569. *Butadienes and Related Compounds. Part I. Conversion of Asymmetric Di-(p-alkoxyphenyl)ethylenes on Bromination into the Corresponding 1 : 1 : 4 : 4-Tetralkoxyphenylbuta-1 : 3-dienes.*

By Wadie Tadros and Gamil Aziz.

1 : 1 : 4 : 4-Tetralkoxyphenylbuta-1 : 3-dienes are prepared by bromination of the *as*-di-(*p*-alkoxyphenyl)ethylenes, heating the di-*p*-alkoxyphenylvinyl chloride or bromide alone, or heating a mixture of the vinyl bromide and *as*-di-(*p*-alkoxyphenyl)ethylenes. The rôles played by temperature, concentration, and mineral acids are demonstrated. The structure of the butadienes is confirmed by ozonolysis.

It has been shown [Robson, Schönberg, and Fahim, *Nature*, 1938, **142**, 292; Schönberg, Robson, Tadros, and Fahim, *J.*, 1940, 1327; Schönberg, Robson, and Tadros, *Nature*, 1942, **150**, 22 (Tadros's name was inadvertently omitted from this publication); Tadros and Schönberg, *J.*, 1943, 394; Tadros and Robson, *Nature*, 1947, **160**, 20; Tadros, Farahat, and Robson, *J.*, 1949, 439) that the replacement of the ethylene hydrogen atom in triarylethylenes by halogen was accompanied by a considerable increase in œstrogenic activity. It was hoped that testing the *as*-di-(*p*-alkoxyphenyl)ethylenes and their halogeno-derivatives might throw light on the relation between structure and œstrogenic activity. Tested on groups of 5 ovariectomised mice (average weight, 25 g.), *as*-di-*p*-methoxyphenylethylene and di-*p*-methoxyphenylvinyl bromide (5 mg. in 0·4 c.c. of sesame oil, injected subcutaneously in 4 doses on 2 days) showed practically no activity.

The *as*-diarylethylenes required by us as intermediates were prepared by treating the diaryl ketones with methylmagnesium iodide (cf. Pfeiffer and Wizinger, *Annalen*, 1928, **461**, 132). The required *as*-diarylvinyl bromides were prepared from the diarylethylenes by treatment with one molecular proportion of bromine in acetic acid, chloroform, carbon tetrachloride, or ether, the solutions being warmed only sufficiently to effect dissolution (otherwise the butadienes may be formed) (cf. Pfeiffer and Wizinger, *loc. cit.*; Bergmann and Szmuszkowicz, *J. Amer. Chem. Soc.*, 1947, **69**, 1777).

Bergmann and Szmuszkowicz (*loc. cit.*), by treatment of *as*-di-*p*-methoxyphenylethylene with two atomic proportions of bromine in acetic acid, obtained a compound, m. p. 206—207°, shown later (Bergmann, Szmuszkowicz, and Dimant, *ibid.*, 1949, **71**, 2968) to be 1 : 1 : 4 : 4-

tetra-*p*-methoxyphenylbuta-1 : 3-diene. We have confirmed this result, which we obtained also on use of chloroform or carbon tetrachloride as solvent, and confirmed the structure by ozonolysis of the product to 4 : 4′-dimethoxybenzophenone and glyoxal. Similar preparations gave also the *p*-ethoxy-, *p*-*n*-propoxy-, *p*-*iso*propoxy-, and *p*-benzyloxy-dienes (structures confirmed by ozonolysis), but some dealkylation occurred in the last two cases. Later we found that use of one atomic proportion of bromine gave higher yields of purer products, except in the case of the benzyloxy-compound the yield of which was always low; we hope to discuss the significance of this observation later.

