725-A):

1-Piperonylsemicarbazide



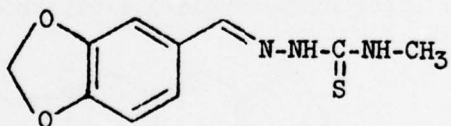
MO-8 (SB-I-49-11, WR-7726-A):

1-Piperonyl-3-hydroxy-1,2,4-triazole



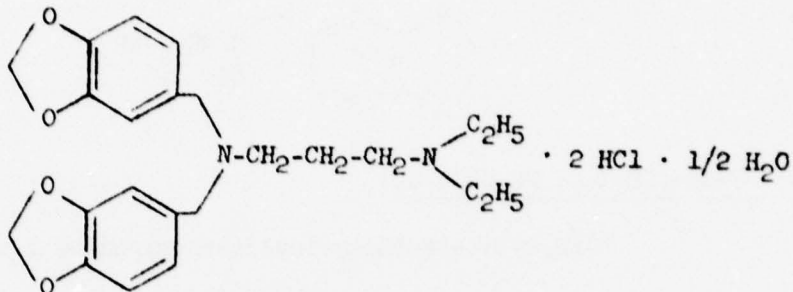
MO-9 (SB-I-51-11, WR-7727-A):

4-N-Methylpiperonal thiosemicarbazone



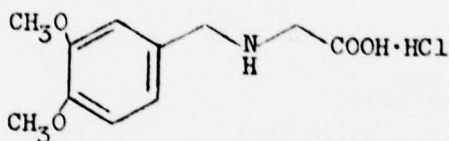
MO-10 (PC-I-29, WR-7728-A):

1-Diethylamino-3-bis(piperonylamino)propane, dihydrochloride, hemihydrate



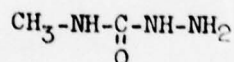
MO-11 (RB-I-74-40, WR-8166-A):

N-(3,4-Dimethoxybenzyl)glycine hydrochloride



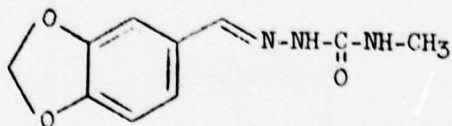
MO-12 (SB-I-70-11, WR-8167-A):

4-N-Methylsemicarbazide



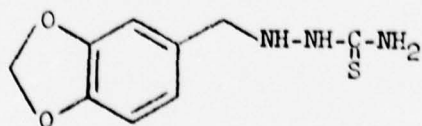
MO-13 (SB-I-72-1, WR-8168-A):

Piperonal 4-N-methylsemicarbazone



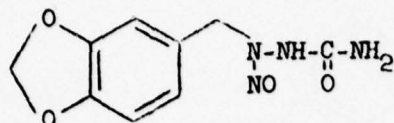
MO-14 (SB-I-75-11, WR-8169-A):

1-N-Piperonylthiosemicarbazide



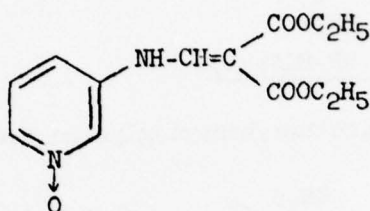
MO-15 (SB-I-73-11, WR-8170-A):

1-N-Nitroso-1-N-piperonylsemicarbazide



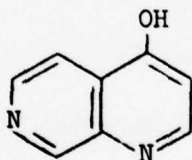
MO-16 (PC-I-8, WR-8171-A):

3-(2,2-Dicarbethoxyvinyl)aminopyridine 1-oxide



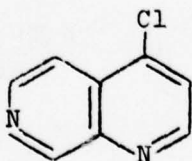
MO-17 (PC-I-10, WR-8630-A):

4-Hydroxy-1,7-naphthyridine



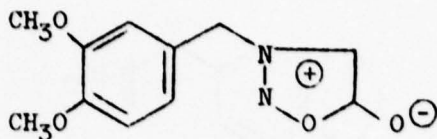
MO-18 (PC-I-14, WR-8631-A):

4-Chloro-1,7-naphthyridine



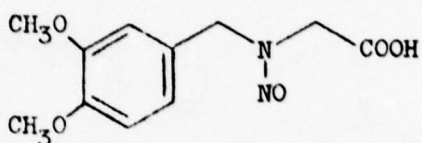
MO-19 (RB-I-87-11, WR-8632-A):

3-(3,4-Dimethoxybenzyl)sydnone



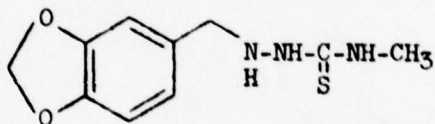
MO-20 (RB-I-85-2, WR-8714-A):

N-Nitroso-N-(3,4-dimethoxybenzyl)glycine



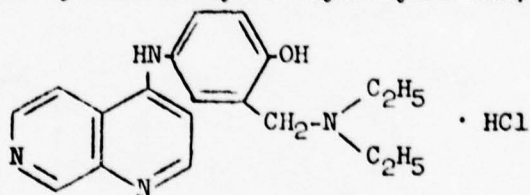
MO-21 (SB-I-96-11, WR-8633-A):

1-Piperonyl-4-methylthiosemicarbazide



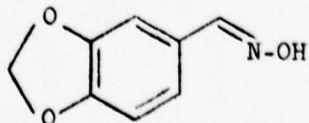
MO-22 (PC-I-35, WR-8715-A):

4-(3-Dimethylaminomethyl-4'-hydroxyanilino)-1,7-naphthyridine



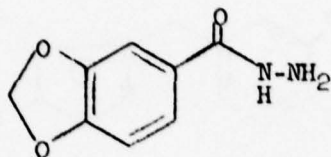
MO-23 (SB-I-112-11, WR-25119-A):

Piperonal oxime



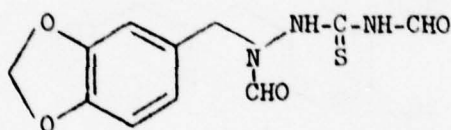
MO-24 (SB-I-124-1, WR-25120-A):

3,4-Methylenedioxybenzoylhydrazine



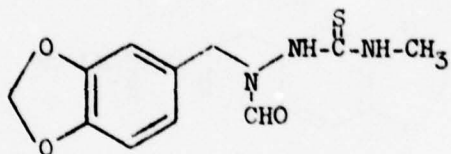
MO-25 (SB-I-107-1, WR-25121-A):

1,4-Diformyl-1-piperonylthiosemicarbazide



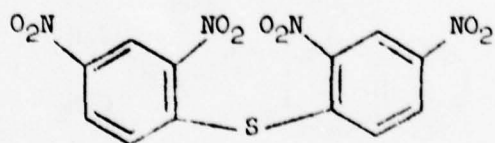
MO-26 (SB-II-12-1, WR-25122-A):

1-Formyl-4-methyl-1-piperonylthiosemicarbazide



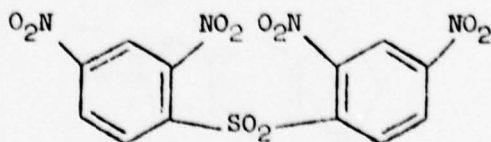
MO-27 (PL-I-40, WR-58-B):

Bis-(2,4-dinitrophenyl)sulfide



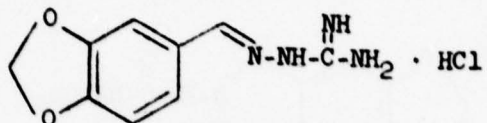
MO-28 (PL-I-43, WR-25123-A):

Bis-(2,4-dinitrophenyl)sulfone



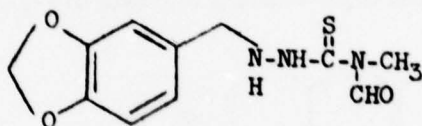
MO-29 (SB-I-141-11, WR-5664-B):

Piperonal guanylhydrazone hydrochloride



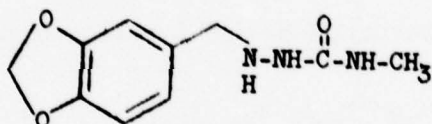
MO-30 (SB-I-137-1, WR-25124-A):

4-Formyl-4-methyl-1-piperonylthiosemicarbazide



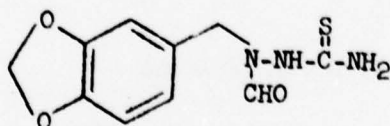
MO-31 (SB-I-136-11, WR-25125-A):

4-Methyl-1-piperonylsemicarbazide



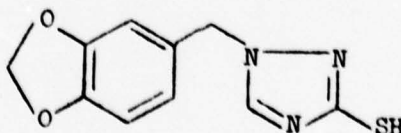
MO-32 (SB-II-36-1, WR-25411-A):

1-Formyl-1-piperonylthiosemicarbazide



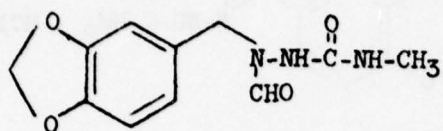
MO-33 (SB-II-33-3, WR-25412-A):

1-Piperonyl-3-mercapto-1,2,4-triazole



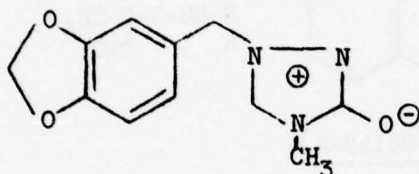
MO-34 (SB-II-28-1, WR-25413-A):

1-Formyl-1-piperonyl-4-methylsemicarbazide



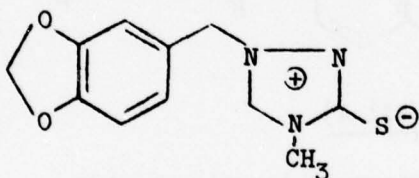
MO-35 (SB-II-32-1, WR-25414-A):

Anhydro-2-piperonyl-4-methyl-5-hydroxy-s-triazolium hydroxide



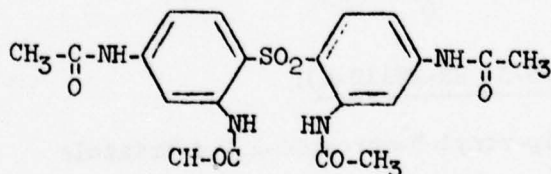
MO-36 (SB-II-35-11, WR-25415-A):

Anhydro-2-piperonyl-4-methyl-5-mercapto-s-triazolium hydroxide



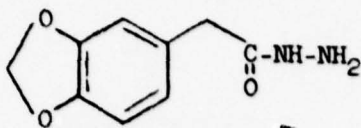
MO-37 (PC-I-54, WR-25873-A):

Bis(2,4-diacetamidophenyl)sulfone



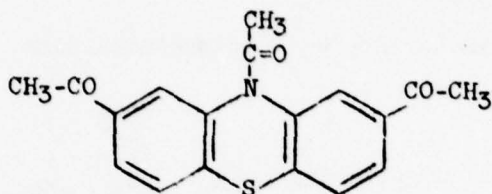
MO-38 (SB-II-50-1, WR-25874-A):

Homopiperonylic acid hydride



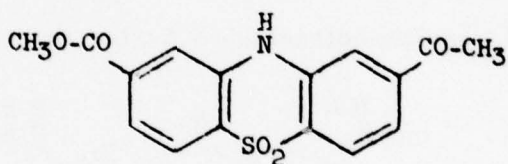
MO-39 (PC-I-57, WR-27012-A):

2,8,10-Triacetylphenothiazine



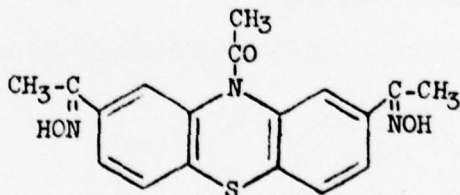
MO-40 (PC-I-64, WR-27013-A):

2,8-Diacetylphenothiazine 5,5-dioxide



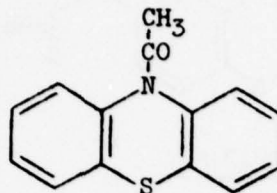
MO-41 (PC-I-62, WR-27014-A):

2,8,10-Triacetylphenothiazine dioxime



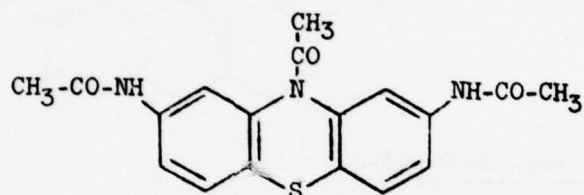
MO-42 (PC-I-58, WR-18038-B):

10-Acetylphenothiazine



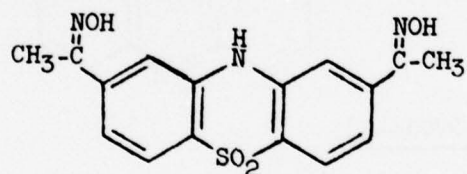
MO-43 (PC-I-67, WR-27015-A):

2,8-Diacetamino-10-acetylphenothiazine



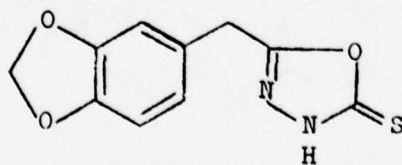
MO-44 (PC-I-75, WR-27797-A):

2,8-Diacetylphenothiazine 5,5-dioxide dioxime



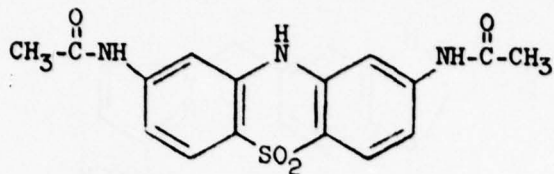
MO-45 (SB-II-104-1, WR-27798-A):

2-Piperonyl- $\Delta^2$ -1,3,4-oxadiazoline-5-thione



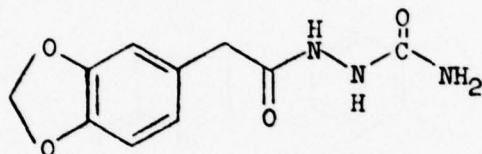
MO-46 (PC-I-74, WR-28450-A):

2,8-Diacetamidophenothiazine 5,5-dioxide



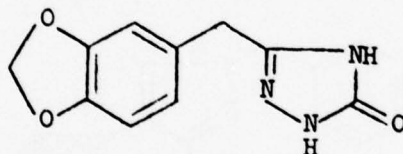
MO-47 (SB-II-102-1, WR-28451-A):

1-Homopiperonyl semicarbazide



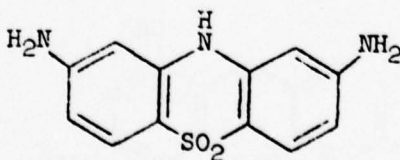
MO-48 (SB-II-120-11, WR-28452-A):

3-Hydroxy-5-piperonyl-1,2,4-triazole



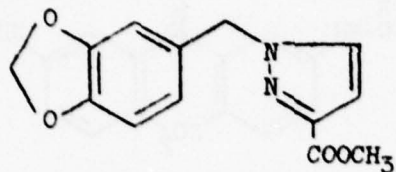
MO-49 (PC-I-87, WR-28776-A):

2,8-Diaminophenothiazine 5,5-dioxide



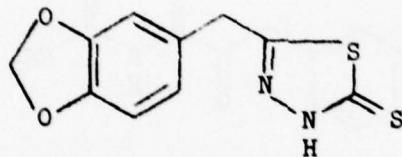
MO-50 (SB-II-132-18, WR-28777-A):

Methyl 1-piperonylpyrazole-3-carboxylate



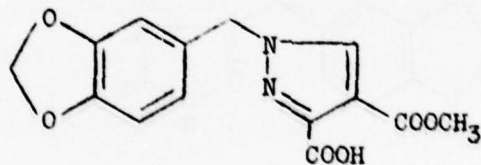
MO-51 (SB-II-147-21, WR-28778-A):

2-Piperonyl- $\Delta^2$ -1,3,4-thiadiazoline-5-thione



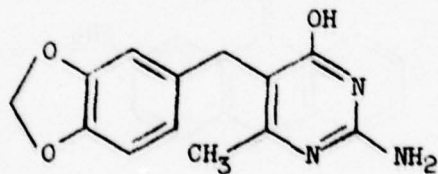
MO-52 (SB-II-49-11, WR-28779-A):

Methyl 1-piperonyl-3-carboxypyrazole-4-carboxylate



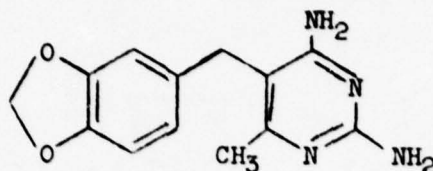
MO-53 (SB-III-23-1, WR-29674-A):

2-Amino-4-hydroxy-5-piperonyl-6-methylpyrimidine



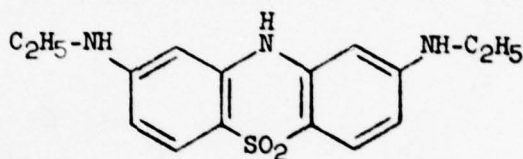
MO-54 (SB-III-27-1, WR-29675-A):

2,4-Diamino-5-piperonyl-6-methylpyrimidine



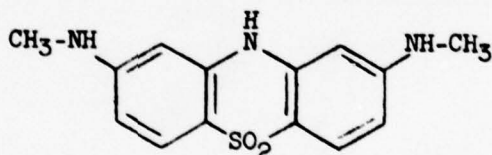
MO-55 (PC-I-92, WR-30210-A):

2,8-Bis(ethylamino)phenothiazine 5,5-dioxide



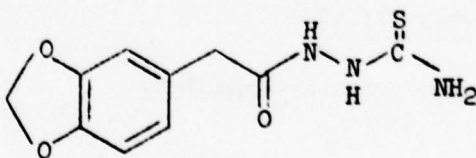
MO-56 (PC-I-94, WR-30211-A):

2,8-Bis(methylamino)phenothiazine 5,5-dioxide



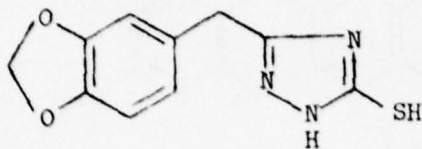
MO-57 (SB-III-25-2, WR-31644-A):

1-Homopiperonylthiosemicarbazide



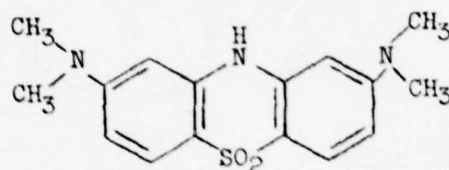
MO-58 (SB-III-33-11, WR-31569-A):

3-Mercapto-5-piperonyl-1,2,4-triazole



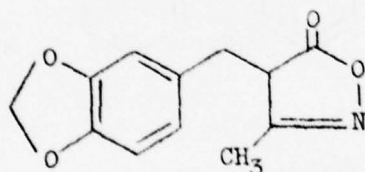
MO-59 (PC-I-101, WR-31872-A):

2,8-Bis(dimethylamino)phenothiazine 5,5-dioxide



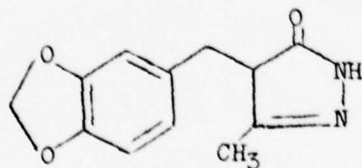
MO-60 (SB-III-31-11, WR-31873-A):

3-Methyl-4-piperonyl-5-isoxazolone



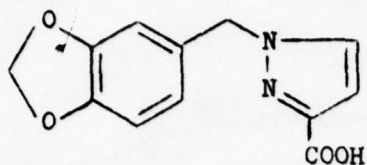
MO-61 (SB-III-28-1, WR-31874-A):

3-Methyl-4-piperonyl-5-pyrazolone



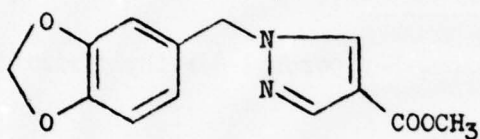
MO-62 (SB-II-146-2; WR-32903-A):

1-Piperonylpyrazole-3-carboxylic acid



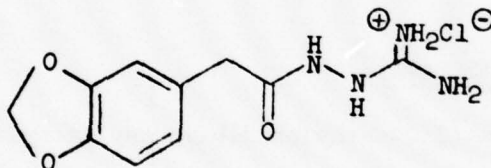
MO-63 (SB-III-18-11; WR-32904-A):

Methyl 1-piperonylpyrazole-4-carboxylate



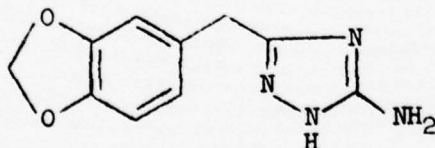
MO-64 (SB-II-152-11; WR-34699-A):

1-Homopiperonylaminoguanidine hydrochloride



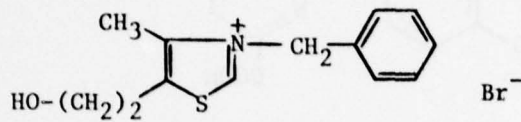
MO-65 (SB-III-68-21; WR-34700-A):

3-Amino-5-piperonyl-1,2,4-triazole



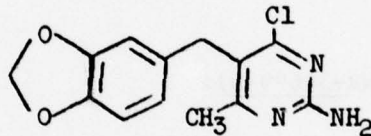
MO-66 (LS-S-877-4; WR-34701-A):

3-Benzyl-4-methyl-5-(2-hydroxyethyl)thiazolium bromide



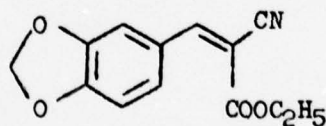
MO-67 (SB-III-26-21; WR-35053-A):

2-Amino-4-chloro-5-piperonyl-6-methylpyrimidine



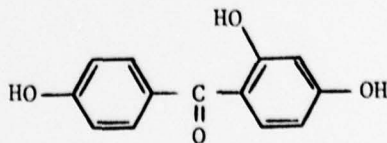
MO-68 (SB-III-74-11; WR-35054-A):

Ethyl  $\alpha$ -cyano- $\beta$ -(3,4-methylenedioxyphenyl)acrylate



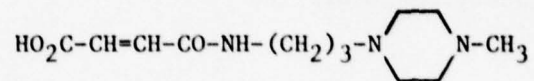
MO-69 (CD-S-878-8; WR-11900-B):

2,4,4'-Trihydroxybenzophenone



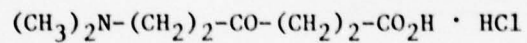
MO-70 (CD-S-878-8A):

N-[3-(4-Methylpiperazino)propyl]maleamic acid



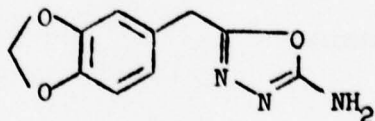
MO-71 (LS-S-877-12; WR-35974-A):

6-(Dimethylamino)-4-ketocaproic acid hydrochloride



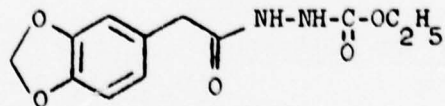
MO-72 (SB-III-96-11; WR-35995-A):

2-Amino-5-piperonyl-1,3,4-oxadiazole



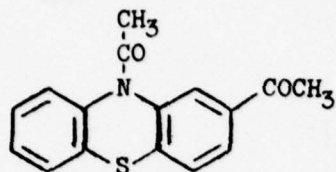
MO-73 (SB-III-86-11; WR-35996-A):

1-Carboethoxy-2-homopiperonylhydrazine



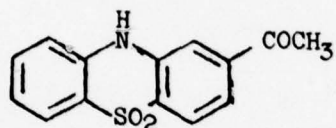
MO-74 (PC-I-89; WR-35997-A):

2,10-Diacetylphenothiazine



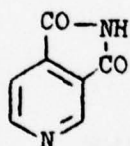
MO-75 (PC-I-103; WR-35998-A):

2-Acetylphenothiazine 5,5-dioxide



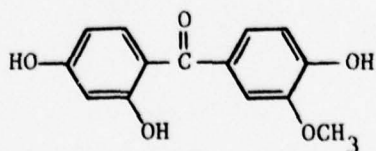
MO-76 (PC-I-112; WR-35999-A):

