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AROMATIC POLYFLUORO-COMPOUNDS—XXXV[1]

1,2,3,4-TETRAFLUOROANTHRAQUINONE AND SOME REACTIONS OF TETRAFLUOROPHTHALIC ACID DERIVATIVES

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Abstract—1,2,3,4-Tetrafluoroanthraquinone has been synthesized and some of its reactions studied Further reactions of tetrafluorophthalic acid and its derivatives are reported.

Previously[2] tetrafluorophthalic acid and some of its reactions have been reported. This paper describes further reactions of the phthalic acid and its derivatives.

Reaction of tetrafluorophthalic acid or its anhydride with benzene under Friedel Crafts conditions[3] gave *o*-benzoyl-tetrafluorobenzoic acid, in good yield, which on heating with sulphuric acid gave 1,2,3,4-tetrafluoroanthraquinone, as pale yellow crystals in reasonable yield. The quinone showed a remarkable similarity to the corresponding hydrocarbon in its U.V. spectrum.

Attempts to reduce the quinone under a variety of conditions either to the 9,10-dihydro- or to 1,2,3,4-tetrafluoroanthracene were unsuccessful. The products obtained were all rapidly re-oxidized to the quinone.

Nucleophilic displacement reactions have been carried out on the quinone; for example reaction with sodium methoxide gave a mixture of products, one constituting about 95% of the whole. The latter was indicated by elemental analysis to be a methoxy-trifluoroanthraquinone, the PMR. spectrum of which was consistent with 2-methoxyl-1,3,4-trifluoroanthraquinone. This result suggests that 1,2,3,4-tetrafluoroanthraquinone is most susceptible to nucleophilic attack in the 2-position, similar to the cases of 1,2,3,4-tetrafluoro-[4] and octafluoronaphthalene,[5] and in accord with the recently published rationlisation of nucleophilic substitution in polyfluoroaromatic compounds.[6]

Tetrafluorophthalic acid or its ethyl ester were readily reduced with LAH to 1,2-bis(hydroxymethyl) tetrafluorobenzene. Bromination of the latter with hydrogen bromide gave the highly lachrymatory 3,4,5,6-tetrafluoro-*o*-xylylene dibromide. The hydrocarbon analogue of the latter has been used as starting material in the synthesis of benzocyclobutene,[7] and it was of interest to establish whether the fluorine atoms in our compound would be used to stabilize benzocyclobutene systems.

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[1] Part XXXIV; J. Burdon, D. R. King and J. C. Tatlow, *Tetrahedron* **22**, 2541 (1966).

[2] B. Gething, C. R. Patrick and J. C. Tatlow, *J. Chem. Soc.* 1574 (1961).

[3] R Hardy, *Colour Trade J.* **9** 184 (1921).

[4] P. L. Coe, G. M. Pearl and J. C. Tatlow to be published.

[5] B. Gething, C. R. Patrick and J. C. Tatlow, *J. Chem. Soc.* 156 (1962).

[6] J Burdon, *Tetrahedron* **21**, 3373 (1965).

[7] M. P. Cava and A. A. Deana, *J. Amer. Chem. Soc.* **81**, 4266 (1959).

Thus reaction between sodium sulphide and the xylylene dibromide gave 1,3-dihydro-3,4,5,6-tetrafluoroisothianaphthene. This compound was found to decompose rapidly in dry air and nitrogen, and further work has so far been impracticable. Tetrafluorophthalamide was readily prepared by reaction of diethyltetrafluorophthalate with ethanolic ammonia. Attempts to dehydrate the amide with a variety of reagents, including acetic anhydride, phosphorus pentoxide, and phosgene, failed to give tetrafluorophthalonitrile, a useful starting material for synthesis of phthalocyanins. In the classical manner heating of tetrafluorophthalic acid and urea also failed to give phthalocyanins.

