

## Reaction of 2,4-Dinitrobenzenediazonium Ions with Thiophens. Part 1. An Acidic Gomberg Reaction

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The reaction of 2,4-dinitrobenzenediazonium ions with a number of thiophen derivatives has been investigated. Under conditions in which 2,4-dinitrobenzenediazonium ions couple with anisole to yield an azo-dye, the same ions interact with thiophen with evolution of nitrogen to yield 2-(2,4-dinitrophenyl)thiophen. Similar arylation occurs with the two monomethylthiophens and with benzo[*b*]thiophen. Other alkylthiophens undergo coupling reactions (see following paper). Mechanisms for the arylation reaction are discussed.

THIOPHEN undergoes electrophilic aromatic substitution much more readily than benzene. Where comparative data are available the similarity in reactivity of anisole and thiophen is striking (see Table). Anisole couples

TABLE I

Partial rate factors for bromination, chlorination, protodesilylation, and nitration of anisole (*para*-position) and thiophen (2-position)

Reaction	Partial rate factors (25 °C)		Ref.
	Thiophen	Anisole	
Bromination	$1.7 \times 10^9$	$1.1 \times 10^{10}$	<i>a, b</i>
Chlorination	$1.3 \times 10^7$	$9.7 \times 10^6$	<i>a, c</i>
Protodesilylation	$5 \times 10^3$	$1.01 \times 10^3$	<i>d</i>
Nitration	$1.5 \times 10^2$	$1.7 \times 10^2$	<i>e</i>

\* G. Marino, *Tetrahedron*, 1965, **21**, 843. <sup>b</sup> R. O. C. Norman and R. Taylor, 'Electrophilic Substitution in Benzenoid Compounds,' Elsevier, Amsterdam, 1965, p. 139. <sup>c</sup> L. M. Stock 'Aromatic Substitution Reactions,' Prentice-Hall, Englewood, 1969, p. 43. <sup>d</sup> F. B. Dean and C. Eaborn, *J. Chem. Soc.*, 1959, 2299, 2303. <sup>e</sup> J. G. Hoggett, R. B. Moodie, and K. Schofield, *J. Chem. Soc. (B)*, 1969, 1.

with 2,4-dinitrobenzenediazonium ions,<sup>1</sup> but until the present work there has been no report of thiophen or any hydrocarbon thiophen derivatives coupling with a diazonium salt. 2-Amino-<sup>2</sup> and 2-acetamido-thiophen<sup>3</sup> couple with diazonium salts to give azo-dyes, and there are a number of reports of 3-hydroxybenzo[*b*]thiophen coupling in the 2-position.<sup>4</sup> The only reactions of thiophen itself with diazonium salts previously reported are arylation reactions. Gomberg and Bachmann, using alkaline conditions, carried out a series of arylations of benzene and thiophen; the yields of substituted biphenyls and phenylthiophens were very similar.<sup>5</sup> More recently a systematic study of thiophen arylation has been undertaken with diaroyl peroxides and nitrosoacetanilides as well as by the Gomberg reaction.<sup>6</sup> In neither of these investigations was any coupling reported; indeed the conditions and particular diazonium salts make coupling unlikely. Since the preliminary account of this work there has been a report of coupling with concurrent decarboxylation of thiophen-3-diazonium-2-carboxylate.<sup>7</sup>

In parallel experiments thiophen and anisole were treated with 2,4-dinitrobenzenediazonium sulphate in

<sup>1</sup> K. H. Meyer, A. Irschick, and H. Schösser, *Ber.*, 1914, **47**, 1741.

<sup>2</sup> O. Stadler, *Ber.*, 1885, **18**, 2316.

<sup>3</sup> C. D. Hurd and H. M. Priestley, *J. Amer. Chem. Soc.*, 1947, **69**, 859.

