# Acylarylnitrosamines. Part VI.[1] Anomalous Reactions with 2,5-Dimethylfuran: † the Formation of 2-Benzyl-5-methylfurans and 3-Acetyl-1-aryl-4-arylazo-5-methylpyrazoles

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Novel reactions of acylarylnitrosamines [$XC_6H_4\cdot N(NO)\cdot COR$; R = Me, X = H, p-CO_2Et, p-MeO, m-CO_2Et, m-MeO, m-Me, or p-Me; R = p-ClC_6H_4, X = H] with 2,5-dimethylfuran in an excess of benzene at room temperature are reported. Interaction of the nitrosamine with the benzene component is minimal, the major products being 2-benzyl-5-methylfurans and/or 3-acetyl-1-aryl-4-arylazo-5-methylpyrazoles. It is tentatively suggested that a key step in the formation of the former is π-complexing of the diazonium cation with 2,5-dimethylfuran, the side chain protons of which then become sufficiently acidic to be removed by the acetate counter ion. In competition with this is azo-coupling at a vacant 3-position, followed by consecutive ring opening, further coupling, and cyclisation under the influence of the diazonium acetate ion pair. The reactions constitute further examples of the recently recognised high basicity of acetate ions in benzene solution.

In Part IV [2] we briefly reported, without explanation, that in the reaction of N-nitrosoacetanilide (NNA) with 2,5-dimethylfuran in an excess of benzene the major identified product was 2-benzyl-5-methylfuran. This reaction was unusual, not only with respect to the preferential reaction with the furan but also because, by
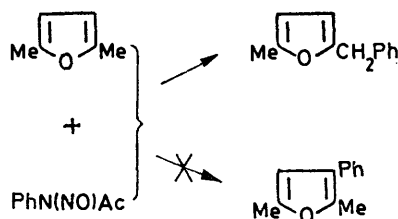
SCHEME 1

analogy with the behaviour of toluene, say, which gives methylbiphenyls,[3] reaction with 2,5-dimethylfuran might have been expected to lead to 2,5-dimethyl-3-phenylfuran (Scheme 1). We now report the results of an

investigation of the mechanism of this unprecedented side-chain phenylation.

EXPERIMENTAL

Gas chromatography was carried out as described earlier.[2]

Materials.—2,5-Dimethylfuran, prepared [4] by dehydration of acetonylacetone with acetic anhydride in the presence of anhydrous zinc chloride, was a mobile liquid, b.p. 93—94° (lit.,[4] 93—94°).

2,3,4,5-*Tetramethylfuran.* 3,4-Dimethylhexane-2,5-dione, prepared [5] by decomposition of dibenzoyl peroxide in butan-2-one, was ring-closed [4] to give the product, b.p. 146—149° (lit.,[4] 146—148°), τ ($CDCl_3$) 8·23 (6H, s, 2- and 5-Me) and 7·92 (6H, s, 3- and 4-Me).

2,5-Dimethyl-3-phenylfuran,[6] b.p. 115—116° at 9 mmHg (lit.,[6] 117° at 11 mmHg), 2,5-di-t-butylfuran,[7] b.p. 60° at 11 mmHg (lit.,[7] 61—62° at 11 mmHg), and 2-methyl-5-phenylfuran,[8] m.p. 41° (lit.,[9] 41—42°) were prepared by reported methods. 2,5-Dimethyl-3-phenylthiophen [10] had

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† Preliminary communication, J. I. G. Cadogan, M. J. P. Harger, J. R. Mitchell, and J. T. Sharp, *Chem. Comm.*, 1971, 1432.

[1] Part V, J. I. G. Cadogan, D. M. Smith, and J. B. Thomson, preceding paper.

[2] D. L. Brydon, J. I. G. Cadogan, J. Cook, M. J. P. Harger, and J. T. Sharp, *J. Chem. Soc.* (*B*), 1971, 1996.

[3] C. S. Rondestvedt and H. S. Blanchard, *J. Amer. Chem. Soc.*, 1955, **77**, 1769.

[4] R. Gaertner and R. G. Tonkyn, *J. Amer. Chem. Soc.*, 1951, **73**, 5872.

[5] C. G. Moore, *J. Chem. Soc.*, 1951, 236.

[6] F. Boberg and G. R. Schultze, *Chem. Ber.*, 1957, **90**, 215.

[7] H. Brown and G. F. Wright, *Canad. J. Chem.*, 1957, **35**, 236.

[8] M. F. March, *Ann. Chim.* (*France*), 1902, **26**, 295.

[9] A. P. Dunlop and F. N. Peters, 'The Furans,' Rheinhold, New York, 1953.

[10] K. E. Schultze, J. Reisch, and D. Bergenthal, *Angew. Chem. Internat. Edn.*, 1965, **4**, 1082.

b.p. 100° at 2 mmHg (lit.,[10] 109° at 1·5 mmHg), τ (CCl$_4$) 7·6 (s, 2 × Me), 3·4br (4-H), and 2·75br (s, Ph).

