Electrophilic Aromatic Reactivity. Part 27.[1] Protiodetritiation of Chrysene

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All six monotritium-labelled chrysenes have been prepared, and their rates of protiodetritiation measured at 70°, using a mixture of trifluoroacetic acid–chloroform (9 : 1 v/v) as the exchanging medium. These lead to the following partial rate factors (positions in parentheses): 975 (1); 186 (2); 307 (3); 696 (4): 2 790 (5); 12 200 (6) and the corresponding σ^+ values are −0.342; −0.259; −0.284; −0.325; −0.394; −0.467. Hückel localization energies predict a positional reactivity order, *viz.* 6 > 1 > 4 > 5 > 3 > 2 and reactivities relative to phenanthrene) close to that observed, only the 5-position being anomalous. Thus as in the case of helicenes, these calculations tend to underestimate the reactivity of the most central position in the molecule, though for chrysene, no localization of electrons at that point through ring distortion can be held responsible. Annelation rules, derived from hydrogen exchange data for other polycyclics, predict that the partial rate factor for the 5-position should be close to that observed. Reactivities in the terminal ring are only half that of the structural isomer benzo[*c*]phenanthrene (tetrahelicene) which further supports the view that distortion in the latter raises the reactivity through destabilization of the ground state. The relative reactivities of the unhindered positions in naphthalene, phenanthrene, and chrysene in acetylation are the inverse of that predicted by hydrogen exchange, and a possible reason for this is considered.

In this series the hydrogen exchange reaction has been used to determine, quantitatively, the electrophilic reactivities, free from steric effects of a range of aromatics (especially polycyclics); this has permitted meaningful evaluation of the theoretical predictions of reactivity, and thus far we have found that simple Hückel calculations are the best indices of reactivity. The reactivity of chrysene is of interest because it is a structural isomer of benzo[*c*]phenanthrene, but differs from it in being virtually planar,[2] so that a comparison of the reactivities of the two molecules should yield further information concerning the effect of distortion upon the reactivity of the former.[3,4] It is also of importance because, like pyrene, its skeleton is present in all the polycyclic aromatics which are highly carcinogenic, *e.g.* benzo[*a*]pyrene. Knowledge of the fundamental electrophilic reactivity of these molecules may lead to a better understanding of the factors which produce carcinogenesis.

To date the only complete study of the reactivity of chrysene has been in acetylation,[5] but here the very considerable steric hindrance to the reaction obscures the electronic contribution to aromatic reactivity, so that under some conditions the positions calculated to be least activated towards substitution, become the most readily acetylated. There have been previous studies, none of them complete, of hydrogen exchange in chrysene. One study, using deuteriation in a complex acid mixture, showed one position, assumed to be 6,† to be much more reactive than a second group of positions, assumed to be 1, 4 and 5,† these latter being equally reactive.[6] However none of the partial rate factors given in ref. 6 for other molecules have ever been reproduced by ourselves[7,8] or others,[9] so that a thorough investigation of chrysene seemed appropriate. The reactivity of the 6-position has previously been determined by Streitwieser *et al.*[9] who obtained a partial rate factor at 70° of *ca.* 11 500 in a mixture of carbon tetrachloride and trifluoroacetic acid; this is close to the value obtained in the present work.

† A non-systematic numbering system was used in the original paper.

RESULTS AND DISCUSSION

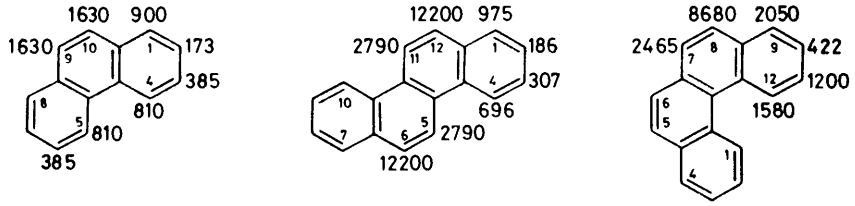
Since chrysene is very insoluble in trifluoroacetic acid (TFA), it proved advantageous to use a co-solvent. Previously one of us found that chloroform is much better than carbon tetrachloride for this purpose and does not interfere with the kinetics in any way except to reduce the exchange rate,[10] and by a factor which we have predetermined using [9-^{3}H]phenanthrene as a standard. For the present work a mixture of chloroform and trifluoroacetic acid (1 : 9 v/v) was used. Good first-order kinetics were obtained for each specifically-labelled isomer and the average values are given in the Table along with that obtained for [9-^{3}H]phenanthrene under the same condition. The partial rate factors under the standard condition (anhydrous TFA at 70 °C) were determined by multiplying the partial rate factor

