Acylarylnitrosamines. Part VII.[1] [^{2}H] Labelling Experiments and the Mechanism of Formation of Benzyne from *N*-Nitrosoacetanilide and Benzenediazonium Acetate

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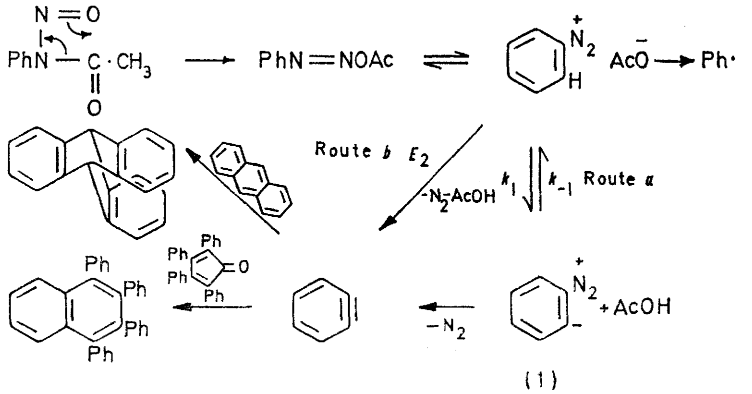
Reaction of *N*-nitroso[2',4',6'-$^2H_3$]acetanilide, formed *in situ* from [2',4',6'-$^2H_3$]acetanilide (99% [$^2H_3$]) and *p*-chlorobenzoyl nitrite, with tetraphenylcyclopentadienone and acetic acid in benzene gave biphenyl, from which no deuterium had been lost, and 1,2,3,4-tetraphenylnaphthalene which had lost one g atom of deuterium. Similar results were obtained from reaction of [2,4,6-$^2H_3$]benzenediazonium fluoroborate (99%[$^2H_3$]) with potassium acetate in benzene. The corresponding reaction using anthracene as a benzyne trap gave similar results. These results exclude the operation of a ' pre-equilibrium ' type of E_1cB mechanism in the formation of benzyne from the benzenediazonium acetate ion pair, but do not allow a distinction to be made between E_1cB (irreversible) or concerted E_2 mechanisms, particularly in view of the low (1·5—1·8) isotope effects observed with [2-^{2}H]benzenediazonium salts.

In previous Parts[2] it was shown that benzyne is formed during the decomposition of *N*-nitrosoacetanilide *via* acetate-induced elimination from the benzenediazonium ion (Scheme 1), and this information has been used to develop a simple one-pot conversion of anilines into the corresponding arynes by *in situ* diazotisation in the presence of a source of acetate ions.[3] There remained, however, the question of the nature of the elimination. This could proceed stepwise *via* a carbanionic E_1cB process (Scheme 1, route *a*) involving either a fully reversible ' pre-equilibrium ' where $k_{-1} \neq 0$, or an irreversible first stage, where $k_{-1} = 0$. Alternatively, reaction could occur *via* a concerted (E_2) elimination (Scheme 1, route *b*) without the intermediacy of the betaine (1). In theory, the choice between these possible mechanisms can be reduced by examining reactions involving deuteriated substrates, and we now report the results of such experiments.



Scheme 1

Thus reaction in benzene of *N*-nitroso[2',4',6'-$^2H_3$]acetanilide (99% [$^2H_3$]), formed by *in situ* reaction of *p*-chlorobenzoyl nitrite with the acetanilide,[3] in the presence of tetraphenylcyclopentadienone (1 mol) acting as a benzyne trap, and acetic acid (2 mol) gave 1,2,3,4-tetraphenylnaphthalene (11%), which had lost only one g atom of deuterium (99% [$^2H_2$]), together with biphenyl (20%), produced *via* the competing radical phenylation of benzene,[2] from which no deuterium had been lost (99% [$^2H_3$]). This result clearly excludes a ' pre-equilibrium ' E_1cB mechanism which would require the loss of more than one g atom of deuterium during benzyne formation on the assumption that the [$^2H_3$]diazonium cation would undergo rapid H–D exchange with acetic acid *via* the betaine (2) (Scheme 2). In the same way, such a mechanism would also lead to the loss of deuterium from biphenyl resulting from radical phenylation of the solvent.

