

to more perfect parallelism of the chains; and since the enhanced birefringence agrees with that of oriented polypeptide chains almost devoid of all but the shortest side-chains, namely, those of natural silk, we have a peculiarly satisfying demonstration, quite apart from the X-ray evidence, that the side-chains do indeed tend to lie perpendicular to the plane of the film, as had already been inferred from monolayer studies<sup>5</sup> and from independent X-ray data<sup>6</sup>.

Finally, we have succeeded in measuring the thickness per monolayer by direct mechanical means. Our first method was to insert the film under one of the feet of a small three-legged interferometer\*, thus altering the angle of an air-wedge included between two pieces of optically flat glass, the upper piece being attached to a balanced metal frame supported by the three legs, and the lower forming the actual table on which rested the film and the three feet. By this means—and it should be noticed that no optical properties of the film itself are invoked—we have measured the thickness of films composed of 600, 800, 1,000, 1,450 and 1,764 monolayers, respectively, and the results all agree in fixing the thickness per monolayer at about  $9\frac{1}{2}$  Å., and not 20 Å., as was first suggested<sup>7</sup>. The value  $9\frac{1}{2}$  Å. agrees well with the side-chain spacing given not only by the films under discussion, but also by  $\beta$ -proteins in general.

The second method was by way of being a *tour de force*, but it was sufficiently accurate to point once again to a thickness per monolayer of about 10 Å. It consisted in measuring the thicknesses of various folded pads of film with a screw micrometer! Needless to say, the thrill of being able for the first time to measure the thickness of a protein chain by such a means far outweighed the satisfaction derived from the more elegant methods.

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<sup>1</sup> Blodgett, K. M., *J. Amer. Chem. Soc.*, **57**, 1007 (1935); Langmuir, I., Schaefer, V. J., and Wrinch, D. M., *Science*, **85**, 76 (1937).

<sup>2</sup> Blodgett, K. M., and Langmuir, I., *Phys. Rev.*, **51**, 964 (1937).

<sup>3</sup> Astbury, W. T., and Sisson, W. A., *Proc. Roy. Soc. A*, **150**, 533 (1935).

<sup>4</sup> Cf. the spinning of fibres from denatured globular protein. Astbury, W. T., Dickinson, S., and Bailey, K., *Biochem. J.*, **29**, 2351 (1935). See numerous papers by Gorter, Rideal, and co-workers.

<sup>5</sup> Astbury, W. T., *Trans. Faraday Soc.*, **29**, 193 (1933); *NATURE*, **137**, 803 (1936); *Chem. Weekbl.*, **33**, 778 (1936).

<sup>7</sup> Langmuir, I., Schaefer, V. J., and Wrinch, D. M., *Science*, **85**, 76 (1937).

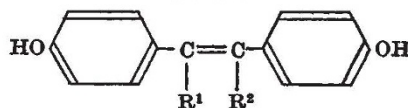
### Estrogenic Activity of Alkylated Stilbcestrols

In a previous communication<sup>1</sup> we described the estrogenic activity of 4:4'-dihydroxy- $\alpha$ : $\beta$ -diethylstilbene (diethylstilbcestrol). It was shown that this substance was fully oestrogenic in doses of 0.004 mgm. given subcutaneously dissolved in oil, and 0.001 mgm. when given by mouth. It is thus several times more potent than oestrone and at least as potent as oestradiol. The following communication is concerned with the activity of a series of compounds in which substituents other than the ethyl group are attached to the  $\alpha$  and  $\beta$  carbon atoms. The method of testing was on ovariectomized rats by the usual technique.

Table 1 indicates the results in this series of compounds and gives the potency of the substances in relationship to oestrone. In view of the fact that maximum activity is represented by diethylstilbcestrol, a number of esters of this substance have been prepared and are being tested.

In Table 2 will be found the activity of a series of derivatives of dihydroxydiphenylbutadienes. Here again the maximum activity is present in 4:4'-dihydroxy- $\gamma$ : $\delta$ -diphenyl- $\beta$ : $\delta$ -hexadiene. This substance appears to possess an activity equal to that of diethylstilbcestrol. The correspondence in the effects of substituents in the two series is noteworthy and the large effects of relatively small changes may be thought to support our view that the middle section of the molecule conforms to the oestrone pattern when the substituents are ethyl or ethylidene groups.

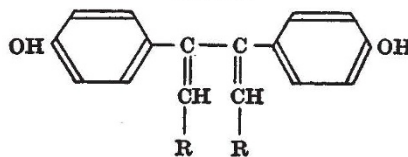
TABLE 1.



R <sup>1</sup>	R <sup>2</sup>	Dose in mgm.	% Positive	Units per gram estimated
H	H	5	80	140
H	H	10	100	
H	C <sub>2</sub> H <sub>5</sub>	0.1	50	5,000
CH <sub>3</sub>	CH <sub>3</sub>	0.02	80	40,000
		0.03	100	
CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	0.0005	30	1,000,000
		0.001	100	
C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	0.0003	80	3,000,000
		0.0004	100	
C <sub>2</sub> H <sub>5</sub>	n-C <sub>3</sub> H <sub>7</sub>	0.001	trace	300,000
		0.01	100	
n-C <sub>3</sub> H <sub>7</sub>	n-C <sub>3</sub> H <sub>7</sub>	0.01	75	50,000
		0.1	100	
n-C <sub>4</sub> H <sub>9</sub>	n-C <sub>4</sub> H <sub>9</sub>	0.01	nil	5,000
		0.1	40	
Monohydroxy-diethylstilbene		0.1	trace	
		1.0	100	

Oestrone administered in oil under the same conditions has activity approx. 700,000 units per gram.

TABLE 2.



	Dose in mgm.	% Positive
4:4'-Dihydroxy- $\beta$ : $\gamma$ -diphenyl-butadiene (R = H)	10	100
	1	trace
4:4'-Dihydroxy- $\gamma$ : $\delta$ -diphenyl- $\beta$ : $\delta$ -hexadiene (R = CH <sub>3</sub> )	0.0005	100
	0.0004	70
4:4'-Dihydroxy- $\delta$ : $\epsilon$ -diphenyl- $\gamma$ : $\sigma$ -octadiene (R = C <sub>2</sub> H <sub>5</sub> )	0.01	100
	0.002	nil
$\beta$ : $\gamma$ -Di(4-hydroxyphenyl)- $\alpha$ : $\delta$ -diphenyl-butadiene (R = C <sub>2</sub> H <sub>5</sub> )	10	nil

The substances mentioned in Table 2 were prepared by dehydration of the appropriate pinacols and the new substituted stilbenes were obtained by applications of the methods previously described.

In the former communication<sup>1</sup> the name of one of us (L. G.) was spelt incorrectly.

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<sup>1</sup> Dodds, Golberg, Lawson and Robinson, *NATURE*, **141**, 247 (1938).