927. *Aromatic Reactivity. Part XXIX.*[1] *Diphenylmethane and Fluorene in Detritiation.*

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Rates of detritiation have been measured for 2-, 3-, and 4-tritiodiphenylmethane, and 1-, 3-, and 4-tritiofluorene in anhydrous trifluoroacetic acid at 70·0°. The results are discussed, and compared with those for other electrophilic aromatic substitutions.

The reactivity of the 2-position of fluorene has been measured in several electrophilic aromatic substitutions,[2-9] but only for nitration in acetic anhydride at 25° are partial

[1] Part XXVIII, Bott, Eaborn, and Greasley, preceding Paper.
[2] Brown and Stock, *J. Amer. Chem. Soc.*, 1962, **84**, 1238; Zimmerman and Berliner, *ibid.*, p. 3953.
[3] Brown and Marino, *J. Amer. Chem. Soc.*, 1962, **84**, 1236.
[4] de la Mare, Hall, Harris, and Hassan, *Chem. and Ind.*, 1958, 1086.
[5] Beaven, de la Mare, Johnson, and Klassen, *J.*, 1962, 988.
[6] Dewar and Urch, *J.*, 1958, 3079.
[7] Brown, Dubeck, and Goldman, *J. Amer. Chem. Soc.*, 1962, **84**, 1229.
[8] Baker, Eaborn, and Sperry, *J.*, 1962, 2382.
[9] Stock and Brown, *Adv. Phys. Org. Chem.*, 1963, **1**, 35.

rate factors available for the less reactive positions.[6]   We have determined the reactivities of the 1-, **3**-, and 4-positions in hydrogen-exchange by measuring the rates of detritiation of 1-, **3**-, and 4-tritiofluorene in anhydrous trifluoroacetic acid at 70·0°.   For comparison we have also measured the rates of detritiation of 3-tritiotoluene and of 2-, 3-, and 4-tritiodiphenylmethane under the same conditions.   The rate factors, f (the rates of detritiation relative to that of tritiobenzene) are shown in the Chart, along with those previously obtained for the 2-position of fluorene,[8] the 2- and 4-positions toluene,[10] and for biphenyl.[11]   Partial rate factors for nitration [6,12-15] of these compounds in acetic anhydride (at 0° for biphenyl, at 30° for toluene, and at 25° for the others), are also shown.
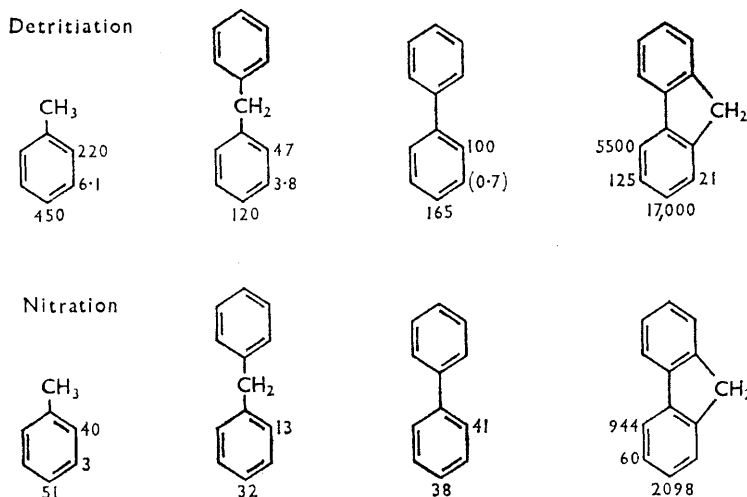

CHART.

In detritiation, the reactivities of the 2- and 4-position of diphenylmethane are about four times smaller than those of the corresponding positions of toluene, while the reactivity of the 3-position is some 1·6 times less than that of the 3-position in toluene.   In free energy terms, however, the change from the methyl to the phenylmethyl substituent has only an insignificantly smaller effect on the 3- than on the 4-position;   thus $(\log f_4{}^{PhCH_2})/(\log f_4{}^{Me}) = 0.78$ and $(\log f_3{}^{PhCH_2})/(\log f_3{}^{Me}) = 0.74$.   The lower reactivity of diphenylmethane than of toluene, which is apparent also in nitration, results from the electron-withdrawing effect of the phenyl group.[13]   It is noteworthy that the value of the ratio $(\log f_2{}^{PhCH_2})/(\log f_4{}^{PhCH_2})$ in nitration (0·74) is smaller than that in detritiation (0·81), possibly partly because of some steric hindrance to *ortho*-substitution in the former reaction (but see ref. 10).