An alternative entry to the benzyne pathway involves reaction of [2,4,6-$^2H_3$]benzenediazonium fluoroborate in the presence of potassium acetate.[2d] Exactly comparable results were obtained using these salts in benzene or 1,2-dichloroethane, in the presence of acetic acid, using both tetraphenylcyclopentadienone and anthracene as benzyne traps. In the last case, for example, the diazonium salt (99% [$^2H_3$]) gave triptycene (5%) (99% [$^2H_2$]) and biphenyl (13%) (99% [$^2H_3$]).

Also in accord with these experiments were the results

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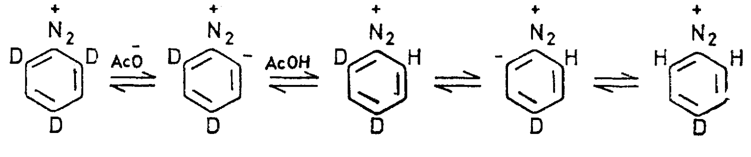
[1] Part VI, J. I. G. Cadogan, J. R. Mitchell, and J. T. Sharp, *J.C.S. Perkin I*, 1972, 1304.

[2] (*a*) D. L. Brydon, J. I. G. Cadogan, D. M. Smith, and J. B. Thomson, *Chem. Comm.*, 1967, 727; (*b*) D. L. Brydon, J. I. G. Cadogan, J. Cook, M. J. P. Harger, and J. T. Sharp, *J. Chem. Soc.* (*B*), 1971, 1996; (*c*) J. I. G. Cadogan, *Accounts Chem. Res.*, 1971, **4**, 186; (*d*) see also C. Ruchardt and C. C. Tan, *Angew. Chem. Internat. Edn.*, 1970, **9**, 522.

[3] B. Baigrie, J. I. G. Cadogan, J. R. Mitchell, A. K. Robertson, and J. T. Sharp, *J.C.S. Perkin I*, 1972, 2563.

of the reverse case involving the reaction of undeuteriated benzenediazonium fluoroborate with potassium acetate and tetraphenylcyclopentadienone in benzene in the presence of acetic [^{2}H]acid. Both the resulting biphenyl (22%) and 1,2,3,4-tetraphenylnaphthalene (6%) contained no deuterium which could be detected by mass spectroscopy. These experiments also show, therefore, that no H–D exchange occurs in the reaction.



(2)

SCHEME 2

In accord with this are the results of experiments involving mono-*ortho*-deuteriated substrates. Thus [2-^{2}H]benzenediazonium fluoroborate (92% [^{2}H]) in the presence of potassium acetate and tetraphenylcyclopentadienone in benzene gave 1,2,3,4-tetraphenylnaphthalene (29%) (55% [^{2}H]) and biphenyl (10%) (92% [^{2}H]). Comparable results were obtained in 1,2-dichloroethane as solvent, while triptycene (58% [^{2}H]) and biphenyl (92% [^{2}H]) were isolated using anthracene as the benzyne trap, in benzene. In the absence of a benzyne trap, biphenyl (36%) (92% [^{2}H]) was obtained. Again, exactly comparable results arose from experiments using [2-^{2}H]benzenediazonium chloride (94% [^{2}H]) in dichloroethane in the presence of acetic acid and anthracene. Additionally, in this case, we isolated 9-phenylanthracene (11%) (94% [^{2}H]). It should be noted that these results are at variance with those of a similar experiment carried out contemporaneously,[4] but now known to be in error,[5] repetition of the work having led to results identical with ours.[5,6]

In these experiments with [2-^{2}H]benzenediazonium salts, slightly more than half the deuterium was retained in the aryne adduct, indicating an isotope effect of 1·5—1·8 (making the assumption, which we have shown to be reasonable, that [^{2}H]benzyne is trapped as efficiently as [^{1}H]benzyne, and that secondary isotope effects approximate to unity). The isotope effects observed are lower than those (2—8) which might be expected for a fully concerted E_2 elimination and the 'irreversible' E_1cB mechanism.[7,8] In summary, therefore, our evidence completely excludes a 'pre-equilibrium' type of E_1cB elimination involving the reversible formation of the betaine (1), which would have given an isotope effect of unity. Our evidence does not permit, of course, a distinction between an E_1cB (irreversible) or a concerted E_2 mechanism which can be distinguished, only if significant isotope effects are observed for cleavage of *both* eliminated groups.[8]