Cincheronimide



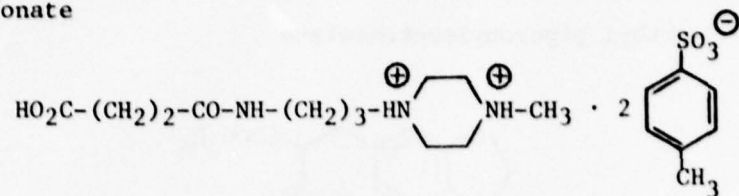
MO-77 (CD-S-878-24; WR-36260-A):

2,4,4'-Trihydroxy-3'-methoxybenzophenone



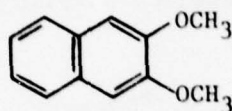
MO-78 (CD-S-878-14; WR-36261-A):

N-[3-(4-Methylpiperazino)propyl]succinamic acid di-p-toluene-sulfonate



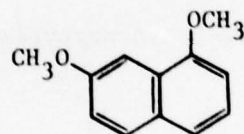
MO-79 (FB-S-882-3):

2,3-Dimethoxynaphthalene



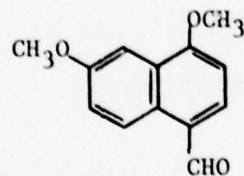
MO-80 (FB-S-882-5):

1,7-Dimethoxynaphthalene



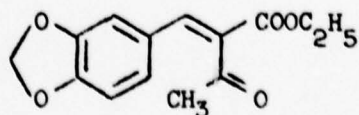
MO-81 (FB-S-882-6):

4,6-Dimethoxy-1-naphthylencarboxaldehyde



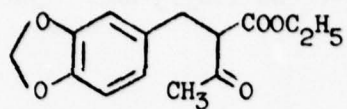
MO-82 (SB-III-115-1; WR-36444-A):

Ethyl piperonylideneacetoacetate



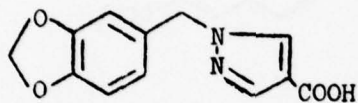
MO-83 (SB-III-22-11; WR-36445-A):

Ethyl piperonylacetoacetate



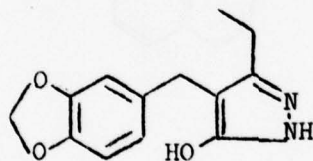
MO-84 (SB-III-79-2; WR-36446-A):

1-Piperonyl-4-pyrazolecarboxylic acid



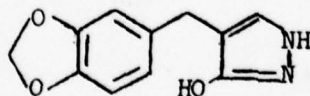
MO-85 (SB-III-51-1; WR-36447-A):

3-Ethyl-4-piperonyl-5-hydroxypyrazole



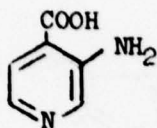
MO-86 (SB-III-109-11; WR-36448-A):

3-Hydroxy-4-piperonylpyrazole



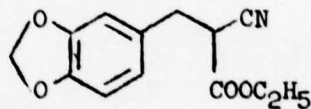
MO-87 (PC-I-124; WR-36449-A):

3-Aminoisonicotinic acid



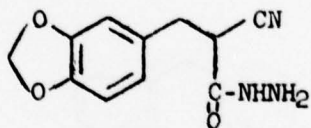
MO-88 (EN-I-48-12; WR-36663-A):

Ethyl piperonylcynoacetate



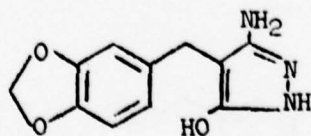
MO-89 (EN-I-41-14; WR-36664-A):

Piperonylcynoacetic acid hydrazide



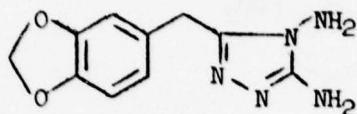
MO-90 (EN-I-49-12; WR-36665-A):

3-Amino-4-piperonyl-5-hydroxypyrazole



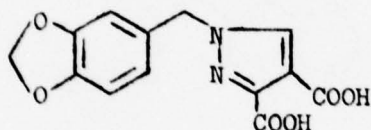
MO-91 (SB-III-125-11; WR-37670-A):

3,4-Diamino-5-piperonyl-1,2,4-triazole



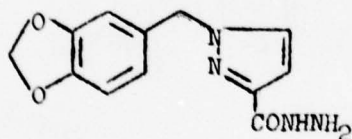
MO-92 (SB-III-127-1; WR-37671-A):

1-Piperonyl-3,4-pyrazoledicarboxylic acid



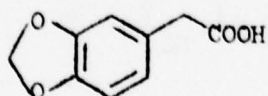
MO-93 (SB-III-130-1; WR-37672-A):

1-Piperonylpyrazole-3-carboxylic acid hydrazide



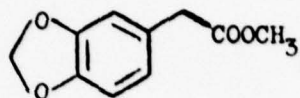
MO-94 (SB-II-149-21):

Homopiperonylic acid



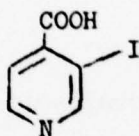
MO-95 (SB-II-39-1; WR-37673-A):

Methyl homopiperonylate



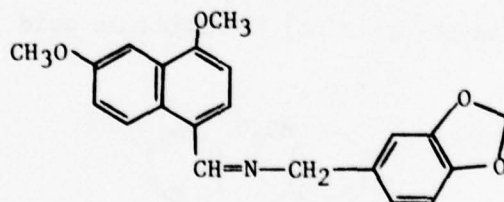
MO-96 (PC-I-129; WR-37674-A):

3-Iodoisonicotinic acid



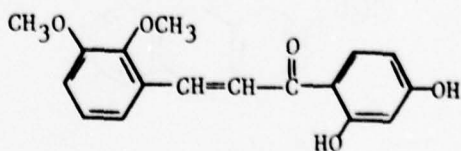
MO-97 (FB-S-882-8):

N-(4,6-Dimethoxynaphthylmethylene)piperonylamine



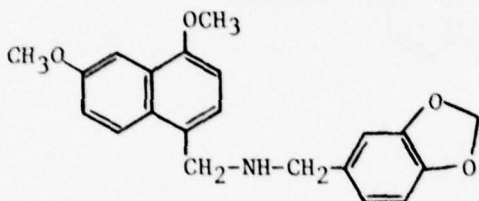
MO-98 (CD-S-878-27):

2,3-Dimethoxy-2',4'-dihydroxychalcone



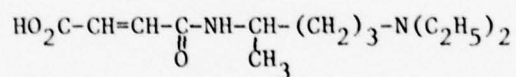
MO-99 (FB-S-882-10):

N-(4,6-Dimethoxynaphthylmethyl)piperonylamine)



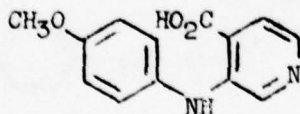
MO-100 (LS-S-877-31):

N-(4-Diethylamino-1-methylbutyl)maleamic acid



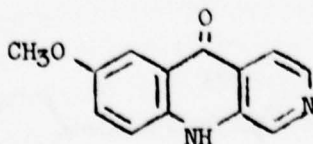
MO-101 (PC-I-131; WR-40065-A):

3-(p-Methoxyphenylamino)-isonicotinic acid



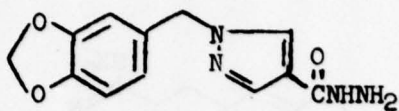
MO-102 (PC-I-133; WR-40066-A):

6-Methoxy-4(1H)-pyrido [3,4-b] quinolone



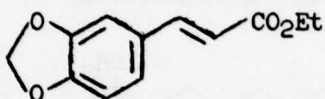
MO-103 (SB-III-139-3; WR-40067-A):

1-Piperonylpyrazole-4-carboxylic acid hydrazide



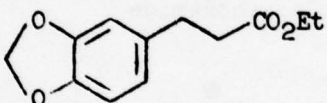
MO-104 (SB-III-137-11; WR-40068-A):

Ethyl piperonylideneacetate



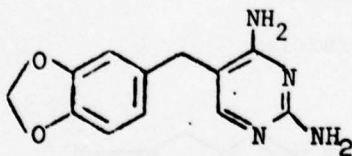
MO-105 (SB-III-142-11; WR-40069-A):

Ethyl piperonylacetate



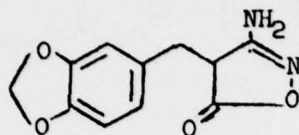
MO-106 (EN-I-65-14; WR-40070-A):

2,4-Diamino-5-piperonylpyrimidine



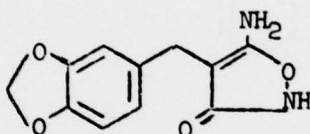
MO-107 (EN-I-58-12; WR-40071-A):

3-Amino-4-piperonyl-5-isoxazolone



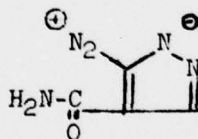
MO-108 (EN-I-73-12; WR-40072-A):

5-Amino-4-piperonyl-5-isoxazolone



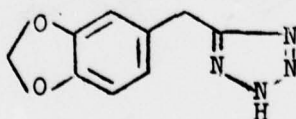
MO-109 (CC-253; WR-45684-A):

3-Diazo-4-pyrazolecarboxamide



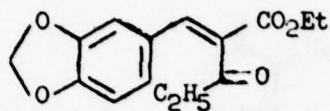
MO-110 (WB-1-10E; WR-43863-A):

5-Piperonyltetrazole



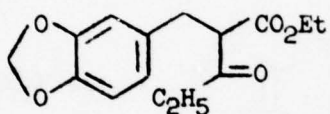
MO-111 (SB-III-49-13; WR-43864-A):

Ethyl  $\alpha$ -piperonylidene- $\beta$ -ketovalerate



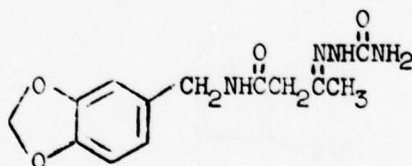
MO-112 (SB-III-50-1; WR-43865-A):

Ethyl  $\alpha$ -piperonyl- $\beta$ -ketovalerate



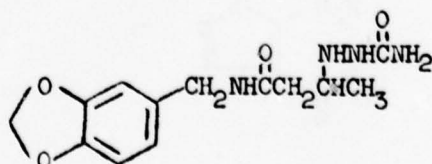
MO-113 (PC-II-6):

Piperonylacetoacetamide semicarbazone



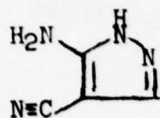
MO-114 (PC-II-8):

N-Piperonyl-3-carbamoylhydrazinobutyramide



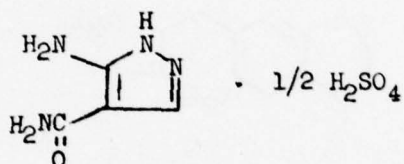
MO-115 (CC-245; WR-10412-B):

3-Amino-4-cyanopyrazole



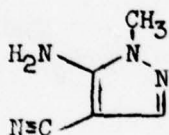
MO-116 (CC-247; WR-10461-B):

3-Amino-4-pyrazolecarboxamide hemisulfate



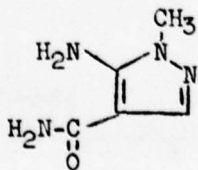
MO-117 (CC-244):

1-Methyl-4-cyano-5-aminopyrazole



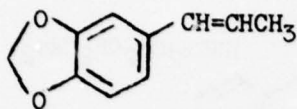
MO-118 (CC-246):

1-Methyl-5-amino-4-pyrazolecarboxamide



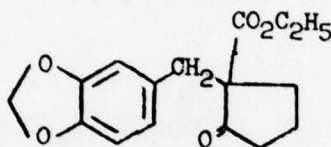
MO-119 (WB-1-33B; WR-22838-B):

Isosafrole



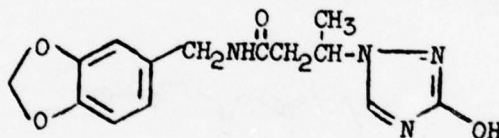
MO-120 (WB-1-47D; WR-47714-A):

Ethyl 1-piperonyl-2-oxocyclopentanecarboxylate



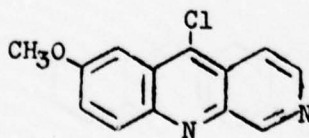
MO-121 (PC-II-15; WR-47713-A):

N-Piperonyl-2-[3-hydroxy-1,2,4-triazol-1-yl]-butyramide



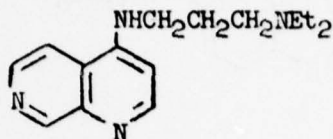
MO-122 (PC-I-135; WR-47712-A):

10-Chloro-6-methoxy-2,9-diazaanthracene



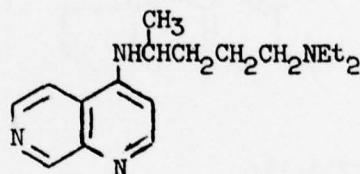
MO-123 (PC-I-104; WR-47710-A):

4-(3-Diethylaminopropylamino)-1,7-naphthyridine



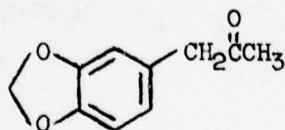
MO-124 (PC-II-16; WR-47714-A):

4-(4-Diethylamino-1-methylbutylamino)-1,7-naphthyridine



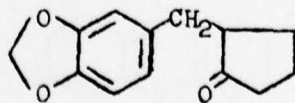
MO-125 (WB-1-52C; WR-47715-A):

Methyl piperonyl ketone



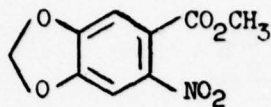
MO-126 (WB-1-61B; WR-51873-A):

2-Piperonylcyclopentanone



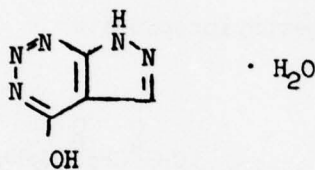
MO-127 (MW-1-19; WR-51901-A):

Methyl 2-nitro-4,5-methylenedioxybenzoate



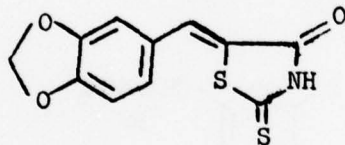
MO-128 (CC-250; WR-51898-A):

4-Hydroxypyrazolo[3,4-d]-v-triazine, hydrate



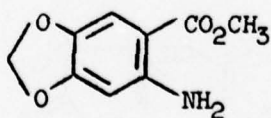
MO-129 (WLB-S-900-3; WR-51886-A):

5-(3,4-Methylenedioxybenzylidene)rhodaine



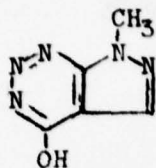
MO-130 (MW-1-21; WR-51904-A):

Methyl 2-amino-4,5-methylenedioxybenzoate



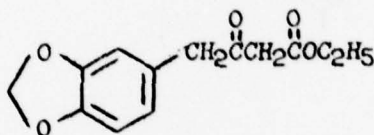
MO-131 (CC-259-III; WR-51897-A):

7-Methyl-4-hydroxypyrazolo [3,4-d]y-triazine



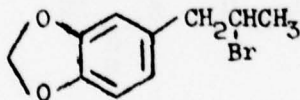
MO-132 (WB-I-87E; WR-51891-A):

Ethyl 3-oxo-3-piperonylpropionate



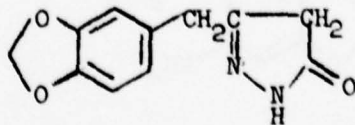
MO-133 (WB-1-94F; WR-51905-A):

1-Bromo-1-piperonylethane



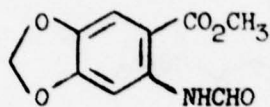
MO-134 (WB-1-106A; WR-52726-A):

3-Piperonyl-5-pyrazolinone



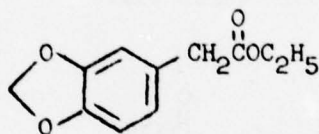
MO-135 (MW-1-45-2; WR-52710-A):

Methyl 2-formylamido-4,5-methylenedioxybenzoate



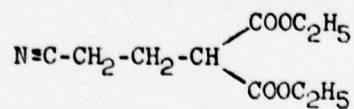
MO-136 (WB-1-17B; WR-52728-A):

Ethyl homopiperonylate



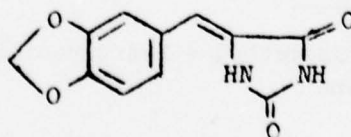
MO-137 (MW-1-41-2B; WR-53739-A):

Diethyl 2-cyanoethylmalonate



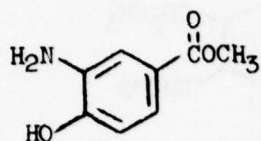
MO-138 (S-900-19A; WR-53740-A):

5-[3,4-Methylenedioxybenzyl]hydantoin



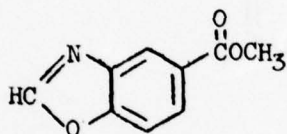
MO-139 (WB-1-118; WR-23063-B):

Methyl 3-amino-4-hydroxybenzoate



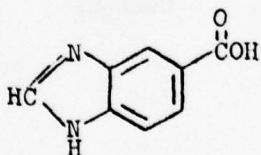
MO-140 (WB-1-121E; WR-56637-A):

Methyl 5-benzoxazole carboxylate



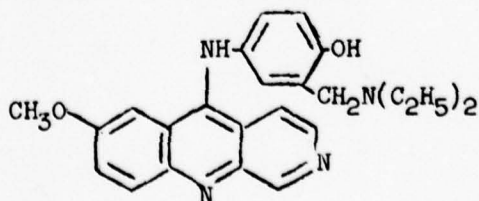
MO-141 (WB-1-123c; WR-56638-A):

5-Benzimidazole carboxylic acid



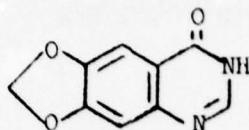
MO-142 (PC-II-17; WR-56636-A):

10-(3-Diethylaminomethyl-4-hydroxyanilino)-6-methoxy-2,9-diazaanthracene



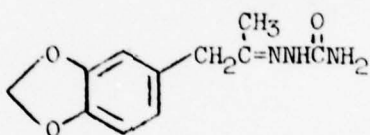
MO-143 (PC-II-23; WR-56635-A):

6,7-Methylenedioxy-4-quinazolone



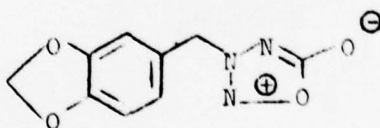
MO-144 (WB-1-135A; WR-57850-A):

3,4-Methylenedioxyphenyl-2-propanone semicarbazone



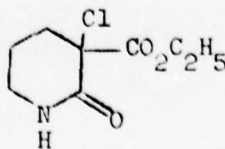
MO-145 (DM-I-19-4; WR-57846-A):

Anhydro-5-hydroxy-3-piperonyl-1,2,3,4-oxatriazolium hydroxide



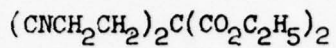
MO-146 (PC-II-36; WR-59545-A):

3-Chloro-3-carbethoxy-2-piperidone



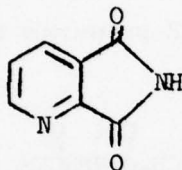
MO-147 (MW-1-53; WR-10985-C):

Diethyl bis(2-cyanoethyl)malonate



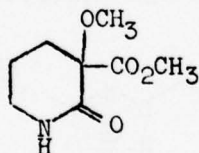
MO-148 (DM-I-14-3; WR-29027-C):

Quinolinimide



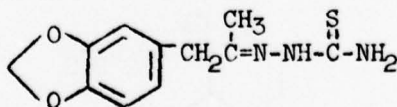
MO-149 (PC-II-37; WR-59545-A):

3-Methoxy-3-carbomethoxy-2-piperidone



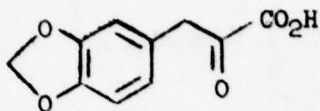
MO-150 (WB-1-134B; WR-59557-A):

3-(3,4-Methylenedioxyphenyl)-2-propanone  
thiosemicarbazone



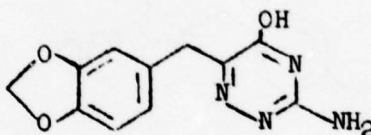
MO-159 (DM-I-30-2; WR-56407-C):

3,4-Methylenedioxyphenylpyruvic acid



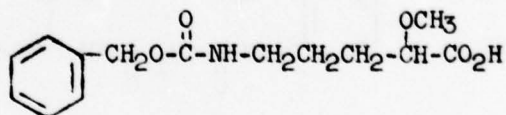
MO-160 (DM-I-32-1; WR-67635-A):

3-Amino-5-hydroxy-6-piperonyl-1,2,4-triazine



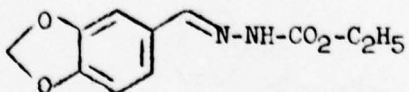
MO-161 (PC-II-52; WR-67824-A):

2-Methoxy-5-carbobenzoylaminovaleric acid



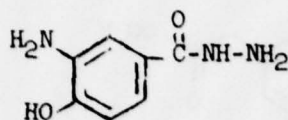
MO-162 (WB-2-46A; WR-67655-A):

Ethyl 2-piperonylidencarbazate



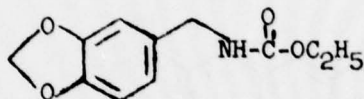
MO-163 (WB-2-23B; WR-67636-A):

3-Amino-4-hydroxybenzoic acid hydrazide



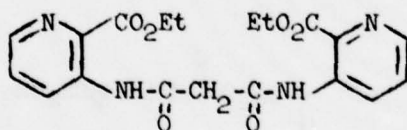
MO-164 (WB-2-48; WR-71486-A):

Ethyl 2-piperonylcarbazate



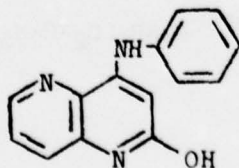
MO-165 (DM-I-28-2; WR-71484-A):

*N,N'*-Bis(2-ethoxycarbonyl-3-pyridyl)malonamide



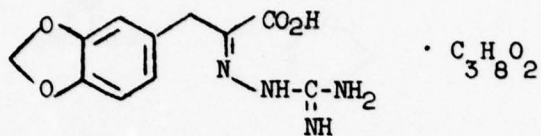
MO-166 (DM-I-33-1; WR-71468-A):

4-Anilino-2-hydroxy-1,5-naphthyridine



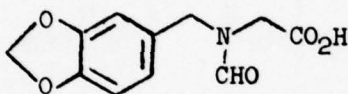
MO-167 (DM-I-31-2; WR-71480-A):

3,4-Methylenedioxyphenylpyruvic acid guanylhyazone  
(Compound with ethyleneglycol monomethyl ether)



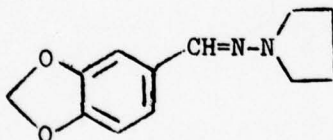
MO-168 (DM-I-34-2; WR-71474-A):

N-Formyl-N-piperonylglycine



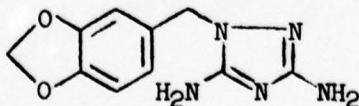
MO-169 (PC-II-67; WR-71472-A):

Piperonal tetramethylenehydrazone



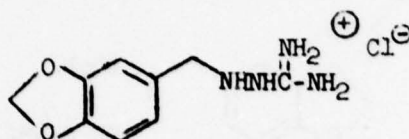
MO-171 (WB-2-65A; WR-74101-A):

1-Piperonyl-3,5-diamino-1,2,4-triazole



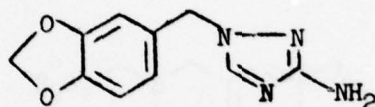
MO-172 (WB-2-75B; WR-74102-A):

Piperonylaminoguanidine hydrochloride



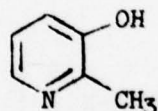
MO-173 (WB-2-76; WR-74103-A):

1-Piperonyl-3-amino-1,2,4-triazole



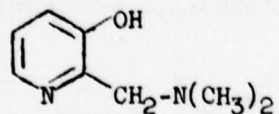
MO-174 (PC-II-76; WR-14710-B):

3-Hydroxy-2-methylpyridine



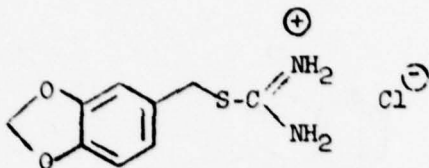
MO-175 (PC-II-81; WR-13796-C):

2-Dimethylaminomethyl-3-hydroxypyridine



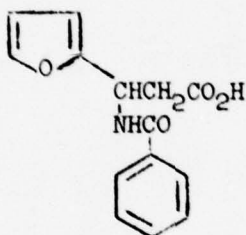
MO-176 (WB-2-89B; WR-74630-A):

