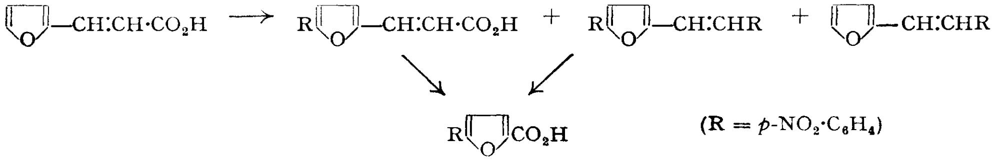
587. *The Reaction of Diazonium Salts with Furylacrylic Acid. Part I.*

By Walter Freund.

The reaction of diazonium salts with furylacrylic acid leads mainly to diarylated compounds (5-aryl-2-styrylfurans). As by-products, 2-styrylfurans and β-(5-aryl-2-furyl)acrylic acids are obtained (Austr. P. 26,725/1949).

As 4-aminostilbene derivatives have been shown to be carcinogenic as well as to have an inhibitory effect on the development of transplanted tumours in the rat, the preparation of compounds in which one benzene nucleus is replaced by a heterocyclic ring such as furan or thiophen was considered of interest. These experiments were carried out in 1946—1947. In the meantime, Brown and Kon (*J.*, 1948, 2150), with the same object, prepared a considerable number of such compounds, amongst them 2-4′-aminostyrylfuran, which they synthesised according to the Meerwein method. *E.g.*, they treated diazotised *p*-nitroaniline and furylacrylic acid in acetone with a sodium acetate buffer in presence of cupric chloride; they obtained only 2-4′-nitrostyrylfuran, in agreement with other reactions of diazonium compounds on αβ-unsaturated carbonyl compounds (Meerwein, Buchner, and van Emster, *J. pr. Chem.*, 1939, **152**, 237; B.P. 480,617). However, this furan is only one of the reaction products: the main product is a diarylated compound, (5?)-4′-nitrophenyl-2-4′-nitrostyrylfuran (Austr. P. 26,725/1949), and an acid of m. p. 262° is also obtained. Oxidation of the diarylated compound with potassium permanganate gave *p*-nitrobenzoic acid and, probably, 5-*p*-nitrophenyl-2-furoic acid. The last acid was obtained by oxidation of the acid of m. p. 262° which is consequently considered to be β-(5-*p*-nitrophenyl-2-furyl)acrylic acid. The relations of the various compounds are shown in the annexed scheme.



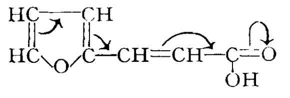
(R = *p*-NO$_2$·C$_6$H$_4$)

On the other hand, diazotised *o*-nitroaniline and furylacrylic acid have so far yielded only one product, an acid. Attempts at decarboxylation gave only resinous masses. If this acid were *trans*-β-2-furyl-α-*o*-nitrophenylacrylic acid, in accordance with the results of Meerwein *et al.* (*loc. cit.*), it should be decarboxylated to *trans*-1-2′-furyl-2-*o*-nitrophenylethylene in the same way as is the isomeric *trans*-α-2′-furyl-*o*-nitrocinnamic acid (Amstutz and Spitzmiller, *J. Amer. Chem. Soc.*, 1943, **65**, 367). The acid has therefore been assigned the structure β-2-furyl-α-*o*-nitrophenylacrylic acid. Oxidation experiments were inconclusive, as no arylfuroic acid could be isolated.

p-Chloroaniline and ethyl *p*-aminobenzoate gave results in agreement with those obtained with *p*-nitroaniline, although the product from the latter could not be crystallised. The diarylated compounds, 5-*p*-chlorophenyl-2-4′-chlorostyrylfuran and 5-*p*-carbethoxyphenyl-2-4′-carbethoxystyrylfuran, gave a deep blue fluorescence in benzene as did the diamine obtained from the dinitro-compound. This amine has, however, not yet been closely investigated.

Sulphanilic and arsanilic acid each yielded only one product, probably the 5-substituted furylacrylic acid (B.P. appln. 7144/1948). The corresponding diarylated compounds could not be purified although they were undoubtedly formed.