It should be noted that in certain previous cases exhibiting isotope effects <2 a so-called E_1cB (ion-pair mechanism) has been invoked,[9] but it is arguable whether our reaction is analogous because the corresponding entity in question would be the betaine (I)–acetic acid complex and not an ion pair.

EXPERIMENTAL

Preparation of Materials.—Benzene (sodium dried) was freshly distilled from calcium hydride while dichloroethane was distilled from phosphorus pentaoxide. Potassium acetate was fused before use and the acetic acid was dried by repeated freezing, filtering, and warming. *p*-Chlorobenzoyl nitrite was prepared by the method described previously.[3]

Deuteriated materials. (i) [2,4,6-^{2}H$_3$]Aniline hydrochloride was prepared by the repeated reaction of aniline hydrochloride with deuterium oxide in a sealed Pyrex tube, using the method of Best and Wilson,[10] τ (D_2O) 2·50 (2H, s, 3- and 5-H). Standard acetylation gave [2′,4′,6′-^{2}H$_3$]acetanilide, m.p. 114—115°, the mass spectrum showing a deuterium content of 99%, τ ($CDCl_3$) 7·86 (3H, s, Me), 2·72 (2H, s, 3- and 5-H), and 1·72 br (1H, s, NH).

(ii) [2,4,6-^{2}H$_3$]Benzenediazonium fluoroborate, prepared from the corresponding [^{2}H$_3$]aniline by diazotisation in aqueous hydrochloric acid followed by treatment with aqueous sodium fluoroborate, after repeated crystallisations from acetone–ether, had m.p. 96—97° (decomp.; Kofler). The only literature [11] m.p. reported is 119—120°. Since repeated preparations in our laboratory are consistent we conclude that the literature report is in error. Our product on treatment with alkaline β-naphthol gave 1-phenylazo-2-naphthol shown by the mass spectrum to have 99% [^{2}H$_3$].

(iii) [2-^{2}H]Aniline was prepared from 2-bromo-[*NN*-^{2}H$_2$]-aniline [12] after the method of Heaney.[13] Distillation afforded a colourless oil (45%), b.p. 52° at 4 mmHg, τ ($CDCl_3$) 2·6—3·6 (4H, complex, aromatic), and 6·5br (2H, s, NH_2).

(iv) [2-^{2}H]Benzenediazonium fluoroborate, m.p. 96—97° (decomp.), was prepared using a procedure analogous to that for the preparation of the trideuteriodiazonium fluoroborate, and was obtained in 61% yield after recrystallisation (×4) from acetone–ether. A sample of the

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[4] P. C. Buxton and H. Heaney, *J.C.S. Chem. Comm.*, 1973, 545.

[5] P. C. Buxton and H. Heaney, personal communication.

[6] J. I. G. Cadogan, C. D. Murray, and J. T. Sharp, *J.C.S. Chem. Comm.*, 1974, 133.

[7] F. G. Bordwell, *Accounts Chem. Res.*, 1972, **5**, 374.

[8] W. H. Saunders and A. F. Cockerill in 'Mechanisms of Elimination Reactions,' Wiley-Interscience, New York, 1972.

[9] W. K. Kwok, W. G. Lee, and S. I. Miller, *J. Amer. Chem. Soc.*, 1969, **91**, 468.

[10] A. P. Best and C. L. Wilson, *J. Chem. Soc.*, 1946, 239.

[11] A. I. Vogel, 'Practical Organic Chemistry,' Longmans, Green and Co., London, 3rd edn., 1956, p. 610.

[12] R. N. Renaud, D. Kovachic, and L. C. Leitch, *Canad. J. Chem.*, 1961, **39**, 21.