Acylarylnitrosamines were prepared as described earlier,[1,2,11] care being taken to ensure complete dryness of the samples.

Reactions of N-Nitrosoacetanilide.—(i) *With 2,5-dimethylfuran in benzene.* N-Nitrosoacetanilide (4·97 g, 30·3 mmol) was stirred overnight in a solution of 2,5-dimethylfuran (5·8 g, 60 mmol) in sodium-dried benzene (28 g, 0·36 mol) at room temperature under anhydrous conditions and in an atmosphere of oxygen-free nitrogen. The nitroso-compound by then had decomposed completely, but in order to ensure removal of the last traces the mixture was boiled under reflux for 1 h, and then examined by g.l.c. (2% NPGS at 127·5°; 2% APL at 140°) with bibenzyl as internal standard. 2-Benzyl-5-methylfuran (27%) and biphenyl (6%) were shown to be present. Preparative g.l.c. (CAR 10% at 186°) gave pure samples of biphenyl, m.p. and mixed m.p. 71° [i.r. (film) spectrum indistinguishable from that of an authentic sample], and 2-benzyl-5-methylfuran, τ (CCl$_4$) 2·87 (s, Ph), 4·29 (s, furan 3-H and 4-H), 6·18 (s, CH$_2$Ph), and 7·79 (s, Me).

A portion of the mixture (20%) was chromatographed on silica (40 g) and eluted with benzene. A yellow oil (0·3 g), which proved to be a mixture of biphenyl and 2-benzyl-5-methylfuran, was obtained, followed by a red oil (0·1 g) to which was assigned the structure 3-acetyl-5-methyl-1-phenyl-4-phenylazopyrazole by an exact mass measurement of the parent ion (Found: M^+, 304·132071. C$_{18}$H$_{16}$N$_4$O requires M, 304·132404); $\nu_{max.}$ (film) 1680 cm^{-1}.

A similar experiment carried out in the presence of added water (1 mol. equiv.) led to the suppression of the formation of 2-benzyl-5-methylfuran (yield 0·3%).

(ii) *With 2,5-dimethylfuran in t-butylbenzene.* N-Nitrosoacetanilide (3·66 g, 22·3 mmol) was stirred overnight at room temperature in a solution of 2,5-dimethylfuran (4·21 g, 44 mmol) in t-butylbenzene (35·3 g, 0·26 mol). The mixture was then boiled under reflux for 1 h. Distillation of a portion (33%) gave a pale yellow oil (0·3 g; b.p. 30—60° at 0·5 mmHg), leaving a tarry residue (0·5 g). Chromatography of the oil on silica gel (30 g), eluting initially with petroleum, and then with petroleum–benzene (15 : 1) gave crystals (70 mg) identified by their g.l.c. retention times (2% PEGA at 147°; 2% APL at 180°) as being a mixture of o-, m-, and p-t-butylbiphenyls (by comparison with a standard mixture of the three isomers). The n.m.r. (CDCl$_3$) spectrum was similar to that of an authentic mixture of the isomers. Continued elution of the column gave a pale yellow oil (0·17 g) whose n.m.r. (CCl$_4$) and i.r. (film) spectra were indistinguishable from those of 2-benzyl-5-methylfuran. Quantitative examination of the reaction mixture by g.l.c. (10% Sil at 180°; naphthalene as internal standard) showed the presence of 2-benzyl-5-methylfuran (17·3%), and g.l.c. (2% APL at 183°) examination with terphenyl as internal standard showed the presence of o-t-butylbiphenyl (1·73%), m-t-butylbiphenyl (3·3%), and p-t-butylbiphenyl (1·5%).

(iii) *With 2,5-di-t-butylfuran in benzene.* N-Nitrosoacetanilide (4·97 g, 30 mmol) was stirred at room temperature overnight in a mixture of 2,5-di-t-butylfuran (10·8 g, 60 mmol) and benzene (28 g, 0·36 mol). The solution was boiled under reflux for 1 h, and a portion (62%) was distilled, to give a dark oil, b.p. 140—160° at 12·0 mmHg (0·5 g), which was chromatographed on silica (60 g). Elution with petroleum gave biphenyl (0·3 g),

m.p. and mixed m.p. 70°, whose i.r. spectrum (film) was indistinguishable from that of an authentic sample. A pale yellow oil (55 mg) was also obtained, identified as 2,5-di-t-butyl-3-phenylfuran (Found: C, 84·7; H, 9·1%; M^+, 256. Calc. for C$_{18}$H$_{24}$O: C, 84·5; H, 9·4%; M^+, 256), τ (CDCl$_3$) 8·78 (s, 2-Bu^t) and 2·56—3·2 (6H, complex, aromatic). G.l.c. (10% Sil at 170·5°) of the mixture with anthracene as internal standard indicated the presence of biphenyl (12·5%) and 2,5-di-t-butyl-3-phenylfuran (11%).