Introduction of two aryl groups by diazo-compounds has so far only been observed with quinones (D.R.-P. 508,395; Kvalnes, *J. Amer. Chem. Soc.*, 1934, **56**, 2478). That the 5-position in furylacrylic acid is the reactive one has already been observed by Gilman and Wright (*ibid.*, 1930, **52**, 3349) who found that ethyl furylacrylate yields a dibromo-compound, which loses hydrogen bromide to yield ethyl β-(5-bromo-2-furyl)acrylate. Marckwald (*Ber.*, 1887, **20**, 2813) found that furylacrylic acid when treated in alcohol with hydrogen chloride yields diethyl γ-ketopimelate; the ease with which the furan nucleus is opened and water added, is not met in other furan derivatives. Furylacrylic acid does not undergo the Diels–Alder reaction in spite of its three conjugated double bonds (van Campen and Johnson, *J. Amer. Chem. Soc.*, 1933, **55**, 430), while furylethylene according to Paul (*Compt. rend.*, 1939, **208**, 1028) adds maleic anhydride between the β-atom of the furan nucleus and the ethylene group. More recently, Herz (*J. Amer. Chem. Soc.*, 1946, **68**, 2732) showed that if the conjugation of furylacrylic acid is destroyed by hydrogenation, as in furylpropionic acid, then a normal Diels–Alder reaction takes place on the furan nucleus. According to Herz, the electronic displacements are represented as inset. A true diene, such as butadiene, adds only one aryl group (Goyner and Ropp, *ibid.*, 1948, **70**, 2283). There can therefore be little doubt that the peculiar polarisation of the double bonds in furylacrylic acid is responsible for the double arylation of this compound which has not been met before in the numerous applications of the Meerwein reaction. It is not in agreement with the theory that organic radicals are involved in the Meerwein reaction as claimed by Waters (*J.*, 1946, 411; "The Chemistry of Free Radicals," London, 1946). The results of reaction



between diazotised amines and furylacrylic acid support Meerwein's suggestion that the polarisation of the double bonds is the governing factor.

Further results with furylacrylic acid, and results with furyl-pentadienoic and -heptatrienoic acid, as well as with β-thienylacrylic acid, will be reported later.

EXPERIMENTAL

M. p.s are uncorrected.

Furylacrylic Acid and p-*Nitroaniline.*—*p*-Nitroaniline (13·8 g.) was diazotised with 25% hydrochloric acid (43 c.c.), ice (20 g.), and sodium nitrite (7·3 g. in water, 20 c.c.). The diazonium solution was filtered and poured into a solution of β-2-furylacrylic acid (13·8 g.) in acetone (200 c.c.) in which crystalline sodium acetate (40 g.) was suspended. The reaction mixture was well shaken. The pH was approx. 6. Gas evolution set in almost immediately and became so violent after addition of a solution of cupric chloride (4·2 g.) in water (12 c.c.) that cooling with ice-water became advisable. The reaction temperature was 23—24° and the gas evolution lasted for about 20 minutes. As the reaction proceeded a red solid separated which was filtered off (6·2 g.) and washed with dilute aqueous ammonia, water, and alcohol. This material melted at 220—225°. It was heated with a small quantity of acetone and allowed to cool. The solid material was filtered off and, recrystallised from acetic acid, formed small red needles, m. p. 234°, which dissolved in benzene with strong green fluorescence. After about 3 weeks in daylight the green fluorescence disappeared. This compound is 5-p-*nitrophenyl*-2-4′-*nitrostyrylfuran* (Found: C, 64·5, 64·5; H, 3·6, 3·7; N, 8·1, 8·3. $C_{18}H_{12}O_5N_2$ requires C, 64·4; H, 3·6; N, 8·3%). It dissolved in concentrated sulphuric acid with a wine-red colour which changed rapidly to dark purple.