Tetra-*p*-alkoxyphenylbutadienes were also prepared by the following methods : (1) Thermal decomposition of the diarylvinyl chloride or bromide. (2) Refluxing of the *as*-diarylethylene and diarylvinyl bromide in acetic acid; this reaction is autocatalytic, a pronounced induction period being removed by addition of a trace of hydrogen bromide—sulphuric acid is also effective. (3) Refluxing of solutions of the diarylvinyl bromide in acetic acid saturated with hydrogen bromide; a small amount of hydrogen bromide has no effect; the vinyl bromide cannot be replaced by the *as*-diarylethylene which is recovered largely unchanged although the solution acquires a green colour (cf. Schmitz-Dumont, Thömke, and Diabold, *Ber.*, 1937, **70**, 175; Bergmann and Szmuszkowicz, *loc. cit.*). (4) Refluxing of a solution of di-*p*-methoxyphenylvinyl bromide in acetic acid or chloroform containing a little iodine. (5) Treatment of di-*p*-methoxyphenylvinyl bromide with stilbene or 2-phenyl-1 : 1-di-*p*-*iso*propylphenylethylene (Tadros, *J.*, 1949, 442) in acetic acid, which gives the tetra-*p*-methoxyphenyl-diene. Brominated by-products were formed in all cases.

A product, m. p. 149° (Brand and Matsui, *Ber.*, 1913, **46**, 2942; Brand and Kercher, *Ber.*, 1921, **54**, 2007; Brand and Horn, *J. pr. Chem.*, 1927, **115**, 351), supposed to be 1 : 1 : 4 : 4-tetra-*p*-methoxyphenylbuta-1 : 3-diene, appears to differ from the compound, m. p. 206—207°, and this is being investigated. The *p*-ethoxy-diene, m. p. 202°, reported from the same school (Brand, Horn, and Bausch, *ibid.*, 1930, **127**, 240), appears to accord with ours of m. p. 207°.

Reference may be made to the ionic mechanism suggested by Bergmann *et al.* (*locc. cit.*) for the formation of 1 : 1 : 4 : 4-tetra-*p*-methoxyphenylbuta-1 : 3-diene from di-*p*-methoxyphenylethylene by bromine, but comment is reserved.

The formation of butadienes is affected by the temperature and the concentration of the reactants. Thus, equimolecular amounts of bromine and *as*-diarylethylenes, in suspension in a small amount of cold solvent, give the vinyl bromides, whereas from the boiling solutions the butadienes are at once formed. The vinyl bromides could also be obtained when larger amounts of solvent were used. But the butadienes may be formed if escape of hydrogen bromide is prevented; and the effect of iodine is evident from the experiments recorded above. Similarly, *as*-di-*p*-methoxy- and -ethoxy-phenylethylene are largely unaffected by chlorine in small amounts of boiling acetic acid (1 g. of the ethylene in 10 c.c.), but use of larger proportions of the solvent (100 c.c. per g.) leads to 1 : 1-dichloro-2 : 2-di-*p*-ethoxy- and 1 : 1-dichloro-2 : 2-di-*p*-*n*-propoxy-phenylethylene together with unchanged ethylene. Di-*p*-ethoxy-(obtained from 1 : 1-dichloro-2 : 2-di-*p*-ethoxyphenylethane by Brand, *Ber.*, 1913, **46**, 2935) and di-*p*-benzyloxy-phenylvinyl chloride were obtained by chlorination of the ethylene in chloroform or carbon tetrachloride.

Finally, we note that Sheibley and Prutton (*J. Amer. Chem. Soc.*, 1940, **62**, 840) obtained small amounts of 1 : 1 : 4 : 4-tetraphenylbuta-1 : 3-diene and stilbene on bromination of 1 : 1-diphenylethane, the former product doubtless being formed by way of 1 : 1-diphenylethylene.

EXPERIMENTAL.

M. p.s are uncorrected. Microanalyses were by Drs. Weiler and Strauss of Oxford.

as-*Di*-p-*alkoxyphenylethylenes*.—Preparation of these compounds is exemplified by the following. 4 : 4′-Di-*p*-ethoxybenzophenone (15 g.) in ether (250 c.c.) was added to methylmagnesium iodide (from magnesium, 3·4 g., and methyl iodide, 19·8 g.) in ether (150 c.c.), with stirring, during 2 hours and the whole was set aside overnight. The mixture was decomposed with aqueous ammonium chloride and extracted with ether or benzene–ether. Crystallisation from benzene gave *as*-di-*p*-ethoxyphenylethylene (10·6 g.), m. p. 142° (Found : C, 80·3; H, 7·4. Calc. for $C_{18}H_{20}O_2$: C, 80·6; H, 7·5%).

