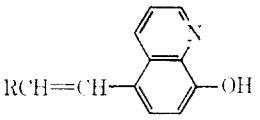
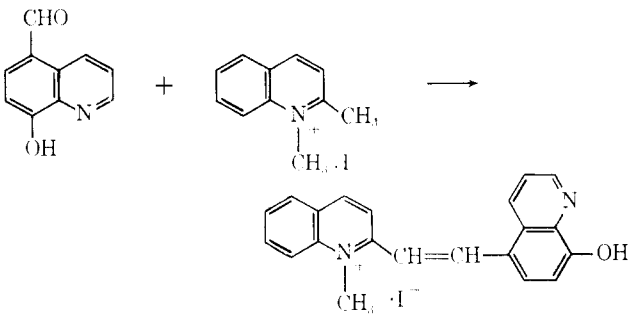
TABLE I
(8-HYDROXY-5-QUINOLYL)VINYL COMPOUNDS



No.	R	Formula	Mp, °C dec	Yield, %	Carbon, % Calcd	Carbon, % Found	Hydrogen, % Calcd	Hydrogen, % Found	Nitrogen, % Calcd	Nitrogen, % Found
1	1-Methyl-8-hydroxy-2-quinolinium chloride	$C_{21}H_{17}ClN_2O_2$	255	60					7.68	7.87
2	1-Methyl-5-ethyl-2-pyridinium iodide	$C_{19}H_{19}IN_2O$	247	65	54.55	54.47	4.58	4.94	6.70	6.43
3	1-Methyl-2-quinolinium iodide	$C_{21}H_{17}IN_2O \cdot H_2O$	220	85	55.03	55.14	4.18	4.43	6.11	6.66
4	1,3,3-Trimethyl-3H-2-indolinium chloride	$C_{22}H_{21}ClN_2O \cdot 3H_2O$	256	70	63.07	62.31	6.50	6.50	6.69	6.47
5	3-Methyl-2-benzothiazolium chloride	$C_{19}H_{15}IN_2OS \cdot H_2O$	239	72	49.14	48.93	3.69	3.64	6.03	6.07
6	3-Methyl-2-benzoselenazolium iodide	$C_{19}H_{15}IN_2OSe \cdot H_2O$	246	71	44.64	45.04	3.35	3.47	5.48	5.60
7	1,3-Dimethyl-2-benzimidazolium iodide	$C_{20}H_{18}IN_3O \cdot 0.5H_2O$	300	32	53.11	53.26	4.23	4.27	9.29	9.33
8	1-Methyl-4-pyridinium iodide	$C_{17}H_{15}IN_2O$	302	86	52.32	52.14	3.87	3.95	7.18	7.19
9	1-Methyl-2-pyridinium iodide	$C_{17}H_{15}IN_2O \cdot 0.5H_2O$	276	81	51.14	50.63	4.04	4.16	7.02	6.88
10	1,6-Dimethyl-2-quinolinium iodide	$C_{22}H_{19}IN_2O \cdot H_2O$	251	79	55.94	55.58	4.48	4.45	5.93	6.02
11	1-Methyl-6-ethoxy-2-quinolinium iodide	$C_{23}H_{21}IN_2O_2$	248	86	57.03	57.09	4.37	4.44	5.78	5.79
12	1-Methyl-4-quinolinium iodide	$C_{21}H_{17}IN_2O$	234	79					6.36	6.69
13	2-Methyl-1-isoquinolinium iodide	$C_{21}H_{17}IN_2O \cdot 0.5H_2O$	250	76	56.13	56.38	4.04	3.94	6.23	6.21

SCHEME I



I

pounds such as I (see Scheme I). Because they contain the 8-quinolinol function these compounds are chelating agents, but they are also merocyanines and thus change color markedly with variations in solvent polarity, a subject discussed elsewhere.[2] All but the first[2] of the compounds listed in Table I are new; like most solvatochromic compounds they are usually obtained as hydrates from solvents containing water.

In the screening program of the Cancer Chemotherapy National Service Center several of these compounds showed considerable toxicity in cell culture tests (see Table II), but testing against cancer in other systems used in the routine *in vivo* screening confirmed toxicity but indicated no significant activity.

Experimental Section

Preparation of Compounds.—Condensations of 5-formyl-8-quinolinol with methiodides of appropriate heterocyclic active methyl compounds gave all of the products described in this paper. A solution containing 0.02 mole of the aldehyde, 0.015 mole of a methiodide, and 1.5 ml of piperidine in 60 ml of 1-propanol was refluxed for 4 hr; on cooling, the crystalline product usually separated and was filtered, washed with ether, and recrystallized from 80% methanol. Compounds **2** and **3** (Table I) were crystallized from ethanol instead, and **4**–**6** were prepared without piperidine as catalyst. Compound **4** had to be precipitated by the addition of HCl and ether to the reaction mixture.

