

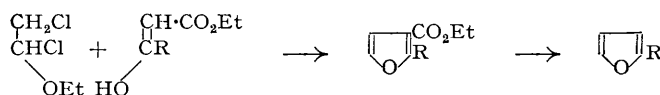
195. *Synthesis of 2-Arylfurans.*

By A. W. JOHNSON.

Interaction of furan with aryldiazonium chlorides in the presence of alkali, or with nitrosoacetanilides, yields 2-arylfurans with minor quantities of 3-arylfurans. By these methods the following have been prepared; 2-phenyl-, 2- and 3-*p*-chlorophenyl-, 2-*p*-nitrophenyl-, 2-*m*-chlorophenyl-, 2-*p*-bromophenyl-, and 2-*a*-naphthyl-furan. The structure of 2-*p*-chlorophenylfuran has been rigidly proved by independent synthesis and by the nature of the Diels-Alder adduct with acetylenedicarboxylic ester. Light-absorption data clearly differentiate between 2- and 3-arylfurans.

2-ARYLFURANS have been prepared previously in small quantities by the two following laborious routes :

(i) The condensation of 1 : 2-dichlorodiethyl ether with aroylacetic esters in the presence of 10% ammonium hydroxide yields a mixture of the 2-arylfuran-3-carboxylic ester together with the pyrrole analogue which is separated by fractionation. Hydrolysis and decarboxylation of the 2-arylfuran-3-carboxylic ester gives the corresponding 2-arylfuran :



The method is based on that of Benary (*Ber.*, 1911, **44**, 493) who synthesised 2-methylfuran from ethyl acetoacetate. 2-Phenylfuran (Kondo and Suzuki, *J. Pharm. Soc. Japan*, 1927, **544**, 501; Fujita, *ibid.*, 1925, **519**, 450) and 2-*p*-chlorophenylfuran (Wibaut and Dhont, *Rec. Trav. chim.*, 1943, **62**, 272) have been synthesised by this method.

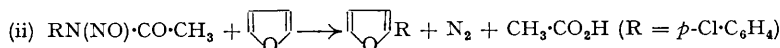
(ii) 4-Benzoyl-2-phenylfuran, obtained by a complicated synthesis, was converted into 2-phenylfuran-4-carboxylic acid by a Beckmann rearrangement of the oxime and hydrolysis of the amide. Decarboxylation of the acid gave 2-phenylfuran (Fuson, Fleming, and Johnson, *J. Amer. Chem. Soc.*, 1938, **60**, 1994). No chemical reactions of the 2-arylfurans have been described.

Other aryl substituted heterocyclic compounds have been prepared by the normal methods for the union of aryl nuclei (Bachmann and Hoffman, "Organic Reactions," 1944, **2**, 224), *e.g.*, arylthiophens (Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1924, **46**, 2339), arylpyrroles (Rinkes, *Rec. Trav. chim.*, 1943, **62**, 116), and arylpyridines (Heilbron, Hey, *et al.*, *J.*, 1940, 349, 355, 358, 372, 1279; 1943, 441). Of these methods the so-called Gomberg reaction is the most common: $\text{ArN}_2\text{OH} + \text{Ar}'\text{H} \longrightarrow \text{Ar}\cdot\text{Ar}' + \text{N}_2 + \text{H}_2\text{O}$. It is known that furan readily couples with aryldiazonium chlorides (Gilman, Wooley, and Vanderwal, *Proc. Iowa Acad. Sci.*, 1932, **29**, 176; Ochiai, *J. Pharm. Soc. Japan*, 1938, **58**, 1025), but the possibility of formation of arylfurans by the reaction of furan with alkaline or neutral solutions of diazonium hydroxides has not been investigated previously.

A modification of the Gomberg reaction as described by Elks, Haworth, and Hey (*J.*, 1940, 1284) was used for the condensation in which the equivalent quantity of aqueous sodium hydroxide or sodium acetate was added to a well-stirred mixture of the aqueous diazonium chloride and furan at 5–10°. In all the cases examined, the main identified product was the 2-arylfuran. The reaction between *p*-chlorobenzenediazonium acetate and furan has been examined in detail, and 3-*p*-chlorophenylfuran has been isolated in 0.7% yield as compared with the 29% yield of 2-*p*-chlorophenylfuran. In addition, traces of a higher-melting product were isolated from the reaction but the structure of this has not been determined.

