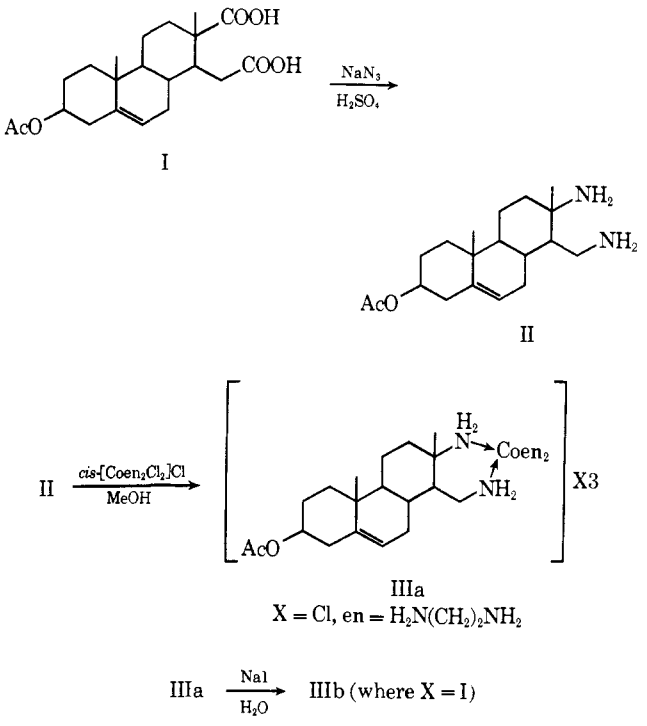
SCHEME I



When II was added to *cis*-dichlorobis(ethylenediamine)cobalt(3+) chloride in MeOH, [7-amino-8-(aminomethyl)-1,2,3,4,4a,4b,5,6,7,8,8a,9-dodecahydro-4a,7-dimethyl-2-phenanthrol]bis(ethylenediamine)cobalt(3+) trichloride β-acetate (ester), IIIa, was produced in 60% yield. The ir and nmr spectra of IIIa were consistent with the assigned structure. Ir maxima reported to be characteristic of Co–N bonds were present.[4] All elemental analyses for IIIa were within experimental error. Aq sols of IIIa gave 4 particle depressions of the freezing point of H_2O, and IIIa was diamagnetic. Reaction of IIIa with aq NaI yielded IIIb. The ir and nmr spectra of IIIb were consistent with the assigned structure, a 4 particle depression of the freezing point of aq sols was observed, the elemental analyses were within experimental error, and the compd was diamagnetic.

Biological Activity.—The capacity of the test compds to interfere with the incorporation of labeled acetate and/or mevalonate into cholesterol by rat liver homogenate was determined *in vitro* by the method of Dvornik, *et al.*[5] Any test compd producing 40% inhibition of cholesterol synthesis at 1×10^{-4} *M* is considered active and worth further work. IIIa was active as a hepatic cholesterogenesis inhibitor displaying 65% inhibition of cholesterol synthesis. II also was screened in identical fashion, but IIIa was more active than II. II showed only 26% inhibition of cholesterol synthesis. Activity testing continues.

Experimental Section[6]

7-Amino-8-(aminomethyl)-1,2,3,4,4a,4b,5,6,7,8,8a,9-dodecahydro-4a,7-dimethyl-2-phenanthrol β-Acetate (Ester) (II).—To a stirred soln of 0.50 g (1.8×10^{-3} mole) of I[1] in 10 ml of $CHCl_3$ was slowly added 3 ml of concd H_2SO_4; 0.5 g of NaN_3 was added very slowly to this mixture at a rate which kept the temp of the soln below 40°. After the addn was complete, the mixt was warmed to 40° for 2 hr, neutralized with concd NH_4OH at 0–5°, and filtered, and the filtrate was extd 4 times with $CHCl_3$. Removal of the solvent from the combined exts and recrystn from ligroin (bp 90–120°) yielded 0.20 g (54%) of product: mp 110–112°; $[\alpha]^{24}D$ −72°. *Anal.* ($C_{19}H_{32}N_2O_2$) C, H, N.