Rate coefficients for detritiation of [*X*-^{3}H]Ar in $CHCl_3$–TFA (1 : 9 v/v) at 70 °C, the derived partial rate factors, σ^+ values, and Hückel localization energies

Ar	*X*	10^7k/ s^{-1}	*f*	σ^+	L_r^+/ $-\beta$
Phenanthrene	9	98.3	1 630 [a]		2.299
Chrysene	1	58.8	975	−0.342	2.302
Chrysene	2	11.2	186	−0.259	2.492
Chrysene	3	18.5	307	−0.284	2.448
Chrysene	4	42.0	696	−0.325	2.349
Chrysene	5	168	2 790	−0.394	2.351
Chrysene	6	736	12 200	−0.467	2.254

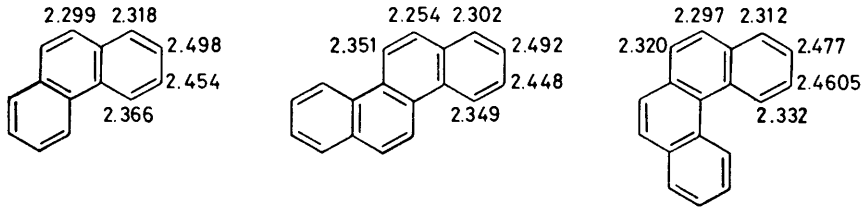
[a] Determined in TFA at 70 °C; the other values in this column are calculated from this (see text).

for the 9-position of phenanthrene under the standard condition by the relative rate coefficients in the TFA–chloroform mixture. This avoided problems arising from the fact that the ρ factor for exchange in the latter medium is not known. The partial rate factors (and the derived σ^+ values) are given in the Table, and are displayed in the Scheme 1 along with those for the related phenanthrene [11] and benzo[*c*]phenanthrene.[3] The main features of these results are as follows.



SCHEME 1 Partial rate factors for protiodetritiation

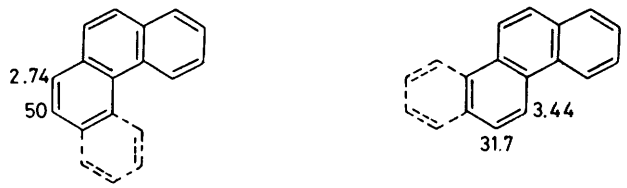
(i) Whereas the reactivities of the corresponding positions of the terminal rings in phenanthrene and chrysene are closely similar, those in benzo[*c*]phenanthrene are approximately twice as great. By contrast, localization energies (calculated by the simple Hückel method, and given in Scheme 2) predict that these corresponding positions in all three molecules should have the same reactivity. This further supports the view that non-planarity increases the reactivity of benzo[*c*]-phenanthrene through loss of ground-state aromaticity.[4]



SCHEME 2 Localization energies/$-\beta$ for electrophilic substitution

(ii) The positional reactivity order in chrysene is $6 > 5 > 1 > 4 > 3 > 2$ whereas localization energies predict $6 > 1 > 5 \simeq 4 > 3 > 2$. The agreement is thus very good except that the position nearest the centre of the molecule is rather more reactive than predicted. One of us observed a similar effect in detritiation of tetra-,[4] penta-,[4] and hexa-helicene [10] and tentatively suggested for these latter molecules [4] that this might be the position where overlap of adjacent *p*-orbitals is poorest, through strain. However, there is little strain in chrysene, so the anomaly may be the manifestation of a more fundamental deficiency of the Hückel calculations.

(iii) This inadequacy of the calculations is confirmed by analysis of the annelation effects produced by a benzo-substituent. Previously, one of us showed that the greater activating effect of a α- *versus* a β-benzo-substituent evident in the reactivity of naphthalene *versus* benzene,[4] is carried through to the helicenes. (Further evidence for this will be published in due course.) In all cases to date both positions are activating with the average $\alpha : \beta$ activation ratio of between 8 and 18. Scheme 3 shows the annelation effects of the benzo-substituents at the positions shown (calculated by dividing the partial rate factors for corresponding positions given in Scheme 1). The ratio of the α- and β-effects is nine-fold and consistent with previous observations. On the other hand, for the calculations to be correct the reactivity of the 5-position would have to be less than that of the 4-position and since the 5-position of chrysene *is* the 4-position of phenanthrene which has been annelated by a β-benzo-substituent, then it follows that this annelation would have to produce *deactivation* which would be difficult to explain.