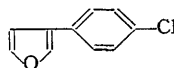
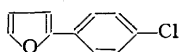
The following 2-arylfurans have also been obtained by this method : 2-phenylfuran (22%), 2-*p*-nitrophenylfuran (20%), 2-*m*-chlorophenylfuran (16%), 2-*p*-bromophenylfuran (15%), 2- α -naphthylfuran (18%) (and its *picrate*). 2-*p*-Aminophenylfuran (isolated as its *phenylurea*) was obtained from 2-*p*-nitrophenylfuran by hydrogenation at room temperature and pressure in the presence of Raney nickel.

Other standard methods of effecting the union of aryl nuclei have been investigated, in particular the reaction of furan with *p*-chloronitrosoacetanilide [obtained according to equation (i) and employed as shown in equation (ii)] (Heilbron, Hey, *et al.*, *J.*, 1940, 369, 372). This method has already been used for the preparation of arylpyridines (Heilbron, Hey, *et al.*, *loc. cit.*) and arylpyrroles (Rinkes, *loc. cit.*). 2-*p*-Chlorophenylfuran, identical with the product obtained by the Gomberg method, was obtained from the reaction in 19% yield :



An attempt to condense 1-*p*-chlorophenyl-3 : 3-dimethyltriazene with furan in the presence of hydrogen chloride or acetic acid (I.G., B.P., 513,846; Elks and Hey, *J.*, 1943, 441) was unsuccessful.

The arylfurans rapidly darkened on standing in air at room temperature and were best preserved in dark bottles. The physical constants of the phenylfuran obtained as the main identified product from the Gomberg reaction agreed closely with the values for 2-phenylfuran given in the literature (Kondo and Suzuki, *loc. cit.*; Fuson, Fleming, and Johnson, *loc. cit.*) but as phenylfuran was a liquid it was decided to study the orientation of the aryl groups of the readily obtainable solid *p*-chlorophenylfurans, the m. p. of the main product (74–75°) being appreciably higher than that given (67°) by Wibaut and Dhont (*loc. cit.*) for 2-*p*-chlorophenylfuran. It is evident that if the *p*-chlorophenyl group is in the 2-position of the furan nucleus, it is conjugated with both of the double bonds of the furan ring, but if it is in the 3-position then only the Δ^2 -double bond is in conjugation with the aryl group :



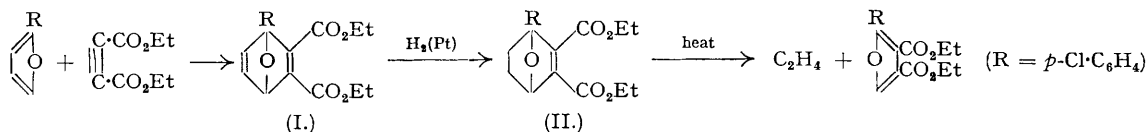
A determination of the ultra-violet absorption spectra of the two isomers in chloroform solution showed that the higher-melting product was the 2-*p*-chlorophenyl isomer and that the lower-melting product was the

3-*p*-chlorophenyl isomer. The ultra-violet absorption spectra of styrene and 1-phenylbutadiene are given for comparison (Dimroth, *Z. angew. Chem.*, 1939, **52**, 545).

	Maximum (A.).	$\epsilon_{\text{max.}}$
Isomer, m. p. 74—75°	2870	20,600
PhCH:CH:CH:CH ₂	2800	24,400
Isomer, m. p. 50—51°	2620	13,200
PhCH:CH ₂	2450	15,000

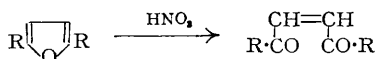
The positions of the maxima of the ultra-violet absorption curves are at a greater wave-length for the *p*-chlorophenylfurans than for the corresponding phenylethylenic hydrocarbons as the double bonds conjugated with the *p*-chlorophenyl group are themselves part of a cyclic system. The chlorine atom has a negligible effect on the absorption spectrum over the wave-lengths under consideration. The presence of a phenyl group in conjugation is roughly equivalent to 1.5 conjugated double bonds (Dimroth, *loc. cit.*).