7-Amino-8-(aminomethyl)-1,2,3,4,4a,4b,5,6,7,8,8a,9-dodecahydro-4a,7-dimethyl-2-phenanthrol β-Acetate (Ester)·2HCl.—II (1 g, 3.13×10^{-3} mole) was dissolved in 15 ml of dry C_6H_6. HCl gas was bubbled through the soln for 5 min. After filtration and recrystn (H_2O-concd HCl), 1.18 g (96%) of product was obtained: mp 225–227°; neut equiv, calcd, 197; found 195, 198. *Anal.* ($C_{15}H_{34}Cl_2N_2O_2$) C, H, Cl, N.

Bis derivatives of II (α-naphthylurea, benzenesulfonamide, *p*-chlorobenzamide) were prepd in the same manner as previously reported analogs:[2] α-naphthylurea, 85% yield (recryst EtOH), mp 230–231° [*Anal.* ($C_{41}H_{46}N_4O_4$) C, H, N]; benzenesulfonamide, 70% yield (recryst EtOH), mp 147–148° [*Anal.* ($C_{31}H_{40}N_2O_6S_2$) C, H, N, S]; *p*-chlorobenzamide, 86% yield (recryst EtOH), mp 111–112° [*Anal.* $C_{33}H_{38}Cl_2N_2O_4$) C, H, Cl, N].

[7-Amino-8-(aminomethyl)-1,2,3,4,4a,4b,5,6,7,8,8a,9-dodecahydro-4a,7-dimethyl-2-phenanthrol]bis(ethylenediamine)cobalt(3+) Trichloride β-Acetate (Ester) (IIIa).—To 0.625 g (2.19×10^{-3} mole) of *cis*-dichlorobis(ethylenediamine)cobalt(3+) chloride in 30 ml of MeOH was added a soln of 0.70 g (2.19×10^{-3} mole) of II in 10 ml of dry C_6H_6. After stirring for 48 hr, the product was filtered and recrystd from H_2O-EtOH. The yield of gold-colored crystals was 0.80 g (60%): mp 215–217°; λ_{max} 472 mμ; $[\alpha]^{28}D$ −7°; cryoscopic particle no., calcd, 4.00; found, 4.14, 4.11. *Anal.* ($CoC_{23}H_{48}Cl_2N_6O_2$) Co, C, H, Cl, N.

[7-Amino-8-(aminomethyl)-1,2,3,4,4a,4b,5,6,7,8,8a,9-dodecahydro-4a,7-dimethyl-2-phenanthrol]bis(ethylenediamine)cobalt(3+) Triiodide β-Acetate (Ester) (IIIb).—IIIa (0.1 g) was dissolved in a min vol of H_2O. A 10-fold excess of NaI was added to the soln. The orange ppt was filtered and recrystd from hot H_2O. The yield of product, mp 256–257°, λ_{max} 475 mμ, was quantitative; cryoscopic particle no., calcd, 4.00; found, 4.02, 4.06. *Anal.* ($CoC_{23}H_{48}I_3N_6O_2$) Co, C, H, I, N.

Acknowledgments.—We are indebted to the National Science Foundation for partial support of this work under Traineeship Grant GE-7878, and we are indebted to Dr. K. L. Loening of the Chemical Abstracts Service for naming compounds II and IIIa for us. Activity testing was done by Ayerst Laboratories.

Where anal. are indicated only by the symbols of the elements or functions, analytical data were within experimental error relative to the calcd values for those elements or functions. Nmr spectra were taken on a Varian A60A spectrometer in $CDCl_3$ or D_2O. Visible spectra were taken on a Perkin-Elmer 202 spectrophotometer. Optical rotations were measured in a Rudolph Model 62 polarimeter in $CHCl_3$.

(4) E. P. Bertin, I. Nakagawa, S. Misushima, T. J. Lane, and J. V. Quagliano, *J. Amer. Chem. Soc.*, **80**, 525 (1958).

(5) D. Dvornik, M. Kraml, and J. Dubue, *Proc. Soc. Exp. Biol. Med.*, **116**, 537 (1964).

(6) Melting points were taken on a hot stage and are corrected. Ir spectra were taken in KBr wafers on a Beckmann IR-12 spectrophotometer.