Piperonyl thiuronium hydrochloride



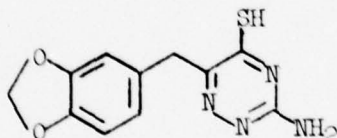
MO-177 (PC-II-83; WR-74631-A):

$\beta$ -Benzamido- $\beta$ -(2-furyl)propionic acid



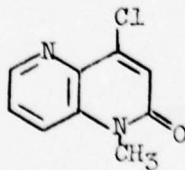
MO-178 (DM-I-35-1; WR-76077-A):

3-Amino-5-mercapto-6-piperonyl-1,2,4-triazine



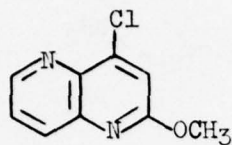
MO-179 (DM-I-39-2A; WR-76065-A):

4-Chloro-1-methyl-1,2-dihydro-1,5-naphthyridine-2-one



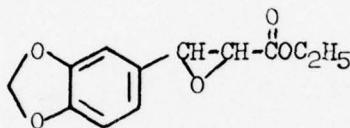
MO-180 (DM-I-40-1; WR-76066-A):

4-Chloro-2-methoxy-1,5-naphthyridine



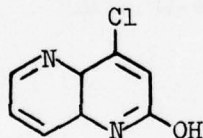
MO-181 (WB-2-96C; WR-76067-A):

Ethyl 3-(3,4-methylenedioxyphenyl)glycidate



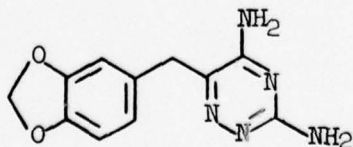
MO-182 (DM-I-38-1; WR-76171-A):

4-Chloro-2-hydroxy-1,5-naphthyridine



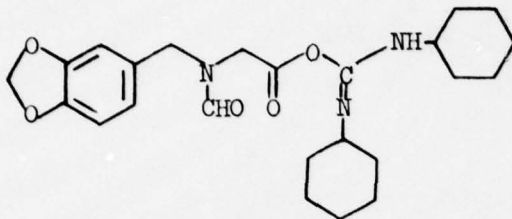
MO-183 (DM-I-36-1; WR-76172-A):

3,5-Diamino-6-piperonyl-1,2,4-triazine



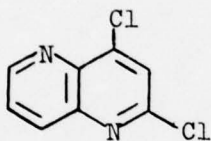
MO-184 (DM-I-41-1; WR-76985-A):

N,N'-Bis(cyclohexyl)-O-(N-formyl-N-piperonyl)glycylisourea



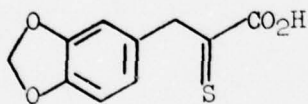
MO-185 (DM-I-37-1; WR-76984-A):

2,4-Dichloro-1,5-naphthyridine



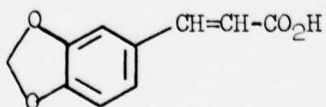
MO-186 (WB-900-71C; WR-80854-A):

3-(3,4-Methylenedioxyphenyl)-2-thiopyruvic Acid



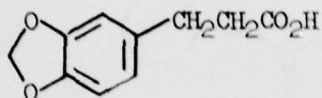
MO-187 (WB-2-117; WR-06338-D):

3-(3,4-Methylenedioxyphenyl)acrylic Acid



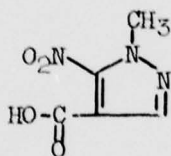
MO-188 (WB-2-119; WR-481790-A):

3-(3,4-Methylenedioxyphenyl)propionic Acid



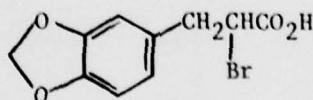
MO-189 (CC-260; WR-81791-A):

1-Methyl-5-nitro-4-pyrazolecarboxylic Acid



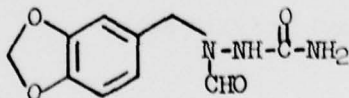
MO-190 (WB-2-128B; WR-81792-A):

2-Bromo-3-(3,4-methylenedioxyphenyl)propionic acid



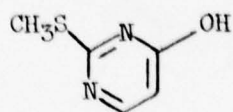
MO-191 (DM-I-46-1; WR-83965-A):

1-Formyl-1-piperonylsemicarbazide



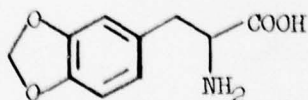
MO-192 (DM-I-43-1; WR-46291-C):

4-Hydroxy-2-methylthiopyrimidine



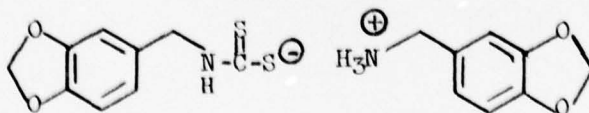
MO-193 (WB-300-68A; WR-83966-A):

3-(3,4-Methylenedioxyphenyl)alanine



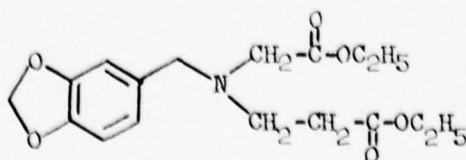
MO-194 (WB-2-146B; WR-83967-A):

Piperonylammonium N-Piperonyldithiocarbamate



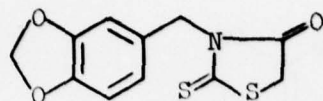
MO-195 (WB-2-145C; WR-83968-A):

N-Piperonyl-N-(2-ethoxycarbonyl)ethylglycine Ethyl Ester



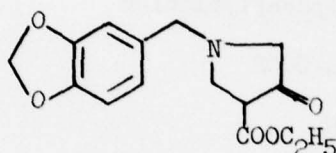
MO-196 (WB-2-137E2; WR-87023-A):

3-Piperonylrhodanine



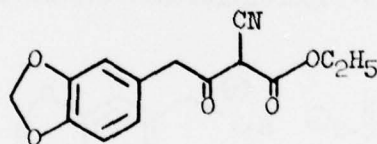
MO-197 (WB-3-111A; WR-87022-A):

3-Ethoxycarbonyl-1-piperonyl-4-pyrrolidone



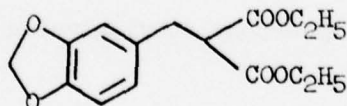
MO-198 (WB-3-108E; WR-87325-A):

Ethyl 2-Cyano-4-(3,4-methylenedioxyphenyl)-3-oxobutyrates



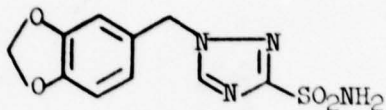
MO-199 (WB-3-117D; WR-87327-A):

Diethyl Piperonylmalonate



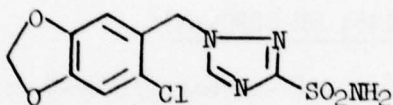
MO-200 (DM-I-49-1; WR-87328-A):

1-Piperonyl-3-sulfamoyl-1,2,4-triazole



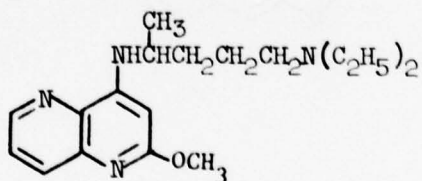
MO-201 (DM-I-48-1; WR-87329-A):

1-(6-Chloropiperonyl)-3-sulfamoyl-1,2,4-triazole



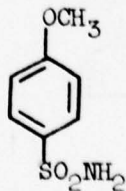
MO-202 (DM-I-50-2; WR-90010-A):

4-(4-Diethylamino-1-methylbutylamino)-2-methoxy-1,5-naphthyridine



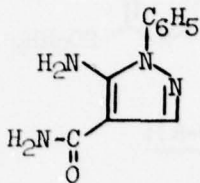
MO-203 (WB-3-129B; WR-15535-C):

p-Methoxybenzenesulfonamide



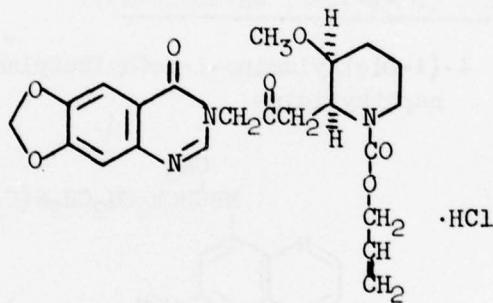
MO-204 (CC-268; WR-10485-C):

5-Amino-1-phenyl-4-pyrazolecarboxamide



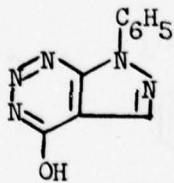
MO-205 (PC II-146; WR-89904-A):

cis-3-[2-Oxo-3-(1-carboallyloxy-3-methoxy-2-piperidyl)-propyl]-6,7-methylenedioxy-4-quinazalone Hydrochloride



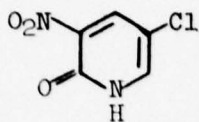
MO-206 (CC-269; WR-90210-A):

1-Phenyl-4-hydroxypyrazolo[3,4-d]-v-triazine



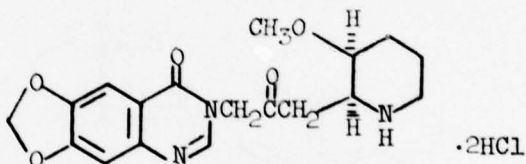
MO-207 (DM-I-53-1; WR-90211-A):

5-Chloro-3-nitro-2(1H)pyridone



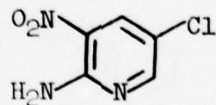
MO-208 (PC-III-7; WR-90212-A):

cis-3-[2-Oxo-3-(3-methoxy-2-piperidyl)propyl]-6,7-methylenedioxy-4-quinazolinone Dihydrochloride



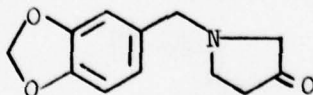
MO-209 (DM-I-52-1; WR-90213-A; AB-14188; WR-51462-C):

2-Amino-5-chloro-3-nitropyridine



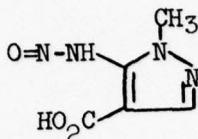
MO-210 (WB-4-37B; WR-92105-A):

1-Piperonyl-3-pyrrolidone



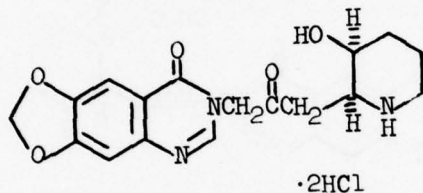
MO-211 (CC-255; WR-92104-A):

1-Methyl-5-nitrosamino-4-pyrazolecarboxylic Acid



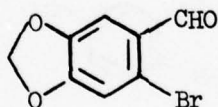
MO-212 (PC-III-10; WR-92103-A):

cis-3-[2-Oxo-3-(3-hydroxy-2-piperidyl)propyl]-6,7-methylenedioxy-4-quinazolinone Dihydrochloride



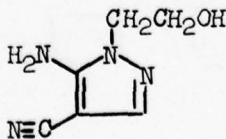
MO-213 (PC-III-14; WR-92444-A):

6-Bromo-3,4-methylenedioxybenzaldehyde



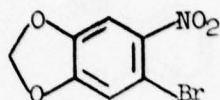
MO-214 (CC-280W; WR-92443-A):

1-(β-Hydroxyethyl)-4-cyano-5-aminopyrazole



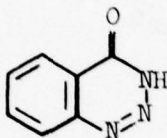
MO-215 (PC-III-16; WR-27298-D):

4-Nitro-5-bromocatechol Methylene Ether



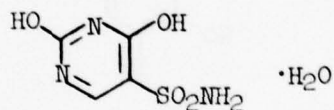
MO-216 (PC-III-12; WR-10009-K):

4-Oxo-3,4-dihydro-1,2,3-benzotriazine



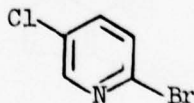
MO-217 (DM-I-54-1; WR-92958-A):

2,4-Dihydroxy-5-sulfamoylpyrimidine Monohydrate



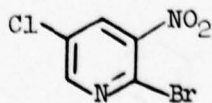
MO-218 (DM-I-55-1; WR-92959-A):

2-Bromo-5-chloropyridine



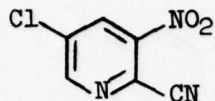
MO-219 (DM-I-56-1; WR-92960-A):

2-Bromo-5-chloro-3-nitropyridine



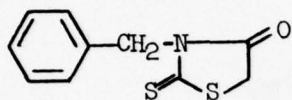
MO-220 (DM-I-57-1; WR-92964-A):

5-Chloro-3-nitropicolinonitrile



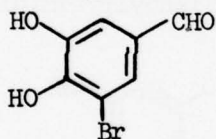
MO-221 (WB-4-47; WR-94290-A):

3-Benzylrhodanine



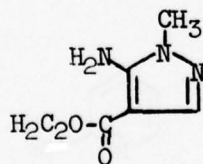
MO-222 (WB-4-58C; WR-94291-A):

3-Bromo-4,5-dihydroxybenzaldehyde



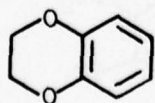
MO-223 (CC-286; WR-94409-A):

Ethyl 1-Methyl-5-aminopyrazole-4-carboxylate



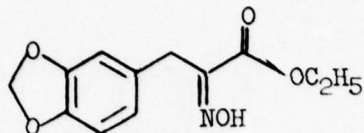
MO-224 (WB-3-110; WR-79235-C):

1,4-Benzodioxan



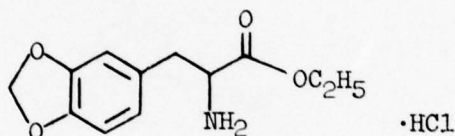
MO-225 (WB-4-64A; WR-94257-A):

Ethyl 2-Oximino-3(3,4-methylenedioxyphenyl)propionate



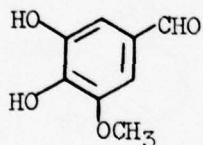
MO-226 (WB-4-66B; WR-94258-A):

Ethyl 2-Amino-3(3,4-methylenedioxyphenyl)propionate  
Hydrochloride



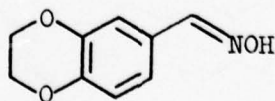
MO-227 (WB-4-68C; WR-13669-C):

3,4-Dihydroxy-5-methoxybenzaldehyde



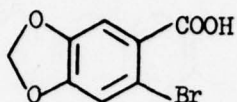
MO-228 (WB-4-76C; WR-95562-A):

1,4-Benzodioxan-6-carboxaldoxime



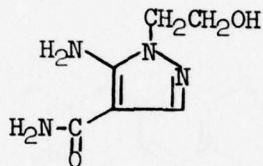
MO-229 (PC-III-22; WR-95563-A):

6-Bromo-3,4-methylenedioxybenzoic Acid



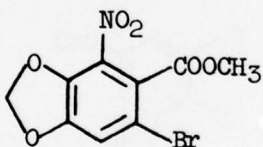
MO-230 (CC-288; WR-95564-A):

1-( $\beta$ -Hydroxyethyl)-5-aminopyrazole-4-carboxamide



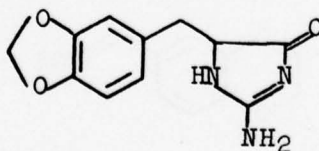
MO-231 (PC-III-25; AC-16730):

Methyl 6-Bromo-3,4-methylenedioxy-2-nitrobenzoate



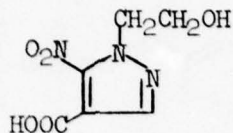
MO-232 (WB-4-86B; AC-16721):

2-Amino-5-piperonyl-4-imidazolinone



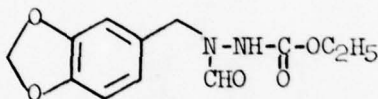
MO-233 (CC-291; AC-16712):

1-( $\beta$ -Hydroxyethyl)-5-nitropyrazole-4-carboxylic Acid



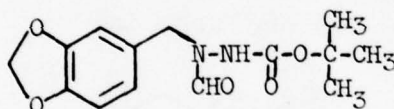
MO-234 (DM-I-58-1; AC-16703):

Ethyl 3-Formyl-3-piperonylcarbazate



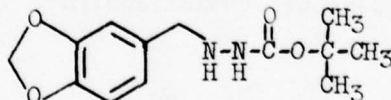
MO-235 (DM-I-62-1; AC-16696):

tert-Butyl 3-Formyl-3-piperonylcarbazate



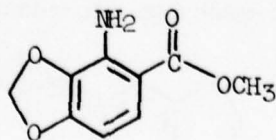
MO-236 (DM-I-61-1; AC-32510):

tert-Butyl 3-Piperonylcarbazate



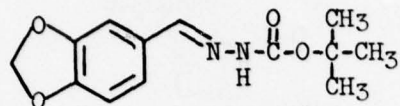
MO-237 (PC-III-32; AC-32529):

Methyl 2-Amino-3,4-methylenedioxybenzoate



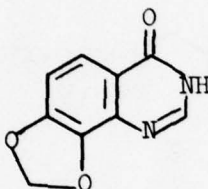
MO-238 (DM-I-60-1; AC-32538):

tert-Butyl 3-Piperonylidene-carbazate



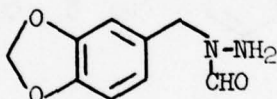
MO-239 (PC-III-35; AC-32547):

7,8-Methylenedioxy-4-quinazolone



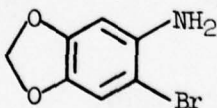
MO-240 (DM-I-63-1; AC-71517):

1-Formyl-1-piperonylhydrazine



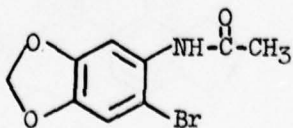
MO-241 (PC-III-33; AC-71526):

2-Bromo-4,5-methylenedioxyaniline



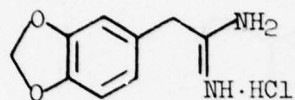
MO-242 (PC-III-38; AC-71535):

2-Bromo-4,5-methylenedioxyacetanilide



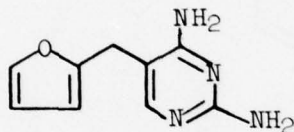
MO-243 (WB-4-121A; AD-00479):

3,4-Methylenedioxyphenylacetamide Hydrochloride



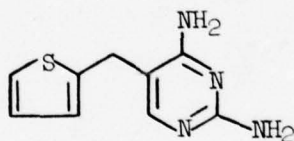
MO-244 (DM-I-66-1; AD-00488):

2,3-Diamino-5-furfurylpyrimidine



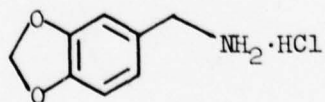
MO-245 (DM-I-65-1; AD-00497):

2,4-Diamino-5-(2-thienyl)pyrimidine



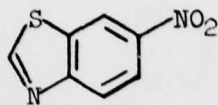
MO-246 (WB-4-104B; AD-21834):

6-Aminomethyl-1,4-benzodioxan Hydrochloride



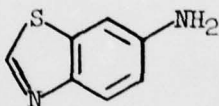
MO-247 (WB-4-115B; AD-21843):

6-Nitrobenzothiazole



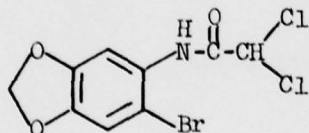
MO-248 (NB-4-127A; AD-21852):

6-Aminobenzothiazole



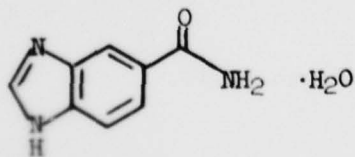
MO-249 (PC-III-4; AD-21861):

2-Bromo-4,5-methylenedioxydichloroacetanilide



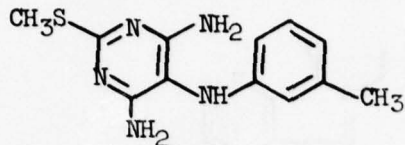
MO-250 (WB-5-12C; AE-47628):

5-Benzimidazolecarboxamide monohydrate



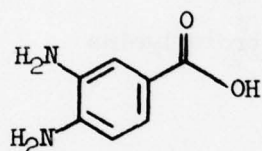
MO-251 (FB-5-856-777R; AE-47637):

4,6-Diamino-2-methylthio-5-(m-toluidino)pyrimidine



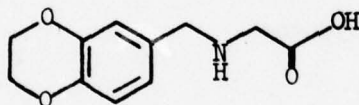
MO-252 (WB-4-123; AE-47646; 013387 AB):

3,4-Diaminobenzoic acid



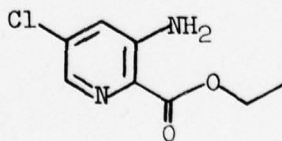
MO-253 (WB-5-27B; AE-92785):

N-(3,4-Ethylenedioxybenzyl)glycine hydrochloride



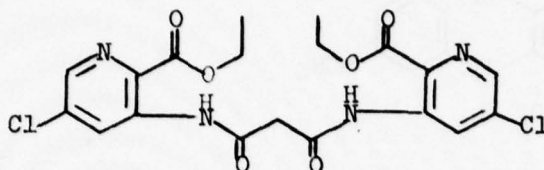
MO-254 (DM-I-68-1; AE-92794):

Ethyl 3-amino-5-chloropicolinate



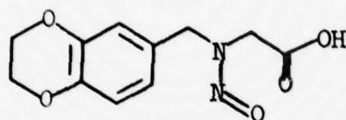
MO-255 (DM-I-71-1; AE-96023):

N,N'-Bis(5-chloro-2-ethoxycarbonyl-3-pyridyl)malonamide



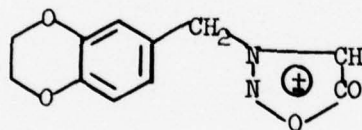
MO-256 (WB-5-34B; AE-96032):

N-(3,4-Ethylenedioxybenzyl)-N-nitrosoglycine



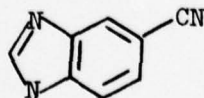
MO-257 (WB-5-43A; AF-11785):

3-(3,4-Ethylenedioxybenzyl)sydnone



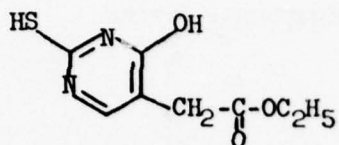
MO-258 (WB-5-41; AF-11776):

5(6)-Cyanobenzimidazole



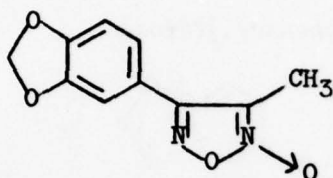
MO-259 (CN-5-12; AF-11794):

2-Thio-4-hydroxy-5-ethoxycarbonylmethylpyrimidine



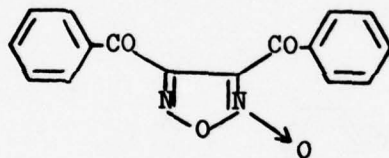
MO-260 (PC-III-52; AF-12657):

3-Methyl-4-(3,4-methylenedioxyphenyl)furoxan



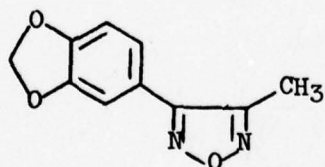
MO-261 (PC-III-54; AF-12648):

Dibenzoylfuroxan



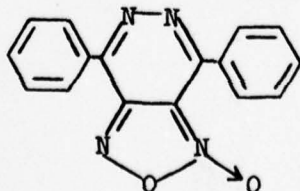
MO-262 (PC-III-55; AF-16011):

3-Methyl-4-(3,4-methylenedioxyphenyl)fuzazan



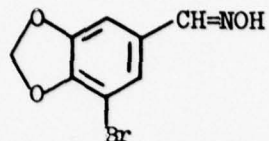
MO-263 (PC-III-57; AF-16020):

Dibenzoylfuroxan azine



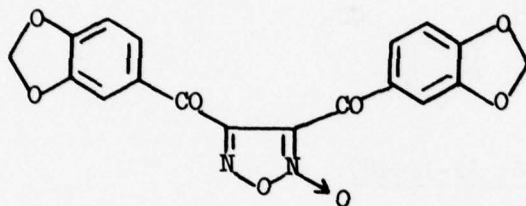
MO-264 (WB-5-48c; AF-16002):