A further proof that the product, m. p. 74—75°, from the Gomberg reaction of furan and *p*-chlorobenzene-diazonium acetate was 2-*p*-chlorophenylfuran was afforded by the Diels-Alder addition to ethyl acetylenedicarboxylate (cf. Alder and Rickert, *Ber.*, 1937, **70**, 1354; Hofmann, *J. Amer. Chem. Soc.*, 1944, **66**, 51, 157; 1945, **67**, 421). The primary addition product (I) was hydrogenated in the presence of Adams's catalyst, when the dihydro-adduct (II) was obtained, which on heating lost ethylene and gave ethyl 2-*p*-chlorophenylfuran-3 : 4-dicarboxylate, m. p. 60—61°. Had the *p*-chlorophenyl group been in the 3-position in the furan ring, *p*-chlorostyrene would have been eliminated with the formation of furan-3 : 4-dicarboxylic ester :



2-*p*-Chlorophenylfuran has been synthesised by a method essentially that of Wibaut and Dhont (*loc. cit.*), and the product proved to be identical with the main product isolated from the reaction of furan with *p*-chlorobenzene-diazonium acetate or *p*-chloronitrosoacetanilide. The 1 : 2-dichlorodiethyl ether required for the synthesis was obtained by the addition of chlorine to ethyl vinyl ether in chloroform solution. An attempted condensation of the more readily available 1 : 2-dichloroethyl isobutyl ether with ethyl *p*-chlorobenzoylacetate was unsuccessful.

Lutz and Wilder (*J. Amer. Chem. Soc.*, 1934, **56**, 978) have described the oxidation of 2 : 5-diarylfurans to 1 : 2-diaroylethylenes, usually in excellent yields, by the action of nitric acid in acetic acid :



All attempts to convert 2-*p*-chlorophenylfuran into β -*p*-chlorobenzoylacrylic acid by this method have been unsuccessful, and *p*-chlorobenzoic acid was obtained in every experiment.

EXPERIMENTAL.

Preparation of Arylfurans.—The amine ($\frac{1}{2}$ mole) in presence of concentrated hydrochloric acid (160 c.c.) and water (90 c.c.) was diazotised in the normal manner with aqueous sodium nitrite. The filtered diazonium solution was added to furan and vigorously stirred at 5—10° while a solution of 5*N*-sodium hydroxide (300 c.c.) (method *A*) or a solution of sodium acetate (160 g. of trihydrate) in water (400 c.c.) (method *B*) was added over $\frac{1}{2}$ hour. Stirring was continued for 48 hours, the reaction being allowed to continue at room temperature after the first 5 hours. The furan layer was then separated, washed with water, and dried. After removal of the excess of furan the residue was purified by distillation under reduced pressure or in steam.

Phenylfuran.—Prepared by method *A*. The crude product (25.7 g.) was distilled in a vacuum and the following fractions obtained : (i) 3.0 g., b. p. 70—80°/15 mm., n_D^{20} 1.5547; (ii) 16.3 g., b. p. 92—95°/10 mm., n_D^{20} 1.5920. Fraction (ii) was 2-phenylfuran (22%) (Fuson, Fleming, and Johnson, *J. Amer. Chem. Soc.*, 1938, **60**, 1994, give b. p. 107—108°/18 mm., n_D^{20} 1.5968, for 2-phenylfuran). Fraction (i) has not been further investigated.

p-Chlorophenylfuran.—Prepared by method *A*. The crude product was distilled in steam (3 hours) and the first 200 c.c. of the distillate kept separate from the remainder. The oil which was obtained in the main distillate rapidly solidified and was separated (25 g.; 29%) and crystallised from aqueous methanol when 2-*p*-chlorophenylfuran was obtained as colourless plates, m. p. 74—75° (Found : C, 67.3; H, 4.2; Cl, 19.6. Calc. for C₁₀H₇OCl : C, 67.2; H, 3.9; Cl, 19.9%). 2-*p*-Chlorophenylfuran slowly darkens in air and gives a permanganate-coloured solution in concentrated sulphuric acid from which the original furan is not precipitated on dilution.