Closure of the five-membered ring on going from diphenylmethane to fluorene leads to a large increase in reactivity at positions *meta*- to the methylene group, because of the considerable conjugation between the rings in fluorene.[4,13,15]   The value of the ratio $(\log f_4{}^{Fl})/(\log f_2{}^{Fl})$ in detritiation (0·88) is virtually identical with that [11] of the ratio $(\log f_o{}^{Ph})/(\log f_p{}^{Ph})$ (0·90) in biphenyl, as might be expected for a reaction in which primary steric hindrance seems [10] to be negligible.*   The ratio $(\log f_4{}^{Fl})/(\log f_2{}^{Fl})$ has the same

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* The symbol $f_x{}^{Fl}$ denotes the partial rate factor for the x-position of fluorene.

[10] Baker, Eaborn, and Taylor, *J.*, 1961, 4927.
[11] Baker, Bott, and Eaborn, *J.*, 1963, 2136.
[12] de la Mare and Ridd, " Aromatic Substitution.   Nitration and Halogenation," Butterworths, London, 1959, p. 88.
[13] Ref. 12, pp. 157—160.
[14] Simamura and Mizuno, *Bull. Chem. Soc. Japan*, 1957, **30**, 196; cf. Billing and Norman, *J.*, 1961, 3885.
[15] Stock and Brown, *J. Amer. Chem. Soc.*, 1962, **84**, 1242.

value in nitration as in detritiation, suggesting that steric effects are absent or small for nitration at the 4-position of fluorene; for nitration of biphenyl in acetic anhydride at 0°, the value of the corresponding ratio $(\log f_o{}^{\text{Ph}})/(\log f_p{}^{\text{Ph}})$ (*viz.*, 1·02),[14] is larger, which is consistent with the suggestion that there may be steric assistance to reaction at the *ortho*-position.[16] *

The reactivity of the 1-position of fluorene is only about half of that of the 2-position of diphenylmethane, and this can be ascribed to the deactivating effect of a *meta*-phenyl substituent. (The deactivation is about 1·5-fold in detritiation of [3-³H]biphenyl at 25° by trifluoroacetic acid containing aqueous perchloric acid.[17]) However, the 3-position of fluorene, which is also *meta* to the phenyl group, is slightly more reactive than the 4-position of diphenylmethane, and it is not clear why this should be so. In nitration, the reactivity of the 3-position of fluorene is almost twice as great as that of the 4-position of diphenylmethane,[6] which, in view of the smaller general spread of rates in nitration, is not in accord with our results.

From the detritiation results, one could expect to obtain substantial quantities of 4-substituted products from fluorene in reactions of fairly low selectivity, such as mercuration, and nitration; † it is known that 80% of 2-substituted product can be obtained in mercuration in glacial acetic acid,[7] but other products are also formed.‡ In molecular chlorination in acetic acid, 9% of 4-, and not more than 69% of 2-chlorofluorene are formed along with substantial amounts of addition products;[5] it might thus at first sight seem surprising that no 4-product is formed in acetylation in ethylene dichloride catalysed by aluminium chloride, which gives " essentially 100% " of 2-acetylfluorene,[3] since this is a reaction of similar selectivity to molecular chlorination. However, this result is consistent with the formation of no detectable 2-acetyl-product from biphenyl under these conditions, presumably because of a steric factor:[3] that steric hindrance to Friedel–Crafts substitution at the 4-position of fluorene is important accords with the alkylation data of Cairns and Hickinbottom.[18] In molecular bromination in acetic acid, a reaction of very high selectivity,[9] virtually 100% of 2-bromofluorene is formed.[2]

In detritiation, the reactivities of the 1- and 3-positions represent 0·1 and 0·5%, respectively, of the total reactivity. Thus in molecular chlorination for example, a reaction of greater selectivity, amounts of 1- and 3-chlorofluorene would be expected to be undetectably small. In nitration, no formation of 1-nitrofluorene was detected,[6] and surprise about this has been expressed.[13] From the detritiation results, however, it seems likely that in nitration the partial rate factor for the 1-position of fluorene would be smaller than that for the 2-position of diphenylmethane, and probably would not be greater than 10, which means that less than 0·3% of 1-nitrofluorene would be formed.