3-Bromo-4,5-methylenedioxybenzaloxime



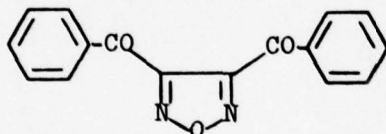
MO-265 (PC-III-59; AF-55698):

Bis-(3,4-methylenedioxybenzoyl)furoxan



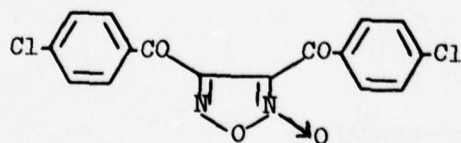
MO-266 (PC-III-61; AF-55689):

Dibenzoylfurazan



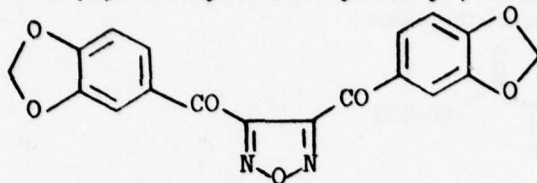
MO-267 (PC-III-62; AF-55670):

Bis-(p-Chlorobenzoyl)furoxan



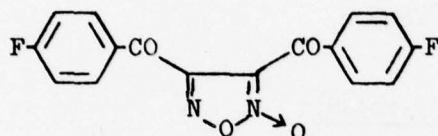
MO-268 (PC-III-64; AF-55661):

Bis-(3,4-methylenedioxybenzoyl) furazan



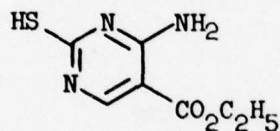
MO-269 (PC-III-65; AF-55652):

Bis-(p-fluorobenzoyl) furoxan



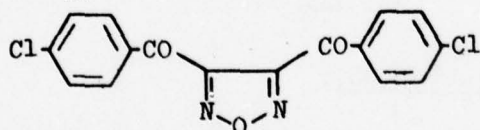
MO-270 (WB-5-57A; AF-55643):

Ethyl 4-Amino-2-mercaptopyrimidine-5-carboxylate



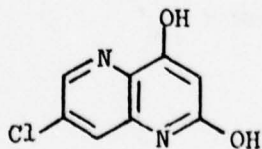
MO-271 (PC-III-63; AF-59445):

Bis-(p-chlorobenzoyl) furazan



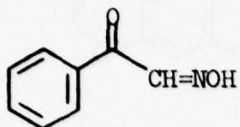
MO-272 (DM-I-71-2; AF-59436):

7-Chloro-2,4-dihydroxy-1,5-naphthyridine



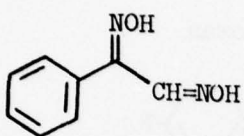
MO-273 (DM-I-72-1; AF-59427):

Isonitrosoacetophenone



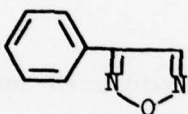
MO-274 (DM-I-73-1; AF-59418):

Phenylglyoxime



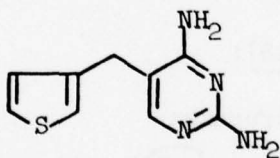
MO-275 (DM-I-74-1; AF-59409):

3-Phenylfuran



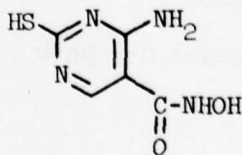
MO-276 (DM-I-77-1; AF-59392):

2,4-Diamino-5-(3-thenyl)pyrimidine



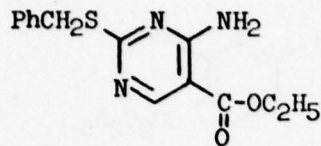
MO-277 (WB-5-67A; AF-59383):

4-Hydroxy-2-mercapto-5-pyrimidinehydroxamic Acid



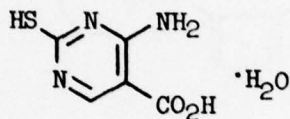
MO-278 (WB-5-69A; AF-59374):

Ethyl 4-Amino-2-benzylthio-5-pyrimidinecarboxylate



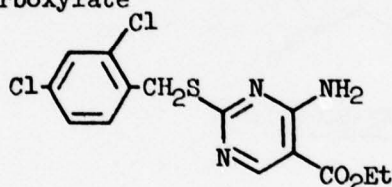
MO-279 (WB-5-71A; AF-93018):

4-Amino-2-mercapto-5-pyrimidinecarboxylic Acid  
Monohydrate



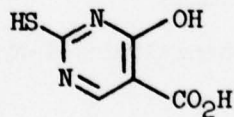
MO-280 (WB-5-82A; AF-93009):

Ethyl 4-Amino-2-(2,4-dichlorobenzylthio)-5-pyrimidine-  
carboxylate



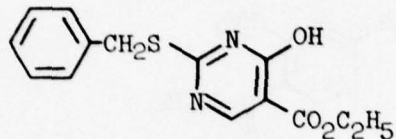
MO-281 (WB-5-73B; AF-93027):

4-Hydroxy-2-mercapto-5-pyrimidinecarboxylic Acid



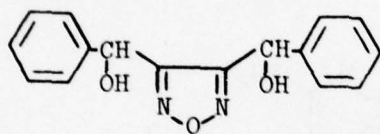
MO-282 (WB-5-77B; AF-93036):

Ethyl 2-Benzylthio-4-hydroxy-5-pyrimidinecarboxylate



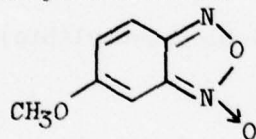
MO-283 (PC-III-67; AF-93045):

Bis-( $\alpha$ -hydroxybenzyl) furazan



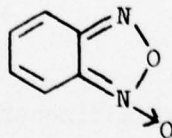
MO-284 (PC-III-68; AF-93054):

6-Methoxybenzofuroxan



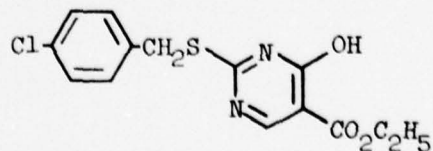
MO-285 (PC-III-70; AF-93063):

Benzofuroxan



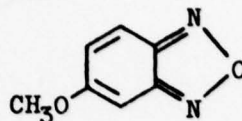
MO-286 (WB-5-93B; AF-93072):

Ethyl 2-(*p*-Chlorobenzylthio)-4-hydroxy-5-pyrimidinecarboxylate



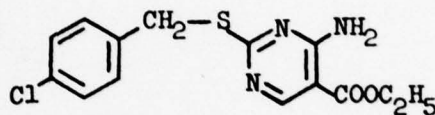
MO-287 (PC-III-71; AS-37015):

5-Methoxybenzofurazan



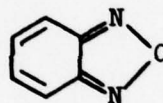
MO-288 (WB-5-91C; AS-37024):

Ethyl 4-Amino-2-(p-chlorobenzylthio)-5-pyrimidinecarboxylate



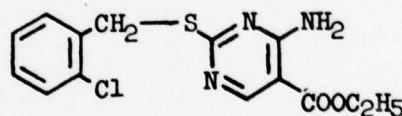
MO-289 (PC-III-72; AS-37033):

Benzofurazan



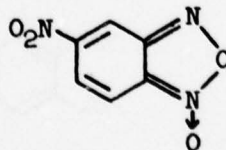
MO-290 (WB-5-95C; AS-37042):

Ethyl 4-Amino-2-(o-chlorobenzylthio)-5-pyrimidinecarboxylate



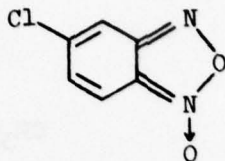
MO-291 (PC-III-74; AS-37051):

5-Nitrobenzofuroxan



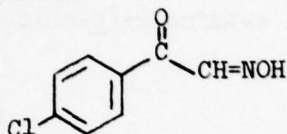
MO-292 (PC-III-75; AS-37060):

5-Chlorobenzofuroxan



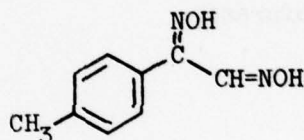
MO-293 (DM-I-78-1; AS-37079):

p-Chloroisnitrosoacetophenone



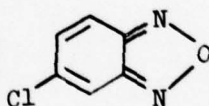
MO-294 (DM-I-82-1; AS-37088):

p-Tolylglyoxime



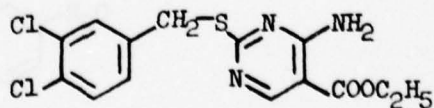
MO-295 (PC-III-76; AS-37097):

5-Chlorobenzofurazan



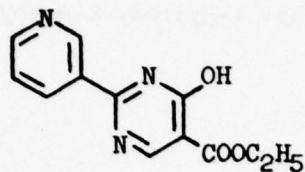
MO-296 (WB-5-101; AS-39920):

Ethyl 4-Amino-2-(3,4-dichlorobenzylthio)-5-pyrimidinecarboxylate



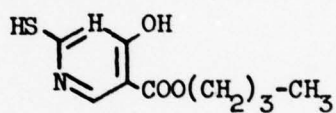
MO-297 (WB-5-100C; AS-39939):

Ethyl 4-Hydroxy-2-(3-pyridyl)-5-pyrimidinecarboxylate



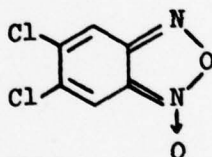
MO-298 (WB-5-102B; AS-39948):

Butyl 4-Hydroxy-2-thio-5-pyrimidinecarboxylate



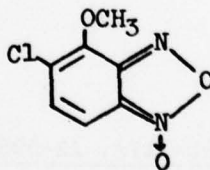
MO-299 (PC-III-77; AS-39957):

5,6-Dichlorobenzofuroxan



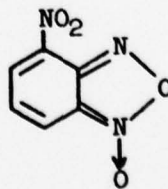
MO-300 (PC-III-78); AS-39966):

5-Chloro-4-methoxybenzofuroxan



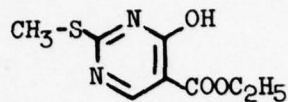
MO-301 (PC-III-80; AS-59459):

4-Nitrobenzofuroxan



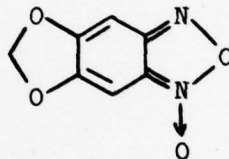
MO-302 (WB-5-103C; AS-59468):

Ethyl 4-Hydroxy-2-methylthio-5-pyrimidinecarboxylate



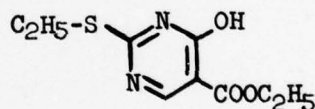
MO-303 (PC-III-81; AS-59477):

5,6-Methylenedioxybenzofuroxan



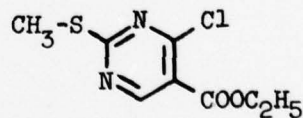
MO-304 (WB-5-109; AS-59486):

Ethyl 2-Ethylthio-4-hydroxy-5-pyrimidinecarboxylate



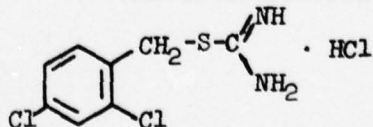
MO-305 (WB-5-IIIA; AS-59495):

Ethyl 4-Chloro-2-methylthio-5-pyrimidinecarboxylate



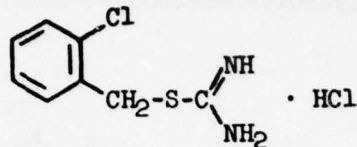
MO-306 (WB-5-117A; AS-59502):

S-(2,4-Dichlorobenzyl)isothiuronium Hydrochloride



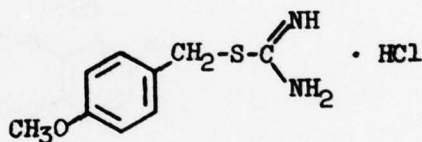
MO-307 (WB-5-115B; AT-16048):

S-(o-Chlorobenzyl)isothiuronium Hydrochloride



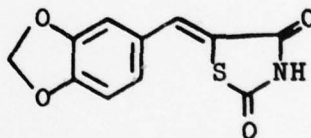
MO-308 (WB-5-128; AT-16039):

S-(p-Methoxybenzyl)isothiuronium Hydrochloride



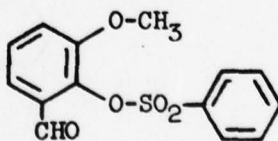
MO-309 (WB-5-135; AT-16020):

5-Piperonylidene-2,4-thiazolidinedione



MO-310 (PC-III-90; AT-16011):

o-Vanillin Benzenesulfonate



AD-A060 471

MIDWEST RESEARCH INST KANSAS CITY MO

F/G 6/15

SYNTHESIS OF RATIONALLY DESIGNED ORGANIC COMPOUNDS FOR MALARIA --ETC(U)

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DAMD17-76-C-6015

UNCLASSIFIED

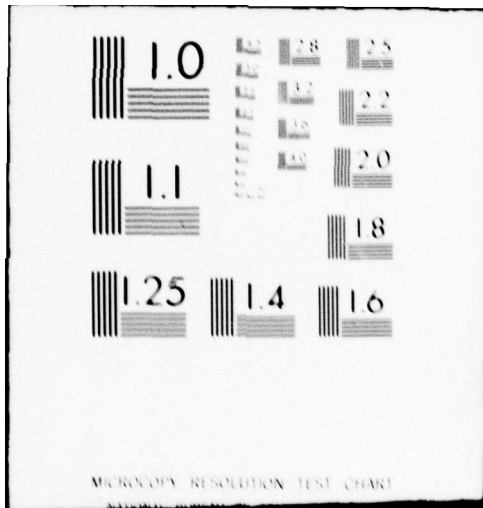
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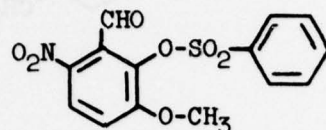
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MICROCOPY RESOLUTION TEST CHART

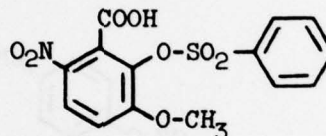
MO-311 (PC-III-85; AT-16002):

2-Hydroxy-3-methoxy-6-nitrobenzaldehyde Benzenesulfonate



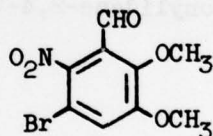
MO-312 (PC-III-86; AT-15998):

2-Hydroxy-3-methoxy-6-nitrobenzoic Acid Benzenesulfonate



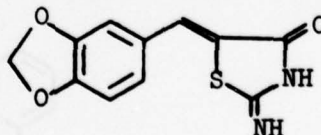
MO-313 (PC-III-83; AT-15989):

5-Bromo-2,3-dimethoxy-6-nitrobenzaldehyde



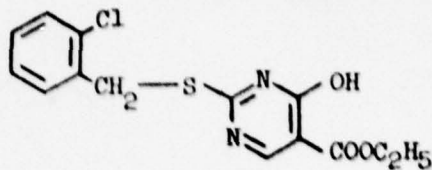
MO-314 (WB-5-133C; AT-15970):

5-Piperonylidenehydantoin



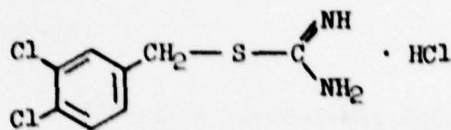
MO-315 (WB-5-132A; AT-15961):

Ethyl 2-(*o*-Chlorobenzylthio)-4-hydroxy-5-pyrimidinecarboxylate



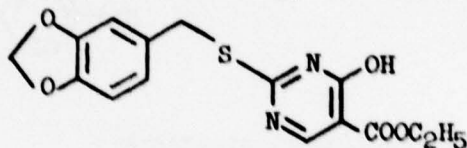
MO-316 (WB-5-140; AT-15952):

S-(3,4-Dichlorobenzyl)isothiuronium Hydrochloride



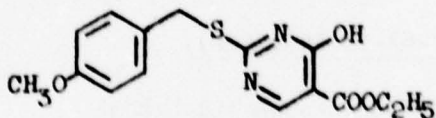
MO-317 (WB-5-127A; AT-15943):

Ethyl 4-Hydroxy-2-piperonylthio-5-pyrimidinecarboxylate



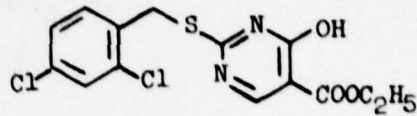
MO-318 (WB-5-136B; AT-17714):

Ethyl 2-(*p*-Methoxybenzylthio)-4-hydroxy-5-pyrimidinecarboxylate



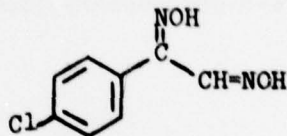
MO-319 (WB-5-123H; AT-17698):

Ethyl 2-(2,4-Dichlorobenzylthio)-4-hydroxy-5-pyrimidinecarboxylate



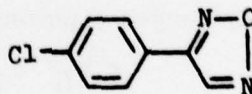
MO-320 (DM-I-79-1; AT-17689):

*p*-Chlorophenylglyoxime



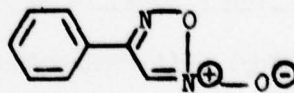
MO-321 (DM-I-80-1; AT-17670):

4-(*p*-Chlorophenyl)furazan



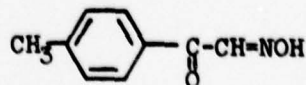
MO-322 (DM-I-83-1; AT-17661):

4-Phenylfuroxan



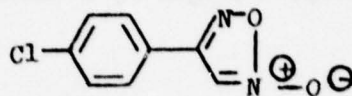
MO-323 (DM-I-81-1; AT-17652):

*p*-Methylisonitrosoacetophenone



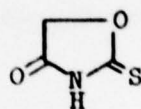
MO-324 (IM-I-84-1; AT-17643):

4-(p-Chlorophenyl)furoxan



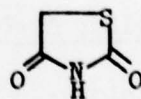
MO-325 (WB-5-149A; AT-17634):

2-Thio-2,4-oxazolidinedione



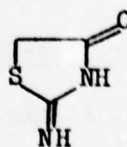
MO-326 (WB-6-1B; AT-17705):

2,4-Thiazolidinedione



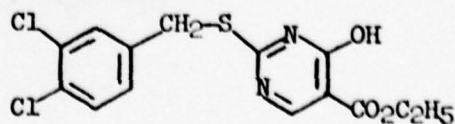
MO-327 (WB-6-1A; AT-70186):

Pseudothiohydantoin



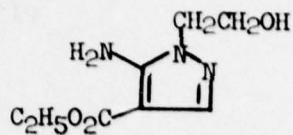
MO-328 (WB-5-148A; AT-70195):

Ethyl 2-(3,4-Dichlorobenzylthio)-4-hydroxy-5-pyrimidinecarboxylate



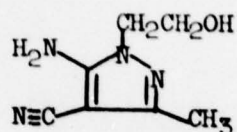
MO-329 (CC-1-303; AT-70202):

Ethyl 1-β-Hydroxy-5-amino-4-pyrazolecarboxylate



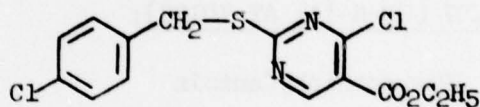
MO-330 (CC-II-2; AT-70211):

1-β-Hydroxyethyl-3-methyl-4-cyano-5-aminopyrazole



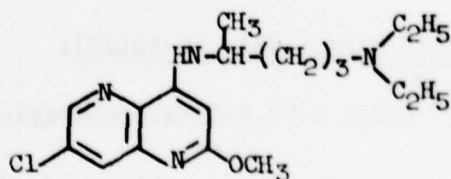
MO-331 (WB-5-113C; AT-70220):

Ethyl 4-Chloro-2-(p-chlorobenzylthio)-5-pyrimidinecarboxylate



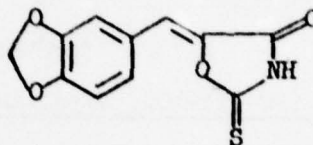
MO-332 (DM-I-86-1; AT-70239):

7-Chloro-4-(4-dimethylamino-1-methylbutylamino)-2-methoxy-1,5-naphthyridine



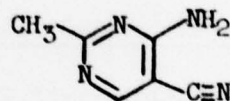
MO-333 (WB-5-146B; AT-70248):

5-Piperonylidene-2-thio-2,4-oxazolidinedione



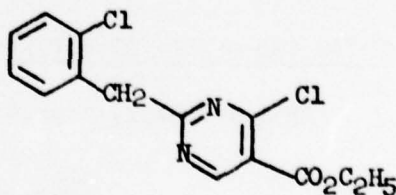
MO-334 (WB-6-15A; AT-88259):

4-Amino-2-methyl-5-pyrimidinecarbonitrile



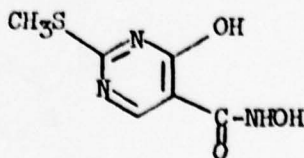
MO-335 (WB-6-10; AT-88268):

Ethyl 4-Chloro-2-(o-chlorobenzylthio)-5-pyrimidinecarboxylate



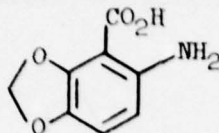
MO-336 (WB-6-16B; AT-88277):

4-Hydroxy-2-methylthio-5-pyrimidinehydroxamic Acid



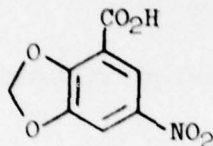
MO-337 (PC-III-99; AT-90731):

6-Amino-2,3-methylenedioxybenzoic Acid



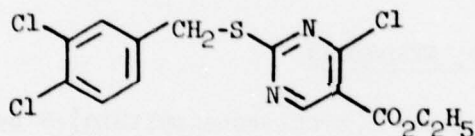
MO-338 (PC-III-100; AT-90722):

2,3-Methylenedioxy-5-nitrobenzoic Acid



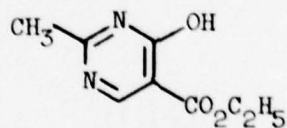
MO-339 (WB-6-21B; AT-90713):

Ethyl 4-Chloro-2-(3,4-dichlorobenzylthio)-5-pyrimidinecarboxylate



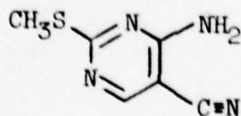
MO-340 (WB-6-32A; AT-90704):

Ethyl 4-Hydroxy-2-methyl-5-pyrimidinecarboxylate



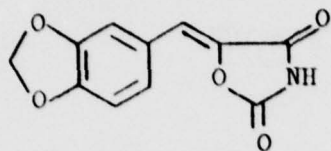
MO-341 (WB-6-37B; AT-90697):

4-Amino-2-methylthio-5-pyrimidinecarbonitrile



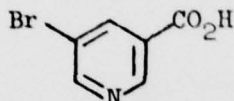
MO-342 (WB-6-34B; AT-90688):

5-Piperonylidene-2,4-oxazolinedione



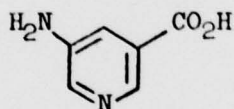
MO-343 (DM-I-87-1; AT-90679):

5-Bromonicotinic Acid



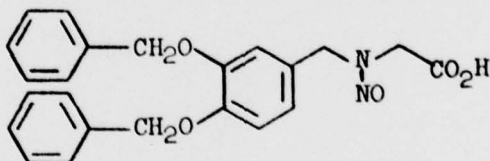
MO-344 (DM-I-88-1; AT-90660):

5-Aminonicotinic Acid



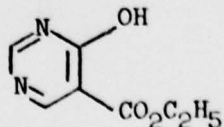
MO-345 (WB-6-45E; AU-13248):

N-(3,4-Dibenzoyloxybenzyl)-N-nitrosoglycine



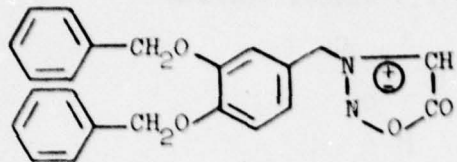
MO-346 (WB-6-50B; AU-13257):

Ethyl 4-Hydroxy-5-pyrimidinecarboxylate



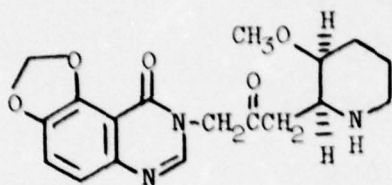
MO-347 (WB-6-53A; AU-13266):

3-(3,4-Dibenzyloxybenzyl)sydnone



MO-348 (PC-III-111; AU-13211):