The oil which was obtained in the first portion of the steam distillation was extracted with ether (3 \times 100 c.c.); the combined ethereal extracts were dried and the solvent was removed. After three days at room temperature the residual oil (2.5 g.) partly solidified and the solid (approx. 1 g.; m. p. 67—69°) separated; this, after crystallisation from aqueous methanol, had m. p. 74—75° alone and in admixture with authentic 2-*p*-chlorophenylfuran. The filtrate was distilled in a vacuum and the main fraction, b. p. 95—115°/10 mm. (0.6 g.), collected. On cooling, the distillate solidified; it had m. p. 50—51° after repeated crystallisations from light petroleum (b. p. 60—80°) (mixed m. p. with 2-*p*-chlorophenylfuran, 38—45°) (Found : C, 67.1; H, 3.8. C₁₀H₇OCl requires C, 67.2; H, 3.9%). The product, 3-*p*-chlorophenylfuran, dissolved in concentrated sulphuric acid to give an orange coloured solution.

The residue from the steam distillation was extracted with benzene (3 \times 150 c.c.); the combined benzene extracts were washed and the solvent was removed. The residue was sublimed in a vacuum at 100°; 2-*p*-chlorophenylfuran (1 g.) was first obtained, followed by an unidentified compound (0.1 g.) which formed colourless needles, m. p. 86—87°, from light petroleum (b. p. 40—60°).

2-p-Nitrophenylfuran.—Prepared by method *B*. The crude product was dissolved in benzene (100 c.c.) and purified by chromatography on alumina. The bright yellow band was eluted with benzene containing 5% of methanol, leaving a dark brown residue, and the solvent was removed from the eluate. The residual product formed yellow needles after crystallisation from aqueous ethanol, m. p. 134—135° (19.0 g.; 19.7%) (Found: C, 63.25; H, 3.45; N, 7.4. $C_{10}H_7O_3N$ requires C, 63.4; H, 3.7; N, 7.4%).

2-m-Chlorophenylfuran.—Prepared by method *A*. The crude product was distilled in steam (3 hours) and the distillate extracted with ether (3×250 c.c.). The combined ethereal extracts were washed with 2*N*-sodium hydroxide and then water, and dried. The residue after removal of solvent was distilled in a vacuum; *2-m-chlorophenylfuran* was thus obtained as a colourless oil (14 g.; 16%), b. p. 137°/15 mm.; n_D^{25} 1.6053 (Found: C, 66.9; H, 4.2; Cl, 19.7. $C_{10}H_7OCl$ requires C, 67.2; H, 3.9; Cl, 19.9%).

2-p-Bromophenylfuran.—Prepared by method *A* on 0.1-mole scale. The crude product was distilled in steam. The yellow solid obtained in the distillate was separated and crystallised from aqueous methanol to yield *2-p-bromophenylfuran* (3.35 g.; 15%) as colourless plates, m. p. 85—86° (Found: C, 54.1; H, 3.4; Br, 35.8. $C_{10}H_7OBr$ requires C, 53.8; H, 3.1; Br, 35.9%).

2-a-Naphthylfuran.—Prepared by method *B*. The residue was distilled in steam (4 hours) and the distillate extracted with ether (3×200 c.c.), and the combined ethereal extracts were washed with 2*N*-sodium hydroxide and water, and dried. After removal of the solvent the residue was distilled in a vacuum. The main fraction, *2-a-naphthylfuran*, was a pale yellow oil (17.3 g.; 18%), b. p. 90—91°/0.02 mm. (Found: C, 86.5; H, 5.0. $C_{14}H_{10}O$ requires C, 86.6; H, 5.2%). The *picrate*, m. p. 105—106°, formed dark red prisms from methanol (Found: C, 56.65; H, 3.0; N, 10.2. $C_{20}H_{13}O_6N_3$ requires C, 56.7; H, 3.1; N, 9.9%). A little naphthalene was obtained as a white sublimate in the condenser in the early stage of the distillation.

