

## Oxidation of Aromatic Substrates. Part 4.<sup>1</sup> Action of Ruthenium Tetraoxide on some Substituted Biphenyls

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Selective cleavage of biphenyls by ruthenium tetraoxide is possible, attack being directed towards the ring carrying an activating substituent; protection is afforded by electron-attracting groups. Aminobiphenyls differ from aliphatic amines (see preceding paper) in that they undergo oxidation in acidic solution, reaction being initiated by the low concentration of free base in the equilibrium mixture. However, formation of the *N*-trifluoroacetyl derivative prevents participation by the N atom and this group is therefore effective in protecting aromatic amines.

In the preceding paper<sup>1</sup> it was shown that the oxidation of anilines was retarded in acidic solution, but that the higher concentration of the free base led to their more rapid degradation than the stronger aliphatic bases. This difference of behaviour is further illustrated by the oxidation of 2-aminobiphenyl to benzoic acid (53% yield) with no detectable formation of 2-aminobenzoic acid. The attack by the tetraoxide is here directed to the activated ring in the free base; the unsubstituted ring in the predominant conjugate acid is protected by its mesomeric interaction with anilinium ion. There is similar evidence<sup>2</sup> of mesomeric inactivation of the unsubstituted ring in the 2- and 4-nitrobiphenyls, where the partial rate factor for 4'-nitration is one-thirtieth of that for biphenyl itself. The over-riding direct effect of the substituents is shown here by the absence of ring disubstitution products. In contrast to the relatively rapid attack on aromatic amines in sulphuric acid (see Table in preceding paper) the unsubstituted ring in 2-nitrobiphenyl was incompletely oxidised, giving *o*-nitrobenzoic acid (70% yield) after 48 h in carbon tetrachloride-sodium hypochlorite containing ruthenium trichloride (0.05 equiv.). G.l.c. showed that destruction of starting material was complete in 72 h, and by prolonging the reaction time both 2- and 4-nitrobiphenyl were converted into the corresponding nitrobenzoic acids in over 80% yield.

Trifluoroacetylation is known<sup>3</sup> to protect amines from attack by the tetraoxide, and trial experiments with the derivatives<sup>4</sup> of *n*-heptylamine and aniline showed that in carbon tetrachloride both resisted attack for several hours at ambient temperature. The 2- and 4-trifluoroacetylaminobiphenyls in carbon tetrachloride were therefore treated with sodium periodate (12 equiv.) in the presence of ruthenium trichloride (0.1 equiv.)

and after quenching with propan-2-ol the 2- and 4-aminobenzoic acids were isolated in 76 and 65% yield, respectively. Trifluoroacetylation is evidently of value for the protection of aromatic amines; a measure of its effectiveness comes from the positive Hammett substituent constants which were determined<sup>5</sup> following potentiometric titration of *m*- and *p*-trifluoroacetylaminobenzoic<sup>6</sup> acids in 50% ethanol-water and 80% methyl cellosolve-water. The values of  $\sigma_m$  (0.30) and  $\sigma_p$  (0.12) obtained show that the group is electron-withdrawing. Further, from the equations  $\sigma_p = 1.14\sigma_I + \sigma_R$  and  $\sigma_m = \sigma_I + 0.33\sigma_R$  a value of  $\sigma_R$  of  $-0.36$  is obtained, indicating a weak mesomeric effect for the  $\text{CF}_3\text{CO}\cdot\text{NH}$  group, similar to that of a chloro-substituent. The protection afforded by trifluoroacetylation is expected to be greater in practice than is implied by the value of  $\sigma_R$ . This follows because the solvents of choice, unlike those used in ref. 5, are not basic and cannot therefore bolster the electromeric effect of the nitrogen atom. These factors probably account for the observation that the degradation of the unsubstituted ring in the trifluoroacetylaminobiphenyls is slow, and similar to that in the 2- and 4-nitrobiphenyls.

Provided that solvolysis is avoided the protective role of the trifluoroacetyl group may be extended. The technique is also attractive for amino-acid synthesis<sup>1</sup> particularly as a g.l.c. procedure for the resolution of racemic mixtures of *N*-trifluoroacetylaminobenzoic acid esters has been published.<sup>7</sup>

### EXPERIMENTAL

The equipment used was as given in the preceding paper save that some of the g.l.c. analyses were carried out with a Pye 104 unit. Micro-analyses were performed by the

<sup>1</sup> Part 3, D. C. Ayres, preceding paper.

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<sup>4</sup> E. J. Bourne, S. H. Henry, C. E. M. Tatlow, and J. C. Tatlow, *J. Chem. Soc.*, 1952, 4014.

<sup>5</sup> O. Exner and J. Lakomy, *Coll. Czech. Chem. Comm.*, 1970, **35**, 1371.

