

Derivatives of 5,4-Dihydro-1,5-Oxazine Condensed with Aromatic Rings in the Position 5,6

by

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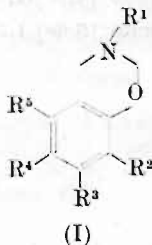
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Recent publications on derivatives of benz-1,3-oxazine [1], [2] prompt us to report on our own investigations which form a continuation of previously published papers [3]–[5].

We prepared namely a number of new derivatives of 3,4-dihydro-1,3-oxazine. The method of preparation consisted in adding a primary amine to a slightly alkaline, cooled solution of formaldehyde in methanol. The solution thus prepared was added to a compound with a phenolic function.

The substances obtained can be classified into several groups, as given below.

(I) Derivatives of substituted phenols of the general formula:



Here:

(Ia) — $R^1 = \text{CH}_2\text{C}_6\text{H}_5$; $R^2 = R^3 = \text{CH}_3$; $R^4 = R^5 = \text{H}$

(Ib) — $R^1 = \text{CH}_2\text{C}_6\text{H}_5$; $R^3 = R^4 = \text{CH}_3$; $R^2 = R^5 = \text{H}$

(Ic) — $R^1 = \text{CH}_2\text{C}_6\text{H}_5$; $R^3 = R^5 = \text{CH}_3$; $R^2 = R^4 = \text{H}$

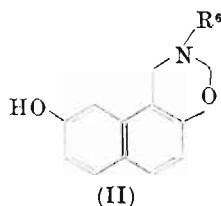
(Id) — $R^1 = \text{CH}_3$; $R^3 = \text{CH}_3$; $R^4 = \text{Cl}$; $R^2 = R^5 = \text{H}$

(Ie) — $R^1 = \text{CH}_2\text{C}_6\text{H}_5$; $R^2 = \text{CH}_3$; $R^5 = \text{iC}_3\text{H}_7$; $R^3 = R^4 = \text{H}$

(If) — $R^1 = \text{CH}_3$; $R^2 = \text{CH}_3$; $R^5 = \text{iC}_3\text{H}_7$; $R^3 = R^4 = \text{H}$

(Ig) — $R^1 = \text{CH}_2\text{C}_6\text{H}_5$; $R^2 = \text{CH}_3$; $R^5 = \text{C}_2\text{H}_5$; $R^3 = R^4 = \text{H}$

(II) Products of the reaction of 2,7-dihydroxynaphthalene with formaldehyde and amines in the molar ratio 1:2:1

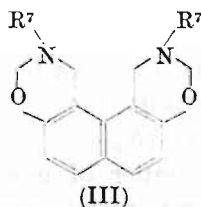


(IIa) — $R^6 = \text{CH}_2\text{C}_6\text{H}_5$

(IIb) — $R^6 = \text{CH}_3$

(IIc) — $R^6 = \text{C}_2\text{H}_5$

(III) Products of the reaction of 2,7-dihydroxynaphthalene with formaldehyde and amines in the molar ratio 1:4:2



(IIIa) — $R^7 = \text{CH}_2\text{C}_6\text{H}_5$

(IIIb) — $R^7 = \text{CH}_3$

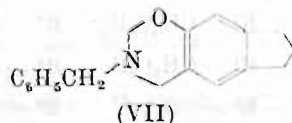
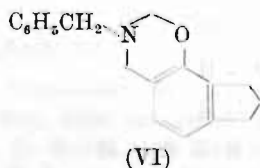
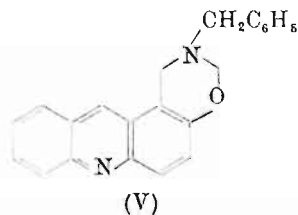
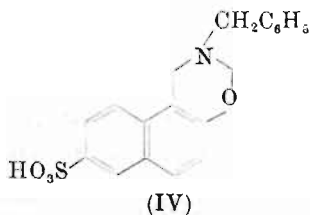
(IIIc) — $R^7 = \text{C}_2\text{H}_5$

Besides, we also obtained the compounds: (IV) 3,4-dihydro-3-benzyl-(6-sulphonaphtho) [1,2e]-1,3-oxazine and its sodium salt (IVa)

(V) 3,4-dihydro-3-benzylacridine [1,2e]-1,3-oxazine

(VI) 3,4-dihydro-3-benzylhydrindo [4,5e]-1,3-oxazine

(VII) 3,4-dihydro-3-benzylhydrindo [5,6e]-1,3-oxazine.



The physical properties of the compounds are tabulated (Table).

We are continuing experiments on the synthesis of analogous compounds by condensing phenols with amines and aldehydes both aliphatic and aromatic.

TABLE

Compound	m. p. or b. p.	m. p. of hydro- chlorides	Required		Analysis		Found		Formula
			%C	%H	%N	%C	%H	%N	
Ia	71–73°	150–153°	70.5 (hydro- chloride)	6.5	—	70.7	7.0	—	C ₁₇ H ₂₀ ONCl
Ib	87–88°								C ₁₇ H ₁₉ ON
Ic	94–97°								C ₁₇ H ₁₉ ON
Id	172–174°	222–225°							C ₁₆ H ₁₆ ONCl
Ie	174–176° ^{0.35 cm} Hg	206–207°	71.9 (hydro- chloride)	7.6	4.4	71.5	7.3	4.6	C ₁₉ H ₂₄ ONCl
If	98° 0.2 m Hg								C ₁₃ H ₁₀ ON
Ig	39–41°								
IIa	139–140°	~240° ^a	78.3 (hydro- chloride)	5.9	4.8	78.6	5.9	4.9	C ₁₈ H ₂₁ ON C ₁₉ H ₁₇ O ₂ N
IIb	~210° d				4.3			4.6	C ₁₉ H ₁₈ O ₇ NCl
IIc	~190° d				6.1			6.4	C ₁₃ H ₁₃ O ₂ N C ₁₄ H ₁₅ O ₂ N
IIIa	123–124°		79.6	6.2	6.6	79.3	6.0	6.6	C ₂₈ H ₂₆ O ₂ N ₂
IIIb	171–173° decomp.								C ₁₆ H ₁₈ O ₂ N ₂
IIIc	133–135°								C ₁₈ H ₂₂ O ₂ N ₂
IV	234–235°		64.2	4.8	4.0	64.1	4.8	4.1	C ₁₉ H ₁₇ O ₄ NS
IVa	does not melt		60.5	4.3	3.7	60.7	4.9	4.0	C ₁₉ H ₁₆ O ₄ NSNa
V	131–132°		81.0	5.6	8.6	81.1	6.0	8.8	C ₂₂ H ₁₉ ON ₂
VI	73–75°								C ₁₈ H ₁₉ ON
VII	97–99°								C ₁₈ H ₁₉ ON

As previously reported [3]–[6] the benz-1,3-oxazine derivatives possess interesting bacteriostatic and antineoplastic activities.

More detailed results including methods of preparation [7] and biologic activities [8], [9] will be reported later.

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