2-p-Aminophenylfuran.—A suspension of *2-p-nitrophenylfuran* (1 g.) in methanol (70 c.c.) was hydrogenated at room temperature and pressure in the presence of Raney nickel (1 g.). The absorption of hydrogen was very rapid, and three equivalents (456 c.c. at N.T.P. Calc. for $C_{10}H_7O_3N \rightarrow C_{10}H_9ON$, 462 c.c.) were absorbed after 14 minutes, when absorption ceased. The catalyst was separated and the solvent removed leaving *2-p-aminophenylfuran* as a pale yellow solid, m. p. 53—54° after crystallisation from light petroleum (b. p. 40—60°). The solid decomposed to a brown oil when kept in air for 2 days, and owing to this fairly rapid decomposition a satisfactory analysis was not obtained. The corresponding *phenylurea*, m. p. 227—228°, formed colourless plates from ethanol (Found: C, 73.5; H, 5.3; N, 10.15. $C_{17}H_{14}O_2N_2$ requires C, 73.2; H, 5.1; N, 10.1%).

Reaction of p-Chloronitrosoacetanilide with Furan.—A mixture of *p*-chloroacetanilide (18 g.), acetic anhydride (80 c.c.), acetic acid (80 c.c.), fused potassium acetate (12 g.), and phosphoric oxide (1 g.) was stirred and cooled to 8°, while a stream of nitrosyl chloride was passed in until excess was present (brown fumes emitted). The mixture was poured into ice-water (1000 c.c.) and the precipitated *p*-chloronitrosoacetanilide rapidly separated and dried on a porous tile. The solid was dissolved in furan (500 c.c.), and the solution dried (Na_2SO_4) and left overnight. Nitrogen was evolved from the solution. The excess of furan was removed on the steam-bath and the residue distilled in steam. *2-p-Chlorophenylfuran* was obtained in the distillate as a pale brown solid which was separated and crystallised from aqueous methanol. The product (3.65 g.; 19%) formed colourless plates, m. p. 74—75° alone and mixed with the product of the Gomberg reaction.

1-p-Chlorophenyl-3:5-dimethyltriazene.—An aqueous solution of diazotised *p*-chloroaniline ($\frac{1}{2}$ mole) was added slowly from a cooled dropping funnel to a cooled stirred mixture of dimethylamine (25%; 100 g.) and sodium carbonate (130 g.) in water (400 c.c.). Stirring was continued for $\frac{1}{2}$ hour and the precipitated *1-p-chlorophenyl-3:3-dimethyltriazene* separated, washed, pressed, and crystallised from aqueous methanol; it formed colourless plates, m. p. 56—57° (78 g.; 85%) (Found: N, 22.5; Cl, 19.3. $C_8H_{10}N_3Cl$ requires N, 22.9; Cl, 19.3%).

Reaction of 1-p-Chlorophenyl-3:3-dimethyltriazene with Furan.—*1-p-Chlorophenyl-3:3-dimethyltriazene* (20 g.) was dissolved in a mixture of furan (200 c.c.) and acetic acid (30 c.c.) and the solution heated under reflux overnight. The excess of furan was removed on the steam-bath and the black tarry residue extracted with ether (3×100 c.c.), and the combined ethereal extracts were washed and dried, and the solvent was removed. The residue was a dark coloured oil which could not be induced to crystallise.

Repetition of the above experiment using excess of dry hydrogen chloride instead of acetic acid also failed to yield any *p*-chlorophenylfuran.