The aqueous-acetone mother-liquor was steam-distilled. This removed *p*-chloronitrobenzene. The dark resinous residue was separated from the hot liquor which contained the bulk of unchanged furylacrylic acid, digested with dilute cold sodium hydrogen carbonate solution, and extracted 3 times with dilute aqueous ammonia. From the united filtered ammoniacal solutions, hydrochloric acid precipitated orange-coloured β-(5-p-*nitrophenyl*-2-*furyl*)*acrylic acid* which was filtered off and recrystallised from acetic acid from which it separated in thick brown prisms, m. p. 262° (3 g.), which dissolved in concentrated sulphuric acid with a golden yellow colour (Found: C, 60·3, 60·3; H, 3·6, 3·5; N, 5·4. $C_{13}H_9O_5N$ requires C, 60·2; H, 3·5; N, 5·3%). It did not fluoresce in any solvent.

The material remaining after the ammoniacal extraction was dried and extracted 3 times with absolute alcohol (150 c.c.), which was allowed to evaporate at room temperature. A brown mass, still somewhat resinous, remained. After two recrystallisations from light petroleum (b. p. 60—80°) and absolute alcohol, brown needles, m. p. 130—131°, of 2-*p*-nitrostyrylfuran were obtained (Brown and Kon, *loc. cit.*, give m. p. 130—131°) (Found: C, 67·1, 67·2; H, 4·3, 4·3; N, 6·6. Calc. for $C_{12}H_9O_3N$: C, 67·0; H, 4·2; N, 6·5%).

Oxidation of 5-p-*Nitrophenyl*-2-4′-*nitrostyrylfuran.*—5-*p*-Nitrophenyl-2-4′-nitrostyrylfuran (3·36 g.) in acetone (200 c.c.) containing crystalline magnesium sulphate (7·5 g.) was oxidised with potassium permanganate (4·5 g.), and then, as oxidation was incomplete, with acetone (100 c.c.), magnesium sulphate (2·5 g.), and potassium permanganate (1·5 g.). The furan nucleus was partly oxidised. The acetone was allowed to evaporate and the dark material freed from manganese dioxide with sulphur dioxide. A light yellow material (2·65 g.) was filtered off and extracted with cold dilute sodium hydrogen carbonate solution which removed *p*-nitrobenzoic acid (2·25 g.; m. p. and mixed m. p. 238—239°).

The reddish-brown solid insoluble in cold bicarbonate solution (0·4 g.) was twice recrystallised from absolute alcohol, yielding β-(5-p-*nitrophenyl*)-2-*furoic acid*, m. p. 204—205° (Found: C, 56·8, 56·8; H, 3·1, 3·1; N, 6·0. $C_{11}H_7O_5N$ requires C, 56·7; H, 3·0; N, 6·0%).

Oxidation of β-(5-p-*Nitrophenyl*-2-*furyl*)*acrylic Acid.*—β-5-*p*-Nitrophenylfurylacrylic acid (2·62 g.), when oxidised as above, gave 5-*p*-nitrophenyl-2-furoic acid, m. p. and mixed m. p. 204—205°.

Furylacrylic Acid and o-*Nitroaniline.*—*o*-Nitroaniline (6·9 g.) was diazotised with 25% hydrochloric acid (20—22 c.c.), ice (20 g.), and sodium nitrite (3·65 g.) in water (10 c.c.). The filtered solution was poured into a solution of furylacrylic acid (6·9 g.) in acetone (80 c.c.) containing crystalline sodium acetate (15—20 g.). The colour of the solution changed from orange-red to brown. There was brisk gas evolution. In spite of cooling, the temperature rose to 20°. Addition of a solution of cupric chloride (2 g.) in water (5 c.c.) did not revive noticeably the gas evolution which lasted for only about 10—15 minutes. The acetone was allowed to evaporate overnight. The dark resinous residue was digested with dilute hydrochloric acid, water, and then dilute cold sodium hydrogen carbonate solution from which on acidification some unchanged furylacrylic acid was recovered. The dark material was then extracted with dilute ammonia solution which was filtered and acidified. The precipitate was washed with cold sodium hydrogen carbonate solution and on crystallistion from benzene yielded β-(5-o-*nitrophenyl-2-furyl)acrylic acid* as brown needles, m. p. 178° (2·7 g.) (Found : N, 5·3, 5·4. $C_{13}H_9O_5N$ requires N, 5·3%).