[13] R. Harrison, H. Heaney, J. M. Jablonski, K. G. Mason, and J. M. Sketchley, *J. Chem. Soc.* (*C*), 1969, 1684.

fluoroborate was coupled with an aqueous alkaline solution of β-naphthol and the resulting 1-phenylazo-2-naphthol showed a deuterium content of 92% [^{2}H].

(v) [2-^{2}H]Benzenediazonium chloride was prepared by the method described by Vogel.[11] The salt was recrystallised (×4) from acetone–ether and the crystals were dried over P_2O_5. Owing to the explosive nature of the product, it was used without further characterisation. The deuterium content of the resulting 1-phenylazo-2-naphthol was 94% [^{2}H].

Mass Spectroscopy.—Mass spectra were recorded using an A.E.I. MS-902 double focusing mass spectrometer and a V.G. Micromass 12, single focusing mass spectrometer–gas chromatograph. The deuterium contents of phenyl radical and benzyne derived products were calculated after the method of Biemann[14] the following assumptions being inherent in the technique. (1) The intensity of the isotope peaks at $M + 1$ and $M + 2$ is the same in both standard and labelled compound. (2) There is no '$M + 1$' peak due to ion–molecule collisions. (3) The electron energy does not change from one sample to another. (4) There are no background or other impurities present that contribute to the peaks being measured. While for some of the samples (both standard and labelled) an electron energy of 12 eV was used (at which the molecular-ion peak is still intense enough to be measured accurately while the fragmentation resulting in the loss of one or more hydrogen atoms is negligible), it was found that identical results were obtained from spectra run at 70 eV.

All decomposition reactions described below were carried out under dry nitrogen.

Reaction of p-*Chlorobenzoyl Nitrite with* [2′,4′,6′-^{2}H$_3$]-*Acetanilide in Benzene in the Presence of Acetic Acid and Tetraphenylcyclopentadienone.*—4-Chlorobenzoyl nitrite (0·30 g, 1·6 mmol) (99% [^{2}H$_3$]) in benzene (2 ml) was added dropwise over 10 min to a mixture of [2′,4′,6′-^{2}H$_3$]acetanilide (0·152 g, 1·1 mmol), tetraphenylcyclopentadienone (0·32 g, 1·1 mmol), and acetic acid (0·13 g, 2·2 mmol) in benzene (20 ml) and the mixture was stirred at room temperature for 3 h and subsequently at 50° for 2 h. Work-up using dry column chromatography gave biphenyl (0·032 g, 20%) (99% [^{2}H$_3$]) and tetraphenylnaphthalene (0·055 g, 11%) (99% [^{2}H$_2$]).

Decomposition of Benzenediazonium Fluoroborate in Benzene in the Presence of Tetraphenylcyclopentadienone and Acetic [^{2}H]*Acid.*—To a mixture of tetraphenylcyclopentadienone (0·192 g, 0·5 mmol), potassium acetate (0·098 g, 1 mmol), and acetic [^{2}H]acid (0·06 g, 1 mmol) in benzene (10 ml), benzenediazonium fluoroborate (0·192 g, 1 mmol) was added in three batches with 30 min between each addition. The temperature of the well stirred mixture was maintained at 60° for a further 1 h. The mixture was chromatographed on alumina (30 g) eluting with cyclohexane. Biphenyl (0·034 g, 22%) and tetraphenylnaphthalene (0·023 g, 6%) were obtained and shown to contain no deuterium.

Decomposition of [2,4,6-^{2}H$_3$]*Benzenediazonium Fluoroborate.*—(i) *In the presence of tetraphenylcyclopentadienone.* To a mixture of tetraphenylcyclopentadienone (0·38 g, 1 mmol), potassium acetate (0·20 g, 2·4 mmol), and acetic acid (0·036 g, 0·6 mmol) in benzene (12 ml), trideuteriobenzenediazonium fluoroborate (0·39 g, 2 mmol) (99% [^{2}H$_3$]) was added as in the previous reaction to give biphenyl (0·044 g, 14%), m.p. and mixed m.p. 70—71°, and tetraphenylnaphthalene (0·305 g, 35%), m.p. and mixed m.p. 203—204°. Mass spectral analysis of the products showed 99% [^{2}H$_3$] retention in the biphenyl and 99% [^{2}H$_2$] in tetraphenylnaphthalene.

