Some New Synthetic Estrogens

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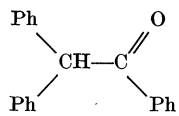
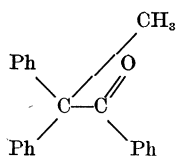
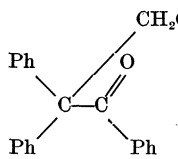
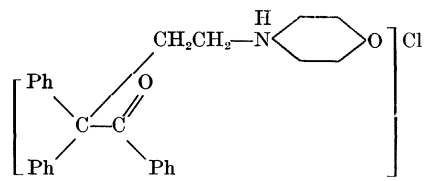
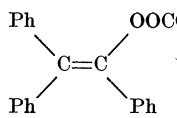
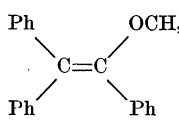
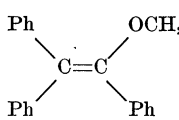
In the course of an investigation[3] on the alkylation of α: α-diphenylacetophenone (*1*) a series of compounds was obtained which, in view of their structural relationship to triphenylethylene, appeared to be of interest as potential estrogens. Table 1 presents the result of the provisional tests for estrogenic activity. Assays were carried out according to standard procedures.

Although the number of compounds investigated is too small to permit general conclusions as to a relationship between chemical constitution and physiological activity, certain regularities can be observed within a series of homologs. Thus, in the ketone series (1, 2, 3, 4) substitution of the α-position by an aliphatic group increases the activity as compared with the parent substance (1). Maximum activity is shown by the methyl-homolog (2). An increase in the chain length, however, drastically reduces activity (3, 4).

In the second series (5–12) etherification of the enol of α: α-diphenylacetophenone gives, as would be expected, compounds more active than the acetate (5), which presumably is hydrolyzed *in vivo* by esterases. Again estrogenic activity decreases rapidly with increasing chain length of the alkyl group involved in ether formation (6, 7, 9, 10, 12). Although the ethyl ether (6) appears to be the most active nonbasic compound of this group, the methyl-homolog might be expected to exhibit maximum activity, but unfortunately

TABLE 1

No.	Structural formula	Assayed in	Estrogenic activity in IU/mg
	Theelin		10,000
1.		Aqu. ethanol	10
		Peanut oil	40
2.		Peanut oil	6000
3.		Peanut oil	1000
4.		Aqu. ethanol	< 100
5.		Aqu. ethanol	400
		Peanut oil	400
6.		Peanut oil	5000
7.		Peanut oil	500

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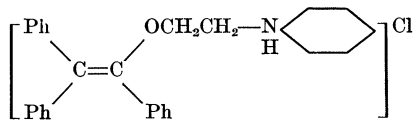
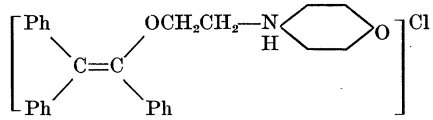
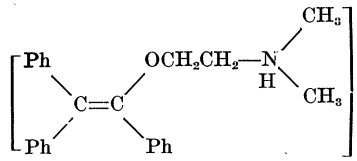
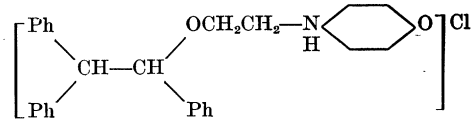
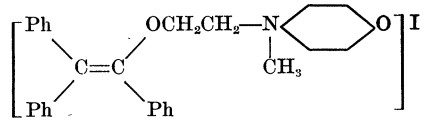
[3] The authors wish to express their sincere thanks to G. Rieveschl for his interest and help in this work.

TABLE 1—(*Continued*)

No.	Structural formula	Assayed in	Estrogenic activity in IU/mg
8.		Peanut oil	3000
9.		Peanut oil	100
10.		Peanut oil	200
11.		Aqu. ethanol	< 400
12.		Aqu. ethanol	< 400
		Peanut oil	< 100

it was not available for testing. The only compound that does not fit this general pattern is the β-piperidinoethyl ether (8). No explanation can at present be offered for its surprisingly high estrogenic potency, which is 15 to 30 times that of the analogously constituted compounds (10) and (9). This was confirmed by several reassays.

Reference

1. RINDERKNECHT, H. *J. Am. Chem. Soc.*, **73**, 5770 (1951).

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Comments and Communications

"Attraction Fields" between Growing Tissue Cultures[1]

GHOSTS have a way of refusing to be laid. One such ghost is the alleged "attraction" for each other's cells supposedly exerted by two growing parts—for instance, two tissue fragments cultured in a common medium. More than 20 years ago I gave the first description of the striking phenomenon of an oriented cell bridge forming, under certain conditions, between two growing centers (*1*); for convenience this may be referred to as the "two-center effect." At the same time, and repeatedly since (e.g., [*2*]), I have pointed out that the superficial impression of "attractions" (in the customary sense of the word) being at play is a sheer illusion. The correct interpretation, gained by stepwise analysis of the factors involved, has been amply documented and published (*2–5*). It has found even wider currency through the publications of other authors (*6, 7*).

It is somewhat perplexing, therefore, to find in a recent article in SCIENCE (**114**, 431 [1951]) the whole phenomenon rediscovered, redescribed and, by the implications of the terms used, again misinterpreted. In the article in question, entitled "Distance as a Factor in the Development of Attraction Fields between Growing Tissues in Culture," the author, Allan A. Katzberg, states that "the term 'attraction field' has been used to describe this phenomenon." This term is absolutely inappropriate and misleading. Its reaffirmation by the author mars what is otherwise a correct, if not altogether novel, presentation. It matters little that the author is only dimly aware of the systematic work that has been done in this field before. After all, his observations fully confirm the known facts. But the way in which he treats them is apt to lead back to

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