Cancer and Arylsulphatase Activity

THREE arylsulphatases (arylsulphate sulphohydrolases *E.C.*3.1.6.1.) are known. Their distribution in the animal kingdom is very wide and their activity is low in such tissues as muscle and skin[1,2] and high in liver and kidney[2,3]. There are some indications that arylsulphatase activity is modified in tumours[2,4,5].

We have investigated the activity of arylsulphatase in cancers of the skin, stomach, colon and mammary gland.

250 mg of cancerous tissue extracted at operation were homogenized in 25 ml. of 0·5 molar acetate buffer, *p*H 5·8, for 3 min. 0·4 ml. of the homogenate was incubated for 24 h at 37° C with 0·4 ml. of 0·016 molar dipotassium 2-hydroxy-5-nitrophenyl sulphate as substrate. The reaction was stopped by adding 3 ml. of 2 per cent phosphotungstate and the liberated 4-nitrocatechol was estimated colorimetrically after adding 5 ml. of a 10 per cent solution of sodium hydroxide containing 0·2 per cent quinol and 5 per cent sodium sulphite. The activity of arylsulphatase was expressed in μmoles of 4-nitrocatechol per 0·4 ml. of 1 per cent homogenate (4 mg of wet tissue). Identical estimations on normal tissue of the organ from which the cancer originated were used as controls.

The cancerous character of the tissues was confirmed by histopathological examination. We have examined a total of nine cases of cancer of the stomach, nine cases of cancer of the colon, seven cases of cancer of the breast, four cases of malignant melanoma and one case of cancer of the skin.

Table 1 shows that in all cases of cancer examined the activity of arylsulphatase was elevated compared with the activity of the control tissue. The most marked increase occurred with malignant melanoma, which had a mean arylsulphatase activity more than eighty times higher than that of normal skin. The activity of arylsulphatase in one case of spino-cellular carcinoma of the skin was only ten times higher than the activity in normal skin.

Table 1. ARYLSULPHATASE ACTIVITY OF SOME CANCEROUS TISSUES EXPRESSED IN μMOLES OF 4-NITROCATECHOL/4 MG OF WET TISSUE

	Skin		Stomach mucous membrane	Colon mucous membrane	Breast
Normal tissue	25		250	230	90
	Melanoma	cancer			
Cancerous tissue	2,150	250	540	670	400

Arylsulphatase in tissue from cancer of the stomach was about twice as active as in normal gastric mucous membrane and five times as active as in the normal muscle layer. The activity of arylsulphatase in cancer of the colon was three times as high as the activity in normal mucous membrane of the colon and about fourteen times as high as that of the muscle layer. Cancer of the breast had an arylsulphatase activity which was about four times higher than the activity of normal mammary tissue.

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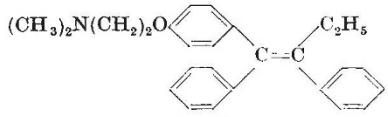
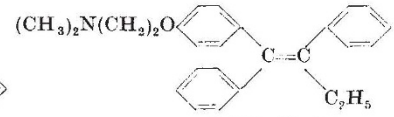
PHARMACOLOGY

Preparation and Identification of *cis* and *trans* Isomers of a Substituted Triarylethylene

WE have prepared a series of 1-(*p*-dialkylamino alkoxyphenyl) 2 alkyl-1,2-diphenylethylenes[1] and in many instances have isolated the respective isomers[2]. The differences in biological activity of one pair of *cis* and *trans* isomers, I.C.I. compounds Nos. 47,699 and 47,644. respectively, have already been described[3].



I.C.I. 47,699
(*cis*-)



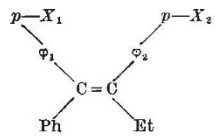
I.C.I. 46,474
(*trans*-)

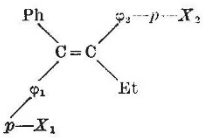
A mixture of these isomers was obtained by dehydration of 1 - (4 - β - dimethylaminoethoxyphenyl) - 1,2 - diphenylbutanol by heating the latter under reflux with ethanolic hydrochloric acid and converting the resulting mixed hydrochloride to base. The crude mixture was slurried with petroleum ether (boiling point 40°–60° C) and the insoluble material crystallized from the petroleum ether (b.p. 60°–80° C). In this way the *trans* isomer (melting point 96°–98° C) was obtained. The *cis* isomer (m.p. 72°–74° C, after crystallization from methanol) separated from the petroleum ether liquors (b.p. 40°–60° C). The preferred method of preparation of the intermediate butanol is by the reaction of phenylmagnesium bromide or phenyl lithium with 4-β-dimethylaminoethoxy-α-ethyldesoxybenzoin.

Table 1. CHEMICAL SHIFTS (τ) OF THE TWO ISOMERS

	NMe_2	$N.CH_2CH_2$	CH_2CH_2O	Aromatic A_2	Aromatic B_2	Phenyl singlets	
I.C.I. 46,474	7·80	7·46	6·17	3·33	3·54	2·91	2·79
I.C.I. 47,699	7·72	7·32	5·98	2·89	3·17	2·93	3·12

Table 2. CHEMICAL SHIFT DATA (τ) AND DIPOLE MOMENTS (DEBYE)





X_1	X_2	Ph	φ_1		φ_2		μ	Ph	φ_1		φ_2		μ
			H_A	H_B	H_A	H_B			H_A	H_B	H_B	H_B	
$Me_2N(CH_2)_2O$	H	2·79	3·33	3·54	2·91	2·91		3·12	2·89	3·17	2·93	2·93	
MeO	H	2·78	3·30	3·55	2·92	2·92		3·14	2·88	3·21	2·94	2·94	
MeO	MeO	2·79	3·29	3·51	3·01	3·37		3·09	2·91	3·21	3·00	3·40	
Cl	Cl	2·79	3·02	3·24	2·90	2·98	2·80	3·06*	2·71	2·88	2·94	2·98	0·94

H_A, Aromatic protons adjacent to the ethylenic double bond. H_B, Aromatic proton adjacent to the substituent.
* Multiplet.