<sup>4</sup> P. Friedlaender, *Monatsh.*, 1909, **30**, 347.

glacial acetic acid at 0 °C for 70 h. 1-(2,4-Dinitrophenylazo)-4-methoxybenzene was isolated in 26% yield from the anisole experiment, whereas from the thiophen experiment no azo-compound was isolated but instead the isolated products were 2-(2,4-dinitrophenyl)thiophen (17%); 2,5-bis-(2,4-dinitrophenyl)thiophen (2.8%), and 2,3,5-tris-(2,4-dinitrophenyl)thiophen (<2%). The occurrence of arylation in a cold acidic diazonium salt solution, under conditions in which the diazonium salt is stable, was most unexpected. The decomposition of the diazonium salt to give 2,4-dinitroaryl radicals appeared to be induced either by thiophen itself or else by some product derived from it. This was confirmed by adding equal portions of the 2,4-dinitrobenzenediazonium salt solution severally to equimolar portions of thiophen, benzene, and anisole. The reaction vessels containing the thiophen and benzene solutions were connected to nitrometers and the evolution of nitrogen was monitored. After 24 h at room temperature no nitrogen had been evolved from the benzene solution, whereas the thiophen solution had evolved 75% of the theoretical maximum. Further evidence that the arylation is initiated by the thiophen nucleus, and not a result of the spontaneous decomposition of the diazonium salt, is provided by the reaction in trifluoroacetic acid. When a solution of thiophen in trifluoroacetic acid was treated with 2,4-dinitrobenzenediazonium trifluoroacetate in the same solvent a rapid evolution of nitrogen ensued almost immediately. The solution developed a deep blue colour and on work-up the principal product was 2-(2,4-dinitrophenyl)thiophen.

2-Methyl- and 3-methyl-thiophen also gave mono-arylation products when treated with 2,4-dinitrobenzenediazonium sulphate in acetic acid at 0 °C. 2-Methylthiophen gave in addition a trace of a bis-(2,4-dinitrophenyl)-2-methylthiophen, and the 3-methylthiophen gave besides 2-(2,4-dinitrophenyl)-3-methylthiophen a trace of a coloured product which was present in too small a yield for complete characterisation; however an accurate mass determination indicated that it was probably 2-(2,4-dinitrophenylazo)-3-methylthiophen. 2-*t*-Butylthiophen and the polymethylthiophens studied all gave azo-coupled products (see following paper).

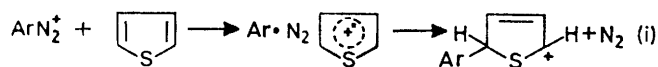
<sup>5</sup> M. Gomberg and W. E. Bachmann, *J. Amer. Chem. Soc.*, 1924, **46**, 2339.

<sup>6</sup> C. M. Camaggi, R. Leardini, M. Tiecco, and A. Tundo, *J. Chem. Soc. (B)*, 1969, 1251, and references therein.

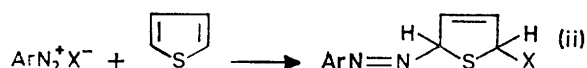
<sup>7</sup> M. G. Reinecke and R. H. Walter, *J.C.S. Chem. Comm.*, 1974, 1044.

Benzo[*b*]thiophen on the other hand behaved like the parent compound and underwent arylation when treated with an acidic solution of 2,4-dinitrobenzene-diazonium salt. 2-Methyl- and 3-methyl-benzo[*b*]thiophen undergo coupling (see following paper).

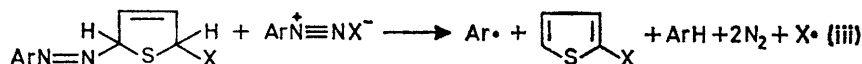
There is little precedent for aromatic compounds initiating the decomposition of aromatic diazonium salts in acidic media. Ferrocene induces the decomposition of benzenediazonium chloride with concomitant phenylation of the ferrocene.<sup>8</sup> The arylation observed in the present studies probably involves 2,4-dinitrophenyl



radicals since the corresponding carbocations would be unlikely to attack a thiophen nucleus which was already substituted by a 2,4-dinitrophenyl group. Furthermore



when an excess of benzene was added some 2,4-dinitro-biphenyl was observed. However 2,4-dinitrobenzene was never present in the products in appreciable yield, nor were significant amounts of 2,2',4,4'-tetranitro-biphenyl isolated. 2-Phenylthiophen was treated with



diazonium salt solution in the expectation that some arylation would occur in the benzene ring. However this compound coupled smoothly to give the azo-dye (see following paper).