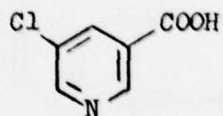
cis-3-[2-Oxo-3-(3-methoxy-2-piperidyl)propyl]-5,6-methylene-  
dioxy-4-quinazalone Dihydrochloride



·2HCl

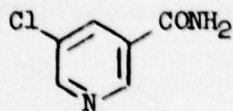
MO-349 (AU-93200; DM-I-89-1):

5-Chloronicotinic acid



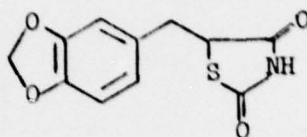
MO-350 (AU-93219; DM-I-90-1):

5-Chloronicotinamide



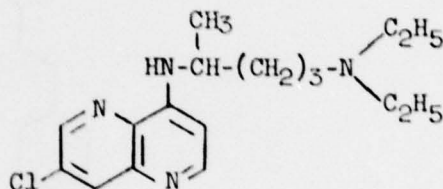
MO-351 (AU-93228; WB-5-144C):

5-Piperonyl-2,4-thiazolidinedione



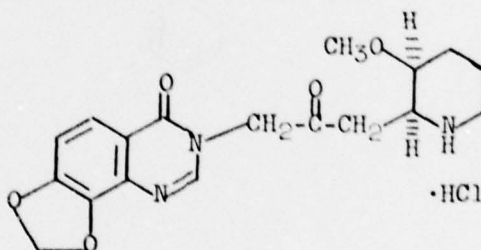
MO-352 (AU-93237; DM-I-95-1):

7-Chloro-4-(4-diethylamino-1-methylbutylamino)-1,5-naphthyridine



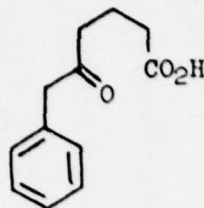
MO-353 (AU-93246; FC-III-114):

*cis*-3-[2-Oxo-3-(3-methoxy-2-piperidyl)propyl]-7,8-methylene-dioxy-4-quinazoline hydrochloride



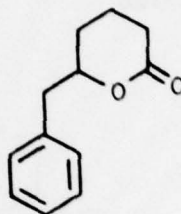
MO-354 (AV-80039; DM-I-97-1):

5-Oxo-6-phenylhexanoic Acid



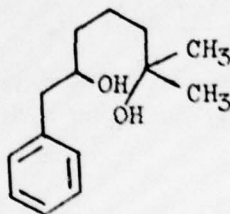
MO-355 (AV-80002; DM-I-98-1):

5-Hydroxy-6-phenylhexanoic Acid  $\delta$ -Lactone



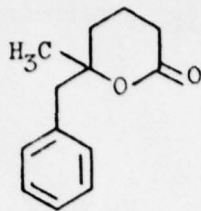
MO-356 (AV-80011; DM-I-99-1):

2-Methyl-7-phenyl-2,6-heptanediol



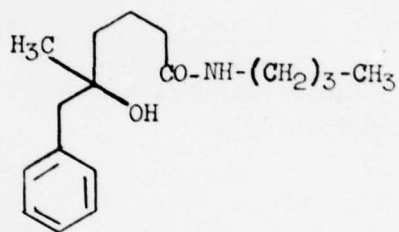
MO-357 (AV-80020; DM-I-100-1):

5-Hydroxy-5-methyl-6-phenylhexanoic Acid  $\delta$ -Lactone



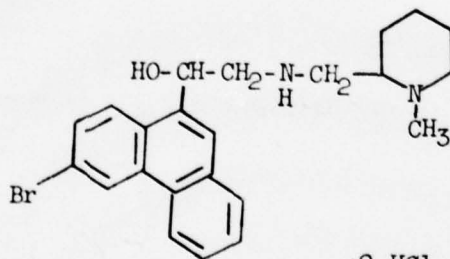
MO-358 (AW-20912; DM-I-101-1):

N-Butyl-5-hydroxy-5-methyl-6-phenylhexamide



MO-359 (AW-20921; DM-I-104-1):

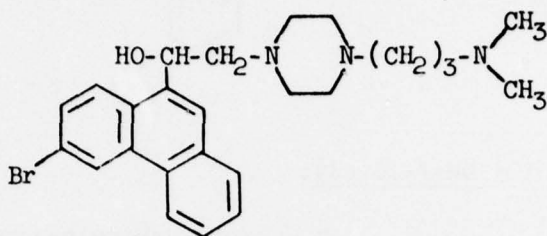
$\alpha$ -[(1-Methyl-2-piperidylmethyl)aminomethyl]-6-bromo-9-phenanthrene-methanol Dihydrochloride



$\cdot 2 \text{ HCl}$

MO-360 (AW-20930; DM-I-105-1):

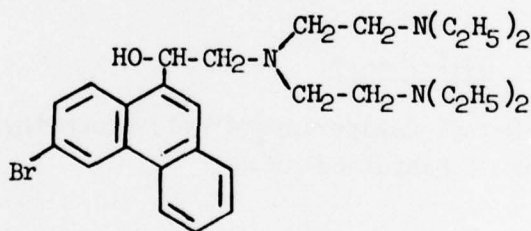
$\alpha$ -[4-(Dimethylaminopropyl)piperazinylmethyl]-6-bromo-9-phenanthrenemethanol  
Trihydrochloride



• 3 HCl

MO-361 (AW-20949; DM-I-106-1):

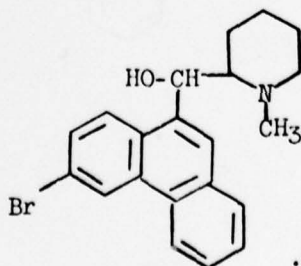
$\alpha$ -{N,N-Bis[2-(diethylamino)ethyl]aminomethyl}-6-bromo-9-phenanthrenemethanol  
Trihydrochloride



• 3 HCl

MO-362 (AW-20958; WB-7-53c)

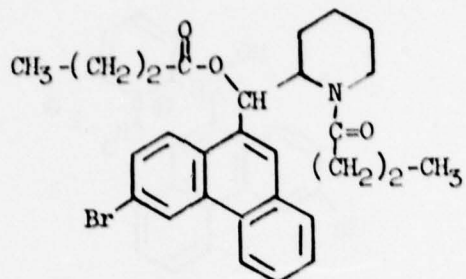
6-Bromo- $\alpha$ [2-(1-methylpiperidyl)]-9-phenanthrenemethanol Hydrochloride  
Hydrate



• HCl • H<sub>2</sub>O

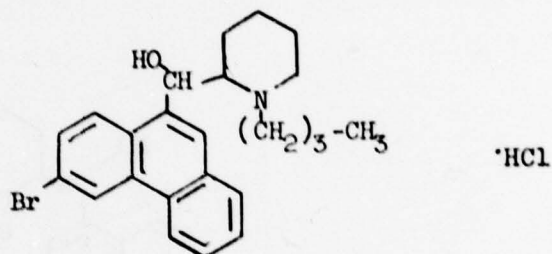
MO-363 (AW-45035; WB-7-59C)

6-Bromo- $\alpha$ -[2-(1-butyrylpiperidyl)]-9-phenanthrenemethanol Butyrate



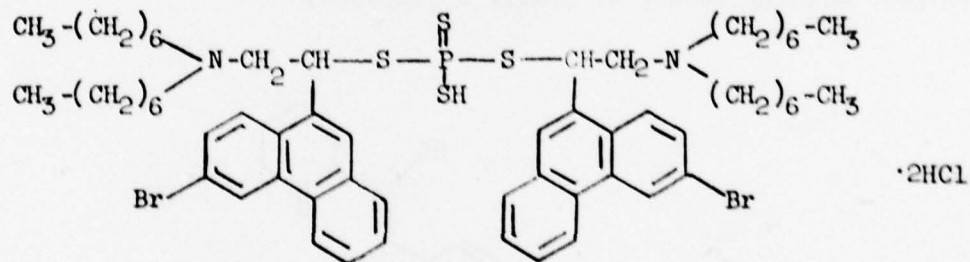
MO-364 (AW-45026; WB-7-65B)

6-Bromo- $\alpha$ -[2-(1-butylpiperidyl)]-9-phenanthrenemethanol Hydrochloride



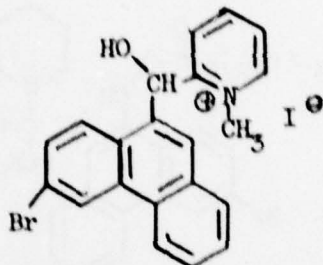
MO-365 (AW-91984, WB-6-84-4B)

S,S-Bis[1-(6-bromo-9-phenanthryl)-2-diheptylamino] ethylphosphorotetra-thioate Dihydrochloride



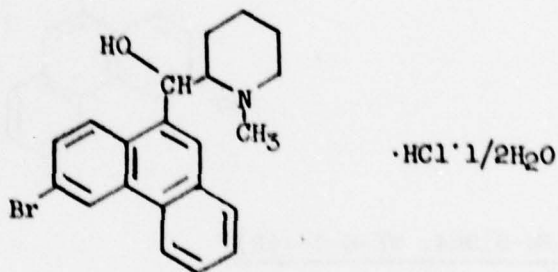
MO-366 (AW-91993; WB-7-51):

6-Bromo- $\alpha$ -(2-pyridyl)-9-phenanthrenemethanol Methiodide



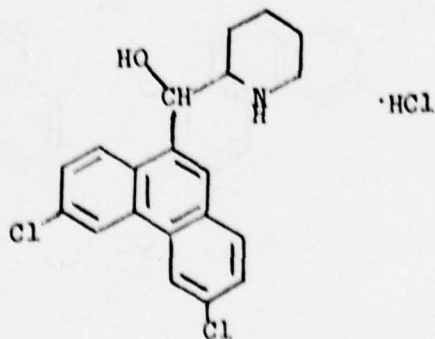
MO-367 (AX-20837; WB-7-55D):

6-Bromo- $\alpha$ -[2-(1-methylpiperidyl)]-9-phenanthrenemethanol Hydrochloride Hemihydrate (lower melting isomer of MO-362)



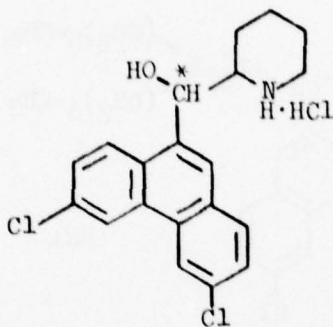
MO-368 (AX-20828; PC-IV-21):

3,6-Dichloro- $\alpha$ -(2-piperidyl)-9-phenanthrenemethanol Hydrochloride (higher melting isomer of Nodiff's compound)



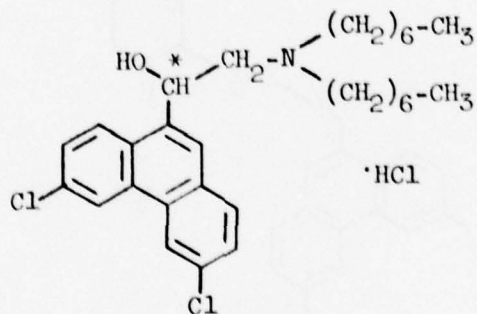
MO-369 (PC-IV-10)

3,6-Dichloro- $\alpha$ -(2-piperidyl)-9-phenanthrenemethanol-C<sup>14</sup> Hydrochloride



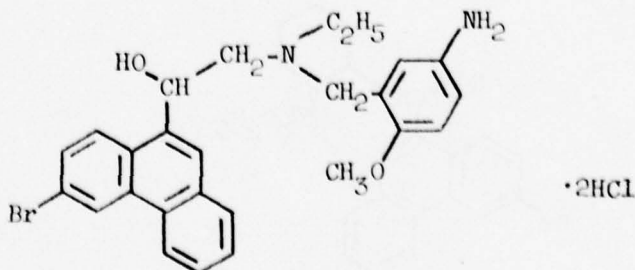
MO-370 (PC-IV-11)

3,6-Dichloro- $\alpha$ -(di-n-heptylaminomethyl)-9-phenanthrenemethanol-C<sup>14</sup>  
Hydrochloride



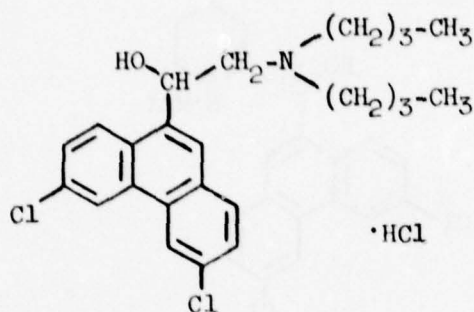
MO-371 (AX-25476; DM-I-111-1)

$\alpha$ -[N-(5-Amino-2-methoxybenzyl)-N-ethyl]aminomethyl-6-bromo-9-phenanthrene-  
methanol Dihydrochloride



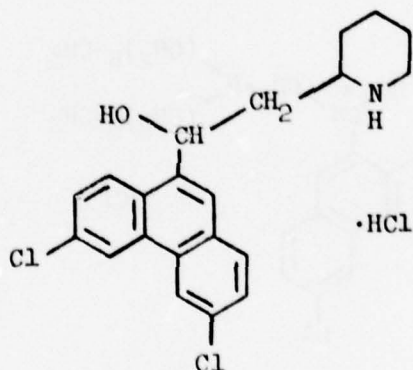
MO-372 (AX-25485; PC-IV-34)

3,6-Dichloro- $\alpha$ -(di-n-butylaminomethyl)-9-phenanthrenemethanol Hydrochloride



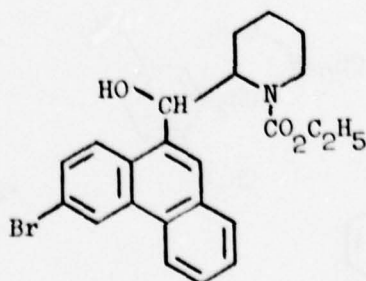
MO-373 (AX-25903; PC-IV-35)

3,6-Dichloro- $\alpha$ -(2-piperidylmethyl)-9-phenanthrenemethanol Hydrochloride



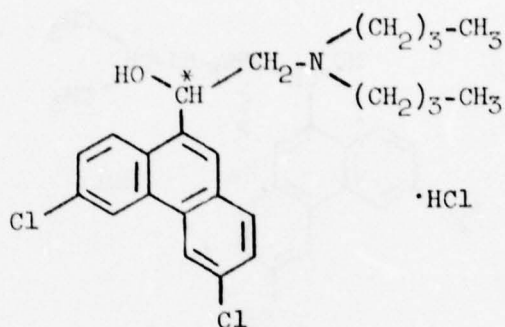
MO-374 (AX-25912; DM-I-110-1)

6-Bromo- $\alpha$ -[2-(1-ethoxycarbonylpiperidyl)]-9-phenanthrenemethanol



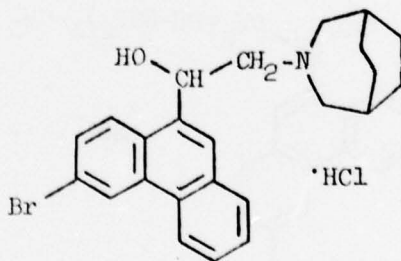
MO-375 (PC-IV-38)

3,6-Dichloro- $\alpha$ -(di-n-butylaminomethyl)-9-phenanthrenemethanol-C<sup>14</sup>  
Hydrochloride



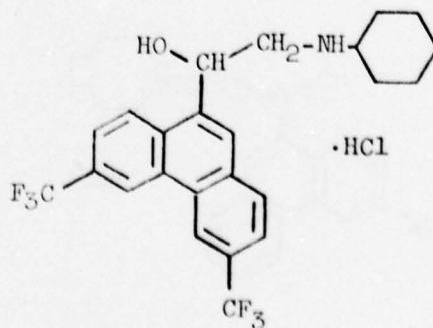
MO-376 (AX-58788; DM-I-114-1)

6-Bromo- $\alpha$ -{3-[3-azabicyclo(3·2·2)nonyl]}-9-phenanthrenemethanol  
Hydrochloride



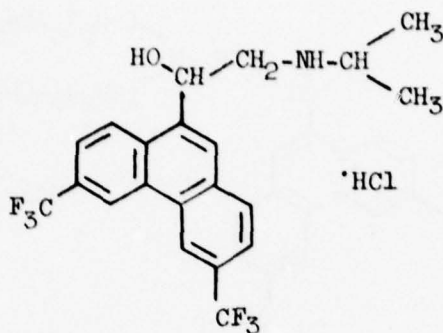
MO-377 (AX-58797; PC-IV-47)

3,6-Bis(trifluoromethyl)- $\alpha$ -(cyclohexylaminomethyl)-9-phenanthrenemethanol  
Hydrochloride



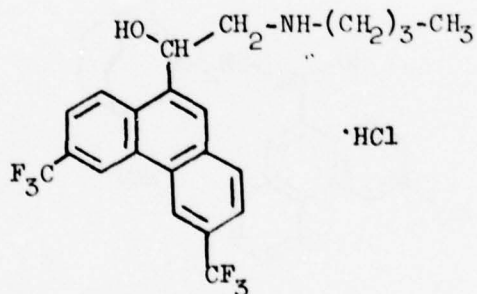
MO-378 (AX-27836; PC-IV-48B)

3,6-Bis(trifluoromethyl)- $\alpha$ -(iso-propylaminomethyl)-9-phenanthrenemethanol  
Hydrochloride



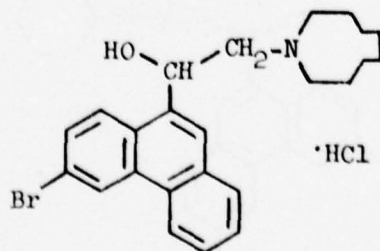
MO-379 (AX-27845; PC-IV-46B)

3,6-Bis(trifluoromethyl)- $\alpha$ -(butylaminomethyl)-9-phenanthrenemethanol  
Hydrochloride



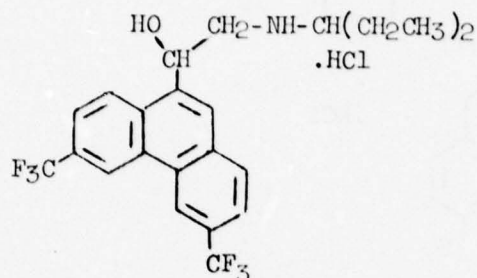
MO-380 (AX-27854; DM-I-117-1)

6-Bromo- $\alpha$ -(N,N-octamethyleneaminomethyl)-9-phenanthrenemethanol  
Hydrochloride



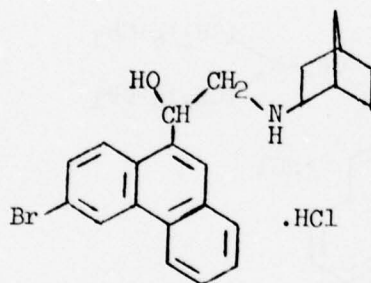
MO-381 (AX-28691; PC-IV-52)

3,6-Bis-(trifluoromethyl)- $\alpha$ -(1-ethylpropylaminomethyl)-9-phenanthrene-methanol Hydrochloride



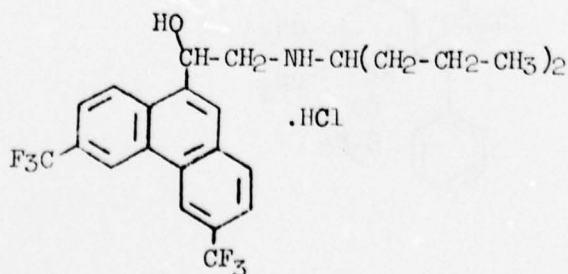
MO-382 (AX-28682; DM-I-118-1)

6-Bromo- $\alpha$ -(endo-2-norbornylamino)-9-phenanthrenemethanol Hydrochloride



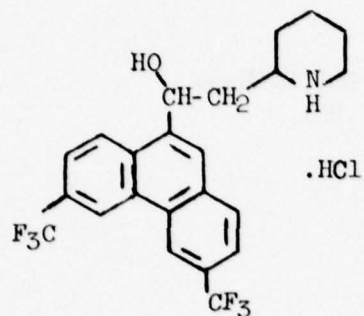
MO-383 (AX-29812; PC-IV-50)

3,6-Bis(trifluoromethyl)- $\alpha$ -(1-propylbutylaminomethyl)-9-phenanthrene-methanol Hydrochloride



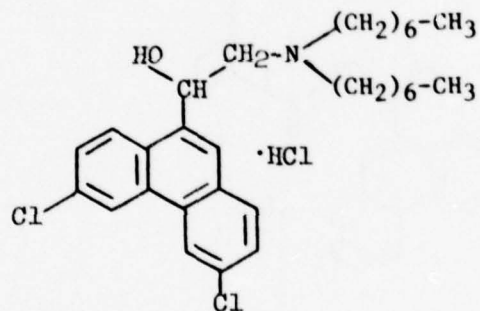
MO-384 (AX-29821; PC-IV-33)

3,6-Bis(trifluoromethyl)- $\alpha$ -(2-piperidylmethyl)-9-phenanthrenemethanol  
Hydrochloride



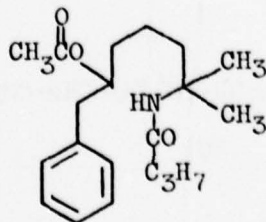
MO-385 (AX-64713; PC-IV-5)

3,6-Dichloro- $\alpha$ -(diheptylaminomethyl)-9-phenanthrenemethanol  
Hydrochloride



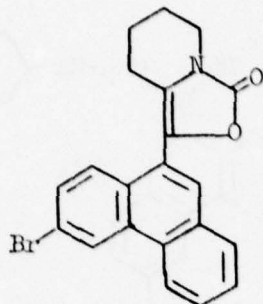
MO-386 (AX-66600; DM-I-115-1)

N-(5-Acetoxy-1,1-dimethyl-6-phenylhexyl)butyramide



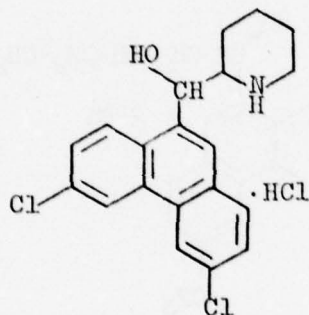
MO-387 (AX-66619; IM-I-113-2)

5-(6-Bromo-9-phenanthryl)-3,4-tetrahydro-2H-pyridin-2-one



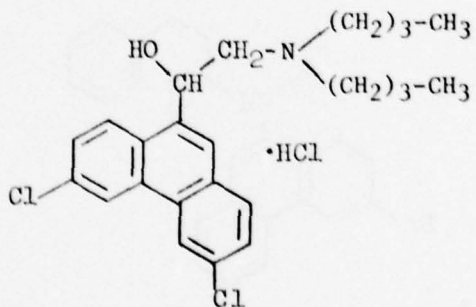
MO-368B (AX-64731; PC-IV-21)

3,6-Dichloro- $\alpha$ -(2-piperidyl)-9-phenanthrenemethanol Hydrochloride



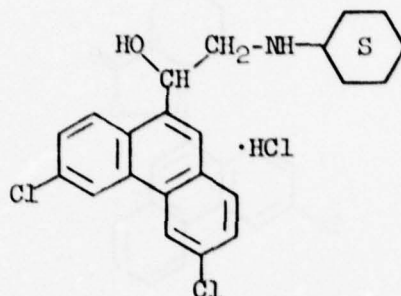
MO-372B (AX-64722; PC-IV-34)

3,6-Dichloro- $\alpha$ -(dibutylaminomethyl)-9-phenanthrenemethanol  
Hydrochloride



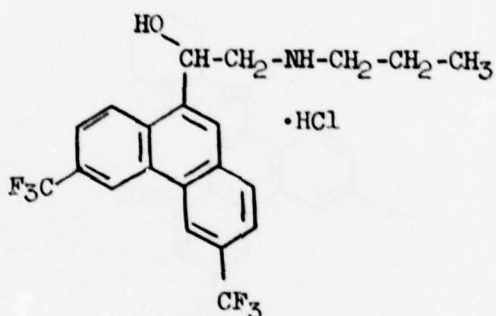
MO-388 (AX-66628; PC-IV-84)

3,6-Dichloro- $\alpha$ -(cyclohexylaminomethyl)-9-phenanthrenemethanol  
Hydrochloride