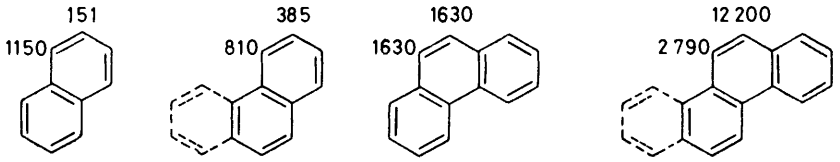


SCHEME 3 Annelation effects products by an adjacent benzo-substituent

(iv) Two other annelation effects may be compared and these are evident in Scheme 4. They operate here through an intervening ring and one (which we denote as a 1,2-benzo-7-interaction since it operates across a naphthalene ring) is consistent in both systems, the annelation producing a substantial increase in reactivity. The other effect (1,2-benzo-8-interaction) is not consistent in both systems, but the reactivity changes produced are relatively small.

(v) Comparison of the hydrogen exchange data with those for acetylation [5] shows good agreement after allowance is made for steric hindrance to the latter reaction. The significant points are as follows. (a) Steric hindrance causes the reactivities of the 1- and 4-

positions to be *less* than those of the 2- and 3-positions in acetylation under all conditions. However, the orders 3 > 2 (equally hindered positions) and 1 > 4 were always obtained as required by our data for those pairs of positions. (b) The 4- and 5-positions are equally hindered so that a substantial 5 : 4-product ratio (38 or greater) was obtained, consistent with the substantial reactivity ratio found in the present work. (c) The 6-isomer was substantially the main product, except under conditions of the severest steric hindrance (when 70% or more of the products consisted of the 2- and 3-isomers). (d)



SCHEME 4 Partial rate factors for protiodetritiation

The hydrogen exchange data predict an overall reactivity order in acetylation of chrysene > phenanthrene > naphthalene as observed. However for unhindered positions the reverse is true and a possible reason lies in the differing demands for resonance between acetylation and hydrogen exchange.

We have reached the stage where the partial rate factors for hydrogen exchange of a wide range of polycyclic molecules and at all positions are now accurately known, *i.e.* for naphthalene,[12] phenanthrene,[11] anthracene,[8] biphenylene,[13] triphenylene,[8] chrysene, pyrene,[6] fluoranthene,[14] coronene,[8] and the helicenes.[3,4,10] With these data it should be possible to refine existing methods of calculating aromatic reactivity and in so doing, be able to determine bond orders on polycyclics with greater precision. This is of importance in studies of carcinogenesis, since it seems very probable that highly localized bonds are the key reactive sites which produce carcinogenic activity in aromatic compounds.

EXPERIMENTAL

Each specifically labelled chrysene was prepared from the bromo-precursor by hydrolysis of the lithium derivative with tritiated water, and purification of the product by column chromatography or recrystallisation. The bromo compounds were prepared as follows.

1-Bromochrysene.— 3-(2-Bromophenyl)-1-(1-naphthyl)-propenoic acid, m.p. 190—191° (lit.,[15] 182—184°) was prepared in 31% yield by the method of Fieser and Joshel,[16] $\nu_{max.}$ (KBr) 1 623 (C=C), 1 682 (C=O), and 3 045 (OH) cm^{-1}, δ ($CDCl_3$) 7.27—7.88 (ArH), 8.43 (s, CH), and 11.62 (s, CO_2H, exchangeable with D_2O). The acid was decarboxylated by the literature method [15] to give after column chromatography (Type H; elution with benzene) 1-(2-bromophenyl)-2-(1-naphthyl)ethylene, m.p. 74—75° (lit.,[15] 74—75°), $\nu_{max.}$ (KBr) 1 588 cm^{-1} (C=C), δ ($CDCl_3$) 6.80—7.86 (m, ArH, olefinic H) and 8.1—8.3 (*peri*-ArH). This compound with identical properties was also prepared in 77% yield by a Wittig reaction between 2-bromobenzaldehyde and 1-naphthylmethyl(triphenyl)phosphonium chloride.

Photocyclization of the above alkene (0.3 g, 1.1 mmol) in redistilled cyclohexane (11) using iodine as a catalyst in the general manner previously described [17] gave after column chromatography (benzene as eluant) and thrice recrystallisation from benzene, *1-bromochrysene* (0.26 g, 74%), m.p. 240—241° (Found: C, 70.1; H, 3.95; Br, 26.0. $C_{18}H_{11}Br$ requires C, 70.4; H, 3.6; Br, 26.0%), δ ($CDCl_3$) 7.26—8.10 (m, ArH), 8.26 (d, *J* 8.1 Hz, 12-H), and 8.55—8.93 (m, 4-, 5-, 10-, and 11-H).