A combination of knowledge of the partial rate factors of the various positions of fluorene, shown in the Chart, with previously obtained information about the transmission of substituent effects from one ring of fluorene to the other,[23] leads to understanding of the position(s) of further substitution of monosubstituted fluorenes. Thus a strongly or fairly-strongly deactivating group (*e.g.*, CF_3, NO_2, CO_2H, Cl, Br) in one ring will cause

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* This discussion neglects, however, for want of relevant facts, the possibility that the relation between $(\log f_o)/(\log f_p)$ and the electron demand may be a factor (cf. refs. 10 and 11).

† From nitration in acetic anhydride, 24% of 4-nitrofluorene can be isolated. This provides a useful route to 4-substituted fluorenes.[19]

‡ Mercuration in acetic acid had previously been said to give the 4-product [20] (but see refs. 21 and 22).

[16] de la Mare and Hassan, *J.*, 1957, 3004.
[17] Eaborn and Taylor, *J.*, 1961, 1012.
[18] Cairns and Hickinbottom, *J.*, 1962, 867.
[19] T. S. Sorensen, personal communication.
[20] Miller and Bachman, *J. Amer. Chem. Soc.*, 1935, **57**, 2447.
[21] Huntress, Pfister, and Pfister, *J. Amer. Chem. Soc.*, 1942, **64**, 2845.
[22] Weisburger, Weisburger, and Ray, *J. Org. Chem.*, 1951, **16**, 1697.
[23] Baker, Bott, Eaborn, and Greasley, *J.*, 1964, 627.

further substitution to take place in the other ring.* For example, a 2-nitro-group will very strongly deactivate 1-, 3-, and 4-positions, and will deactivate the 5- and 7-positions by much smaller, though still large, amounts. (The 2-nitro-group deactivates the 7-position by about 2500 times in detritiation.[23]) Since the 5- and 7-position will be affected to much the same extent, substitution at these positions would be expected in a ratio somewhat similar to that in which 4- and 2-substitution occurs in the same reaction with fluorene; in agreement, some 60% of 2,7- and 22% of 2,5-dinitrofluorene were isolated from nitration of 2-nitrofluorene.[24] A similar ratio of 5- and 7-product (these being predominant) would be expected also in nitration of 1-, 3-, and 4-nitrofluorene (provided no unusual steric effect operates in the last case).

Strongly electron-releasing groups, such as amino and hydroxyl, in the 2-position will have little effect on the 4-position, but will activate the 1- and 3-positions by a large factor and the 5- and 7-positions by a much smaller factor, so that the inherently large reactivity of the 7-position will be more than compensated. Substitution should thus occur at the 3- and 1-position, in much the same ratio as it occurs at these positions in the same reaction with fluorene itself. In other words, along with a large amount of 3-substitution a detectable amount of 1-substitution might also be expected unless the reaction is of very high selectivity.†

In reactions of 1-amino- or 1-hydroxy-fluorene, further substitution would be expected to occur predominantly at the 4-position (unless there is a special tendency to *ortho*-substitution, as is sometimes the case with substituents of this general type in nitration under some conditions). In reactions of 3-amino- and 3-hydroxy-fluorene, 4- and 2-substitution would be expected (special steric effects being absent) in much the same ratio as in the same reaction of fluorene.†

In nitration of 1-methylfluorene, substitution should occur mainly at the 2-, but also to a substantial extent at the 4-position. Nitration of 3-methylfluorene should give 2- and 4-product in roughly a 2 : 1 ratio (unless there is special steric hindrance to 4-substitution). In both cases, very little substitution would take place in the other ring.

With 2-methylfluorene, the picture is a little more complex. If in detritiation the 2-methyl group activates the 3- and 4-positions to the same extent as the methyl group in toluene activates the *ortho*- and *meta*-positions, respectively, the partial rate factors will be about 28,000 and 33,000. The factor for the 7-position of 2-methylfluorene is known[23] to be about 64,000, so we would expect hydrogen-exchange to occur about twice as often at the 7- as at the 3- and at the 4-position. In nitration, by similar reasoning, factors of about 2400 and 2800 would be expected for the 3- and 4-positions, and one for the 7-position little greater than in fluorene itself, *viz.*, 2100, so that similar amounts of 3-, 4-, and 7-substitution would be expected.