(ii) *In the presence of anthracene.* To a mixture of anthracene (0·18 g, 1 mmol), potassium acetate (0·20 g, 2·4 mmol), and acetic acid (0·036 g, 0·6 mmol) in benzene (12 ml) was added the benzenediazonium fluoroborate (0·39 g, 2 mmol) (99% [^{2}H$_3$]) in three batches with 30 min between each addition. The temperature was maintained at 60° and stirring continued for a further 1 h. The volume of the reaction mixture was reduced on a rotary evaporator and chlorobenzene (17 ml) and maleic anhydride (0·2 g) were added. The mixture was boiled under reflux for a further 24 h. Chromatography of the mixture on alumina (50 g) eluting with cyclohexane afforded biphenyl (0·041 g, 13%), m.p. and mixed m.p. 69—70°, and triptycene (0·022 g, 5%), m.p. and mixed m.p. 255—256°, which was shown to be pure by g.l.c. after recrystallisation from light petroleum (b.p. 60—80°) containing a little benzene. The biphenyl and triptycene obtained showed deuterium contents of 99% [^{2}H$_3$] and 99% [^{2}H$_2$] respectively.

Decomposition of [2-^{2}H]*Benzenediazonium Fluoroborate.*—(i) *In benzene in the presence of tetraphenylcyclopentadienone.* Reaction, as described above, of a mixture of *tetraphenylcyclopentadienone* (0·19 g, 0·5 mmol), potassium acetate (0·10 g, 1·2 mmol), and acetic acid (0·02 g, 0·03 mmol) in benzene (10 ml) with [2-^{2}H]benzenediazonium fluoroborate (0·195 g, 1 mmol) (92% [^{2}H]) in benzene at 60° gave biphenyl (0·015 g, 10%) and tetraphenylnaphthalene (0·121 g, 29%) showing deuterium contents of 92% [^{2}H] and 55% [^{2}H] respectively.

(ii) *In dichloroethane in the presence of tetraphenylcyclopentadienone.* To a mixture of tetraphenylcyclopentadienone (0·19 g, 0·5 mmol), potassium acetate (0·10 g, 1·2 mmol), and acetic acid (0·02 g, 0·03 mmol) in 1,2-dichloroethane (10 ml), [2-^{2}H]benzenediazonium fluoroborate (0·195 g, 1 mmol) (92% [^{2}H]) was added in three batches with 30 min between each addition. The temperature of the well stirred mixture was maintained at 60° for a further 1 h. Tetraphenylnaphthalene (0·061 g, 15%) was isolated by dry column chromatography and shown to have a deuterium content of 55% [^{2}H].

(iii) *In benzene in the presence of anthracene.* Reaction of a mixture of anthracene (0·09 g, 0·5 mmol), potassium acetate (0·10 g, 1·2 mmol), and acetic acid (0·02 g, 0·03 mmol) in benzene (10 ml) with [2-^{2}H]benzenediazonium fluoroborate (0·195 g, 1 mmol) (92% [^{2}H]) as above, gave biphenyl (0·023 g, 15%). Triptycene was isolated by preparative g.l.c. (3% SE30; 230°). The yield of triptycene (6%) was established by quantitative g.l.c. examination of the reaction mixture (5% SE30; 220°) using fluoranthene as internal standard. Biphenyl had 92% [^{2}H] and triptycene 58% [^{2}H].

(iv) *In benzene in the absence of a trap.* Reaction, in benzene (10 ml), of a mixture of potassium acetate (0·05 g 0·6 mmol), acetic acid (0·01 g, 0·015 mmol), and [2-^{2}H]-benzenediazonium fluoroborate (0·1 g, 0·5 mmol) (92% [^{2}H]) gave biphenyl (0·028 g, 36%) (92% [^{2}H]).