The simplest conceivable mechanism for the arylation reaction involves electron transfer followed by decomposition of the diazonium salt and coupling of the aryl radical with the thiophen radical cation [reaction (i)]. Loss of a proton would then lead to the product. The objections to this mechanism are two-fold. When the diazonium salt is treated with an excess of thiophen the yield of monoarylthiophen is ca. 45% (based on the diazonium salt). If electron transfer were the initial step then the polyalkylthiophens should undergo arylation too, since electron transfer would be expected to be faster than the coupling reaction. A mechanism consistent with the yield in the presence of an excess of thiophen involves coupling followed by addition of an anion (*i.e.* 2,5-electrophilic addition, characteristic of furan) [reaction (ii)]. The resulting adduct would be very susceptible to oxidation, and 2,4-dinitrobenzene-diazonium ions are powerful oxidizing agents [reaction (iii)]. This mechanism, though consistent with the stoichiometry, can be ruled out because little 2,4-dinitrobenzene was found and no product corresponding to the substituted thiophen (X = HSO<sub>4</sub> or AcO) was

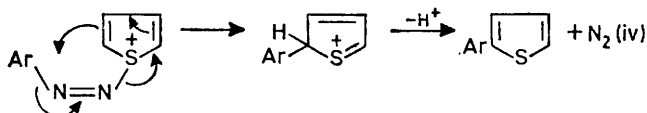
observed [except with benzo[*b*]thiophen, from which a trace of 3-hydroxy-2-(2,4-dinitrophenylazo)-derivative was obtained, which could be a by-product from such a mechanism]. A third alternative mechanism would involve coupling through the sulphur [reaction (iv)].

The great difficulty in elucidating the mechanism has been the incomplete recovery of the starting materials. When the reaction mixture is poured into water the insoluble products, consisting mainly of the arylated thiophens, are easily extracted and purified by chromatography. However other trace products remain on the column, and in addition the water-soluble products are almost impossible to isolate from the aqueous solution which contains sulphuric and acetic acids.

The fact that coupling occurs with polyalkylthiophens suggests that there is competition between arylation and coupling, and if the nucleus is sufficiently activated coupling is preferred. However it is hard to accept that either the *t*-butyl group or the phenyl group is more activating than a methyl group, and yet 2-*t*-butyl- and 2-phenyl-thiophen undergo coupling, whereas 2-methylthiophen is arylated. These results suggest that steric hindrance may play some part in the reaction and provide some support for the mechanism involving coupling through the sulphur.

The mechanism of the arylation remains uncertain, and the reaction represents a new type of aromatic

substitution which has no exact parallel. The nearest appears to be the interaction of arenediazonium tetrafluoroborates with 2,4,6-trisubstituted λ<sup>3</sup>-phosphorins.



Two arylation products are formed from 2,4,6-triphenyl-λ<sup>3</sup>-phosphorin, 1-aryl-1-methoxy-2,4,6-triphenyl-λ<sup>3</sup>-phosphorin and the analogous compound with the 4-phenyl arylated in the *para*-position.<sup>9</sup>

#### EXPERIMENTAL

**Diazotisation of 2,4-Dinitroaniline.**—Sodium nitrite (7.0 g) was added gradually to concentrated sulphuric acid (110 cm<sup>3</sup>) and the mixture was heated to 70 °C. The resultant solution was allowed to cool to 35 °C before 2,4-dinitroaniline (18.3 g) was added, then stirred at room temperature for 1.5 h, and poured onto crushed ice (200 g). The aqueous solution (containing 0.1 mol of diazonium salt) was filtered before use in coupling experiments.

**Coupling with Anisole.**—The diazonium salt solution (0.05 mol of diazonium salt) was added to anisole (5.4 g) in glacial acetic acid (200 cm<sup>3</sup>) and the combined solution maintained at 0 °C for 68 h with stirring. A red precipitate (3.5 g) was filtered off and recrystallised from acetone-petroleum (b.p. 60–80 °C) to give 1-(2,4-dinitrophenylazo)-4-methoxybenzene as orange needles, m.p. 177–178° (lit.,<sup>1</sup>

<sup>8</sup> G. D. Broadhead and P. L. Pauson, *J. Chem. Soc.*, 1955, 367.

<sup>9</sup> O. Schaffer and K. Dimroth, *Chem. Ber.*, 1975, 108, 3281.

177<sup>+</sup>), *m/e* 302 ( $M^+$ ) (Found: C, 51.5; H, 3.2; N, 18.35. Calc. for  $C_{13}H_{10}N_4O_5$ : C, 51.65; H, 3.3; N, 18.55%). The filtrate was diluted with water and extracted with chloroform; the extract was washed with aqueous sodium hydrogen carbonate and water, dried ( $MgSO_4$ ), and evaporated. The resulting red oil (0.8 g) which was chromatographed on alumina to yield further azo-dye (0.4 g; total yield 26%) and impure 2,4-bis-(2,4-dinitrophenyl)-1-methoxybenzene (0.02 g), *m/e* 440 ( $M^+$ ).