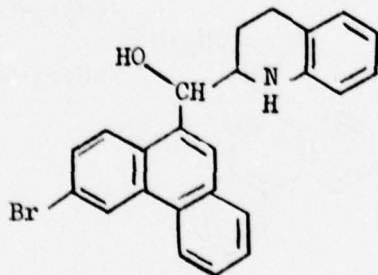
MO-389 (AX-68033; PC-IV-90):

3,6-Bis(trifluoromethyl)- $\alpha$ -(propylaminomethyl)-9-phenanthrenemethanol  
Hydrochloride



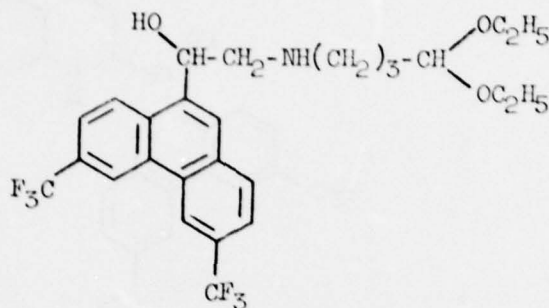
MO-390 (AX-68042; DM-I-121-4):

6-Bromo- $\alpha$ -[2-(1,2,3,4-tetrahydroquinolyl)]-9-phenanthrenemethanol



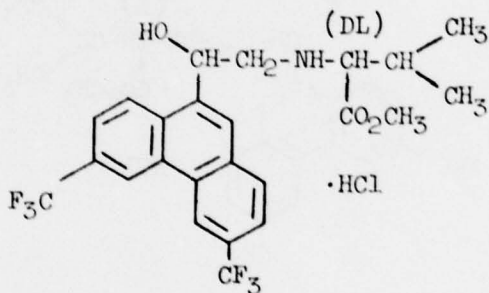
MO-391 (AY-61388; PC-V-3):

3,6-Bis(trifluoromethyl)- $\alpha$ -(4-diethoxybutylaminomethyl)-9-phenanthrenemethanol



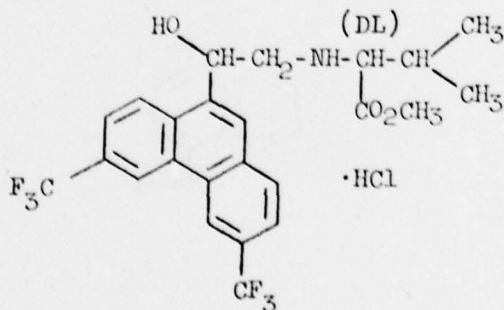
MO-392 (AY-61397; PC-IV-95):

3,6-Bis(trifluoromethyl)- $\alpha$ -(DL-1-carbomethoxy-2-methylpropylaminomethyl)-9-phenanthrenemethanol Hydrochloride (lower melting isomer)



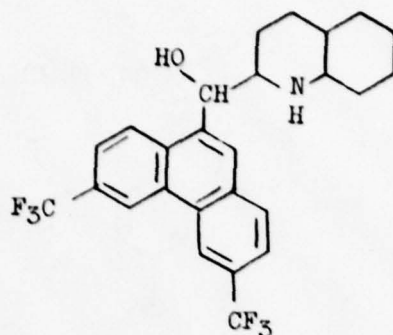
MO-393 (AY-61404; PC-IV-95A):

3,6-Bis(trifluoromethyl)- $\alpha$ -(DL-1-carbomethoxy-2-methylpropylaminomethyl)-9-phenanthrenemethanol Hydrochloride (higher melting isomer)



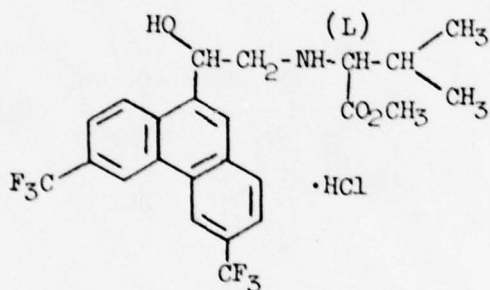
MO-394 (AY-62367; DM-1-125-1):

3,6-Bis(trifluoromethyl)- $\alpha$ -(2-decahydroquinolyl)-9-phenanthrene-  
methanol



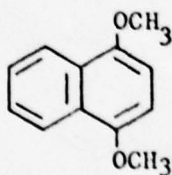
MO-395 (AY-62376; PC-V-5):

3,6-Bis(trifluoromethyl)- $\alpha$ -(L-1-carbomethoxy-2-methylpropylamino-  
methyl)-9-phenanthrenemethanol Hydrochloride (higher melting isomer)



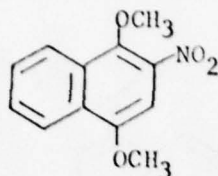
MO-396 (AY-64549; DM-1-126-1):

1,4-Dimethoxynaphthalene



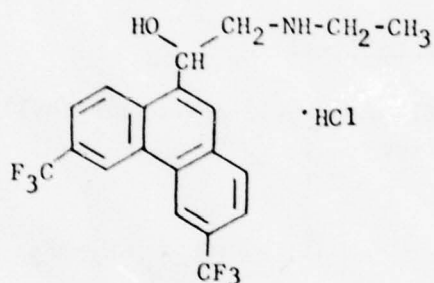
MO-397 (AY-64558; DM-I-127-1):

1,4-Dimethoxy-2-nitronaphthalene



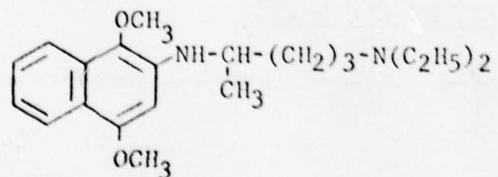
MO-398 (AY-64567; PC-V-19):

3,6-Bis(trifluoromethyl)- $\alpha$ -(ethylaminomethyl)-9-phenanthrene-methanol Hydrochloride



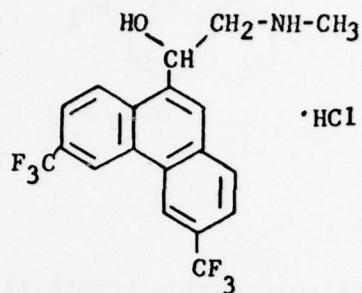
MO-399 (AY-64576; DM-I-130-1):

2-(4-Diethylamino-1-methylbutylamino)-1,4-dimethoxynaphthalene



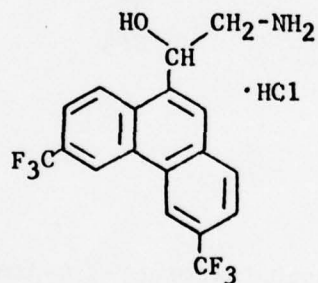
MO-400 (AY-64779; PC-V-23):

3,6-Bis(trifluoromethyl)- $\alpha$ -(methylaminomethyl)-9-phenanthrene-  
methanol Hydrochloride



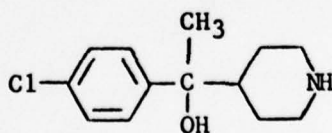
MO-401 (AY-64760; PC-V-25):

3,6-Bis(trifluoromethyl)- $\alpha$ -(aminomethyl)-9-phenanthrenemethanol  
Hydrochloride



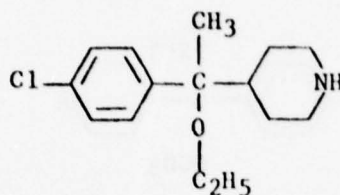
MO-402 (AY-91386; DM-I-135-1):

$\alpha$ -(4-Chlorophenyl)- $\alpha$ -methyl-4-piperidinemethanol



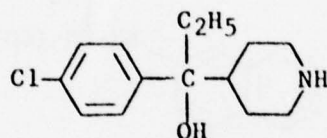
MO-403 (AY-91395; DM-I-139-1):

4-[1-(4-Chlorophenyl)-1-ethoxyethyl]piperidine



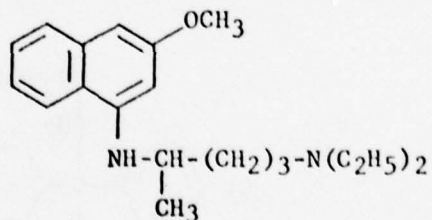
MO-404 (AY-95571; DM-I-137-1):

$\alpha$ -(4-Chlorophenyl)- $\alpha$ -ethyl-4-piperidinemethanol



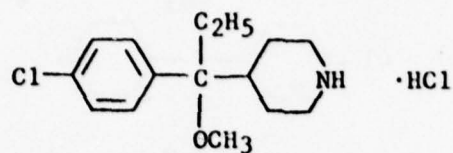
MO-405 (AY-95580; PC-V-32):

1-(4-Diethylamino-1-methylbutylamino)-3-methoxynaphthalene



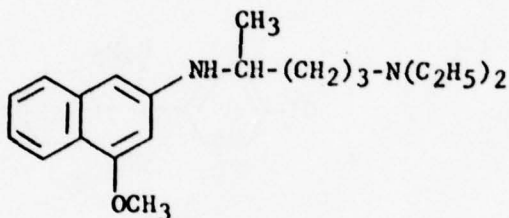
MO-406 (AY-96112; DM-1-141-2):

4-[1-(4-Chlorophenyl)-1-methoxypropyl]piperidine Hydrochloride



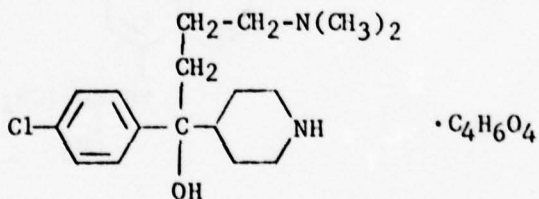
MO-407 (AY-96121; DM-1-138-1):

3-(4-Diethylamino-1-methylbutylamino)-1-methoxynaphthalene



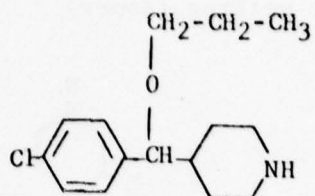
MO-408 (AY-98652; DM-1-144-1):

4-[ $\alpha$ -(4-Chlorophenyl)- $\alpha$ -(3-dimethylaminopropyl)]piperidinemethanol  
Fumarate



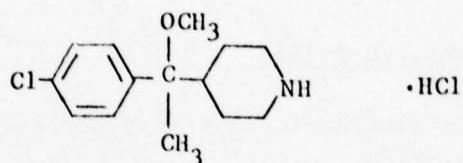
MO-409 (AY-99695; DM-I-149-1):

4-[( $\alpha$ -Propoxy)-*p*-chlorobenzyl]piperidine



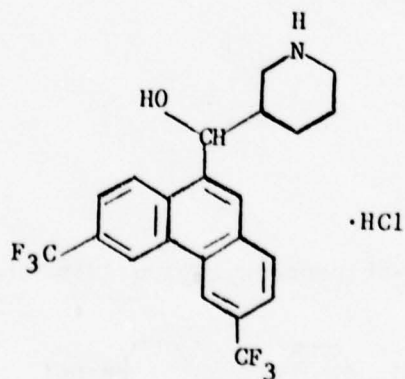
MO-410 (AY-99926; DM-I-151-2):

4-[( $\alpha$ -methoxy- $\alpha$ -methyl)-*p*-chlorobenzyl]piperidine Hydrochloride



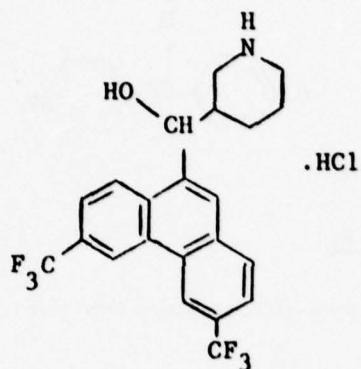
MO-411 (AY-99935; PC-V-45):

3,6-Bis(Trifluoromethyl)- $\alpha$ -(3-piperidyl)-9-phenanthrenemethanol  
Hydrochloride



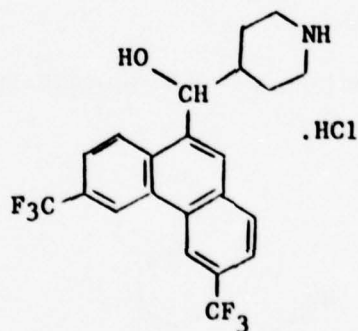
MO-412 (BB-41189; PC-V-49):

3,6-Bis(Trifluoromethyl)- $\alpha$ -(3-piperidyl)-9-phenanthrenemethanol Hydrochloride (lower melting isomer)



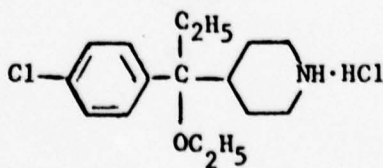
MO-413 (BB-41563; PC-V-59):

3,6-Bis(Trifluoromethyl)- $\alpha$ -(4-piperidyl)-9-phenanthrenemethanol Hydrochloride



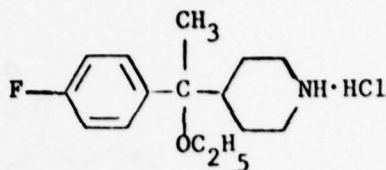
MO-414 (BB-41670; DM-II-3-2):

4-[ $\alpha$ -Ethoxy- $\alpha$ -ethyl]-p-chlorobenzyl]piperidine Hydrochloride



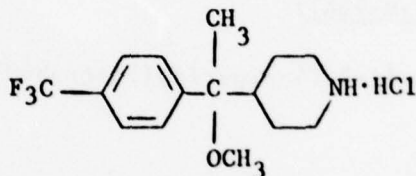
MO-415 (BB-41689; DM-II-6-1):

4-[ $\alpha$ -Ethoxy- $\alpha$ -methyl)-p-fluorobenzyl]piperidine Hydrochloride



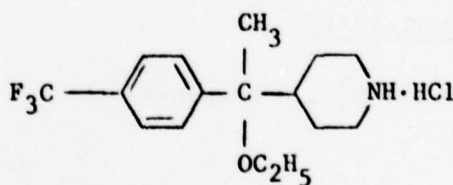
MO-416 (BB-42211; DM-II-10-1):

4-[ $\alpha$ -Methoxy- $\alpha$ -methyl)-p-(trifluoromethyl)benzyl]piperidine Hydrochloride



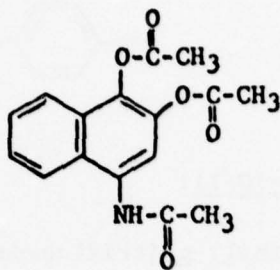
MO-417 (BB-43030; DM-II-13-1):

4-[ $\alpha$ -Ethoxy- $\alpha$ -methyl)-p-(trifluoromethyl)benzyl]piperidine Hydrochloride



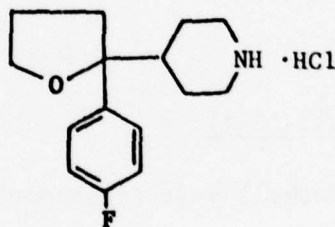
MO-418 (BB-44055; PC-V-63):

4-Acetamido-1,2-diacetoxynaphthalene



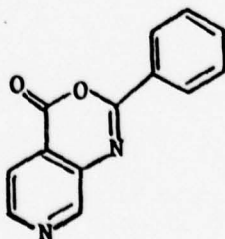
MO-419 (BB-44064; WB-B-93A):

2-(p-Fluorophenyl)-2-(4-piperidyl)tetrahydrofuran Hydrochloride



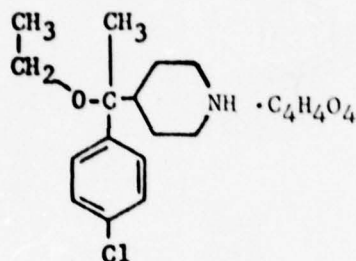
MO-420 (BB-47449; DM-II-15-1):

2-Phenylpyrido[3,4-d]-1,3-oxazin-4-one



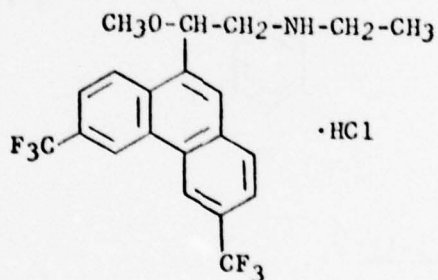
MO-421 (BB-45605; DM-I-139-3):

4-[1-(4-Chlorophenyl)-1-ethoxyethyl]piperidine Fumarate



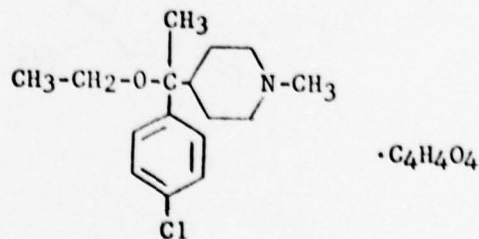
MO-422 (BB-48099; PG-V-86):

3,6-Bis(trifluoromethyl)- $\alpha$ -(propylaminomethyl)-9-phenanthrenemethanol  
Methyl Ether Hydrochloride



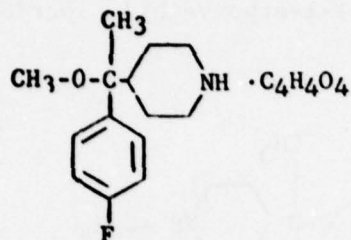
MO-423 (BB-48428; DM-II-22-1):

4-[ $\alpha$ -(Ethoxy- $\alpha$ -methyl)-p-chlorobenzyl]-1-methylpiperidine Fumarate



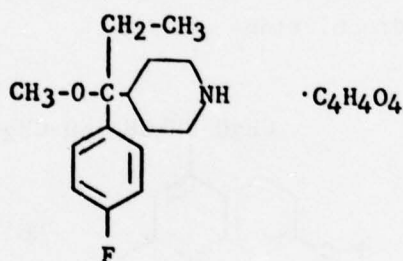
MO-424 (BB-48437; DM-II-26-1):

4-[( $\alpha$ -Methoxy- $\alpha$ -methyl)-p-fluorobenzyl]piperidine Fumarate



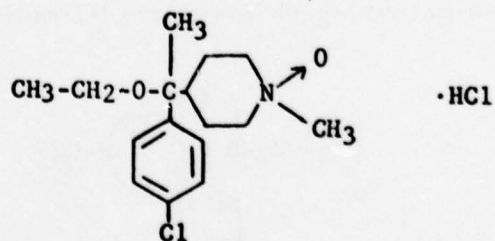
MO-425 (BB-48446; DM-II-27-1):

4-[( $\alpha$ -Ethyl- $\alpha$ -methoxy)-p-fluorobenzyl]piperidine Fumarate



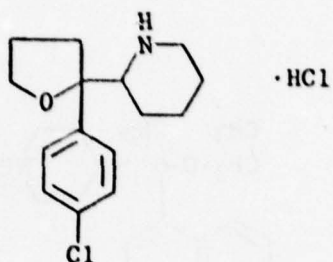
MO-426 (BB-49434; DM-II-31-1):

4-[( $\alpha$ -Ethoxy- $\alpha$ -methyl)-p-chlorobenzyl]-1-methylpiperidine N-oxide  
Hydrochloride



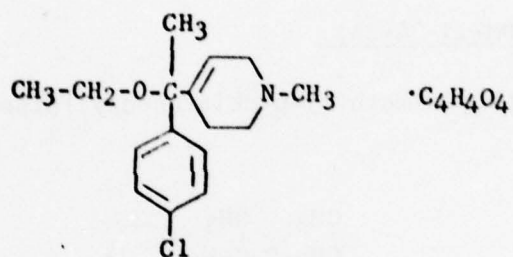
MO-427 (BC-06578; WB-9-45A):

2-(p-Chlorophenyl)-2-(2-piperidyl)tetrahydrofuran Hydrochloride



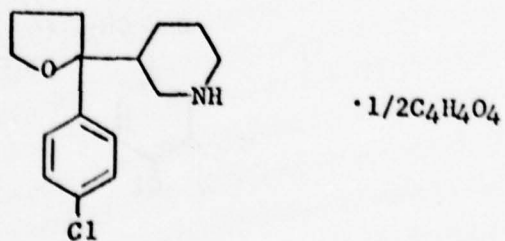
MO-428 (BC-06676; DM-II-30-1):

4-[ $\alpha$ -Ethoxy- $\alpha$ -methyl]-p-chlorobenzyl]-1-methyl-1,2,3,6-tetrahydropyridine Fumarate



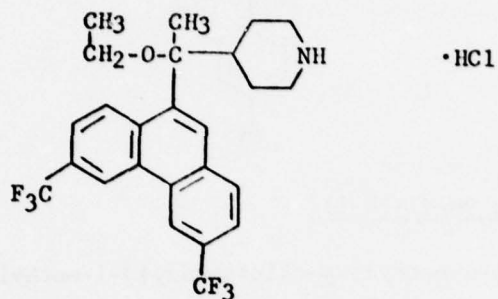
MO-429 (BC-07351; WB-9-39D):

2-(p-Chlorophenyl)-2-(3-piperidyl)tetrahydrofuran Hemifumarate



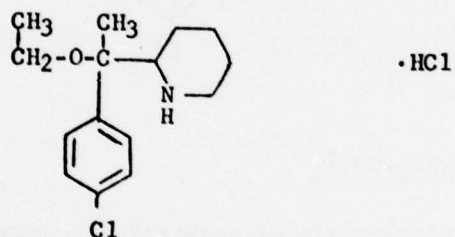
MO-430 (BC-07897; PC-V-93):

1-[3,6-Bis(trifluoromethyl)-9-phenanthryl]-1-(4-piperidinyloxy)ethanol  
Ethyl Ether



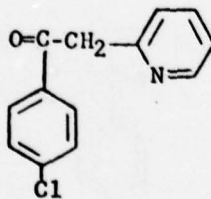
MO-431 (BC-08330; DM-II-34-2b):

2-[( $\alpha$ -Ethoxy- $\alpha$ -methyl)-*p*-chlorobenzyl]piperidine Hydrochloride



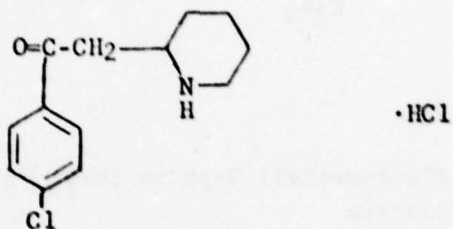
MO-432 (BC-09659; WB-9-50A):

*p*-Chloro-2-(2-pyridyl)acetophenone



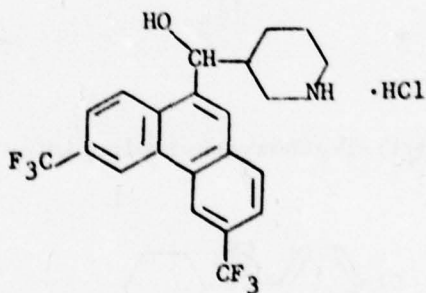
MO-433 (BC-09668; WB-9-52):

p-Chloro-2-(2-piperidyl)acetophenone Hydrochloride



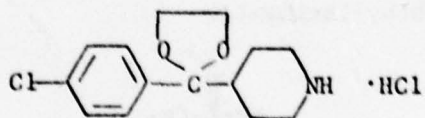
MO-434 (BC-58901; PC-VI-9):

3,6-Bis(trifluoromethyl)- $\alpha$ -(3-piperidyl)-9-phenanthrenemethanol Hydrochloride (lower melting isomer)



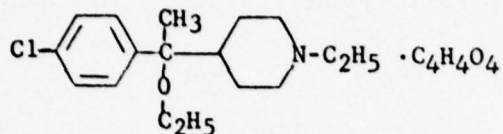
MO-435 (BC-59024; WB-9-86C):

2-(p-Chlorophenyl)-2-(4-piperidyl)-1,3-dioxolane Hydrochloride



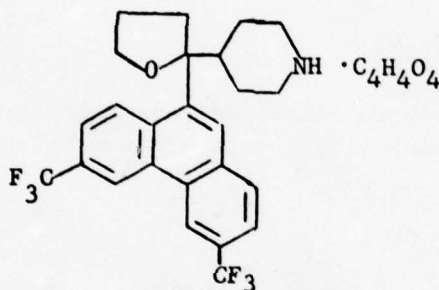
MO-436 (BC-59211; DM-II-38-1):

4- [1-(p-Chlorophenyl)-1-ethoxyethyl] -1-ethylpiperidine Fumarate



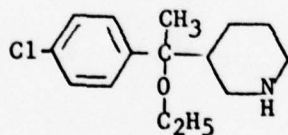
MO-437 (BC-99420; PC-VI-6):