Tetrafluoroanthranilic acid has previously been prepared[7] but the method was not satisfactory. A reported method for anthranilic acid synthesis is the decomposition of N-hydroxyphthalimides.[8] Thus tetrafluoro-N-hydroxyphthalimide was easily prepared by reaction of tetrafluorophthalic anhydride with hydroxylamine. Decomposition of the product under a variety of conditions, which gave anthranilic acid from N-hydroxyphthalimide, failed to give any of the desired tetrafluoroanthranilic acid, in all cases tetrafluorophthalic acid itself was obtained. It is thought that the reaction, which is essentially a Lössen rearrangement, fails at the dehydration of the intermediate hydroxamic acid. This is closely similar to the failure to dehydrate tetrafluorophthalimide, and clearly reflects the electron-withdrawing effect of the tetrafluoro-substituted benzene ring. Such effects of fluorinated groups are well known, for example in the difficulty of dehydration of partly fluorinated alcohols.[9]

Tetrafluorophthalide and tetrafluorophthalimidine were prepared by reduction of tetrafluorophthalic anhydride and tetrafluorophthalimide, respectively, with zinc in glacial acetic acid. Hydrolyses of these compounds to give 2-hydroxymethyl and 2-aminomethyl-3,4,5,6-tetrafluorobenzoic acid, respectively, were unsuccessful, and only unchanged starting materials were obtained.

Many attempts were made to prepare tetrafluorophenolphthalein and tetrafluorofluorscein. Products were obtained which showed some of the expected indicator properties, but elemental analysis and PMR spectroscopy always revealed an excessive carbon and hydrogen content. It would seem that the basic skeleton of the two compounds was formed but the nucleophilic attack by the phenate and resorcinate anions took place readily to give complex productions.

This work shows that the reactivities of tetrafluorophthalic acid and its derivatives may differ materially, and often disadvantageously from those of their hydrocarbon analogues. It is unfortunate that attempts to prepare representatives of the phthaleins and cyanins were unsuccessful, since the effect of fluorine substitution on the colour and related behaviour is of interest. Novel methods of synthesis for such compounds may need to be developed, and it may prove that polyfluorophthaleins are unexpectedly unstable.

EXPERIMENTAL

o-*Benzoyl-tetrafluorobenzoic acid.* Tetrafluorophthalic anhydride[7] (10 g) and $AlCl_3$ (18·9 g) were heated under reflux in dry benzene (120 ml) for 16 hr. Most of the excess benzene was removed by distillation and the residue washed with $NaHCO_3$aq (500 ml). The soln obtained was filtered. The filtrate was acidified with 50% H_2SO_4 and extracted with ether (3 × 100 ml). The combined extract were dried ($MgSO_4$) and the ether distilled off to leave a white solid (12·6 g). Recrystallization from

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[7] Bösler Chemische Fabrik German Patent 130. 301.

[8] B. K. Campbell, K. N. Campbell and J. A. Knoblock, *J. Amer. Chem. Soc.* 72, 4380 (1950).

benzene gave *o-benzoyltetrafluorobenzoic acid* (11·0 g) m.p. 151–153°. (Found; C, 56·9; H, 2·3 $C_{14}H_6F_4O_3$ requires: C, 56·5; H, 2·0%.) The acid gave an S-benzylthiouronium salt m.p. 183–184° (Found: C, 56·8; H, 3·2. $C_{22}H_{16}F_4N_2O_3S$ requires: C, 57·0; H, 3·5%) in the normal manner.

1,2,3,4-*Tetrafluoro*-9,10-*anthraquinone*. *o*-Benzoyltetrafluorobenzoic acid (12·6 g) was heated at 100° for 2 hr with conc H_2SO_4 (150 ml). The mixture was poured into water (500 ml) and the water heated at 80° for 1 hr to coagulate the ppt. The solid was filtered off and washed with water and sat $NaHCO_3$aq. After being dried, the residue was sublimed *in vacuo* (130°/0·1 mm Hg) to give 1,2,3,4-tetrafluoro-9,10-anthraquinone (10·8 g) m.p. 189–191°. (Found: C, 60·0; H, 1·5; F, 27·0. $C_{14}H_4F_4O_2$ requires: C, 60·0; H, 1·4; F, 27·2%) UV (EtOH) λ_{max} 250 mμ ε = 50, 200 λ_{max} 328 mμ ε = 10,500.

2-*Methoxy*-1,3,4-*trifluoro*-9,10-*anthraquinone*. 1,2,3,4-Tetrafluoro-9,10-anthraquinone (1 g) and MeONa (0·3 g) were heated in dry MeOH (15 ml) for 15 hr. Most of the MeOH was distilled off, and water (100 ml) was added. The aqueous soln was extracted with ether (3 × 50 ml), the combined extracts dried ($MgSO_4$) and the ether removed to yield a yellow solid (0·9 g) Chromatography on a silica gel column (3 × 50 cm) using benzene as eluent gave 2-*methoxy*-1,3,4-*trifluoro*-9,10-*anthraquinone* (0·7 g) m.p. 143–144°, (Found: C, 61·8; H, 2·4; F, 19·1 $C_{15}H_7F_3O_3$ requires: C, 61·7; H, 2·4; F, 19·5%.) PMR gave a triplet centered at 4·11 ppm, J_{HF} = 1·8 c/s downfield from TMS (external) and a complex multiplet at 7·3 ppm. The triplet is consistent with a methoxy-group flanked by two fluorine atoms i.e. a 2-methoxy substituent.