**Reaction with Thiophen.**—Freshly prepared diazonium salt solution (0.05 mol of diazonium salt) was added to a solution of thiophen (4.2 g) in glacial acetic acid (200 cm<sup>3</sup>), and the combined solution was stirred at 0 °C for 70 h. The solution was then diluted and a red oily precipitate which separated was taken up in chloroform, and washed with water and aqueous sodium hydrogen carbonate. After drying the solution was evaporated to yield a red oil (1.8 g). The main filtrate was also extracted with chloroform and the extract after similar treatment yielded a red oil (3.7 g). The two crude products were separately chromatographed on alumina. Benzene eluted 2-(2,4-dinitrophenyl)thiophen, m.p. 60°, *m/e* 250 ( $M^+$ ) (Found: C, 48.3; H, 2.4; N, 11.2.  $C_{10}H_6N_2O_4S$  requires C, 48.0; H, 2.4; N, 11.2%);  $\delta$  7.17 (2 H, m), 7.54 (1 H, dd, *J* 4 and 1 Hz), 7.76 (1 H, d, *J* 9 Hz), 8.38 (1 H, dd, *J* 9 and 1 Hz), and 8.55 (1 H, d, *J* 2 Hz). More benzene eluted 2,5-bis-(2,4-dinitrophenyl)thiophen, m.p. 172°, *m/e* 416 ( $M^+$ ) (Found: C, 46.45; H, 1.9; N, 13.3.  $C_{16}H_8N_4O_8S$  requires C, 46.15; H, 1.9; N, 13.45%). Chloroform eluted a red oil which crystallised from benzene-petrol to give impure red crystals; the mass spectrum indicated the presence of 2,3,5-tris-(2,4-dinitrophenyl)thiophen, *m/e* 582 ( $M^+$ ). Analysis showed this product was contaminated with monoarylated material. The total yields from both columns were: 2-(2,4-dinitrophenyl)thiophen 2.1 g (17%); bis-2,4-(2,4-dinitrophenyl)thiophen 0.58 g (2.8%); impure tris-(2,4-dinitrophenyl)thiophen 0.6 g. The experiment was repeated on a larger scale in order to complete the identification of the minor product. However 2-(2,4-dinitrophenyl)thiophen is light-sensitive and attempts to purify the minor products further were unsuccessful. The mass spectra of the minor products gave no evidence for high molecular weight polymers. The experiment was twice repeated [(a) thiophen (8.4 g, 0.1 mol) and diazonium salt (0.01 mol); (b) thiophen (0.84 g, 0.01 mol) and diazonium salt (0.05 mol)]. Experiment (a) yielded 1.31 g of 2-(2,4-dinitrophenyl)thiophen and experiment (b) yielded 0.48 g.

**Reaction with 2-Methylthiophen.**—The diazonium salt solution (0.01 mol) was added to a solution of 2-methylthiophen (0.98 g) in glacial acetic acid (40 cm<sup>3</sup>). The combined solution was stirred for 24 h at room temperature during which time a tarry precipitate was formed. The mixture was diluted and the whole extracted with chloroform. After washing and drying ( $Na_2SO_4$ ), evaporation left a crude product which was separated by chromatography on alumina. The principal product eluted by benzene was 2-(2,4-dinitrophenyl)-5-methylthiophen, m.p. 73.5–74°,  $\lambda_{max}$  208 ( $\epsilon$   $1.6 \times 10^4$ ), 235 ( $1.5 \times 10^4$ ), and 350 nm ( $8.9 \times 10^3$ ),  $\delta$  2.7 (3 H, s), 6.75 (1 H, m), 7.02 (1 H, d, *J* 3.5 Hz), 7.69 (1 H, d, *J* 8.5 Hz), 8.33 (1 H, dd, *J* 8.5 and 2.5 Hz), and 8.5 (1 H, d, *J* 2.5 Hz); irradiation at  $\delta$  2.7 ( $CH_3$ ) caused the multiplet at  $\delta$  6.75 to collapse to a doublet, thus confirming that the second substituent was at the 5-position; *m/e*

264 ( $M^+$ ) (Found: C, 49.9; H, 3.05; N, 10.2.  $C_{11}H_8N_2O_4S$  requires C, 50.0; H, 3.05; N, 10.6%). Further, trace fractions were eluted by chloroform and methanol. The second fraction appeared to contain 3,5-bis-(2,4-dinitrophenyl)-2-methylthiophen from the mass spectrum (*m/e* 430) and from micro-cell n.m.r. which indicated a proportion of two 2,4-dinitrophenyl residues to one of 2-methylthiophen. There was insufficient material for further purification. The total yield of 2-(2,4-dinitrophenyl)-5-methylthiophen was 0.68 g (24.6%).