2- [3,6-Bis(trifluoromethyl)-9-phenanthryl]-2-(4-piperidyl) tetrahydrofuran Fumarate



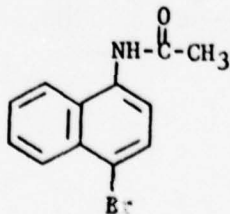
MO-438 (BC-99439; DM-II-39-1):

3- [p-Chlorophenyl)-1-ethoxyethyl] piperidine



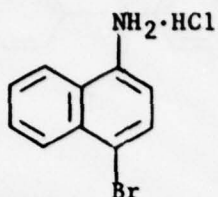
MO-439 (BD-23752; WB-8-40B):

N-1-(4-Bromonaphthyl)acetamide



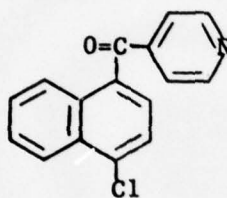
MO-440 (BD-23761; WB-8-41B):

4-Bromo-1-naphthylamine Hydrochloride



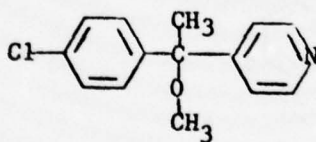
MO-441 (BD-23770; WB-8-59B):

4-Chloro-1-naphthyl 4-Pyridyl Ketone



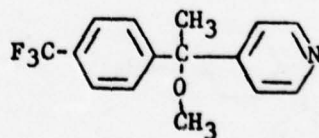
MO-442 (BD-23789; DM-I-151-1):

4-[1-(p-Chlorophenyl)-1-methoxyethyl]pyridine



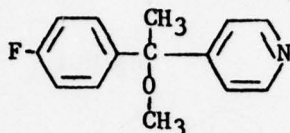
MO-443 (BD-23798; DM-II-8-1):

4-[1-(p-Trifluoromethylphenyl)-1-methoxyethyl]pyridine



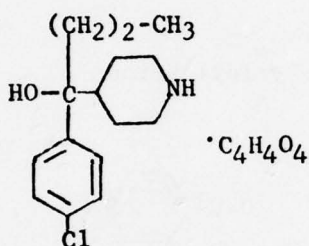
MO-444 (BD-23805; DM-II-23-1):

4-[1-(p-Fluorophenyl)-1-methoxyethyl]pyridine



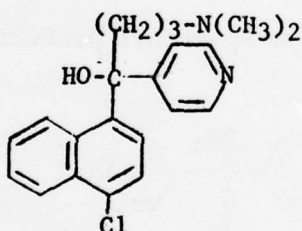
MO-445 (BD-27170; PC-VI-38):

1-(p-Chlorophenyl)-1-(4-piperidyl)butanol Fumarate



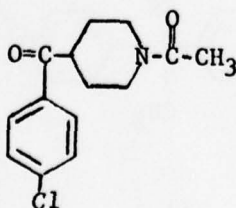
MO-446 (BD-27189; WB-8-65B):

4-Dimethylamino-1-(4-chloro-1-naphthyl)-1-(4-pyridyl)-1-butanol



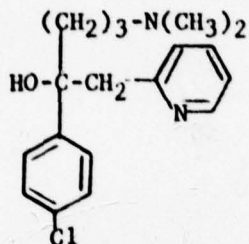
MO-447 (BD-27625; PC-VI-41):

1-Acetyl-4-(p-chlorobenzoyl)piperidine



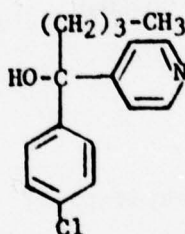
MO-448 (BD-27634; WB-10-19C):

1-(p-Chlorophenyl)-4-dimethylamino-1-(2-pyridylmethyl)butanol



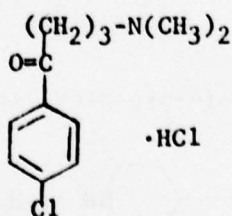
MO-449 (BD-27803; PC-VI-42):

1-(p-Chlorophenyl)-1-(4-pyridyl)butanol



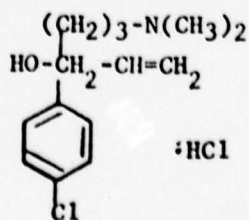
MO-450 (BD-27796; WB-10-22B):

p-Chlorophenyl 3-Dimethylaminopropyl Ketone Hydrochloride



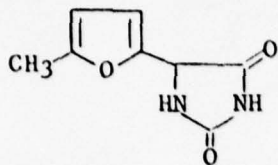
MO-451 (BD-27787; CW-7-10):

4-(p-Chlorophenyl)-7-dimethylamino-1-hepten-4-ol Hydrochloride



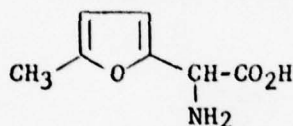
MO-451B (BD-28980; CW-13-28):

5-(5-Methylfurfur-2-yl)hydantoin



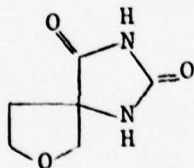
MO-452 (BD-28999; CW-16-26):

(5-Methylfurfur-2-yl)glycine



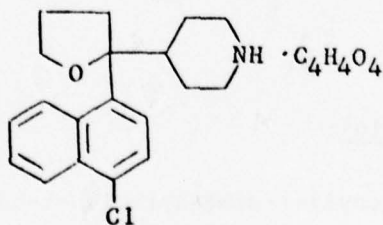
MO-453 (BD-29978; CW-25-29):

Spiro [tetrahydrofuran-3,5'-hydantoin]



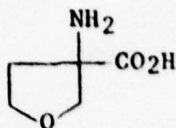
MO-454 (BD-29987; WB-10-49):

2-(4-Chloro-1-naphthyl)-2-(4-piperidyl)tetrahydrofuran Fumarate



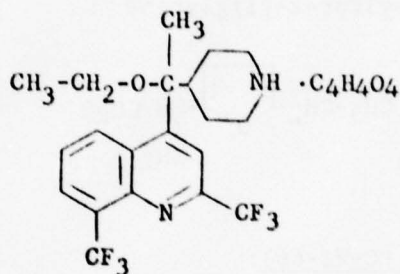
MO-455 (BD-54220; CW-30-12):

3-Amino-3-tetrahydrofurancarboxylic Acid



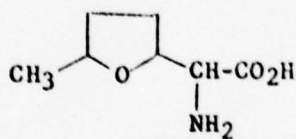
MO-456 (BD-54453; PC-VI-58):

1-[2,8-Bis(trifluoromethyl)quinolyl]-1-(4-piperidyl)ethanol  
Ethyl Ether Fumarate



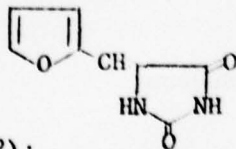
MO-457 (BD-54462; CW-19-25):

(5-Methyl-2,3,4,5-tetrahydrofur-2-yl)glycine



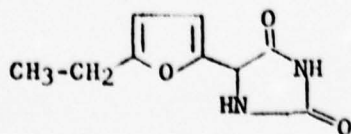
MO-458 (BD-54864; WB-10-53B):

5-Furfurylidenehydantoin



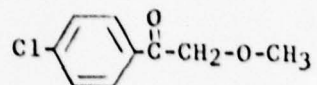
MO-459 (BD-54873; CW-38-22):

5-(5-Ethylfur-2-yl)hydantoin



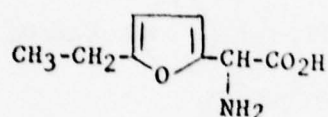
MO-460 (BD-55101; PC-VI-64):

p-Chloro-2-methoxyacetophenone



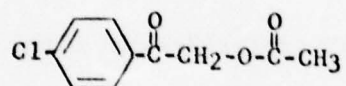
MO-461 (BD-55110; CW-43-11):

(5-Ethylfurf-2-yl)glycine



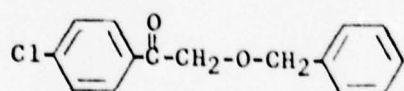
MO-462 (BD-56760; PC-VI-66):

2-Acetoxy-p-chloroacetophenone



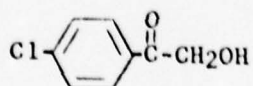
MO-463 (BD-56779; PC-VI-68):

2-Benzyloxy-p-chloroacetophenone



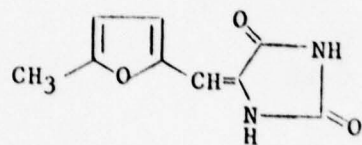
MO-464 (BD-56788; PC-VI-67):

p-Chloro-2-hydroxyacetophenone



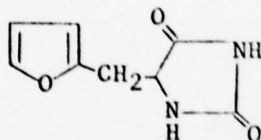
MO-465 (BD-56797; WB-10-68C):

5-(5-Methylfurfurylidene)hydantoin



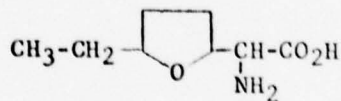
MO-466 (BD-57016; WB-10-60B):

5-Furfurylhydantoin



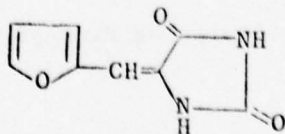
MO-467 (BD-57025; CW-49-22):

(5-Ethyl-1,2,3,4-tetrahydrofuran-2-yl)glycine



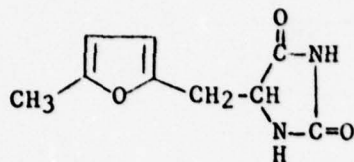
MO-468 (BD-57034; WB-10-71A):

5-Furfurylidene-2-thiohydantoin



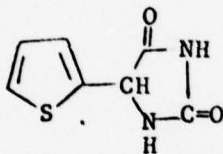
MO-469 (BD-57347; WB-10-74C):

5-(5-Methylfurfuryl)hydantoin



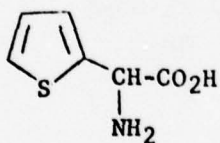
MO-470 (BD-57356; CW-50-15):

5-(2-Thienyl)hydantoin



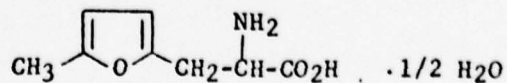
MO-471 (BD-57481; CW-53-15):

(2-Thienyl)glycine



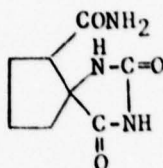
MO-472 (BD-57490; WB-10-80B):

$\beta$ -(5-Methyl-2-furyl)alanine Hemihydrate



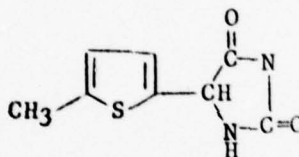
MO-473 (BD-59725; WB-10-84):

1,3-Diazaspiro[4.4]-2,4-dioxononane-6-carboxamide



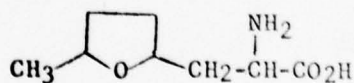
MO-474 (BD-59734; WB-10-87A):

5-(5-Methyl-2-thienyl)hydantoin



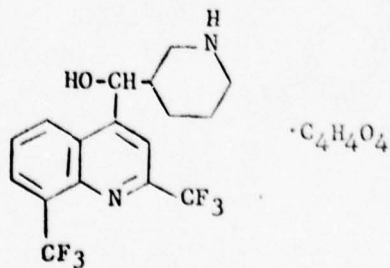
MO-475 (BE-10698; WB-10-88A):

$\beta$ -(5-Methyl-2-tetrahydrofuranyl)alanine



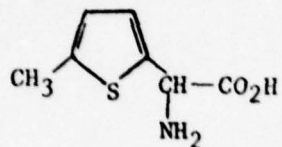
MO-476 (BE-10705; PC-V-77):

2,8-Bis(trifluoromethyl)- $\alpha$ -(3-piperidyl)quinolinemethanol Fumarate



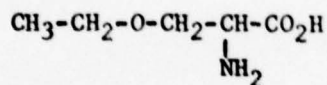
MO-477 (BE-12174; WB-10-94):

(5-Methyl-2-thienyl)glycine



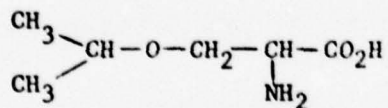
MO-478 (BE-12183; WB-10-97):

$\beta$ -Ethoxy- $\alpha$ -alanine



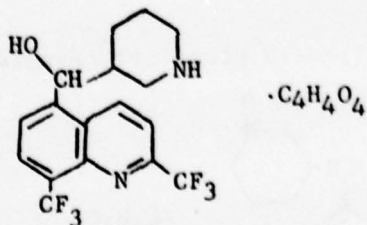
MO-479 (BE-13153; WB-11-11B):

3-Isopropoxyalanine



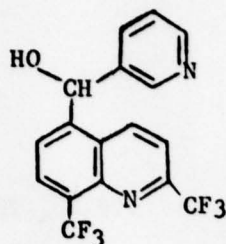
MO-480 (BE-13868; PC-VI-82):

2,8-Bis(trifluoromethyl)- $\alpha$ -(3-piperidyl)-4-quinolinemethanol  
Fumarate (Higher melting isomer)



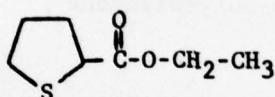
MO-481 (BE-13902; PC-BI-76):

2,8-Bis(trifluoromethyl)- $\alpha$ -(3-pyridyl)-4-quinolinemethanol



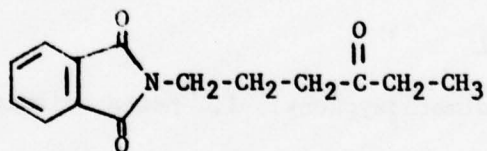
MO-482 (BE-16930; WB-11-15A):

Ethyl Tetrahydrothienyl-2-carboxylate



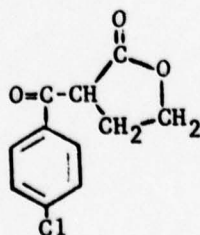
MO-483 (BE-16949; Y-I-51):

N-(4-Oxohexyl)phthalimide



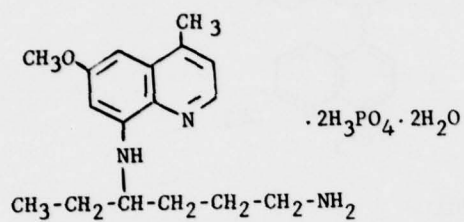
MO-484 (BE-16958; PC-VII-12):

$\alpha$ -p-Chlorobenzoyl- $\gamma$ -butyrolactone



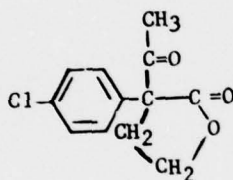
MO-485 (BE-16967; Y-I-79):

8-(6-Amino-3-hexylamino)-6-methoxy-4-methylquinoline  
Diphosphate Dihydrate



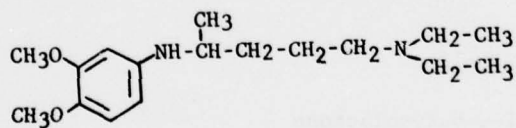
MO-486 (BE-17535; PC-VII-17):

$\alpha$ -Acetyl- $\alpha$ -(p-chlorobenzoyl)- $\gamma$ -butyrolactone



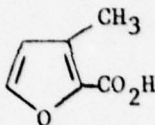
MO-487 (BE-17544; WB-11-40C):

N<sup>1</sup>,N<sup>1</sup>-Diethyl-N<sup>4</sup>-(3,4-dimethoxyphenyl)-1,4-pentanediamine



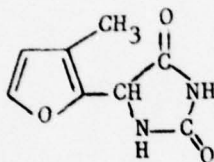
MO-488 (BE-17553; Y-I-82-2):

3-Methyl-2-furoic Acid



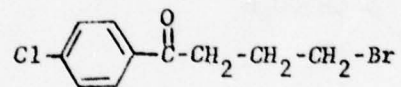
MO-489 (BE-17562; Y-I-85-1):

5-(3-Methyl-2-furyl)hydantoin



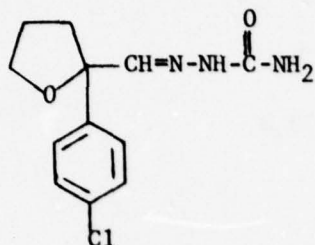
MO-490 (BE-17571; PC-VII-22):

4-Bromo-4'-chlorobutyrophenone



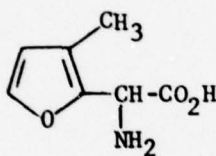
MO-491 (BE-18014; PC-VII-25):

2-(p-Chlorophenyl)tetrahydrofuran-2-carboxaldehyde Semicarbazone



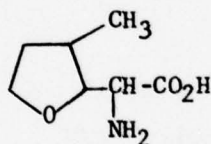
MO-492 (BE-18023; Y-I-90):

2-Amino-2-(3-methyl-2-furyl)acetic acid



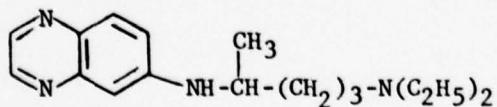
MO-493 (BE-18103; Y-I-94):

2-Amino-2-(3-methyl-2-tetrahydrofuryl)acetic acid



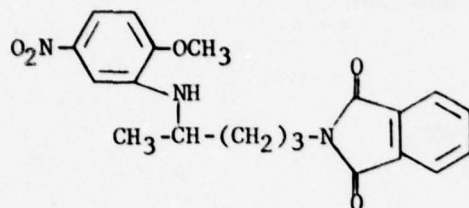
MO-494 (BE-19995; Y-I-95):

6-[(5-Diethylamino-2-pentyl)amino]quinoxaline



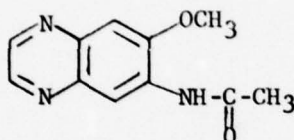
MO-495 (BE-45119; PC-VII-35):

2-Methoxy-5-nitro-N-(1-phthalimido-4-pentyl)aniline



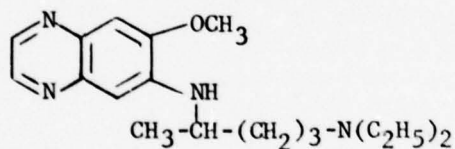
MO-496 (BE-45128; Y-II-11):

6-(N-Acetamido)-7-methoxyquinoxaline



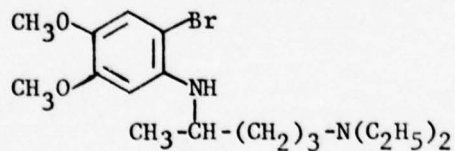
MO-497 (BE-50030; Y-II-20):

6-[(5-Diethylamino-2-pentyl)amino]-7-methoxyquinoxaline



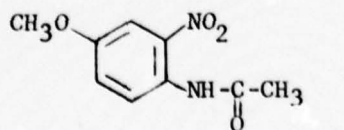
MO-498 (BE-66387; Y-II-26):

2-Bromo-4,5-dimethoxy-N-(5-diethylamino-2-pentyl)aniline



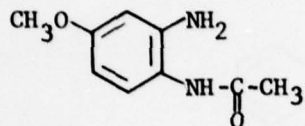
MO-499 (BE-66458; Y-II-2):

4-Methoxy-2-nitroacetanilide



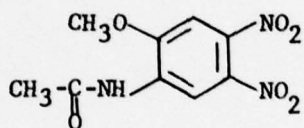
MO-500 (BE-66467; Y-II-19):

2-Amino-4-methoxyacetanilide



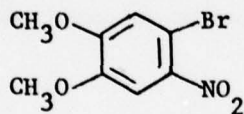
MO-501 (BE-66476; Y-II-12):

4,5-Dinitro-2-methoxyacetanilide



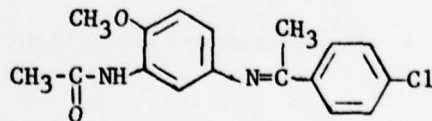
MO-502 (BE-66485 ; Y-II-265; WB-11-67):

6-Bromo-3,4-dimethoxy-1-nitrobenzene



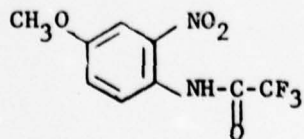
MO-503 (BE-66798; PC-VII-40):

3-Acetamido-N-[(p-chloro-1-methyl)benzylidene]-4-methoxyaniline



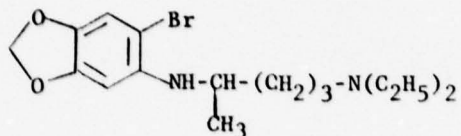
MO-504 (BE-66805; Y-II-28):

4-Methoxy-2-nitrotrifluoroacetanilide



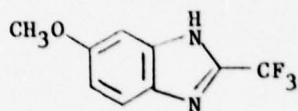
MO-505 (BE-55884; Y-II-49):

2-Bromo-4,5-methylenedioxy-N-(5-diethylamino-2-pentyl)aniline



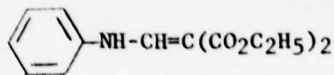
MO-506 (BE-57575; Y-II-28):

5-Methoxy-2-(trifluoromethyl)benzimidazole



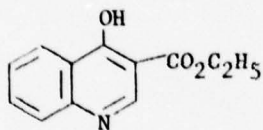
MO-507 (BE-57584; PC-VII-48):

Diethyl anilinomethylenemalonate



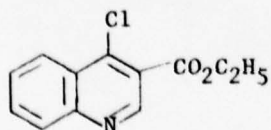
MO-508 (BE-58778; PC-VII-49):

Ethyl 4-hydroxy-2-quinolinecarboxylate



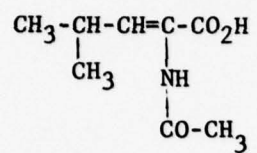
MO-509 (BE-58787; PC-VII-51):

Ethyl 4-chloro-2-quinolinecarboxylate



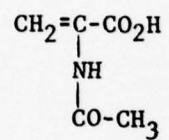
MO-510(BE-58796; Y-11-66):

N-Acetyldehydroleucine



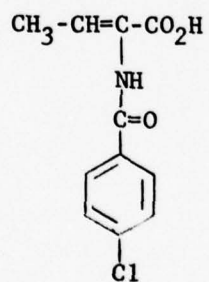
MO-511(BE-58803; Y-11-A):

2-Acetamidoacrylic Acid



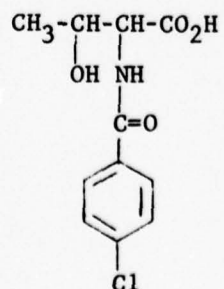
MO-512(BE-58812; Y-11-68):

2-(p-Chlorobenzamido)crotonic Acid



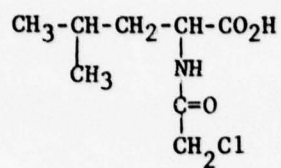
MO-513(BE-58821; Y-11-64):

N-(p-Chlorobenzoyl)-D,L-threonine



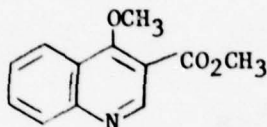
MO-514 (BE-58830; Y-11-63):

N-(Chloroacetyl)-D,L-leucine



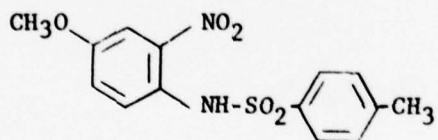
MO-515 (BE-76061; PC-VII-53):

Methyl 4-Methoxy-3-quinolinecarboxylate



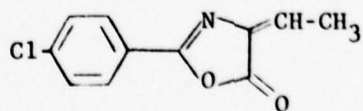
MO-516 (BE-76070; WB-11-72A):

N-(2-Nitro-4-anisyl)-p-toluenesulfonamide



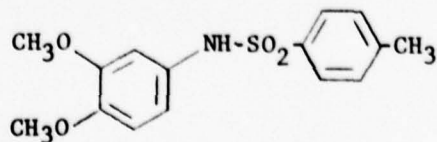
MO-517 (BE-76089; Y-II-67):

2-(p-Chlorophenyl)-4-ethylideneoxazol-5-one



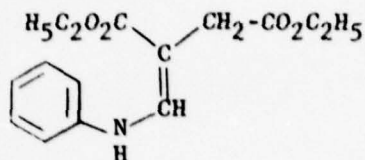
MO-518 (BE-77817; BW-11-73B):