(2) A. Mueller, J. T. Leach, and J. P. Phillips, *Talanta*, **10**, 1087 (1963).

TABLE II
CELL CULTURE TEST DATA[a]

No.[b]	Slope	ED_{50}, mg/kg
2	−0.31	0.16
3	−1.16	3.5
4	−0.23	0.83
6	−0.50	7.6
10	−1.5	1.5
11	−0.66	2.2
13	−0.40	0.63

[a] Testing was performed by the CCNSC on KB 90. [b] Numbers are the same as in Table I.

Acknowledgment.—This work was supported in part by a grant (CA 07403-02) from the National Cancer Institute.

Some Hydrazones of 5-Phenyl-2,4-thiazolidinedione

ALEKSEY A. SIROTENKO AND PETER A. CIAVARRI, JR.[1]

Department of Chemistry, St. John Fisher College, Rochester, New York

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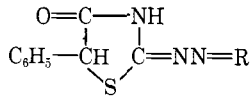
Compounds having structures similar to the hydrazones of 5-phenyl-2,4-thiazolidinedione have exhibited antituberculous,[2]

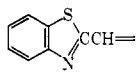
(1) Abstract in part from the B.S. Thesis of Peter A. Ciavarri, Jr.

(2) H. Taniyama, S. Takemura, B. Yasui, and H. Uchida, *J. Pharm. Soc. Japan*, **74**, 113 (1954).

TABLE I

SOME HYDRAZONES OF 5-PHENYL-2,4-THIAZOLIDINEDIONE



R	Mp, °C	Yield, %	Formula	% calcd C	% calcd H	% calcd N	% found C	% found H	% found N
$CON(C_6H_5)N(CH_3)C(CH_3)=CCH=$	259–260	90.02	$C_{21}H_{19}N_5O_2S$	62.21	4.72	17.28	62.52	4.90	17.01
$CON(C_6H_5)N(CH_3)C(CH_3)=CNHCH=$	254	56.00	$C_{21}H_{20}N_6O_2S$	59.99	4.80	19.99	59.42	5.07	20.10
$CH_2CH_2OCH_2CH_2NCH=$	275	18.32	$C_{14}H_{16}N_3O_2S$	58.00	5.50	14.50	57.81	4.94	14.79
	250	38.40	$C_{17}H_{12}N_4OS_2$	57.95	3.43	15.90	57.20	3.98	15.81

antianemia, and antithyroid action.[3-6] Some 5,5-dialkyl derivatives possess hypnotic properties.[7-10] The methods for the preparation of both the parent compound[11] and many of its derivatives are described in literature.[7-10,12-15] Four new analogs are listed in Table I.

Experimental Section[16]

4-Formylantipyrine Hydrazone of 5-Phenyl-2,4-thiazolidinedione.—4-Antipyrine carboxylate (4.0 g, 0.02 mole) was dissolved in ethanol and made basic with NaOH. Thiosemicarbazide (1.8 g, 0.02 mole) was then added. After allowing the mixture to stand for 10 min ethyl phenylchloroacetate (4.0 g, 0.02 mole) was added and the mixture was shaken. Sodium acetate (1.6 g, 0.02 mole) and 6.0 ml of dilute acetic acid were then added and the mixture was refluxed for 30 min. Upon cooling a yellow crystalline solid was filtered off, air dried, and recrystallized from ethanol The hydrazones of N-formylaminoantipyrine, N-formylmorpholine, and 2-formylbenzythiazole were prepared and purified in the same manner.

(3) E. V. Vladzimirskaya, N. M. Turkevich, *Zh. Obshch. Khim.*, **25**, 2150 (1955); *Chem. Abstr.*, **50**, 8605*b* (1956).

(4) N. M. Turkevich, E. V. Vladzimirskaya, *Zh. Obshch. Khim.*, **24**, 2010 (1954); *Chem. Abstr.*, **49**, 14737*i* (1955).

(5) S. M. Kapustyak, *Farm. Zh.*, **14**, No. 3, 6 (1959); *Chem. Abstr.*, **55**, 5650*i* (1961).

(6) N. M. Turkevich, K. M. Serdyuk, and Sechkorez, *Farm. Zh.*, **14**, No. 3, 13 (1959); *Chem. Abstr.*, **55**, 1923*h* (1961).

(7) H. Erlenmeyer and H. v. Meyenburg, *Helv. Chim. Acta*, **20**, 1388 (1937); **21**, 1013 (1938).