The following were similarly prepared, in 70% yield : as-*di*-p-n-*propoxyphenylethylene*, m. p. 134° (from benzene) (Found : C, 80·8; H, 8·0. $C_{20}H_{24}O_2$ requires C, 81·1; H, 8·1%), as-*di*-*p*-iso*propoxyphenylethylene*, m. p. 54° (from alcohol) (Found : C, 81·6; H, 8·0%), as-*di*-p-*benzyloxyphenylethylene*, m. p. 186° (from acetic acid) (Found : C, 85·6; H, 5·8. $C_{28}H_{24}O_2$ requires C, 85·7; H, 6·1%).

Di-p-*alkoxyphenylvinyl Bromide*.—These were prepared by adding an equimolecular quantity of bromine dissolved in acetic acid, chloroform, carbon tetrachloride, or ether to the *as*-di-*p*-alkoxyphenylethylene dissolved in a comparatively large quantity of the solvent (1 g. of the ethylene in 100 c.c. of solvent). When acetic acid was used, the mixture was diluted with water and neutralised with sodium carbonate. When other solvents were used, the solutions were shaken with aqueous sodium carbonate, then with water, dried ($CaCl_2$), and filtered, and the solvent was then distilled off. The residues crystallised from alcohol from which they separated in colourless crystals.

Thus were prepared di-*p*-methoxyphenylvinyl bromide, m. p. 84°, di-*p*-ethoxyphenylvinyl bromide, m. p. 64°, *di*-p-n-*propoxyphenylvinyl bromide,* m. p. 42° (Found : C, 64·2; H, 5·9; Br, 21·3. $C_{20}H_{23}O_2Br$ requires C, 64·0; H, 6·1; Br, 21·4%), and *di*-p-*benzyloxyphenylvinyl bromide,* m. p. 119—120° (Found : C, 71·3; H, 4·7; Br, 17·2. $C_{28}H_{23}O_2Br$ requires C, 71·3; H, 4·9; Br, 17·0%).

Di-p-*alkoxyphenylvinyl Chlorides.*—*Di*-p-*benzyloxyphenylvinyl chloride.* A solution of chlorine (0·181 g.) in carbon tetrachloride (3·2 c.c.) was added to a solution of *as*-di-*p*-benzyloxyphenylethylene (1 g.) in the same solvent (150 c.c.) at room temperature. Washing the mixture with aqueous sodium carbonate and then water, and distilling off the solvent, gave an oily residue which crystallised from alcohol. The *vinyl chloride* had m. p. 98—99° (0·92 g.) (Found : C, 78·0; H, 5·0; Cl, 8·8. $C_{28}H_{23}O_2Cl$ requires C, 78·7; H, 5·4; Cl, 8·3%).

The di-*p*-ethoxyphenylvinyl chloride, similarly prepared, had m. p. 76° (from alcohol) (Found : C, 71·5; H, 6·5; Cl, 12·1. Calc. for $C_{18}H_{19}O_2Cl$: C, 71·4; H, 6·3; Cl, 11·7%).

Di-*p*-*n*-propoxyphenylvinyl chloride was obtained only as an oil.

1 : 1-*Dichloro*-2 : 2-*di*-p-*ethoxyphenylethylene.*—Chlorine (0·511 g.) in acetic acid (10 c.c.) was added to a solution of *as*-di-*p*-ethoxyphenylethylene (2 g.) in the same solvent (100 c.c.), and the mixture refluxed for 3 hours, then cooled, diluted with water, and neutralised with sodium carbonate, giving a product of m. p. 132°. This was fractionally crystallised from acetic acid whereby unchanged *as*-di-*p*-ethoxyphenylethylene (0·9 g.), m. p. 142° (not depressed on admixture with an authentic sample), and 1 : 1-dichloro-2 : 2-di-*p*-ethoxyphenylethylene (0·52 g.), m. p. 104—105° [not depressed on admixture with an authentic sample (Fritsch and Feldmann, *Annalen*, 1899, **306**, 72)] (Found : C, 65·0; H, 5·4; Cl, 20·4. Calc. for $C_{18}H_{18}O_2Cl_2$: C, 64·1; H, 5·3; Cl, 21·1%), were obtained.