1:2-Dichlorodiethyl Ether.—A solution of chlorine (18 g.) in carbon tetrachloride (200 c.c.) was added slowly to a solution of ethyl vinyl ether (20 g.) in carbon tetrachloride (50 c.c.) with stirring and ice cooling. The mixture was stirred overnight and the solvent then removed on the steam-bath. The residue was distilled in a vacuum, and *1:2-dichlorodiethyl ether* was obtained as a colourless oil (18 g.; 45%), b. p. 43—45°/15 mm. [Wildman and Gray (*J. Amer. Chem. Soc.*, 1919, **41**, 1122) give b. p. 66—69°/45 mm.]. There was a considerable black residue after the distillation.

Condensation of 1:2-Dichlorodiethyl Ether and Ethyl p-Chlorobenzoylacetate.—Ethyl *p*-chlorobenzoylacetate, m. p. 37—38° [Thorpe and Brunskill (*J. Amer. Chem. Soc.*, 1915, **37**, 1261) give m. p. 38°], was prepared in 45% yield by the condensation of ethyl *p*-chlorobenzoate and ethyl acetoacetate according to the method of McElvain and Weber (*Org. Synth.*, 1943, **23**, 35).

The condensation of ethyl *p*-chlorobenzoylacetate and *1:2-dichlorodiethyl ether* was effected in the presence of 10% ammonia solution, the method and extraction being essentially that described by Wibaut and Dhont (*Rec. Trav. chim.*, 1943, **62**, 272). The ethyl *2-p-chlorophenylfuran-3-carboxylate*, b. p. 125—130°/0.1 mm., was not purified but the crude product was hydrolysed to the corresponding acid, m. p. 193—194° (from light petroleum, b. p. 80—100°) [Wibaut and Dhont (*loc. cit.*) give m. p. 194°]. *2-p-Chlorophenylfuran-3-carboxylic acid* (0.2 g.) was heated in a sealed tube at 275° overnight. The product was extracted with ether (3×20 c.c.); the combined ethereal extracts were washed with sodium hydrogen carbonate solution and dried, and the solvent was removed. The residue was crystallised from aqueous methanol with carbon clarification and yielded *2-p-chlorophenylfuran* (0.08 g.), m. p. 70—71° alone and on admixture with the product of the Gomberg reaction. Lack of material prevented the complete purification of this product.

1:2-Dichloroethyl isoButyl Ether.—A solution of chlorine (15 g.) in carbon tetrachloride (150 c.c.) was added to a solution of *isobutyl vinyl ether* (20 g.) in carbon tetrachloride (20 c.c.) at 0° with stirring. The addition was very rapid and, after 15 minutes' stirring, the solvent was removed on the steam-bath and the residue distilled in a vacuum to yield *1:2-dichloroethyl isobutyl ether* (30.2 g.) as a colourless oil, b. p. 85°/43 mm., 82°/37 mm., n_D^{21} 1.642 (Found: Cl, 41.4. $C_8H_{12}OCl_2$ requires Cl, 41.5%).

Reaction of 2-p-Chlorophenylfuran and Ethyl Acetylenedicarboxylate.—*2-p-Chlorophenylfuran* (9.6 g.) and ethyl acetylenedicarboxylate (9.1 g.) were heated at 100° overnight. The crude product was dissolved in ethyl acetate (70 c.c.) and hydrogenated over Adams's platinum catalyst (0.5 g.) at room temperature and pressure. Absorption of hydrogen had almost ceased after 5½ hours when approximately $\frac{1}{4}$ of the theoretical volume of hydrogen for one equivalent (1200 c.c.) had been taken up. The reaction was then discontinued, the catalyst separated, and the residue distilled

in a vacuum. The main fraction, b. p. 168—170°/0.2 mm. (5.9 g.), solidified on cooling and after crystallisation from light petroleum (b. p. 60—80°) had m. p. 60—61°; it was *ethyl 2-p-chlorophenylfuran-3:4-dicarboxylate* (Found: C, 59.1; H, 4.45; Cl, 11.3. $C_{18}H_{15}O_5Cl$ requires C, 59.5; H, 4.65; Cl, 11.0%).

The author is indebted to Mr. J. D. Rose for advice throughout the work, and to Dr. A. Lambert who made the original suggestion that 2-arylfurans might be obtained by the methods described.

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