349. *The Relative Reactivity of Aromatic Double Bonds. Part II.* Addition of Osmium Tetroxide to Substituted* 1 : 2-*Benzanthracenes.*

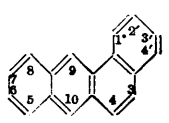
By G. M. Badger and K. R. Lynn.

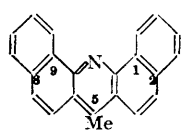
The effect of various *meso*-substituents on the rate of addition of osmium tetroxide to the 3 : 4-double bond of 1 : 2-benzanthracene has been investigated. Methyl, acetoxymethyl, and phenyl groups were found to facilitate the reaction, and bromo-, acetoxy-, and cyano-, substituents to retard the addition. *meso*-Methoxy-groups were found to exert little effect. The rate of addition to 5-methyl-1 : 2-8 : 9-dibenzacridine has also been studied.

9-Methoxy-1 : 2-benzanthracene has been prepared by cyclisation of *o*-2-naphthylmethylbenzoic acid to 9-acetoxy-1 : 2-benzanthracene, followed by cleavage with Grignard reagent and methylation with methyl sulphate.

Three compounds appear to function as " double-bond " reagents: ozone, diazoacetic ester, and osmium tetroxide. These reagents readily react with ethylenic double bonds to form addition compounds, and they also attack certain aromatic double bonds. Ozone is the most vigorous reagent, even benzene and pyridine being readily, if slowly, attacked. Diazoacetic ester also reacts with benzene, with elimination of nitrogen. With polycyclic compounds, the selective addition of ozone, and of diazoacetic ester, to the more reactive double bonds only may be brought about. Under the conditions so far employed, osmium tetroxide does not attack benzene, but reacts only with aromatic bonds which have pronounced double-bond character. Unlike the usual electrophilic reagents, such as NO_2^+ and Br^+, etc., these double-bond reagents do not attack the most reactive centres in a polycyclic molecule, except in those cases in which the most reactive centres are situated at the extremities of the most reactive *bond* (Badger, *J.*, 1949, 456; Cook and Schoental, *J.*, 1948, 170; *idem*, *Nature*, 1948, **161**, 237).

The use of osmium tetroxide to determine the relative reactivity of aromatic double bonds has been described previously by one of us (Badger, *loc. cit.*; Badger and Reed, *Nature*, 1948, **161**, 238). The method has been used to study the rate of addition of osmium tetroxide to a series of cancer-producing compounds, especially the methyl derivatives of 1 : 2-benzanthracene (I). The substitution of methyl groups in this molecule was found to increase the rate of addition to the 3 : 4-bond, the magnitude of the increase being dependent on the position of substitution. It was also found that a cyano-group markedly reduced the rate of addition. A further series of compounds has now been examined, in an attempt to evaluate the effect of other substituent groups on the density of π electrons on the 3 : 4-bond. In the earlier work it was found that methyl groups exerted the maximum effect when present as *meso*-substituents. For this reason most of the compounds in the present series are *meso*-substituted benzanthracenes. The rate of addition to 5-methyl-1 : 2-8 : 9-dibenzacridine (II) has also been examined.

(I.) 



(II.)

The reactions were carried out, as previously reported, in pure chloroform containing 4% pyridine at 20°. The progress of the reaction was followed by removing aliquot portions at

* *J.*, 1949, 456, is regarded as Part I of this series.

suitable intervals and estimating the colour intensity of the solution (and hence the concentration of the complex) with a Spekker absorptiometer. The rate constants for the present series of compounds are given in the accompanying table, the constants for 1 : 2-benzanthracene and its 10-methyl and 9 : 10-dimethyl derivatives being included for reference.

The earlier work showed clearly that methyl substituents facilitate the addition of osmium tetroxide, whilst the cyano-substituent definitely slows the reaction, presumably by withdrawing electrons from the double bond. The present work confirms the activating influence of the methyl group. For example, 10-acetoxy-9-methyl-1 : 2-benzanthracene reacted more rapidly than 10-acetoxy-1 : 2-benzanthracene, and 10-bromo-9-methyl-1 : 2-benzanthracene reacted more rapidly than 10-bromo-1 : 2-benzanthracene. Furthermore, 5-methyl-1 : 2-8 : 9-dibenzacridine (II) reacted with osmium tetroxide more rapidly than 1 : 2-benzanthracene. This is interesting, for the activating influence of the methyl group is offset to some extent by the deactivating influence of the heterocyclic nitrogen atom, and the addition was found to take place only slightly less rapidly than with 10-methyl-1 : 2-benzanthracene.