(8) W. J. Doran and H. A. Shonle, *J. Org. Chem.*, **3**, 193 (1938).

(9) E. R. H. Jones, F. A. Robinson, and M. N. Strachan, *J. Chem. Soc.*, 91 (1946).

(10) C.-P. Lo, E. Y. Shropshire, and W. J. Croxall, *J. Am. Chem. Soc.*, **75**, 4845 (1953).

(11) W. Heintz, *Ann.*, **136**, 223 (1865).

(12) H. L. Wheeler and B. Barnes, *Am. Chem. J.*, **24**, 61 (1900).

(13) H. L. Wheeler and T. B. Johnson, *ibid.*, **28**, 121 (1902).

(14) H. Beckurts and H. Frerichs, *Arch. Pharm.*, **253**, 233 (1915).

(15) D. Liebermann, *Nature*, **160**, 903 (1947).

(16) Melting points were determined in the Thomas–Hoover capillary melting point apparatus and are uncorrected.

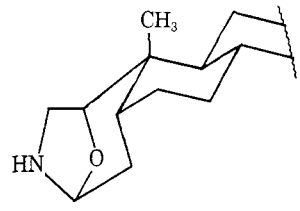
The Chemistry of Samandarine Model Compounds[1]

H. FRANKE AND R. PARTCH[2]

Department of Chemistry, Clarkson College of Technology, Potsdam, New York

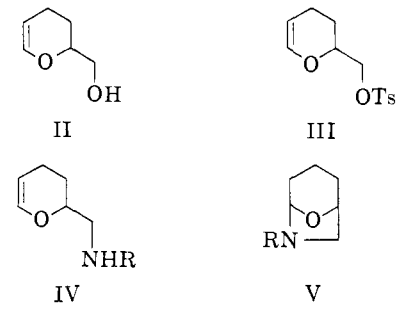
Received February 5, 1966

The salamander toxin,[3,4] samandarine (partial structure I), has still not been synthesized.[5,6] Since it is unusual to have potent neurotoxic and convulsive activity in a "steroidlike" molecule, we undertook the synthesis and physiological evaluation of the heterocyclic portion of the alkaloid. We suspected it to be responsible for the uncommon activity.[7]



I

The synthesis of 6-axa-8-oxabicyclo[3.2.1]octane (Va) and N-substituted derivatives is described in Figure 1.[8] Interesting aspects of the infrared spectra of the bicyclic oxazolidines are: (1) the C–O absorption in V is near 1025 cm^{-1}, whereas it is near 1075 cm^{-1} in IV;[9] and (2) the multiple absorptions of the oxazolidine nucleus between 800 and 900 cm^{-1}.[10] The nmr spectra for Va and Vb strongly support the structures shown.[11]



II III IV V

Figure 1.

(1) Portions of this paper were presented at the 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965.

(2) (a) To whom inquiries should be addressed. (b) Part of the data of this manuscript were obtained at New Mexico Highlands University, Las Vegas, N. M. (c) The authors gratefully acknowledge support of this work by the National Institutes of Health.

(3) O. Gessner, *Arch. Expil. Pathol. Pharmakol.*, **129**, 261 (1928); **167**, 244 (1932); **179**, 39 (1935).

(4) Ed. St. Faust, *ibid.*, **41**, 229 (1898); **43**, 84 (1899).

(5) E. Wolfel, C. Schopf, G. Weik, and G. Habermehl, *Chem. Ber.*, **94**, 2361 (1961).

(6) See ref 5, footnote 1.

(7) Compare O. Gessner, *Arch. Exptl. Pathol. Pharmakol.*, **187**, 378 (1937); **205**, 1 (1948); J. Peters, *J. Pharmacol Exptl. Therap.*, **118**, 90 (1956); P. Mantegazzini, *Arch. Intern. Pharmocodyn.*, **107**, 397 (1956).

(8) Compare H. Guest, H. Stansbury, and B. Kiff, U. S. Patent 3,008,946 (1959); *Chem. Abstr.*, **56**, 8719 (1962).

(9) Compare the absorptions of tetrahydropyran (1080 cm^{-1}) and 8-oxabicyclo[3.2.1]octane (1027 cm^{-1}): A. Cope, *J. Am. Chem. Soc.*, **87**, 3119 (1965).

(10) Compare G. Habermehl, *Chem. Ber.*, **96**, 2029 (1963); M. Senkus *J. Am. Chem. Soc.*, **67**, 1515 (1945).

(11) Nmr data are being obtained from Dr. L. Colebrook, University of Rochester, N. Y. Spin coupling analyses are contemplated.