Furylacrylic Acid and p-*Chloroaniline*.—*p*-Chloroaniline (12·75 g.), diazotised as above, was treated with furylacrylic acid (13·8 g.) at pH 6. Gas evolution set in at once and became violent after addition of a solution of cupric chloride (3 g.) in water (10 c.c.), but ceased after approx. 40 minutes. Working up, as above, yielded from the ammoniacal solution, a small amount of β-(5-p-*chlorophenyl-2-furyl)acrylic acid*, m. p. 196—198° (Found : Cl, 14·5. $C_{13}H_9O_3Cl$ requires Cl, 14·3%).

The dark ammonia-insoluble material was steam-distilled. 2-p-*Chlorostyrylfuran* which volatilised crystallised from light petroleum as yellowish rods, m. p. 97—98° (Found : C, 70·5, 70·6; H, 4·4, 4·5; Cl, 17·3. $C_{12}H_9OCl$ requires C, 70·4; H, 4·4; Cl, 17·4%).

The material involatile in steam was extracted with 3 × 200 c.c. of hot light petroleum (b. p. 70—90°). From these extracts small amounts of crystalline material were obtained of varying m. p. (118° to 125°). The mother-liquor after evaporation deposited material, from which crystallisation from methyl alcohol yielded a little 5-p-*chlorophenyl-2-4′-chlorostyrylfuran*, m. p. 135—136° (Found : C, 68·7, 68·7; H, 3·9, 3·9; Cl, 22·4. $C_{18}H_{12}OCl_2$ requires C, 68·6; H, 3·8; Cl, 22·5%).

A similar experiment (with Dr. A. Komzak), benzene being used instead of light petroleum for extraction, gave, as purest compound, material of m. p. 139—140°.

Furylacrylic Acid and Ethyl p-*Aminobenzoate* [with E. R. Stove].—Ethyl *p*-aminobenzoate (8·25 g.), diazotised in the usual way, was added to a solution of furylacrylic acid (6·9 g.), etc., as above. Gas evolution set in at once, was fastest after approx. 7 minutes, and then soon ceased. No cupric chloride was used. The mixture was poured into aqueous sodium hydrogen bicarbonate (15 g. in 150 c.c.), and the acetone was allowed to evaporate. The solution was filtered and the solid washed with water and cold dilute aqueous ammonia, and then extracted with dilute aqueous ammonia at 50°. Acidification yielded (?)β-(5-p-*carbethoxy-2-furyl)acrylic acid* as a brown solid which crystallised from benzene in sheafs of buff-coloured needles, m. p. 202—203° (2 g.) (Found : C, 67·4, 67·1; H, 5·1, 5·0; EtO, 15·6. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9; EtO, 15·7%).

The residue from the ammonia extraction was dried in a vacuum-desiccator and then extracted with methyl alcohol (500 c.c.), which on evaporation left crystals embedded in a resin. The crystals were separated mechanically, washed with a small amount of acetone, and recrystallised from absolute alcohol, yielding prisms, m. p. 135—140°. After a further recrystallisation from methyl alcohol, prisms with a golden sheen were obtained having m. p. 144° and soluble in benzene with a gentian-blue fluorescence. This compound is 2-p-*carboethoxyphenyl-5-4′-carbethoxystyrylfuran* (Found : EtO, 23·2. $C_{24}H_{22}O_5$ requires EtO, 23·1%).

Furylacrylic Acid and Sulphanilic Acid.—Diazotised sulphanilic acid (17·3 g.) was treated with furylacrylic acid (13·8 g.) at pH approx. 6. Cupric chloride was added. Gas evolution became rapid at 18—-20° and lasted for about 45 minutes. After a few hours, the mixture was steam-distilled and then allowed to cool. A solid crystallised which was filtered off and washed with cold alcohol which removed unchanged furylacrylic acid. β-(5-p-*Sulphophenyl-2-furyl)-acrylic acid* (1·2 g.) remained as a grey solid which crystallised from water in rods and plates, m. p. >300° (Found : C, 53·2, 53·1; H, 3·5, 3·3. $C_{13}H_{10}O_6S$ requires C, 53·1; H, 3·4%). Concentration of the mother-liquor gave crystals which fluoresced blue in acetic (characteristic of the diarylated compounds), but no pure material free from nitrogen was obtained.

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