Synthesis and Hypoglycemic Activity of 3-Aryl(or Pyridyl)-5-alkyl(or aryl)amino-1,3,4-thiadiazoles and Some Sulfonylurea Derivatives of 4*H*-1,2,4-Triazoles

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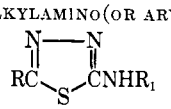
We have described[1,2] the synthesis and study of 1,2,4-triazole derivatives and have shown that many

(1) M. Y. Mhasalkar, M. H. Shah, S. T. Nikam, K. G. Anantanarayanan, and C. V. Deliwala, *J. Med. Chem.*, **13**, 672 (1970).

(2) M. Y. Mhasalkar, M. H. Shah, S. T. Nikam, K. G. Anantanarayanan, and C. V. Deliwala, *ibid.*, **14**, 260 (1971).

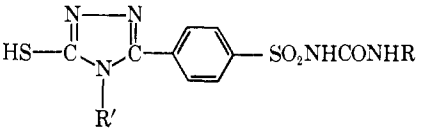
TABLE I: 2-ARYL-5-ALKYLAMINO(OR ARYLAMINO)THIADIAZOLES



No.	R_1	Mp, °C[a] (uncor)	Formula	Analyses	Maximum blood sugar redn at 25 mg/kg dose level in rats, % (hr)[b]
			R = C_6H_5		
1	n-C_3H_7	82–83	$C_{11}H_{13}N_3S$	C, H, N	21.7 (7)
			R = 4-ClC_6H_4		
2	C_2H_5	186–187	$C_{10}H_{10}ClN_3S$	C, H, N, S	10.2 (7)
3	C_3H_5	173–174	$C_{11}H_{10}ClN_3S$	N, S	15.3 (7)
4	n-C_3H_7	153–154	$C_{11}H_{12}ClN_3S$	N, S	16.8 (7)
5	i-C_3H_7	173	$C_{11}H_{12}ClN_3S$	C, H, N, S	
6	n-C_4H_9	145–146	$C_{12}H_{14}ClN_3S$	C, H, N, S	21.7 (7)
7	i-C_4H_9	174–175	$C_{12}H_{14}ClN_3S$	C, H, N, S	
8	C_6H_{11}	209–211	$C_{14}H_{16}ClN_3S$	C, H, N, S	15.3 (7)
			R = 3-ClC_6H_4		
9	C_2H_5	149–150	$C_{10}H_{10}ClN_3S$	C, H, N, S	11.7 (7)
10	C_3H_5	116–117	$C_{11}H_{10}ClN_3S$	C, H, N, S	15.9 (7); 16.7 (24)
11	n-C_3H_7	123–124	$C_{11}H_{12}ClN_3S$	C, H, N, S	
12	i-C_3H_7	115	$C_{11}H_{12}ClN_3S$	C, H, N	18.5 (7)
13	n-C_4H_9	109–110	$C_{12}H_{14}ClN_3S$	C, H, N, S	10.5 (5)
14	i-C_4H_9	103–104	$C_{12}H_{14}ClN_3S$	C, H, N, S	24.3 (5)
15	C_6H_{11}	144–145	$C_{14}H_{16}ClN_3S$	N, S	
			R = 2-ClC_6H_4		
16	C_2H_5	120–121	$C_{10}H_{10}ClN_3S$	C, H, N, S	12.3 (7)
17	n-C_3H_7	82–83	$C_{11}H_{12}ClN_3S$	C, H, N, S[c]	24.8 (5)
			R = 3,4,5-$(OCH_3)_3C_6H_2$		
18	C_2H_5	177–178	$C_{13}H_{17}N_3O_3S$	C, H, N, S	17.3 (7)
19	n-C_3H_7	128	$C_{14}H_{19}N_3O_3S$	C, H, N, S	13.8 (7)
20	i-C_3H_7	145–146	$C_{14}H_{19}N_3O_3S$	C, H, N, S	
21	n-C_4H_9	167–169	$C_{15}H_{21}N_3O_3S$	N, S	
22	i-C_4H_9	163	$C_{15}H_{21}N_3O_3S$	C, H, N, S[d]	15.8 (7)
23	C_6H_{11}	166–167	$C_{17}H_{23}N_3O_3S$	N, S	
24	C_6H_5	191–192	$C_{17}H_{17}N_3O_3S$	C,[e] H, N, S	
			R = 2-OH-5-BrC_6H_3		