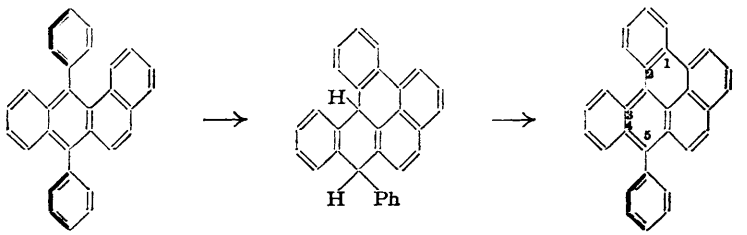
Rate of addition of osmium tetroxide to substituted 1 : 2-*benzanthracenes, in* 4% *pyridine in chloroform, at* 20°. (k_2 in g.-mol.$^{-1}$sec.$^{-1}$l.)

Compound.	$10^3 k_2$.	Compound.	$10^3 k_2$.
9 : 10-Dimethyl-1 : 2-benzanthracene	2·7*	9-Methoxy-1 : 2-benzanthracene	0·55
10-Methyl-1 : 2-benzanthracene	0·91 *	1 : 2-Benzanthracene	0·48 *
5-Methyl-1 : 2-8 : 9-dibenzacridine	0·88	9 : 10-Dimethoxy-1 : 2-benzanthracene...	0·46
10-Bromo-9-methyl-1 : 2-benzanthracene	0·74	10-Cyano-9-methyl-1 : 2-benzanthracene	0·40
9 : 10-Diphenyl-1 : 2-benzanthracene	0·70	10-Acetoxy-1 : 2-benzanthracene	0·34
10-Acetoxy-9-methyl-1 : 2-benzanthracene	0·62	10-Bromo-1 : 2-benzanthracene	0·27
10-Acetoxymethyl-1 : 2-benzanthracene...	0·61	9 : 10-Diacetoxy-1 : 2-benzanthracene ...	0·22

* Badger (*J.*, 1949, 456.)

The acetoxymethyl group is also activating, although less so than the methyl group, for 10-acetoxymethyl-1 : 2-benzanthracene formed the addition complex with osmium tetroxide more rapidly than 1 : 2-benzanthracene, but less rapidly than 10-methyl-1 : 2-benzanthracene. *meso*-Acetoxy- and *meso*-bromo-groups were found to retard the addition, and *meso*-methoxy-groups had little or no effect on the rate of reaction. *meso*-Phenyl groups appear to activate the 3 : 4-bond, the rate of addition to 9 : 10-diphenyl-1 : 2-benzanthracene being greater than that to unsubstituted benzanthracene.

In some respects, these results may seem surprising. For example, it is well known that in electrophilic substitutions of benzene derivatives, the methoxy-group is very strongly activating and *ortho-para* directing, whereas in the present case it seems to exert little or no effect. Moreover, the acetoxy-group is usually regarded as a weak activating group, yet it seems to act as a deactivating substituent in the present reaction. It must be remembered, however, that



(III.) (IV.) (V.)

methoxy- and acetoxy-groups have inductive and tautomeric effects which are opposite in sign, so that it is impossible to estimate, with any degree of certainty, the net effect on a reaction rate. It is known, however, that the $+T$ effect of the methoxy-group is almost wholly a polarisability effect (Bunton, Minkoff, and Reed, *J.*, 1947, 1416), and in almost all the known cases this $+T$ effect easily predominates over the $-I$ effect. The explanation for the present results may well be that in anthracene derivatives, *meso*-methoxy- and *meso*-acetoxy-groups cannot be coplanar with the ring system (Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2127; Spruit, *Rec. Trav. chim.*, 1949, **68**, 325). Moreover, in benzanthracene derivatives the interference with the " benz " ring is very considerable indeed. In these circumstances it is not surprising that these groups do not exert the same activating effects as in simple benzene derivatives.

