

Letters to the Editor

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NOTES ON POINTS IN SOME OF THIS WEEK'S LETTERS APPEAR ON P. 1027.

CORRESPONDENTS ARE INVITED TO ATTACH SIMILAR SUMMARIES TO THEIR COMMUNICATIONS.

Photo-oxides of Carcinogenic Hydrocarbons

SUGGESTIONS have sometimes been made that the biological action of carcinogenic hydrocarbons is preceded by conversion, probably by oxidation, into water-soluble derivatives which may more readily be conceived as able to exert a direct action on the cells which eventually become malignant than the water-insoluble parent hydrocarbons. The photo-sensitivity of solutions of some of the more potent carcinogenic hydrocarbons (namely, 3:4-benzpyrene and 20-methylcholanthrene) is apparent to those accustomed to work with them; moreover, Boyland¹ found that alkaline extracts of photo-oxidized carcinogenic hydrocarbons arrest the activity of certain enzymes, and Maisin and de Jonghe² observed that light accelerates the production of skin tumours in mice by 3:4-benzpyrene. Most of the known carcinogenic hydrocarbons are anthracene derivatives and are therefore related to the group of compounds which have been shown by Dufraisse and his collaborators³ to undergo facile photo-oxidation to oxides which are peroxidic in character.

With the view of determining whether oxides of this type are involved in the biological action of carcinogenic hydrocarbons, we have attempted to isolate the photo-oxides of some of these hydrocarbons. Such photo-oxides would naturally be insoluble in water and hence would represent merely one stage in the oxidation process envisaged as a prelude to biological action. During the earlier stages of our work, Velluz⁴ reported that no absorption of oxygen occurred when solutions of 1:2:5:6-dibenzanthracene and 20-methylcholanthrene were exposed to sunlight. We have ourselves been unable to obtain photo-oxides from 1:2:5:6-dibenzanthracene and 3:4-benzpyrene; in the latter case, dark-coloured unidentified products were obtained. With 1:2-benzanthracene we found indications of the formation of a photo-oxide; but contamination with dark-coloured by-products hindered its isolation.

The most rapidly acting carcinogenic hydrocarbon now known is 9:10-dimethyl-1:2-benzanthracene⁵, and the superior *meso* additive reactivity of this hydrocarbon towards maleic anhydride⁶ suggested that a photo-oxide might be more readily formed than in the case of the hydrocarbons previously mentioned. This has proved to be so. Oxygen was passed through 500 c.c. of a 0.05 per cent solution of 9:10-dimethyl-1:2-benzanthracene in carbon disulphide, exposed to the light of a 200-watt gas-filled lamp. The solution was kept cool by immersion in a bath of running water. After some four hours, the blue fluorescence had disappeared, and the solvent was removed under reduced pressure, in the dark. The resulting *photo-oxide* crystallized from carbon

disulphide in colourless needles, m.p. 193–194°. Photo-oxides having the melting points given in parenthesis were also obtained with approximately equal facility from the following related hydrocarbons: 5:9:10-trimethyl-1:2-benzanthracene (212–213°), 6:9:10-trimethyl-1:2-benzanthracene (205–206°), 5:6:9:10-tetramethyl-1:2-benzanthracene (228–229°), and 9:10-dimethyl-1:2:5:6-dibenzanthracene (222–223°). Two of the hydrocarbons have not been described (6:9:10-trimethyl-1:2-benzanthracene, m.p. 157–158°, and 5:6:9:10-tetramethyl-1:2-benzanthracene, m.p. 132–133°) and their synthesis, and also full descriptions of the photo-oxides, will be published elsewhere.

The compounds thus made available should suffice to show whether oxides of this nature are intermediate products in carcinogenesis by the hydrocarbons, although the lack of correspondence between the carcinogenic activity of a compound and its ability to form a photo-oxide does not support this view.

The ultra-violet absorption spectrum of the photo-oxide of 9:10-dimethyl-1:2-benzanthracene has been examined. It is intermediate between a benzene and a naphthalene type of absorption as shown by their complex derivatives. That is, the bands are similar in position to those of a *meso*-dihydro derivative of 1:2:5:6-dibenzanthracene, but have only about half the intensities. On irradiation with the mercury arc, a hexane solution of the photo-oxide is decomposed and the spectrum of the parent hydrocarbon with its long wave-length band system (3200–4000 Å.) reappears. Prolonged irradiation results in further change in the spectrum leading to a continuous absorption rising towards the region of shorter wave-length, and the same change is observed when the parent hydrocarbon, 9:10-dimethyl-1:2-benzanthracene, is similarly treated. The spectrum of 9:10-dihydroxy-9:10-dimethyl-9:10-dihydro-1:2-benzanthracene, examined for comparison with that of the photo-oxide, shows bands of the same order of intensity as the photo-oxide, but shifted about 180 Å. towards the far ultra-violet.

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¹ Boyland, E., *NATURE*, **130**, 274 (1932); *Biochem. J.*, **27**, 791 (1933).

² Maisin, J., and de Jonghe, A., *C.R. Soc. Biol.*, **117**, 111 (1934).

³ See, for example, Dufraisse, C., *Bull. Soc. Chim.*, (v) **16**, 422 (1930).

⁴ Velluz, L., *C.R.*, **203**, 1514 (1933).

⁵ Bachmann, W. E., Kennaway, E. L., and Kennaway, N. M., *Yale J. Biol. and Med.*, **11**, 97 (1933).

⁶ Bachmann, W. E., and Chernerda, J. M., *J. Amer. Chem. Soc.*, **60**, 1023 (1938).