25	C_2H_5	189–191	$C_{10}H_{10}BrN_3OS$	C, H, N, S	18.8 (7)
26	C_3H_5	186–188	$C_{11}H_{10}BrN_3OS$	N, S	
27	i-C_3H_7	183–184	$C_{11}H_{12}BrN_3OS$	N, S	17.3 (7)
28	n-C_4H_9	197–198	$C_{12}H_{14}BrN_3OS$	N, S	15.6 (7)
29	i-C_4H_9	198–199	$C_{12}H_{14}BrN_3OS$	N, S	
30	C_6H_{11}	188–190	$C_{14}H_{16}BrN_3OS$	N, S	
31	C_6H_5	292 dec	$C_{14}H_{10}BrN_3OS$	N, S	
			R = 4-$NH_2SO_2C_6H_4$		
32	C_2H_5	263	$C_{10}H_{12}N_4O_2S_2$	C, H, N	18.6 (7); 10.7 (24)
33	C_3H_5	214	$C_{11}H_{12}N_4O_2S_2$	N, S	12.2 (7)
34	n-C_3H_7	239–240	$C_{11}H_{14}N_4O_2S_2$	C, H, N	31.1 (7); 5.7 (24)
35	i-C_3H_7	251	$C_{11}H_{14}N_4O_2S_2$	C, H, N	17.9 (7)
36	n-C_4H_9	207–208	$C_{12}H_{16}N_4O_2S_2H_2O$	C, H, N	16.5 (7)
37	i-C_4H_9	252	$C_{12}H_{16}N_4O_2S_2$	C, H, N	24.6 (7)
38	C_6H_{11}	271–272	$C_{14}H_{18}N_4O_2S_2$	C, H, N	31.3 (7)
39	C_6H_5	277	$C_{14}H_{12}N_4O_2S_2$	N, S	18.3 (7)
			R = 3-Pyridyl		
40	C_2H_5	184–185	$C_9H_{10}N_4S$	C, H, N, S	
41	C_3H_5	175–176	$C_{10}H_{10}N_4S$	N, S	
42	n-C_3H_7	162–163	$C_{10}H_{12}N_4S$	C, H, N, S	19.4 (7)
43	i-C_3H_7	123–124	$C_{10}H_{12}N_4S$	C, H, N, S	
44	n-C_4H_9	152–153	$C_{11}H_{14}N_4S$	C, H, N, S	
45	i-C_4H_9	205	$C_{11}H_{14}N_4S$	C, H,[f] N, S	
46	C_6H_{11}	142–143	$C_{13}H_{16}N_4S$	C, H, N, S	16.2 (7)
47	C_6H_5	231–233	$C_{13}H_{10}N_4S$	N	
			R = 4-Pyridyl		
48	C_2H_5	174–175	$C_9H_{10}N_4S$	C, H,[g] N, S	25.5 (7); 14.0 (24)
49	C_3H_5	138	$C_{10}H_{10}N_4S$	C, H, N, S	
50	n-C_3H_7	135–136	$C_{10}H_{12}N_4S$	N, S	11.5 (7)
51	i-C_3H_7	145–146	$C_{10}H_{12}N_4S$	C, H, N, S	18.8 (7)
52	n-C_4H_9	151–152	$C_{11}H_{14}N_4S$	C, H, N, S	15.7 (7)
53	i-C_4H_9	188–190	$C_{11}H_{14}N_4S$	C, H, N, S	7.3 (7)
54	C_6H_{11}	217–218	$C_{13}H_{16}N_4S$	C, H, N, S	15.8 (7)
55	C_6H_5	219–220	$C_{13}H_{10}N_4S$	C, H, N	30.3 (7); 16.8 (24)[h]
			R = 4-$NO_2C_6H_4$		
56	i-C_3H_7	169–170	$C_{11}H_{12}N_4O_2S$	N	28.1 (7); 14.6 (24)[i]

[a] All compds are crystd from dil EtOH. [b] Mean values of 6 rats. [c] *Anal.* S calcd, 12.62; found, 12.04. [d] *Anal.* S calcd, 9.90; found, 9.43. [e] *Anal.* C calcd, 59.32; found, 59.88. [f] *Anal.* H calcd, 5.98; found, 5.39. [g] *Anal.* H calcd, 4.85; found, 5.36. [h] All mice survived at 3 g/kg dose (oral). [i] All mice survived at 1 g/kg, and 50% and 80% mortality at 2 and 3 g/kg doses (oral), resp.