N-(3,4-Dimethoxyphenyl)-p-toluenesulfonamide



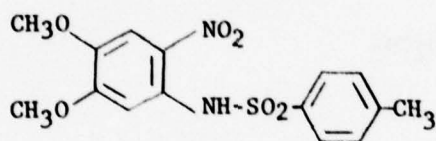
MO-519 (BE-77826; PC-VII-58):

Diethyl Anilinomethylenesuccinate



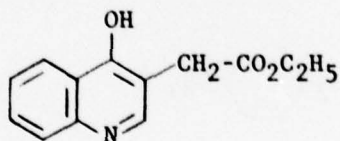
MO-520 (BE-82756; WB-11-75B):

N-(4,5-Dimethoxy-2-nitrophenyl)-p-toluenesulfonamide



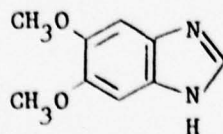
MO-521 (BE-76034; PC-VII-59):

Ethyl 4-Hydroxy-3-quinolyacetate



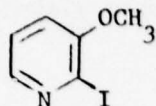
MO-522 (BG-04029; WB-11-88B):

5,6-Dimethoxybenzimidazole



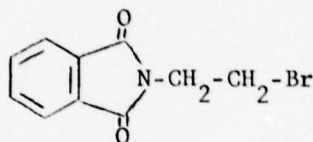
MO-523 (BG-04038; Y-II-92-2):

2-Iodo-3-methoxypyridine



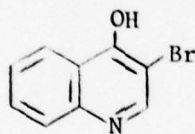
MO-524 (BG-04047; Y-I-21-1):

2-(Phthalimido)bromoethane



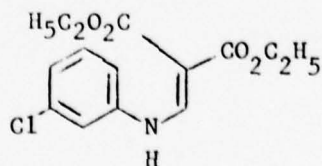
MO-525 (BG-09202; PG-VII-74):

3-Bromo-4-hydroxyquinoline



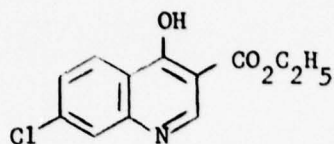
MO-526 (BG-09211; CC-II-31):

Diethyl (m-chloroanilino)methylenemalonate



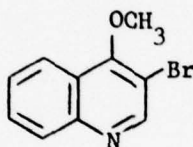
MO-527 (BG-10750; GC-II-33):

Ethyl 7-chloro-4-hydroxy-3-quinolinecarboxylate



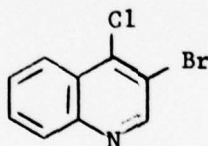
MO-528 (BG-10769; PC-VII-76):

3-Bromo-4-methoxyquinoline



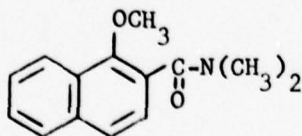
MO-529 (BG-11640; PC-VII-75):

3-Bromo-4-chloroquinoline



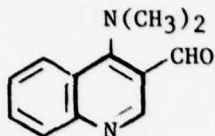
MO-530 (BG-11659; PC-VII-63):

3-Dimethylaminocarbonyl-4-methoxyquinoline



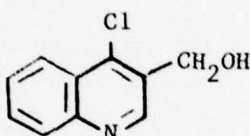
MO-533 (BG-44201; PC-VIII-9):

4-Dimethylamino-3-quinolinecarboxaldehyde



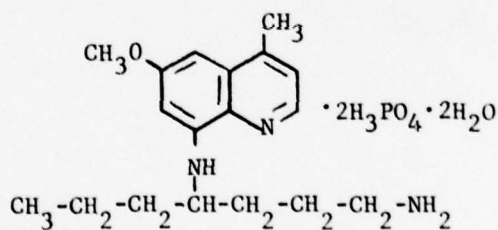
MO-534 (BG-44210; PC-VIII-12):

4-Chloro-3-quinolinemethanol



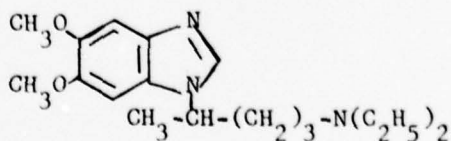
MO-535 (BG-46885; Y-3-84):

6-Methoxy-4-methyl-8-(1-propyl-4-aminobutylamino)-  
quinoline Diphosphate Dihydrate



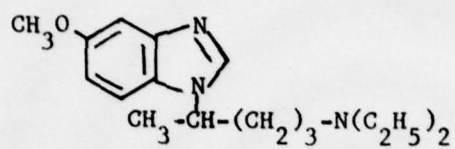
MO-531 (BG-21904; WB-12-18c):

1-(5-Diethylamino-2-pentyl)-5,6-dimethoxybenzimidazole



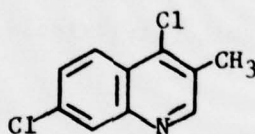
MO-532 (BG-39059; WB-12-24):

1-(5-Diethylamino-2-pentyl)-5-methoxybenzimidazole



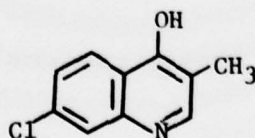
MO-536 (BG-60705; PC-VIII-35):

4,7-Dichloro-3-methylquinoline



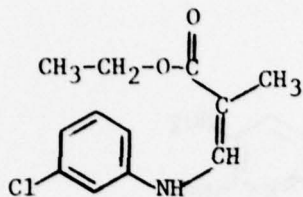
MO-537 (BG-60714; PC-VIII-34):

7-Chloro-4-hydroxy-3-methylquinoline



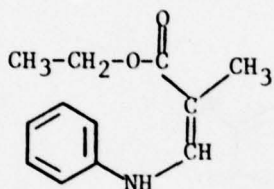
MO-538 (BG-60723; PC-VIII-33):

Ethyl 2-(3-Chlorophenylaminomethylene)propionate



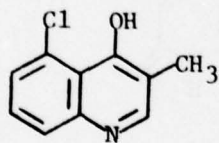
MO-539 (BG-60732; PC-VIII-36):

Ethyl 2-(Anilinomethylene)propionate



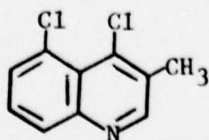
MO-540 (BG-63626; PC-VIII-38):

5-Chloro-4-hydroxy-3-methylquinoline



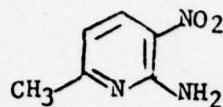
MO-541 (BG-63635; PC-VIII-39):

4,5-Dichloro-3-methylquinoline



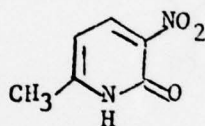
MO-542 (BG-78752; PC-VIII-55):

2-Amino-6-methyl-3-nitropyridine



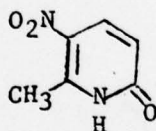
MO-543 (BG-78761; PC-VIII-56):

6-Methyl-3-nitro-1,2-dihydropyridin-2-one



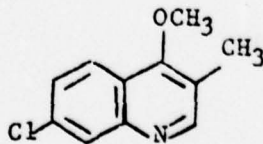
MO-544 (BG-78770; PC-VIII-58):

6-Methyl-5-nitro-1,2-dihydropyridin-2-one



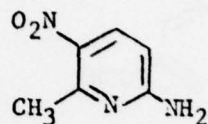
MO-545 (BG-78789; PC-VIII-40):

7-Chloro-4-methoxy-3-methylquinoline



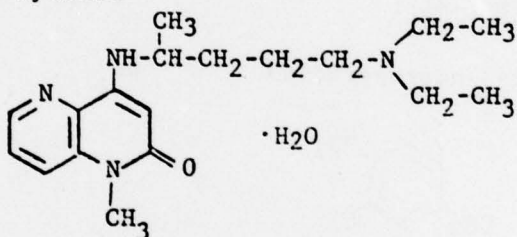
MO-546 (BG-78798; PC-VIII-61):

1-Amino-6-methyl-5-nitropyridine



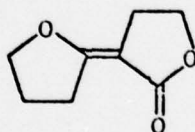
MO-547 (BG-39344; PC-VIII-78):

4-(5-Diethylamino-2-pentyl)amino-1-methyl-2-oxo-1,2-dihydro-1,5-naphthyridine Hydrate



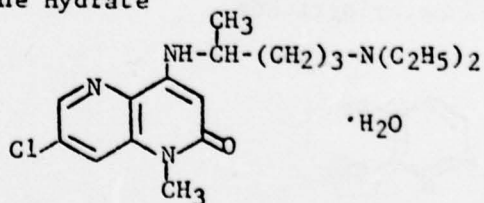
MO-548 (BG-94890; S-I-35):

$\alpha$ -(2-Tetrahydrofurylidene)- $\gamma$ -butyrolactone



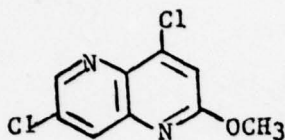
MO-549 (BH-03027; PC-VIII-80):

7-Chloro-4-(5-diethylamino-2-pentyl)amino-1-methyl-2-oxo-1,2-dihydro-1,5-naphthyridine Hydrate



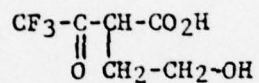
MO-550 (BH-03036; PC-VIII-78):

4,7-Dichloro-2-methoxy-1,5-naphthyridine



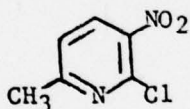
MO-551 (BH-03045; S-I-77):

4-Hydroxy-2-(trifluoroacetyl)butyric Acid



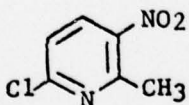
MO-552 (BH-03054; PC-VIII-81):

2-Chloro-6-methyl-3-nitropyridine



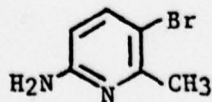
MO-553 (BH-07810; PC-VIII-84):

6-Chloro-2-methyl-3-nitropyridine



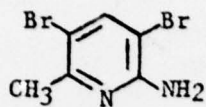
MO-554 (BH-10479; PC-VIII-85):

6-Amino-3-bromo-2-methylpyridine



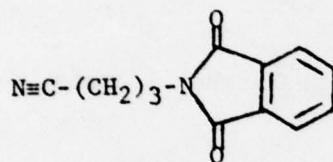
MO-555 (BH-10488; PC-VIII-86):

2-Amino-3,5-dibromo-6-methylpyridine



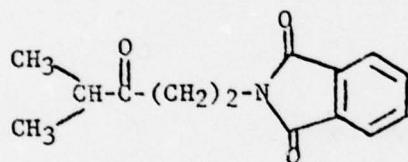
MO-556 (BH-17594; PC-IX-1):

4-Phthalimidobutyronitrile



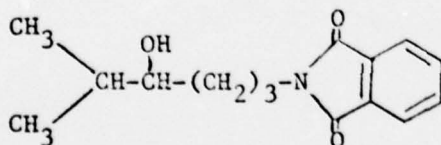
MO-557 (BH-17601; PC-IX-4):

2-Methyl-6-(phthalimido)hexan-3-one



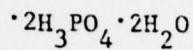
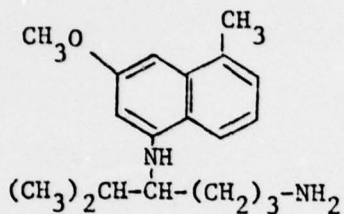
MO-558 (BH-31192; PC-IX-7):

2-Hydroxy-2-methyl-6-phthalimidohexane



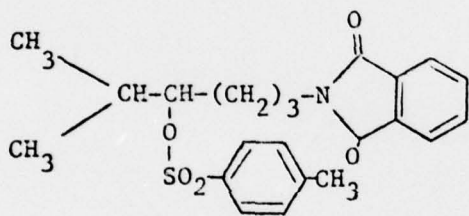
MO-559 (BH-31209; PC-IX-14):

4-Methyl-6-methoxy-8-(1-isopropyl-4-aminobutylamino)-  
quinoline, Diphosphate Dihydrate



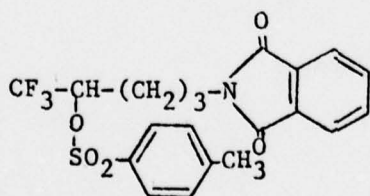
MO-560 (BH-35243; PC-IX-9):

3-Hydroxy-2-methyl-6-phthalimido-hexane-*p*-toluenesulfonate



MO-561 (BH-35252; PC-IX-C7):

2-Hydroxy-5-phthalimido-1,1,1-trifluoropentane  
*p*-toluenesulfonate



#### IV. PUBLICATIONS

Following is a list of publications resulting from our work done in connection with the malaria study.

1. "3-Piperonylsydnone. A New Type of Antimalarial Agent," W. H. Nyberg and C. C. Cheng, J. Med. Chem., 8, 531-553 (1965).
2. "2,8-Bis(substituted amino)phenothiazine 5,5-Dioxides," P.-L. Chien and C. C. Cheng, J. Med. Chem., 9, 960-962 (1966).
3. "Structural Modification Studies of 3-Piperonylsydnone. I. Synthesis of Piperonyl-Substituted Pyrazoles, Isoxazoles, Triazoles, Oxadiazoles, and Thiadiazoles," S. G. Boots and C. C. Cheng, J. Heterocyclic Chem., 4, 272-283 (1967).
4. "Synthesis and Antimalarial Evaluation of Some 1,7-Naphthyridines and 2,9-Diazaanthracenes," P.-L. Chien and C. C. Cheng, J. Med. Chem., 11, 164-167 (1968).
5. "Pyrazoles I. Synthesis of 4-Hydroxypyrazolo[3,4-d]-v-triazine. A New Analog of Hypoxanthine," C. C. Cheng, R. K. Robins, K. C. Cheng, and D. C. Lin, J. Pharm. Sci., 57, 1044-1045 (1968).
6. "Pyrazoles II. Reactions of 1-Methyl-5-amino-4-pyrazolecarboxamide and Nitrous Acid. Introduction of a Nitro Group at Position 5 in the Pyrazole Ring," C. C. Cheng, J. Heterocyclic Chem., 5, 195-197 (1968).
7. "1,5-Naphthyridines: Synthesis of 7-Chloro-4-(4-diethylamino-1-methyl-butylamino)-2-methoxy-1,5-naphthyridine and Related Compounds," D. J. McCaustland and C. C. Cheng, J. Heterocyclic Chem., 7, 467-473 (1970).
8. "Structural Modification of Febrifugine. Some Methylenedioxy Analogs," P.-L. Chien and C. C. Cheng, J. Med. Chem., 13, 867-870 (1970).
9. "Structural Modification Studies of 3-Piperonylsydnone. II. Synthesis of Piperonyl-Substituted Hydantoin, Thiohydantoin, Thiazolidinedione, Rhodanine, Imidazolinone and Related Compounds," W. H. Burton, W. L. Budde, and C. C. Cheng, J. Med. Chem., 13, 1009-1012 (1970).
10. "Structural Modification Studies of 3-Piperonylsydnone. III. Some Analogs of 3-Piperonylsydnone and 2,4-Diamino-5-piperonylpyrimidine," D. J. McCaustland, W. H. Burton, and C. C. Cheng, J. Heterocyclic Chem., 8, 89-97 (1971).

11. "Structure and Antimalarial Activity of Aminoalcohols and 2-(Chlorophenyl)-2-(4-piperidyl)tetrahydrofuran," C. C. Cheng, J. Pharm. Sci., 60, 1596-1598 (1971).
12. "Structure-Activity Relationship Studies on Antimalarial Phenanthrene Amino Alcohols. Modification of the Side Chain," P.-L. Chien, D. J. McCaustland, W. H. Burton, and C. C. Cheng, J. Med. Chem., 15, 23-33 (1972).
13. "Synthesis of Three <sup>14</sup>C-Labeled Phenanthrene Aminomethanols," P.-L. Chien and C. C. Cheng, Mikrochim. Acta, 401-412 (1973).
14. "Further Side Chain Modification of Antimalarial Phenanthrene Amino Alcohols," P.-L. Chien and C. C. Cheng, J. Med. Chem., 16, 1093-1096 (1973).
15. "Deaza Analogs of Some 4-, 6-, and 8-Aminoquinolines," D. J. McCaustland, P.-L. Chien, C. C. Cheng, J. Novotny, W. L. Schreiner, and F. W. Starks, J. Med. Chem., 16, 1311-1314 (1973).
16. "Novel Common Structural Feature Among Several Classes of Antimalarial Agents," C. C. Cheng, J. Pharm. Sci., 63, 307-310 (1974).
17. "A Structural Modification Study of the Antimalarial 2-(p-Chlorophenyl)-2-(4-piperidyl)tetrahydrofuran," D. J. McCaustland, P.-L. Chien, W. H. Burton, and C. C. Cheng, J. Med. Chem., 17, 993-1000 (1974).
18. "Difference in Antimalarial Activity Between Certain Aminoalcohol Diastereomers," P.-L. Chien and C. C. Cheng, J. Med. Chem., 19, 170-172 (1976).
19. "Structural Similarity Between Febrifugine and Chloroquine," C. C. Cheng, J. Theoretical Biol., 59, 497-501 (1976).
20. "Potential Causal Prophylactic Antimalarial Agents. Synthesis of Quinoxaline, Benzimidazole, and Alkoxybenzene Derivatives Containing a Novoldiamine Moiety," S. J. Yan, W. H. Burton, P.-L. Chien, and C. C. Cheng, J. Heterocyclic Chem., 15, 297-300 (1978).

V. INFORMATION ON PERSONNEL RECEIVING CONTRACT SUPPORT

C. C. CHENG  
Principal Advisor for Chemistry  
Program Manager, Medicinal Chemistry

Dr. Cheng has over 20 years experience in synthetic organic chemistry and medicinal chemistry. In his present position, he plans, coordinates and manages the research and development activities of programs on biologically active compounds.

He and his associates perform research projects for a variety of corporate clients as well as for various government agencies. These projects encompass the areas of the synthesis as well as the structural and biological evaluation of antibiotics (toxoflavin, ferverulin, bacimethrin, echinomycin, streptonigrin, etc.), alkaloids (camptothecin, coralyne, nitidine, ungeremine, etc.), vitamin analogs (thiamine, riboflavin, pyridoxine, folic acid, etc.), alkylating agents (nitrogen mustards, aziridines, etc.), antimetabolites, herbicides, nucleic acid derivatives, heterocyclic compounds (pyrimidines, purines, pyridazines, naphthyridines, phenothiazines, 1,2,4-triazines, 1,2,5-triazines, pyrazoles, pyrazolo[3,4-d]pyrimidines, pyrimido[4,5-b]diazepines, isoxazoles, 1,3,4-triazoles, etc.), mesoionic compounds (sydnones,  $\psi$ -1,2,4-triazoles, etc.), and others.

Before joining the MRI staff in 1959, he was a research associate in the Department of Chemistry at Princeton University, where he conducted research on the synthesis of purines and pteridines. Prior to that he spent three years as a research associate in the Department of Chemistry at New Mexico Highlands University where he conducted research on the synthesis of pyrazolo[3,4-d]pyrimidine derivatives for cancer chemotherapy studies.

Dr. Cheng is the author of over 150 scientific publications pertaining to medicinal and organic chemistry. As a member of the American Chemical Society, he served as a tour speaker during 1963-1964 and 1970, was elected to the Editorial Board in 1963, and two years later became Assistant Editor of the International Journal of Heterocyclic Chemistry. In 1967, he was elected as an Academician of the China Academy, Republic of China. He was appointed visiting professor in the School of Pharmacy (1967) and the Department of Chemistry (1972) at the University of Missouri-Kansas City. He has been a member of the National Institutes of Health Medicinal Chemistry A Study Section during 1973-1977 as well as a Special Study Section. In 1973, he received the MRI Council of Principal Scientists "Science Award." Other professional affiliations include the American Association for the Advancement of Science, New York Academy of Sciences, and Sigma Xi, The Scientific Research Society of North America. He graduated from the National University of Chekiang, China, with B.S. in Chemistry (1948), and received both the M.S. (1951) and the Ph.D. (1954) in Organic Chemistry from the University of Texas-Austin.

PING-LU CHIEN  
Senior Chemist

Dr. Chien specializes in synthetic organic chemistry, radiosynthesis, medicinal chemistry, physicochemical characterization, spectroscopy, and chromatography. He has over 12 years experience in the syntheses of organic compounds for use as antimalarial agents, including 1,7-naphthyridines, 2,9-diazaanthracenes, phenothiazines, febrifugine analogs, and phenanthrene amino alcohols, as well as several C<sup>14</sup> labeled compounds. In addition, he has studied the chemistry of *o*-di-*t*-butylbenzene, the photochemical isomerization of di-*t*-butylbenzene, and synthesized a variety of steroids and bicyclohydantoin. Currently, he is assigned to the program sponsored by the National Cancer Institute for the synthesis of radioactive retinoids for metabolic and pharmacologic studies relating to prevention of lung cancer and other epithelial cancers.

Prior to joining the MRI staff in 1965, Dr. Chien was a research associate in the Department of Medicinal Chemistry, University of Kansas from 1964 to 1965, where he conducted research in the synthesis of bicyclic hydanturans and barbiturates. From 1955 to 1959, he was a chemist with Union Industrial Research Institute in Taiwan. His research there involved the synthesis of 2-ethylhexanol, plasticizers, and organosilicone compounds.

Dr. Chien has published 12 papers in his areas of expertise and is a member of the American Chemical Society and Sigma Xi. He graduated with a B.S. in Chemistry from National Taiwan University in 1952, and received the Ph.D. in Organic Chemistry from the University of Kansas in 1964.

SHOU-JEN YAN  
Associate Organic Chemist

Dr. Yan specializes in the synthesis of pharmaceuticals, biochemicals and organic compounds. He applies this expertise to the synthesis of organic compounds for cancer and malaria chemotherapeutic studies. He is experienced in the use of NMR, IR, UV, and mass spectrographs and paper, ion exchange, column, thin-layer, gas and liquid chromatography.

Prior to joining MRI early in 1974, Dr. Yan was a postdoctoral research associate at the University of Georgia where he was involved in stereospecific synthesis of deuterium-labeled intermediates for the study of stereochemistry of enzyme reactions and the total synthesis of lycorine alkaloids. From 1968 to 1973, he conducted research for his Ph.D. dissertation on the determination of absolute configuration of amino acid bio-synthetic intermediates by chemical correlation and stereospecific synthesis of deuterium-labeled substrates for enzyme reactions. Specifically, his dissertation was concerned with stereochemical aspects of isoleucine and valine biosynthesis. Prior to that he was research chemist at the Institute of Chemistry, Academia Sinica, Taiwan from 1964 to 1968 where he synthesized a variety of organic compounds, explored new organic reactions, and isolated and identified natural products from a plant in an attempt to produce pharmaceuticals that might cure ulcers.

Dr. Yan has 13 publications in his areas of expertise. His professional affiliations include membership in the American Chemical Society, and the Chinese Chemical Society. He received the B.S. in Chemistry (1965) from National Taiwan Normal University and the Ph.D. in Organic Chemistry (1973) from the University of Georgia.

WILLIAM H. BURTON  
Associate Chemist

Mr. Burton specializes in organic synthesis and the use of instrumental methods of analysis such as gas chromatography and spectroscopy. In programs for the Environmental Protection Agency and industrial clients he has developed methods for analysis of air pollutants including hydrocarbons, nitrous oxides and ozones. For an industrial client he was involved in the separation, purification and identification of flavor components of ground coffee. He contributed to the development of insecticides through the synthesis and purification of isomers of benzene hexachloride and determined the relative effectiveness of these isomers as insecticides. In the area of insect repellents, he was involved in the correlation of structure with the activity of the compounds. He was responsible for formulation of silicone elastomers for high temperature applications and the synthesis of high temperature, nitrogen-containing heterocyclic compounds with a wide liquid range. In the area of medicinal chemistry he was involved in the synthesis of amino acid analogs and nitrogen heterocyclic compounds as antitumor agents and the synthesis of various antimalarial compounds.

Prior to joining the MRI staff in 1954, Mr. Burton was an assistant chemist for a period of two years with the Ford Motor Company where he developed complete analytical methods for iron ores, steel, aluminum and magnesium alloys. From 1951 to 1952 he was a chemist with Sinclair-Valentine Ink Company working on the formulation of printing inks. From 1950 to 1951 he was an assistant chemist with the Kansas City Power and Light Company performing analyses on coal, fuel oil, natural gas, turbine deposits, and boiler water.

Mr. Burton is coauthor of 11 publications in the field of organic chemistry. He received the B.S. in Chemistry (1949) from the University of Kansas and the M.S. in Chemistry (1963) from the University of Missouri-Kansas City.

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