On the other hand, 9 : 10-diphenyl-1 : 2-benzanthracene (III) must also be non-coplanar,

and the phenyl groups cannot be conjugated with the ring system to any marked extent. Nevertheless, *meso*-phenyl groups do increase the rate of addition of osmium tetroxide. In this connection it was thought of interest to examine the rate of addition of osmium tetroxide to 5-phenyl-1 : 2-3 : 4-dibenzpyrene (V). This compound is theoretically derived from 9 : 10-diphenyl-1 : 2-benzanthracene (III) by the loss of two hydrogen atoms. It must be admitted, however, that this conversion could not be brought about directly by heating with dehydrogenating agents. Clar's method (*Ber.*, 1930, **63**, 119), involving the isomerisation of (III) to (IV) with aluminium chloride, followed by dehydrogenation, was found to give excellent results. In 5-phenyl-1 : 2-3 : 4-dibenzpyrene, only one phenyl group is non-coplanar, and the conversion of (III) into (V) was found to cause a profound redistribution of the π electrons, for (V) reacted so slowly with osmium tetroxide that its rate could not be accurately measured by the present procedure.

It is of some interest to compare the present results with those of similar experiments on the addition of maleic anhydride, and the photo-addition of oxygen, to the *meso*-positions of anthracene derivatives. Bachmann and Kloetzel (*J. Amer. Chem. Soc.*, 1938, **60**, 481), for example, found that whilst *meso*-methyl and -ethyl groups increased the rate of addition of maleic anhydride, *meso*-phenyl groups had a retarding influence. On the other hand, Dufraisse and Bras (*Compt. rend.*, 1943, **216**, 60) found that *meso*-phenyl groups increased the rate of photo-oxidation of anthracene derivatives. *meso*-Acetoxy-groups were found to retard the addition, as was the case with the usual deactivating groups such as cyano-, carbethoxy-, and carbamyl (Dufraisse and Mathieu, *Bull. Soc. chim.*, 1947, 307). It is also noteworthy that 9 : 10-dimethoxyanthracene was the most easily photo-oxidised compound studied by Dufraisse and Priou (*Bull. Soc. chim.*, 1939, **6**, 1649).

For the preparation of 9-methoxy-1 : 2-benzanthracene, *o*-2-naphthoylbenzoic acid was prepared from 2-bromonaphthalene by Weizmann, Bergmann, and Bergmann's method (*J.*, 1935, 1367). Reduction with activated zinc dust and dilute sodium hydroxide gave *o*-2-naphthylmethylbenzoic acid, which was cyclised by zinc chloride and acetic anhydride to **9-*acetoxy*-1 : 2-*benzanthracene*** (compare Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1937, **59**, 1028). The same acetoxybenzanthracene was also obtained, with some difficulty, by acetylation of crude 1 : 2-benz-9-anthrone prepared by reduction of 1 : 2-benzanthraquinone with aluminium powder in sulphuric acid (Cook, *J.*, 1930, 1094). The desired 9-methoxy-derivative was obtained from acetoxybenzanthracene by cleavage with *n*-butylmagnesium bromide, followed by methylation with methyl sulphate (compare Fieser and Hershberg, *loc. cit.*).

9 : 10-*Diacetoxy*-1 : 2-*benzanthracene* was obtained by reductive acetylation of 1 : 2-benzanthraquinone with zinc dust and acetic anhydride, and 9 : 10-dimethoxy-1 : 2-benzanthracene by reductive methylation (Berenblum and Schoental, *Cancer Res.*, 1943, **3**, 686).

Experimental.

o-2-*Naphthylmethylbenzoic Acid.*—*o*-2-Naphthoylbenzoic acid (10 g.) (Weizmann, Bergmann, and Bergmann, *loc. cit.*) was added to a suspension of zinc dust (15 g.) (which had been activated by contact with a 3% solution of copper sulphate for 5 minutes) and 2N-sodium hydroxide solution (225 c.c.), and the resulting mixture was heated on the water-bath for 18 hours. *o*-2-Naphthylmethylbenzoic acid (4·2 g.) formed colourless crystals, m. p. 135°, from toluene. Barnett and Campbell (*J.*, 1935, 1031) give m. p. 135°.