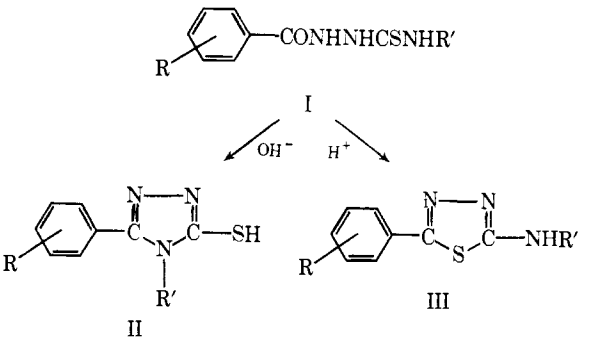
TABLE II
5-*p*-(1-ALKYLUREIDOSULPHONYL)PHENYL-4-ALKYL-4*H*-1,2,4-TRIAZOLE-3-THIOLS



No.	R	R′	Mp, °C (uncor)	Formula[a]	Max blood sugar redn at a dose level of 25 mg/kg in rats, % (hr)[b]
57	*n*-C_4H_9	C_2H_5	205	$C_{15}H_{21}N_5O_3S_2$	20.8 (5); 5.6 (24)
58	C_6H_{11}	C_2H_5	195–196	$C_{17}H_{23}N_5O_3S_2$	17.6
59	*n*-C_4H_9	*n*-C_3H_7	204–205	$C_{16}H_{23}N_5O_3S_2$	14.3 (7)
60	C_6H_{11}	*n*-C_3H_7	205–206	$C_{18}H_{25}N_5O_3S_2$	7.9 (5)
61	*n*-C_4H_9	*n*-C_4H_9	197	$C_{17}H_{25}N_5O_3S_2$	14.5 (7)
62	C_6H_{11}	*n*-C_4H_9	194–195	$C_{19}H_{27}N_5O_3S_2$	13.2 (7)
63	*n*-C_4H_9	C_6H_{11}	213–214	$C_{19}H_{27}N_5O_3S_2$	15.9 (7)
64	C_6H_{11}	C_6H_{11}	215–216	$C_{21}H_{29}N_5O_3S_2$	9.5 (5)

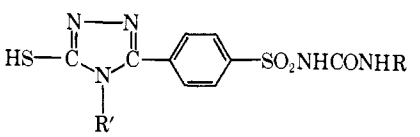
[a] Analyzed correctly for C, H, N and yields varied from 58 to 84%. [b] Tested by the method described.[1]

among them possess blood sugar lowering properties. 5-*p*-Chlorophenyl-4-ethyl-4*H*-1,2,4-triazole-3-thiol (II, R = *p*-Cl; R′ = C_2H_5) and 4-ethyl-5-*p*-sulfamoylphenyl-4*H*-1,2,4-triazole-3-thiol (II, R = *p*-SO_2NH_2; R′ = C_2H_5) were the most active and had prolonged duration of action.[1] The intermediate thiosemicarbazides, whose cyclization under alkaline condition gave these 2 active compds, were also found to possess significant activity. Hence it was thought interesting to cyclize various thiosemicarbazides (I) under acidic condition to obtain thiadiazoles (III) and study them for possible hypoglycemic property. Also, the SO_2NH_2



II III

group of II (R = *p*-SO_2NH_2; R′ = C_2H_5) offered the possibility of being converted into the corresponding sulfonylureas, a class of substances which have already afforded clinically useful hypoglycemic agents. Accordingly, compds of type IV have also been prepared and studied.



IV

R = *n*-C_4H_9 or C_6H_{11}
R′ = C_2H_5, *n*-C_4H_7, *n*-C_5H_{11} or C_6H_{11}

Chemistry.—The requisite 1,4-disubstituted thiosemicarbazides[1-5] were cyclized by heating with concd H_2SO_4 at 50° by the method of Hoggarth[6] (Table I). The sulfonylureas (Table II) were prepared by condensing the 4-ethyl-5-*p*-sulfamoylphenyl-4*H*-1,2,4-triazole-3-thiol with the requisite isocyanates by lit. methods[7] (Table II).

Hypoglycemic Activity.—All compds were tested for hypoglycemic activity in normal fasting rats by the method already described.[1] Many compds from the first series showed significant blood sugar lowering, while in the second series, the conversion of the sulfamoyl group into sulfonylureas led to considerable loss of activity.