<sup>6</sup> F. Weygand and E. Leising, *Chem. Ber.*, 1954, **87**, 248.

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London School of Pharmacy and by Dr. B. Stephenson, Research School of Chemistry, Australian National University. Mass spectra were obtained by the Physico-chemical Measurements Unit, Harwell.

**Oxidation of 2-Aminobiphenyl.**—This compound (1.69 g, 10 mmol) was dissolved in 40% sulphuric acid (40 ml) and added during 1 h at 20 °C to a stirred solution of sodium periodate (24 g) in water (15 ml) containing ruthenium trichloride (0.1 g of  $\text{RuCl}_3 \cdot 3\text{H}_2\text{O}$ ); next morning residual tetraoxide was destroyed with propan-2-ol (3 ml). The mixture was diluted with water (40 ml) and filtered, and benzoic acid (0.64 g, 53%) was extracted from the filtrate with ethyl acetate. The product was characterised by mixed m.p. and i.r. spectrum.

**Oxidation of 2- and 4-Nitrobiphenyls.**—These isomers (1.99 g, 10 mmol) were treated separately with ruthenium tetraoxide in carbon tetrachloride–sodium hypochlorite as described previously.<sup>8</sup> However, the products were not isolated by evaporation of the liquor but by extracting it with ethyl acetate. A reaction period of 48 h at 20 °C led to the isolation of 2-nitrobenzoic acid (0.62 g, 70% allowing for recovery of 1.0 g), m.p. and mixed m.p. 145°, identical (i.r. spectrum) with an authentic sample. G.l.c. (5% Apiezon L on Chromosorb W, 60–80 mesh, at 180 °C) showed that the 2- and 4-nitrobiphenyls were oxidised at similar rates and that 72 h were needed for completion under the above conditions. When the reaction time was extended, the yield of 2-nitrobenzoic acid<sup>9</sup> was increased to 82% and an 85% yield (1.50 g; m.p. 238°) of 4-nitrobenzoic acid<sup>9</sup> was obtained with no recovery of starting material.

**Trifluoroacetyl Derivatives of Amines.**—The reactions between trifluoroacetic anhydride and the amines were all carried out in dry ether at 0 °C for up to 1 h and worked up as described previously.<sup>4</sup>

2-Trifluoroacetylaminobiphenyl (84%) had m.p. 111° (lit.,<sup>10</sup> 101°) (Found: C, 63.0; H, 3.8; N, 5.3. Calc. for  $\text{C}_{14}\text{H}_{10}\text{F}_3\text{NO}$ : C, 63.4; H, 3.8; N, 5.3%). 4-Trifluoroacetylaminobiphenyl (74%) had m.p. 197° (lit.,<sup>10,11</sup> 200,

201°). *N*-Trifluoroacetanilide (90%) had m.p. 89° (lit.,<sup>4</sup> 89°). *N*-Trifluoroacetylheptylamine (78%) was recrystallised from petroleum (b.p. 40–60 °C) to m.p. 16–16.5° in a cold room (Found: C, 51.0; H, 7.8; F, 27.7.  $\text{C}_9\text{H}_{16}\text{F}_3\text{NO}$  requires C, 51.4; H, 7.6; F, 27.1%) (lit.,<sup>10</sup> liquid, b.p. 135° at 11 mmHg).

These substances were further characterised by their i.r. and mass spectra. Molecular ions and daughter ions typical of loss of  $\text{CF}_3$ ,  $\text{CF}_3\cdot\text{CO}$ , and  $\text{CF}_3\cdot\text{CO}\cdot\text{NH}$  were prominent.

**Action of Ruthenium Tetraoxide on the Trifluoroacetyl-amino-compounds.**—Both the aniline and heptylamine derivatives were recovered in over 90% yield after 4 h at 20 °C in carbon tetrachloride containing an excess of oxidant.

2-Trifluoroacetylaminobiphenyl (1.24 g, 5 mmol) in carbon tetrachloride (100 ml) was added to sodium periodate solution (12 equiv., 12.9 g in 150 ml of water) containing ruthenium trichloride (0.15 g). The mixture was stirred in a closed system for 72 h at 20 °C before separation of the two liquid phases. No material was obtained by extraction of the aqueous layer, nor was any product isolated from the carbon tetrachloride layer following destruction of the excess of tetraoxide with propan-2-ol (2 ml). However, extraction of the dried ruthenium dioxide precipitate with hot sodium hydroxide solution (10%; 40 ml), neutralisation to pH 6.0, and extraction with ethyl acetate gave *o*-aminobenzoic acid (0.52 g, 76%), m.p. and mixed m.p. 145° (lit.,<sup>12</sup> 145°).

In a similar experiment 4-trifluoroacetylaminobiphenyl was converted into *p*-aminobenzoic acid (65%), m.p. and mixed m.p. 188° (lit.,<sup>12</sup> 189°).

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