Decomposition of [2-^{2}H]*Benzenediazonium Chloride.*—(i) *In dichloroethane in the presence of anthracene.* To a mixture of anthracene (0·27 g, 1·5 mmol), potassium acetate (0·30 g, 3·6 mmol), and acetic acid (0·06 g, 0·09 mmol) in dichloroethane (20 ml), [2-^{2}H]benzenediazonium

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[14] K. Biemann, 'Mass Spectrometry: Organic Chemical Applications,' McGraw-Hill, New York, 1972.

chloride (0·42 g, 3·0 mmol) (92% [^{2}H]) was added in three batches over a period of 1 h. The mixture was vigorously stirred and the temperature maintained at 60°. Stirring was continued for a further 4 h. The products were isolated by column chromatography on alumina (75 g), eluting with light petroleum (b.p. 40—60°). The triptycene fraction was purified by treatment with maleic anhydride in chlorobenzene. Recrystallisation from light petroleum (b.p. 60—80°) gave crystals, m.p. and mixed m.p. 255—256°. The yield of triptycene (10%) was established in a separate experiment by quantitative g.l.c. examination of the reaction mixture (5% SE30; 220°) using fluoranthene as internal standard. The yield of 9-phenylanthracene (11%) was established using the calculated yield of triptycene as a standard. The deuterium content of the triptycene and 9-phenylanthracene products were found to be 59 and 92% [^{2}H] respectively.

A similar experiment carried out under conditions identical with those of Buxton and Heaney [5] was as follows. To a mixture of anthracene (0·45 g, 2·5 mmol), potassium acetate (0·9 g, 9 mmol), and acetic acid (0·05 g, 0·8 mmol) in dichloroethane (25 ml) [2-^{2}H]benzenediazonium chloride (0·5 g, 3·5 mmol) (94% [^{2}H]) was added in three batches over a period of 1 h. The reaction mixture was vigorously stirred throughout and the temperature maintained at 70°. The mixture was then heated under reflux for 16 h, filtered, and the solvent removed. The products were isolated by column chromatography on alumina (75 g) eluting with light petroleum (b.p. 40—60°). Triptycene was purified as before and the yield (12%) established by quantitative g.l.c. The yield of 9-phenylanthracene (12%) was calculated as above. Triptycene showed a deuterium content of 58% [^{2}H]. 9-Phenylanthracene showed a deuterium content of 94% [^{2}H].

Control Experiments and Calculation of the Isotope Effect.— Three competitive experiments using benzenediazonium fluoroborate, its [2,4,6-^{2}H$_3$] analogue, tetraphenylcyclopentadienone, potassium acetate, and acetic acid in benzene were carried out as described above. The mixture of 1,2,3,4-tetraphenylnaphthalene and its [^{2}H$_2$] analogue was analysed using mass spectrometry (Table). The mean value of k_H/k_D (1·3) so obtained indicates the magnitude of the isotope effect leading to the slightly greater ease of formation of benzyne from the undeuteriated benzenediazonium fluoroborate. Since, in the monodeuteriated cases employed in the diagnostic experiments above, the starting monodeuteriated benzenediazonium salts contained between 6 and 8% of non-deuteriated material we are now able to correct for the fact that slightly more [^{1}H]benzyne will be formed from this component than from the monodeuteriated part. In practice this correction factor was low. Thus in the five experiments, isotope effects calculated on the assumption that the D and H precursors partition equally into benzyne and non-benzyne paths were 1·49, 1·49, 1·71, 1·69, and 1·61. Allowing for the effect summarised in the Table these figures become 1·53, 1·53, 1·83, 1·78, and 1·70, giving a spread of k_H/k_D of 1·5—1·8.

Reactions of PhN_2BF_4 and $[2,4,6\text{-}^2H_3]C_6H_2N_2BF_4$ in the presence of tetraphenylcyclopentadienone (TC)

	Molar ratios		
PhN_2BF_4 : TC	1	0·5	0·2
$[2,4,6\text{-}^2H_3]PhN_2$: $[2,4,6\text{-}^1H_3]PhN_2$	0·97	1·07	0·97
[^{2}H$_2$]TPN : [^{1}H]TPN	0·75	0·785	0·73
k_H/k_D	1·29	1·36	1·33

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