Contrary to our earlier observations in the triazole series,[1] in which C_2H_5 as substituent gave the most active compds, here it afforded the least active ones. Among the substituents at position 2 of the thiadiazole ring, the activity was in the order of *p*-sulfamoylphenyl > 4-pyridyl > *p*-nitrophenyl. Compounds **34**, **38**, **55**, and **56** were the most active in the present series. It was interesting to note that N^1-*p*-chlorophenyl-N^4-ethylthiosemicarbazide which reduced the blood sugar level by 25%, on cyclization under alkaline condition gave a mercaptotriazole derivative possessing increased activity (53.7% lowering)[1] while its thiadiazole derivative (**2**) had much lower activity (10.2% lowering). Similarly, N^1-*p*-sulfamoylphenyl-N^4-ethylthiosemicarbazide, possessing good hypoglycemic activity, (32% lowering) on conversion to the thiadiazole derivative (**32**) was rendered less active (18.6% lowering), while its triazole derivative was highly active (45% blood sugar lowering).[1]

Isoxazole and pyrazole derivatives with potent hypoglycemic activity have been described as rapidly producing resistance.[8] We have, therefore, examined **55** for possible development of resistance. No significant difference in activity was seen after continued administration of the drug for 9 days (29.5% lowering), but thereafter a rapid emergence of resistance was noted. On the 11th day, the activity was almost half (15.0% lowering) as much as in the first 9 days. Withdrawal of the drug for a week and restarting it showed the resistance to be progressive (only 11.7% lowering on 19th day).

(3) M. H. Shah, M. Y. Mhasalkar, and V. M. Patiki, *J. Sci. Ind. Res., Sect. C*, **19**, 68 (1960).
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(6) E. Hoggarth, *J. Chem. Soc.*, 1963 (1949).
(7) S. Petersen, *Ber.*, **83**, 551 (1950).
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Experimental Section[9]

2-(4-Pyridyl)-5-*n*-propylaminothiadiazole.—N^1-Isonicotinoyl-N^4-*n*-propylthiosemicarbazide (2.38 g, 0.01 mole) was added to concd H_2SO_4 (5 ml) in small portions. The mixt was shaken vigorously to form an homogeneous soln and set aside (30 min). It was then poured in ice water and neutralized (Na_2CO_3). The product was collected and crystd (EtOH), to form yellow shining needles. Other compds (Table I) were prepd similarly.

5-*p*-(1-Cyclohexylureidosulfonyl)phenyl-4-ethyl-4*H*-1,2,4-triazole-3-thiol.—4-Ethyl-5-*p*-sulfamoyl-phenyl-4*H*-1,2,4-triazole-3-thiol (2.15 g, 0.01 mole) was dissolved in dry Me_2CO (50 ml). To this soln were added anhyd K_2CO_3 (4.0 g) and cyclohexyl isocyanate (1.5 ml), and the mixt was refluxed on steam bath for 8 hr. Acetone was distd off, and the residue was dissolved in H_2O, filtd, cooled, and acidified (HCl), when a sticky material sepd which solidified after long standing. It was filtd, washed (H_2O), and crystd (EtOH). Other sulfonylureas were prepd by following the above procedure.

Acknowledgments.—We wish to thank Mr. M. T. Jaokar and coworkers for the microanalyses and Dr. N. K. Dutta, Director, Haffkine Institute, for his interest in this work.

(9) The melting points are capillary melting points and are uncor. Analyses indicated by symbols of the elements were within ±0.4% of the theor values.

Potential Acetylcholinesterase Reactivators. *p,p'*-Biphenyl and 1,4-Benzene Disubstituted Oximes[1a,b]

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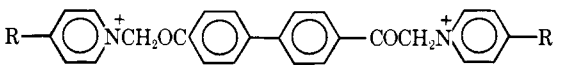
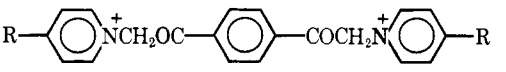
In 1954 Long and Schueler[2] reported the potent AChE inhibition caused by *p,p'*-bis(pyridiniumacetyl)-biphenyl dibromide (**1a**). Later, the relative AChE inhibition of a series of substituted pyridinium and *N*-methylpiperidinium compds was determined.[3] These studies suggested that *p,p'*-bis(substituted acetyl)-biphenyl possessed desirable features for binding with AChE.



