TABLE I.—CHROMATOGRAPHIC DATA FOR THE ALKALOIDS OF *S. carniolica*

Alkaloid	Paper[a]	Thin-Layer[b]
Cuscohygrine	0.08	0.00; 0.63[c]
Pseudotropine	0.15	0.13
Scopolamine	0.26	0.52
Unidentified alkaloid	0.31	0.63
Tropine	0.34	0.22
Hyoscyamine	0.48	0.43
3-α-Tigloyloxytropane	0.84	0.63

[a] Whatman No. 1 paper (0.5 *M* KCl); *n*-butanol–HCl (98:2) water-saturated. [b] Aluminum oxide G; benzene–methanol (9:1). [c] Aluminum oxide G; benzene–methanol–diethylamine (99:1:5).

comparison of R_f values of compounds in extracts when analyzed by paper and thin-layer chromatographic procedures with authentic compounds, and color reactions.

The data indicate the presence of at least seven alkaloids. Identification of hyoscyamine, scopolamine, and tropine corroborates the studies of previous workers. This work has succeeded in the tentative identification of 3-α-tigloyloxytropane, the first reported occurrence of this compound in the genus *Scopolia;* it extends the distribution to still another genus of the family *Solanaceae* along with *Datura* (6), *Withania* (5), and *Physalis* (9). It also broadens the knowledge of the existence of cuscohygrine in plants containing tropane alkaloids. Pseudotropine was the sixth alkaloid to be identified. One other alkaloid remains to be identified. Failure to confirm the presence of scopine and solanidine in this sample was due to a lack of authentic reference compounds.

Work is continuing and complete details on the extraction, isolation, and characterization will be published at a later date.

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Synthesis of *N,N'*-Haloacyl Analogs of *p,p'*-Oxydianiline as Potential Antineoplastic Agents

By WILLIAM D. ROLL

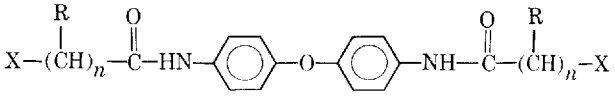
A series of eight new haloacetyl and halopropionyl derivatives of *p,p'*-oxydianiline have been synthesized for evaluation of anticarcinogenic activity.

AS AN INTEGRAL part of this continuing cancer chemotherapy research project, another series of bis-haloamide analogs of a parent diamine molecule have been prepared. Based upon the screening data obtained in this laboratory (1–3) and that from others in the field (4–7), the chemotherapeutic activity of such compounds is deserving of further study. This report concerns itself with the synthesis of a series of bis-haloacetyl and bis-halopropionyl derivatives of *p,p'*-oxydianiline (I).

This type of alkylating agent may inhibit the growth of cancer cells through selective inhibition of vital metabolic activities within tumor cells (8–15). By varying the carrier moieties of these active, relatively nontoxic compounds, it is hoped that some insight will be gained as to structure–activity relationships as regards their alkylating abilities.

DISCUSSION

An anhydrous chloroform solution of the diamine, *p,p'*-oxydianiline[1] (I), was treated with a chloroform solution of chloroacetyl chloride, 2-chloropropionyl chloride, and 3-chloropropionyl chloride to form,



X = Br, Cl, and I
R = H, *n* = 1,2
R = CH_3, *n* = 1

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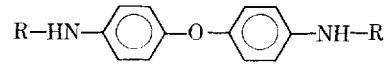
[1] Supplied by The Dow Chemical Co., Midland, Mich.

TABLE I.—*N,N'*-HALOACYL ANALOGS OF *p,p'*-OXYDIANILINE



Compd.	R	M.p., °C.	Yield, %	Anal. Calcd.	Anal. Found	Infrared ν cm.$^{-1}$ (KBr) (C=O amide)
II	$-COCH_2Cl$	231–232	80	C, 54.40 H, 4.00 Cl, 20.08 N, 7.93	C, 54.45 H, 3.96 Cl, 19.98 N, 7.99	1670
III	$-COCH(Cl)CH_3$	235–236	71	C, 56.70 H, 4.76 Cl, 18.60 N, 7.36	C, 56.68 H, 4.79 Cl, 18.52 N, 7.45	1670
IV	$-CO(CH_2)_2Cl$	227–228	75	C, 56.70 H, 4.76 Cl, 18.60 N, 7.36	C, 56.73 H, 4.80 Cl, 18.51 N, 7.30	1660
V	$-COCH_2Br$	216–217	75	C, 43.46 H, 3.19 Br, 36.14 N, 6.34	C, 43.39 H, 3.25 Br, 36.20 N, 6.29	1650
VI	$-COCH(Br)CH_3$	247–248	69	C, 46.98 H, 3.94 Br, 34.73 N, 6.08	C, 46.95 H, 3.93 Br, 34.80 N, 6.13	1660
VII	$-CO(CH_2)_2Br$	225–226	74	C, 46.98 H, 3.94 Br, 34.73 N, 6.08	C, 46.94 H, 3.92 Br, 34.70 N, 5.99	1650
VIII	$-COCH_2I$	239–240	70	C, 35.78 H, 2.62 I, 47.26 N, 5.22	C, 35.79 H, 2.61 I, 47.20 N, 5.18	1650
IX	$-CO(CH_2)_2I$	226–227	78	C, 38.32 H, 3.22 I, 44.98 N, 4.96	C, 38.40 H, 3.24 I, 45.03 N, 5.00	1660

respectively, *N,N'*-bis(chloroacetyl)-*p,p'*-oxydianiline (II), *N,N'*-bis(2-chloropropionyl)-*p,p'*-oxydianiline (III), and *N,N'*-bis(3-chloropropionyl)-*p,p'*-oxydianiline (IV). Similarly, the reaction of I with bromoacetyl bromide, 2-bromopropionyl bromide, and 3-bromopropionyl chloride gave the corresponding diamides, compounds V, VI, and VII, respectively. Compounds V and VII were converted into the iodoamides, compounds VIII and IX, respectively, by treating the former with sodium iodide in acetone.

EXPERIMENTAL

The procedure used for the synthesis of these compounds has been previously related (2). Reference may be made to Table I for the results of this synthetic work and properties of the compounds prepared. The melting points were determined with a Fisher-Johns melting point apparatus and are corrected. The infrared spectra were obtained with a Perkin Elmer Infracord.

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