9-*Acetoxy*-1 : 2-*benzanthracene.*—(*a*) A solution of the naphthylmethylbenzoic acid (5 g.) and zinc chloride (0·4 g.) in glacial acetic acid (30 c.c.) and acetic anhydride (20 c.c.) was boiled under reflux for 1½ hours. The solution was diluted with a large volume of water, and the resulting precipitate dissolved in benzene. After extraction of the benzene solution with dilute sodium carbonate solution, and then water, the solvent was removed. 9-*Acetoxy*-1 : 2-*benzanthracene* (2·2 g.) formed almost colourless micro-prisms, m. p. 141—142°, from alcohol (Found : C, 83·9; H, 5·0. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%).

(*b*) The same product was obtained, in poor yield, when crude 1 : 2-benz-9-anthrone (Cook, *loc. cit.*) was boiled for 1 hour with acetic anhydride and sodium acetate.

9-*Methoxy*-1 : 2-*benzanthracene.*—9-Acetoxy-1 : 2-benzanthracene (2 g.) was added to a solution of *n*-butylmagnesium bromide (from 3·84 c.c. of *n*-butyl bromide) in anhydrous ether, and the mixture refluxed for 1 hour. Methyl sulphate (14·2 g.) in dry toluene (50 c.c.) was then added, and the mixture heated on the steam-bath, for 4 hours, allowing the ether to distil. Water was added, and the product was heated with stirring for a further hour to decompose the excess of reagent. The washed toluene layer was diluted with benzene, dried, and passed through a column of alumina to remove unchanged anthranol. Crystallisation of the residue from light petroleum gave 9-*methoxy*-1 : 2-*benzanthracene* (0·4 g.) as colourless plates, m. p. 104° (Found : C, 88·5; H, 5·6. $C_{19}H_{14}O$ requires C, 88·3; H, 5·4%). The *picrate* formed dark red-brown elongated prisms, m. p. 117—118°, from alcohol (Found : C, 61·6; H, 3·7. $C_{19}H_{14}O,C_6H_3O_7N_3$ requires C, 61·6; H, 3·5%).

9 : 10-*Diacetoxy*-1 : 2-*benzanthracene.*—A mixture of 1 : 2-benzanthraquinone (5 g.), zinc dust (20 g.), and acetic anhydride (50 c.c.) was boiled under reflux for 1 hour. After being poured into water, the

product was left to separate. Next morning, the solid was collected and extracted with alcohol and then benzene, the mixed solvent evaporated, and the product recrystallised from benzene. 9 : 10-*Diacetoxy*-1 : 2-*benzanthracene* (4·1 g.) formed colourless needles, m. p. 217—218° (Found : C, 76·85; H, 4·5. $C_{22}H_{16}O_4$ requires C, 76·7; H, 4·7%).

9 : 10-*Dimethoxy*-1 : 2-*benzanthracene*.—A mixture of benzanthraquinone (7 g.), zinc dust (28 g.), and dilute sodium hydroxide solution was treated alternately with small portions of methyl sulphate and sodium hydroxide solution, at 100°, until the colour of the vat was completely discharged. The product (extracted from the zinc dust with alcohol) formed small colourless prisms, m. p. 136—137° (Found : C, 83·4; H, 5·5. Calc. for $C_{20}H_{16}O_2$: C, 83·3; H, 5·6%). Berenblum and Schoental (*loc. cit.*) give m. p. 137—138°. Hydrolysis of its complex with osmium tetroxide (cf. Cook and Schoental, *loc. cit.*) gave 3 : 4-*dihydroxy*-9 : 10-*dimethoxy*-3 : 4-*dihydro*-1 : 2-*benzanthracene* as colourless needles, m. p. 184—186° (decomp.) (Found : C, 74·5; H, 5·6. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6%).

Reaction Rates.—The rates of reaction were determined by the method described previously (Badger, *loc. cit.*).

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