·2Br⁻

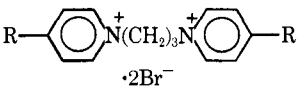
1a, R = H
1b, R = CH=NOH

As part of our continuing studies on AChE reactivators, *p,p'*-bis(pyridinium-4-aldoxime acetyl)biphenyl dibromide (**1b**) and *syn,syn*-1,4-bis(pyridinium-4-carbaldoxime acetyl)benzene (**2a**) were synthesized, the oxime configurations assigned, and the reactivator potency determined relative to TMB-4 (**3a**), 2- and 4-pyridinecarbaldoximes methylhalides (PAM's).



·2Br⁻

2a, R = CH=NOH
2b, R = H



·2Br⁻

3a, R = CH=NOH
3b, R = H

The configuration assignment are based upon the work of Poziomek and coworkers[4] who synthesized and characterized *syn*- and *anti*-4-pyridinecarbaldoxime and the corresponding methiodides. Kirtz, *et al.*,[5] reported that 4-PAM had 0.01 the potency of 2-PAM. In our labs,[1a] the *syn*-4-PAM was found to be 0.01 the potency of 2-PAM. Using combined nmr and biochemical assay techniques, it was possible to determine that **2a** and **3a** are syn,syn'. Since the starting oxime and the method of synthesis are the same for **1b**, it may be inferred that the configuration of **1b** is also syn,syn'.

1b, **2a**, and **3a** were evaluated for their ability to reactivate electric eel AChE inhibited with diethyphosphorylthiocholine according to the procedure previously described.[1a] Pralidoxime (2-pyridinecarbaldoxime methyl chloride, 2-PAM) was utilized as the standard. Since the effectiveness of an AChE reactivator is limited by its ability to inhibit AChE, the inhibitor potency of **1b**, **2a**, **3a**, and 2-PAM together with the inhibitor potency of the corresponding noroximino compds (**1a**, **2b**, and **3b**) was determined. The reactivation and inhibition data is summarized in Table I.

TABLE I
REACTIVATION AND INHIBITION OF ELECTRIC EEL ACHE

	Relative potency as reactivator	ID_{50}[b]
2-PAM	1.0	8.1×10^{-4}
1b	0.63 (0.62–0.64)[a]	9.9×10^{-7}
1a		6.6×10^{-9}
2a	0.55 (0.46–0.64)[a]	2.7×10^{-6}
2b		8.7×10^{-7}
3a	4.8 (4.2–5.4)[a]	6.4×10^{-4}
3b		1.9×10^{-3}

[a] 95% fiducial limits. [b] Molar concentration at which the enzyme is 50% inhibited.

TABLE II

No.	% yield	Mp, °C	Formula[a]	Synthesis method
1b	70	235–237	$C_{28}H_{24}N_4O_4Br_2$	A
2a	75	203–205 dec	$C_{22}H_{20}N_4O_4Br_2$	A
2b	80	220 dec	$C_{20}H_{18}N_2O_2Br_2$	A
3a		246[b]		*b*
3b	51	228–231[c]	$C_{13}H_{16}N_2Br_2$	A

[a] All compds analyzed corrected for C, H, N. [b] Lit. 238–241° [E. J. Poziomek, B. F. Hackley, and G. M. Steinberg, *J. Org. Chem.*, **23**, 714 (1958)]. [c] Lit. 220–221° [J. Hartwell and M. H. Pogorelsken, *J. Amer. Chem. Soc.*, **72**, 2040 (1950)].

(1) (a) Previous paper: C. F. Barfknecht, F. W. Benz, and J. P. Long, *J. Pharm. Sci.*, **60**, 138 (1971); (b) this work was supported in part by National Institutes of Health Research Grants NB-01396 and NB-4430.

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(3) F. W. Benz and J. P. Long, *J. Pharmacol. Exp. Ther.*, **166**, 225 (1969).

(4) E. J. Poziomek, D. N. Kramer, W. A. Mosher, and H. O. Michel, *J. Amer. Chem. Soc.*, **83**, 3916 (1961).

(5) R. J. Kirtz, S. Ginsberg, and I. B. Wilson, *Biochem. Pharmacol.*, **14**, 1471 (1965).