EXPERIMENTAL

[2-³H]*Diphenylmethane.*—The Grignard reagent from *o*-bromochlorobenzene (19·1 g.) in ether[25] was treated with tritiated water (1·8 ml., 180 mc) and then with excess of water (cf. ref. 26). The usual working-up and fractionation gave [2-³H]chlorobenzene (5·2 g., 46%), b. p. 132°.

The tritiated chlorobenzene, diluted with inactive chlorobenzene (total 11·3 g.), was converted into a Grignard reagent in tetrahydrofuran, and treated with benzaldehyde to give [2-³H]diphenylmethanol (4·6 g., 25%), b. p. 185—186°/23 mm. The carbinol (1·2 g.) was reduced with lithium aluminium hydride–aluminium chloride[27] in ether, to give material which

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* We assume that reactions of normal selectivity are involved, such as halogenation or nitration by commonly used reagents.

† Summaries of previous experimental work relevant to these conclusions have been removed at the suggestion of referees, but can be obtained from the authors.

[24] Anantakrishman and Hughes, *J.*, 1935, 1607.
[25] Wittig and Pohmer, *Chem. Ber.*, 1956, **89**, 1334.
[26] Eaborn and Taylor, *J.*, 1960, 3301; 1961, 247.
[27] Nystrom and Berger, *J. Amer. Chem. Soc.*, 1958, **80**, 2896.

was purified, by chromatography of its light petroleum solution on alumina, to give [2-³H]di-phenylmethane (0·56 g., 51%), m. p. 26°, n_D^{25} 1·5754.

[3-³H]*Diphenylmethane.*—A solution of n-butyl-lithium (0·1 mole) in ether (50 ml.) was added with stirring to a refluxing solution of *m*-bromochlorobenzene (19·1 g., 0·1 mole) in ether (50 ml.). The mixture was allowed to cool, then treated with tritiated water (1·8 ml., 180 mc), followed by excess of aqueous hydrochloric acid. The usual working-up and fractionation gave [3-³H]chlorobenzene (6·3 g., 56%), b. p. 132°. This was converted into the [3-³H]diphenyl-methane by the method used for the 2-isomer, but the product was further purified, by zone melting in a vacuum, to give material of m. p. 26°, n_D^{25} 1·5756.

[1-³H]*Fluorene.*—A mixture of 1-bromofluoren-9-one (2·2 g.), m. p. 136·5° (Found: C, 60·1; H, 2·8; Br, 30·8. Calc. for $C_{13}H_7BrO$: C, 60·3; H, 2·7; Br, 30·8%) (made by Huntress, Pfister, and Pfister's method [21]) with 99—100% hydrazine hydrate (7·7 ml.) and diethylene glycol (15 ml.) was kept at 100—110° for 1 hr. then at 170—190° for 5 hr., and was then added to water. The solid which separated was purified by chromatography of its light petroleum solution on alumina to give 1-bromofluorene (1·55 g., 74%), m. p. 67·5° (lit.,[28] 59—60°) (Found: C, 63·7; H, 3·8; Br, 32·6. Calc for $C_{13}H_9Br$: C, 63·7; H, 3·7; Br, 32·6%).

The Grignard reagent from 1-bromofluorene in ether (prepared by the entrainment method, involving use of a molar equivalent of n-propyl bromide) was treated with tritiated water to give tritiated fluorene, which was purified by chromatography on alumina of its light petroleum solution to give tritiated fluorene, m. p. 115·5°. Any tritium which might have entered the 9-position (cf. ref. 8) was removed by refluxing a solution of the solid in 20% ethanolic sodium hydroxide for 18 hr. The solution was added to water, and the precipitated solid was purified by chromatography and vacuum sublimation to give [1-³H]fluorene, m. p. 115·5°.