The experiment was repeated with a coupling time of 68 h at 0 °C. The only product isolated was 2-(2,4-dinitrophenyl)-5-methylthiophen; the trace products appeared similar to those obtained before.

**Reaction with 3-Methylthiophen.**—3-Methylthiophen (0.58 g) in acetic acid (24 cm<sup>3</sup>) was added to the diazonium salt solution (0.01 mol); the mixture was stirred for 71 h at 0 °C then filtered, and the precipitate was taken up in chloroform and thoroughly washed and dried ( $Na_2SO_4$ ). Evaporation left a black oil (1.85 g) which was chromatographed on silica. Benzene eluted 2-(2,4-dinitrophenyl)-3-methylthiophen (0.5 g, 33.3%), m.p. 92–93°;  $\lambda_{max}$  233 ( $\epsilon$   $1.8 \times 10^4$ ) and 335 nm ( $4.8 \times 10^3$ );  $\delta$  2.8 (3 H, s), 6.94 (1 H, d, *J* 5 Hz), 7.38 (1 H, d, *J* 5 Hz), 7.70 (1 H, d, *J* 9 Hz), 8.45 (1 H, dd, *J* 9 and 2.2 Hz), and 8.83 (1 H, d, *J* 2.2 Hz). The coupling of the thiophen protons is within the range 4.6–5.8 Hz expected for 2,3-proton coupling, rather than 1.0–1.3 Hz expected for 2,4-proton coupling (*i.e.* the dinitrophenyl group is in the 2-position). This assignment is confirmed by the mass spectrum: *m/e* 264 ( $M^+$ ), 249 ( $M^+ - CH_3$ ), and 247 ( $M^+ - OH$ ). Loss of OH is only possible if the methyl and the 2,4-dinitrophenyl are in *ortho*-positions (Found: C, 50.3; H, 2.9; N, 10.3.  $C_{11}H_8N_2O_4S$  requires C, 50.0; H, 3.05; N, 10.6%). The mass spectrum of a trace product suggested that 2-(2,4-dinitrophenylazo)-3-methyl-5-(3-methyl-2-thienyl)thiophen was present, but there was insufficient for proper characterisation.

**Reaction with Benzo[b]thiophen.**—A solution of the diazonium salt (0.05 mol) was added to a solution of benzo[b]thiophen (6.7 g) in glacial acetic acid (200 cm<sup>3</sup>) and the mixture was stirred at 0 °C for 52 h. A small amount of precipitate formed, which was filtered off and crystallised from benzene-petrol (b.p. 60–80°) to give a bright orange compound (0.2 g) tentatively identified as 2-(2,4-dinitrophenylazo)benzo[b]thiophen-3-ol, m.p. 290° (decomp.); *m/e* 344 ( $M^+$ ), 167, and 134 (Found: C, 48.7; H, 2.35; N, 16.35.  $C_{14}H_8N_4O_5S$  requires C, 48.85; H, 2.35; N, 16.3%). No sharp O–H band was observed in the i.r. spectrum but this is probably owing to hydrogen bonding with the azo-group. The main filtrate was diluted with water, and extracted with chloroform. The extract was washed with water and aqueous sodium hydrogen carbonate until neutral. Evaporation left a red oil (9.2 g) which was chromatographed on alumina. Elution with benzene gave unchanged benzo[b]thiophen (3.2 g) and 2-(2,4-dinitrophenyl)benzo[b]thiophen as yellow-orange needles (3.9 g), m.p. 104°; *m/e* 300 ( $M^+$ ) (Found: C, 56.25; H, 2.85; N, 9.1.  $C_{14}H_8N_2O_4S$  requires C, 56.0; H, 2.65; N, 9.35%). Elution with chloroform gave 2,3-bis-(2,4-dinitrophenyl)benzo[b]thiophen as yellow crystals (1.6 g), m.p. 120°, *m/e* 466 ( $M^+$ ) (Found: C, 51.0; H, 2.4; N, 11.5.  $C_{20}H_{10}N_4O_8S$  requires C, 51.5; H, 2.15; N, 12.0%).

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