2- and 4-Bromochrysene.—*1-(2-Bromophenyl)-2-(1-naphthyl)ethylene* was prepared by a Wittig reaction between *m*-bromobenzaldehyde and 1-naphthyl(triphenyl)-phosphonium chloride. and was obtained in 37% yield, m.p (after column chromatography and recrystallisation from methanol) 77—78° (Found: C, 69.9; H, 4.35; Br, 25.8. $C_{18}H_{13}Br$ requires C, 69.9; H, 4.25; Br, 25.8%), $\nu_{max.}$ (KBr) 1 590 cm^{-1} (C=C) δ ($CDCl_3$) 6.87 (d, *J* 16.2 Hz, 2-H), 7.14 (d, *J* 16.2 Hz, 1-H), 7.27—7.93 (m, ArH), and 8.21 (m, *peri*-ArH).

Photocyclization of this alkene as described above gave after column chromatography, a mixture of 2- and 4-bromochrysenes in *ca.* 4 : 1 ratio, as indicated by g.l.c. analysis. The lower yield of the 4-isomer reflects steric hindrance to bond formation adjacent to the bromine atom, rather than to an electronic effect since a similar effect was produced by a methyl substituent in formation of 2- and 4-methylphenanthrenes from the corresponding alkenes.[17] Crystallisation from chloroform gave silvery plates of *2-bromochrysene* (42%), m.p. 261—262° (Found: C, 70.4; H, 3.95; Br, 25.8%), δ ($CDCl_3$) 7.25—7.95 (m, ArH), 8.08 (d, *J* 2.0 Hz, 1-H), and 8.56—8.70 (m, 4-, 5-, 10-, and 11-H).

Resolution of the mixture of 2- and 4-isomers was effected by h.p.l.c. using aqueous dioxan as eluant giving 4-bromochrysene as an oil which could not be crystallized. G.l.c. analysis of this oil indicated it to be >98% pure.

3-Bromochrysene.—A Wittig reaction between 1-naphthylmethyl(triphenyl)phosphonium chloride and *p*-bromobenzaldehyde gave, after column chromatography, pale yellow plates of *1-(4-bromophenyl)-2-(1-naphthyl)ethylene* (44%), m.p. 102—103° (Found: C, 70.2; H, 4.44; Br, 25.4%), $\nu_{max.}$ (KBr) 1 588 cm^{-1} (C=C), δ ($CDCl_3$) 7.11 (d, *J* 16.5 Hz, 1-H), and 7.33—8.36 (m, ArH).

Photocyclization of this alkene as described above gave, after crystallization from acetone, 3-bromochrysene (89%), m.p. 182.5—183° (lit.,[18] 195—196°) (Found: C, 70.4; H, 3.75; Br, 25.7%), δ ($CDCl_3$) 7.65—8.10 (m, ArH), 8.60—8.80 (m, 5-, 10-, and 11-H), and 8.92 (d, *J* 1.9 Hz, 4-H).

5-Bromochrysene.—This was prepared by the method of Newman *et al.*[19] (in which 4-bromophenanthrene was obtained from the corresponding carboxylic acid). A mixture of chrysene-5-carboxylic acid (0.30 g, 1.1 mmol) and mercury(II) acetate (0.35 g) in *N*-methylpyrrolidone

(5 ml) was heated at 100° during 6 h. The resulting yellow solution was cooled to 50°, and bromine (0.35 g) in *N*-methylpyrrolidone (5 ml) was added. The cooled dark mixture was diluted with water (75 ml), shaken with chloroform, and the extract washed with water and dried (Na_2SO_4). Removal of the solvent gave a light brown solid, purified by t.l.c. (1 mm thick silica gel, benzene eluant) to give, after recrystallisation from ethanol, fine needles of 5-*bromochrysene* (41%), m.p. 98° (Found: C, 70.5; H, 3.85; Br, 25.9%), δ ($CDCl_3$) 7.58—8.23 (m, ArH), 8.50 (s, 6-H), 8.65 (d, *J* 9.5 Hz, 11-H), 8.67 (m, 10-H), and 9.95 (m, 4-H).

6-*Bromochrysene*.—Direct bromination of chrysene according to the literature [20] method gave 6-bromochrysene, m.p. 154—155° (lit.,[20] 153.6—155°) after recrystallization from benzene, δ ($CDCl_3$) 7.71—8.47 (m, ArH), 8.77—9.10 (m, 4-, 10-, and 11-H), and 9.20 (s, 5-H).

Exchange-rate Measurements.—The general procedure has been described previously,[13,21] and was modified in the present work in that a mixture of AnalaR chloroform and purified trifluoroacetic acid (1:9 v/v) was used as the exchanging medium. Very good first-order kinetics were obtained for each isomer indicating them to be specifically labelled. Rate coefficients for each isomer could be duplicated to better than ±1%.

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