1 : 1-Dichloro-2 : 2-di-*p*-*n*-propoxyphenylethylene, similarly prepared (0·45 g. from 1 g.), m. p. 78° (from alcohol) [not depressed on admixture with an authentic sample (Stephenson and Waters, *J.*, 1946, 339)] (Found: C, 66·0; H, 5·9; Cl, 19·0. Calc. for $C_{20}H_{22}O_2Cl_2$: C, 65·7; H, 6·1; Cl, 19·4%), was accompanied by 0·11 g. of the unchanged *as*-di-*p*-*n*-propoxyphenylethylene, m. p. 134° (not depressed on admixture with an authentic sample).

1 : 1 : 4 : 4-*Tetra*-p-*alkoxyphenylbuta*-1 : 3-*dienes.*—(*a*) Preparation of 1 : 1 : 4 : 4-tetra-*p*-methoxyphenylbuta-1 : 3-diene by adding bromine (0·6 g., 1 mol.) in acetic (2 c.c.) to boiling solution of the *as*-di-*p*-methoxyphenylethylene (1 g.) in the same solvent (10 c.c.) gave only 0·2 g. (about 20%) of the pure butadiene (contrast Bergmann *et al., loc. cit.*, 1947). Use of chloroform or carbon tetrachloride gave similar results. The solvent was distilled off on the water bath and the residue crystallised from acetic acid from which it separated in pale yellow crystals, m. p. 205—206°. On concentration of the mother-liquor, dark brown brominated by-products were obtained. The experiments were repeated with 0·5 mol. of bromine and only 5 c.c. as a solvent; the yield (0·7 g.) of the pure butadiene was then about 70%. On concentration of the mother-liquor, a little of the brominated by-product was obtained. Either a brown or an olive-green colour developed during the formation of the butadiene.

(*b*) A solution of di-*p*-methoxyphenylethylene (0·48 g., 1 mol.) and di-*p*-methoxyphenylvinyl bromide (0·64 g., 1 mol.) in acetic acid (10 c.c.) was refluxed for 0·5 hour, at the end of which a brown colour developed; on cooling, the butadiene (0·8 g.) was obtained. The butadiene was not formed after 10—15 minutes' refluxing. On the addition of 5 drops of acetic acid containing hydrobromic acid the reaction proceeded at once and the butadiene was formed within 1 minute.

(*c*) Experiment (*b*) was repeated, but without solvent. Evolution of gases started at 160—165° and a brown viscid mass was formed within 10 minutes. Crystallisation from acetic acid gave the butadiene (0·45 g.), m. p. 204—205° not depressed on admixture with an authentic sample.

(*d*) Experiment (*b*), but with stilbene or 2-phenyl-1 : 1-di-*p*-*iso*propoxyphenylethylene (Tadros, *loc. cit.*) instead of di-*p*-methoxyphenylethylene, gave a brown colour after 3 hours' refluxing, but the yield of butadiene was poor.

(*e*) Di-*p*-methoxyphenylvinyl bromide (1 g.) was heated alone. Evolution of hydrogen bromide started at 160—165°, and the mass became dark brown. The pure butadiene (0·21 g.), m. p. 204—205°, was obtained.

(*f*) When a solution of di-*p*-methoxyphenylvinyl bromide (1 g.) in acetic acid (10 c.c.) was boiled there was no change in colour and the vinyl bromide was recovered unchanged. Addition of 5 drops of acetic containing hydrogen bromide in a similar experiment did not alter the result. However, when a solution of the bromide (1 g.) in acetic acid (10 c.c.) saturated with hydrogen bromide was refluxed, a brown colour developed and the butadiene (0·52 g.) was formed within 1 minute.

(*g*) Refluxing a solution of di-*p*-methoxyphenylvinyl bromide (1 g.) in acetic acid (10 c.c.) containing iodine (10 mg.) gave the pure butadiene within 1·25 hours. When iodine (50 mg.) was added, the butadiene (0·3 g.) was obtained within 0·5 hour. In all the above experiments brominated by-products were isolated from the acetic acid mother-liquors after crystallisation. Use of chloroform in the last experiment gave the butadiene within 2 hours.