[3-³H]*Fluorene.*—2-Aminofluoren-9-one [29] was converted into 2-amino-3-bromofluoren-9-one,[30] which was deaminated by diazotization and treatment with hypophosphorous acid to give 3-bromofluoren-9-one, m. p. 161—163° (lit.,[30] m. p. 165·5—166°), and this was reduced with hydrazine (as described for 1-bromofluoren-9-one) to give 3-bromofluorene, m. p. 90—92° (lit.,[20] m. p. 90—91°).

The Grignard reagent was prepared from the 3-bromofluorene in ether by entrainment [31] with ethylene dibromide, and treatment with tritiated water followed by the usual working-up gave tritiated fluorene, which was purified by chromatography and treated with ethanolic alkali as described for the 1-isomer above. Chromatography on alumina, recrystallization from acetic acid and from ethanol, and sublimation *in vacuo* gave [3-³H]fluorene, m. p. 115·5°.

[4-³H]*Fluorene.*—Diphenic acid [32] was treated with sulphuric acid at 140° for 12 min. to give 4-carboxyfluoren-9-one, which was converted into its amide, and this was treated with aqueous potassium hypobromite to give 4-aminofluoren-9-one, m. p. 138—140° (lit.,[21] m. p. 138—139°), which was converted into 4-bromofluoren-9-one, m. p. 124—126° (lit.,[21] 125—126°) by the Sandmeyer method. Clemmensen reduction [20] gave 4-bromofluorene, m. p. 57—58° (lit.,[33] m. p. 60—61°).

In an alternative synthesis, 4-nitrofluorene, m. p. 75—77° (lit.,[34] 75—76°), was obtained in 15% yield by chromatography on alumina of the light petroleum–benzene solution of nitro-fluorenes obtained by treatment of fluorene with nitric acid and acetic anhydride at 30°.[19] The nitro-compound was reduced with calcium chloride, zinc dust, water, and ethanol [34] to give 4-aminofluorene (79%), m. p. 115—117° (lit.,[34] 115—116°), which was converted into 4-bromo-fluorene by Bachmann and Boatner's method.[35] Chromatography on alumina of a light petroleum solution of the product gave 4-bromofluorene (50%), m. p. 59·5—60·5°. A mixed m. p. with the sample obtained from diphenic acid was undepressed.

4-Bromofluorene was converted into [4-³H]fluorene, m. p. 115·5°, as described for the 3-isomer above.

Rate Measurements.—These were carried out as previously described.[26] About 5 mg. of aromatic compound in about 10 g. of the trifluoroacetic acid was used for each run. In the

[28] Suzuki and Kojigaeshi, *Bull. Chem. Soc. Japan*, 1962, **35**, 408.
[29] Arcus and Coombs, *J.*, 1954, 3977.
[30] Fletcher and Hsi-Lung Pan, *J. Amer. Chem. Soc.*, 1956, **78**, 4812.
[31] Pearson, Cowan, and Beckler, *J. Org. Chem.*, 1959, **24**, 504.
[32] Atkinson and Law, *Org. Synth.*, Coll. Vol. I, 2nd edn., 1941, 222.
[33] Grantham, Weisburger, and Weisburger, *J. Org. Chem.*, 1961, **26**, 1008.
[34] Weisburger, Weisburger, and Morris, *J. Amer. Chem. Soc.*, 1952, **74**, 4540.
[35] Bachmann and Boatner, *J. Amer. Chem. Soc.*, 1936, **58**, 2194.

approximate method used to allow for the return of a small quantity of the tritium to the aromatic compound, for [X-^{3}H]diphenylmethanes, [Y-^{3}H]fluorenes and [Z-^{3}H]toluenes, the following number, N, of positions was assumed to be available for tritium at 10 times the half-life of the detritiation:

X	2	3	4	Y	1	3	4	Z	3
N	6	10	3	N	8	6	4	N	5

First-order rate constants, k_1, at 70·0° were as follows:

Position	($X =$)	2	3	4 *	($Y =$)	1	3	4	($Z =$)	3
$10^7 k_1$ (sec.$^{-1}$)		4·5	0·36	11·05		2·03	11·8	520		0·577

* Measured by R. Baker.

In the long runs necessary with the relatively unreactive [1-^{3}H]fluorene, first-order kinetics were observed for only about 55% of the detritiation, an apparent fall-off in rate subsequently occurring, probably because of side reactions. The rate constant for this compound is thus less reliable than for the others, but is probably accurate to within ±5%.

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