o-Naphthoyltetrafluorobenzoic acid. Tetrafluorophthalic anhydride (3 g) and naphthalene (217 g) in dry benzene (50 ml) were added to a stirred mixture of $AlCl_3$ (8·5 g) in dry benzene (20 ml). The mixture was heated under reflux for 6 hr, the excess benzene was then distilled off and the residue poured into sat $NaHCO_3$aq. The soln was acidified with H_2SO_4 and the aqueous layer extracted with ether (3 × 100 ml). The combined extracts were dried ($MgSO_4$) and the ether distilled to leave a dark material (4·5 g) which was recrystallized from benzene. A sample (0·3 g) was treated in the usual way with S-benzylthiouronium chloride to give S-benzylthiouronium-*o*-naphthoyltetrafluorobenzoate (0·3 g) m.p. 211–213° with dec. (Found: C, 61·1; H, 3·6. $C_{26}H_{18}F_4N_2O_3S$ requires: C, 60·7; H, 3·5%)

Diethyl tetrafluorophthalate. Tetrafluorophthalic acid (20 g) and fuming H_2SO_4 (16 ml) were heated in refluxing EtOH for 16 hr. The soln was poured into water (500 ml) and the product extracted with ether (3 × 100 ml). The combined extracts were dried ($MgSO_4$) and distilled to give a viscous oil which solidified on standing. Distillation *in vacuo* gave *diethyltetrafluorophthalate* (20·0 g) m.p. 29°, b.p. 134°/0·05 mm. (Found: C, 49·0; H, 3·0. $C_{12}H_{10}F_4O_4$ requires: C, 49·0; H, 3·4%.) In a similar experiment but using conc H_2SO_4 tetrafluorophthalic acid (10 g) gave as well as diethyltetrafluorophthalate (8 g) some 2-carbethoxy-3,4,5,6-tetrafluorobenzoic acid (1·0 g) m.p. 93°. (Found; C, 45·2; H, 1·8. $C_{10}H_6F_4O_4$ requires: C, 45·2; H, 2·2%.)

1,2-*Bis*(*hydroxymethyl*)*tetrafluorobenzene*. Diethyltetrafluorophthalate (19·3 g) in dry ether (100 ml) was added over 30 min to a stirred suspension of LAH (2·8 g) in dry ether (100 ml). The soln was refluxed for 1 hr and the cooled 4N H_2SO_4 (100 ml) was carefully added. The ether layer was separated, the aqueous layer extracted with ether (3 × 25 ml) and the combined ether layers dried ($MgSO_4$). Distillation of the ether gave a white solid (12·8 g) which gave, on recrystallization from benzene–light petroleum (1/1,) 1,2-*bis*(*hydroxymethyl*)*tetrafluorobenzene* (11·5 g) m.p. 101–102°. (Found: C, 45·9; H, 2·9. $C_8H_6F_4O_2$ requires: C, 45·7; H, 2·9%.)

3,4,5,6-*Tetrafluoro*-o-*xylylene dibromide*. 1,2-Bis(hydroxymethyl)tetrafluorobenzene (10 g), 48% HBraq (20·8 g) and conc H_2SO_4 (7·0 g) were heated together under reflux for 16 hr. The soln was poured into water and a heavy oily layer was formed. The aqueous layer was extracted with ether (3 × 50 ml) which dissolved the oil. The combined ether layers were dried ($MgSO_4$) and the ether distilled to give a highly lachrymatory liquid (16·5 g). Distillation *in vacuo* gave 3,4,5,6-*tetrafluoro*-o-*xylylene dibromide* (14·1 g) b.p. 76°/·01 mm. (Found: C, 28·9; H, 1·3; F, 22·5. $C_8H_4Br_2F_4$ requires: C, 28·6; H, 1·2; F, 22·6%.)