1 : 1 : 4 : 4-Tetra-*p*-ethoxyphenylbuta-1 : 3-diene, similarly prepared by methods (*a*), (*b*), (*c*), (*e*), (*f*), and (*g*), crystallised from acetic acid in yellow crystals, m. p. 207° (Found : C, 80·8; H, 7·1. Calc. for $C_{36}H_{38}O_4$: C, 80·9; H, 7·1%). Yields corresponded to those obtained above. It was also obtained by heating di-*p*-ethoxyphenylvinyl chloride (0·5 g.) alone at 200—220° for 10 minutes.

1 : 1 : 4 : 4-*Tetra*-p-n-*propoxyphenylbuta*-1 : 3-*diene*, prepared by methods (*a*) and (*e*) and similarly crystallised, formed pale yellow crystals (*ca.* 15—20%), m. p. 198—199° (Found : C, 81·4; H, 7·6. $C_{40}H_{46}O_4$ requires C, 81·4; H, 7·8%).

1 : 1 : 4 : 4-*Tetra*-p-iso*propoxyphenylbuta*-1 : 3-*diene*, prepared as in (*a*) and (*e*), was contaminated with dealkylated products which were separated by treatment with sodium hydroxide solution. It crystalllised from acetic acid in yellow crystals (about 40%), m. p. 187—188° (Found : C, 81·2; H, 7·5%).

1 : 1 : 4 : 4-*Tetra*-p-*benzyloxyphenylbuta*-1 : 3-*diene* was obtained, contaminated with dealkylated products which were separated as above, on addition of bromine (0·42 g.) in acetic acid (2 c.c.) to *as*-di-*p*-benzyloxyphenylethylene (2 g.) suspended in the same solvent (5 c.c.) at the b. p. Boiling was continued for 20 seconds. The diene crystallised from acetic acid in pale yellow crystals (*ca.* 8%), m. p. 225° (Found : C, 85·5; H, 5·9. $C_{56}H_{46}O_4$ requires C, 85·9; H, 5·9%).

When equimolecular quantities of bromine were added to the *as*-di-*p*-alkoxyphenylethylenes suspended in acetic acid (10 c.c.) at room temperature, a mixture of unchanged ethylene and vinyl bromide, which could be separated by fractional crystallisation, was obtained.

Ozonolyses.—A stream of dry ozonised oxygen (3%) was passed through a cold solution of the butadienes in carbon tetrachloride until the reaction was almost complete. Raney nickel sludge (5 g.) in distilled water was added and the mixture warmed on the water-bath for 10 minutes and filtered (cf. Cook and Whitmore, *J. Amer. Chem. Soc.*, 1941, **63**, 3540). The aqueous layer which contained nickel chloride was treated with 2 : 4-dinitrophenylhydrazine in hydrochloric acid (1 : 1), and the glyoxal bis-2 : 4-dinitrophenylhydrazone thus formed was filtered off. It crystallised from nitrobenzene in orange crystals, m. p. 318° alone or mixed with an authentic sample. The carbon tetrachloride layer was washed twice with water, then distilled on the water-bath after addition of distilled water. The residue was extracted with water from which another crop of dinitrophenylhydrazone could be obtained. The di-*p*-substituted benzophenone which did not dissolve in hot water crystallised from alcohol or acetic acid. No other products could be isolated. The following di-*p*-substituted benzophenones were obtained on ozonolysis of the corresponding butadienes : 4 : 4′-dimethoxy-, m. p. and mixed m. p. 142° (3·1 g. from 4 g.), 4 : 4′-diethoxy-, m. p. and mixed m. p. 131° (1·5 g. from 2 g.), 4 : 4′-di-*p*-*n*-propoxy-, m. p. and mixed m. p. 127° (0·7 g. from 1 g.), 4 : 4′-di*iso*propoxy-, m .p. and mixed m. p. 72° (0·75 g. from 1 g.), and 4 : 4′-di-*p*-benzyloxy-benzophenone, m. p. and mixed m. p. 188° (0·7 g. from 1 g.).

FOUAD I UNIVERSITY, ABBASSIA, CAIRO, EGYPT.

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