1,3-*Dihydro*-4,5,6,7-*tetrafluoroisothionaphthene*. 3,4,5,6-tetrafluoro-*o*-xylylene dibromide (5 g) in EtOH (50 ml) was added over 20 min to a refluxing sol of $Na_2S.9H_2O$ (4·0 g) in EtOH (50 ml). The soln was refluxed for 30 min and then most of the EtOH evaporated. The residue was poured into water (250 ml) and the aqueous layer extracted with ether (3 × 50 ml). The ether layers were dried

($MgSO_4$) and distilled to leave a yellow solid (2·8 g). Purification by steam distillation and sublimation *in vacuo* gave the unstable 1,3-dihydro-4,5,6,7-tetrafluoroisothianaphthene (0·5 g) m.p. 33–34°. (Found: C, 46·0; H, 1·8. $C_8H_4F_4S$ requires: C, 46·2; H, 1·9%.)

Tetrafluorophthalamide. Diethyltetrafluorophthalate (3·0 g) in EtOH (15 ml) was treated with gaseous ammonia for 4 hr. Evaporation of the EtOH *in vacuo* afforded a sticky white solid (1·5 g), recrystallization from EtOH gave tetrafluorophthalamide (0·9 g) m.p. 192–194° with dec. (Found: C, 40·8; H, 1·7; N, 12·1. $C_8H_4F_4N_2O_2$ requires: C, 40·7; H, 1·7; N, 11·9%.) On heating at its m.p. the amide decomposes quantitatively to tetrafluorophthalimide, identified by IR spectroscopy.

*Tetrafluoro-*N*-hydroxyphthalimide.* Tetrafluorophthalic anhydride (5·0 g) was added to a stirred soln of hydroxylamine hydrochloride (1·6 g) and K_2CO_3 (1·6 g) in water (100 ml) at room temp. After 12 hr the precipitated yellow solid was filtered off, washed (H_2O) and dried to give crude tetrafluoro-N-hydroxyphthalimide (3·5 g). Recrystallization from benzene–EtOH (1:1) gave tetrafluoro-N-hydroxyphthalimide (2·4 g) m.p. 166–167°. (Found: C, 41·1; H, 0·4; N, 6·9. $C_8HF_4NO_3$ requires: C, 40·8; H, 0·4; N, 6·9%.) The hydroxyimide on treatment with K_2CO_3aq at 100° gave tetrafluorophthalic acid.

Tetrafluorophthalide. Zn dust (6 g) was added with stirring to a refluxing sol of tetrafluorophthalic acid (3 g) in glacial AcOH (21 ml). After being refluxed for 16 hr the mixture was filtered hot and the residue washed with hot glacial AcOH (3 × 10 ml). Most of the AcOH was distilled *in vacuo* from the filtrate and the resulting soln poured into $NaHCO_3$aq. Continuous ether extraction of the aqueous layer followed by evaporation of the ether gave *tetrafluorophthalide* (0·7) m.p. 67–69° purified by sublimation *in vacuo.* (Found: C, 46·9; H, 1·0; $C_8H_2F_4O_2$ requires: C, 46·7; H, 1·0%.)

Tetrafluorophthalimidine. Zn dust (1·75 g) was added with stirring to a soln of tetrafluorophthalimide (1·0 g) in glacial AcOH (12·5 ml) kept at 60°. The soln was then heated under reflux for 4 hr and was then filtered hot. The filtrate and the AcOH washings of the residue were distilled *in vacuo*, and the residue neutralized with $NaHCO_3$. The aqueous layer was continuously extracted with ether for 16 hr, the ether layer dried ($MgSO_4$) and distilled to give a brown solid. Sublimation *in vacuo* gave tetrafluorophthalimidine (0·2 g) m.p. 207–208° with dec. (Found: C, 47·1; H, 1·6. $C_8H_3F_4NO$ requires: C, 46·8; H, 1·5%.)

N-*carbethoxymethyltetrafluorophthalimide.* Potassium tetrafluorophthalimide (2·2 g) was added to a sol of ethyl chloroacetate (1·1 g) in dimethylformamide (25 ml). The sol was stirred for 1 hr and then poured into water. The precipitated solid was filtered off, and the aqueous layer extracted with ether and the ether layer dried ($MgSO_4$). Evaporation of the ether gave a solid identical to the ppt. All the solid was dissolved in acetone and passed down a column of silica gel (2 × 30 cm). The only fraction eluted was recrystallized from EtOH to yield N-carbethoxymethyltetrafluorophthalimide (1·6 g) m.p. 186–187° with dec. (Found: C, 47·1; H, 2·8. $C_{12}H_7F_4NO_4$ requires: C, 47·2; H, 2·3%.)

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