(iv) *With tetramethylfuran in benzene.* N-Nitrosoacetanilide (3·34 g, 20·2 mmol) was stirred overnight at room temperature in a mixture of 1,2,3,4-tetramethylfuran (4·98 g, 40·2 mmol) and benzene (18·8 g, 0·24 mol). The mixture was then boiled under reflux for 1 h, and a portion (86%) was chromatographed on silica (80 g) with petroleum-benzene (1 : 50) as eluant. Biphenyl (55 mg) was collected [m.p. and mixed m.p. 71° i.r. spectrum (film) indistinguishable from that of an authentic sample] followed by an oil (0·1 g) which proved to be a mixture (ca. 9 : 1) of 2-benzyl-3,4,5-trimethylfuran and 3-benzyl-2,4,5-trimethylfuran (Found: C, 83·75; H, 8·3. Calc. for C$_8$H$_{12}$O: C, 84·0; H, 8·0%), τ (CDCl$_3$) 8·4 (s, 2- and 5-Me), 8·1 (s, 3- and 4-Me), 6·43 (s, 2-CH$_2$), 6·64 (s, 3-CH$_2$), and 3·1 (s, aromatic). Quantitative examination of the mixture by g.l.c. (10% Sil, 143°) with anthracene as internal marker gave the combined yields of the 2- and 3-isomers as 31 mol %. G.l.c. on 2% APL at 133° showed furthermore that the ratio of the 2- to the 3-isomer was 8·6 : 1.

(v) *With 2-methylfuran in benzene.* N-Nitrosoacetanilide (2·5 g, 15·25 mmol) was stirred overnight in a mixture of 2-methylfuran (2·46 g, 30·0 mmol) and benzene (14 g, 0·18 mol) under the standard conditions already given. Distillation of the bulk of the mixture gave a yellow oil (0·25 g; b.p. 90—120° at 0·5 mmHg) which proved (g.l.c. on 2% APL at 120° and on 2% NPGS at 110°) to be a mixture of biphenyl and an unknown compound. Preparative g.l.c. (10% NPGS at 175°) afforded pure samples of biphenyl [m.p. and mixed m.p. 71°; i.r. spectrum (film) indistinguishable from that of an authentic sample], and 2-methyl-5-phenylfuran [n.m.r. (CCl$_4$) and i.r. spectra (film) indistinguishable from those of an authentic sample].

Quantitative examination of the reaction mixture by g.l.c. (10% APL at 170°) with bibenzyl as internal standard showed the presence of biphenyl (4·8%) and 2-methyl-5-phenylfuran (7·6%).

(vi) *With 2,5-dimethylthiophen in benzene.* N-Nitrosoanilide (4·97 g, 30·3 mmol) was stirred in a solution of 2,5-dimethylthiophen (6·72 g, 60 mmol) in benzene (28·1 g, 0·36 mol) under the standard conditions. Distillation gave an oil (0·5 g), b.p. 60—100° at 0·2 mmHg, which proved (g.l.c. on 2% APL at 140°) to be a mixture of two compounds. Preparative g.l.c. afforded pure samples of biphenyl [m.p. and mixed m.p. 71°, i.r. (film) spectrum indistinguishable from an authentic sample] and 2,5-dimethyl-3-phenylthiophen [n.m.r. (CCl$_4$) and i.r. (film) spectra indistinguishable from those of an authentic sample]. Quantitative examination by g.l.c. (10% APL at 170°) with naphthalene as internal standard showed the presence of biphenyl (12%) and 2,5-dimethyl-3-phenyl-thiophen (3%). The residue (2 g) from the distillation of the reaction mixture was an intractable tar.

Reactions of Substituted Acylarylnitrosamines with 2,5-Dimethylfuran in Benzene.—(i) *General procedure.* The acylarylnitrosamine (30 mmol) was stirred overnight in a

[11] J. W. Haworth and D. H. Hey, *J. Chem. Soc.*, 1940, 361.

solution of 2,5-dimethylfuran (5·8 g, 60 mmol) in benzene (28 g, 0·36 mol) under anhydrous conditions and in an atmosphere of oxygen-free nitrogen. This was sufficient to decompose the nitroso-amide but all traces were removed by boiling the mixture under reflux for 1 h. If liquid, the nitroso-amides were extracted into cold benzene and dried (MgSO$_4$, followed by P$_2$O$_5$ for a few minutes) and the requisite amounts of 2,5-dimethylfuran and benzene were added after estimation of the quantity of nitroso-amide present.

(ii) *4-Chloro-N-nitrosobenzanilide.* G.l.c. (2% NPGS at 125°; 2% APL at 140°) showed the presence of 2-benzyl-5-methylfuran (30%) and 1,4-epoxy-1,4-dihydro-1,4-dimethylnaphthalene (1%) (by comparison with an authentic specimen [2]). The presence of these compounds was confirmed and established beyond doubt by mass spectrum–g.l.c. analysis.

(iii) *4-Methoxy-N-nitrosoacetanilide.* A portion (28%) of the reaction mixture was chromatographed on silica (40 g). Elution with benzene gave 4-methoxybiphenyl (90 mg; m.p. and mixed m.p. 80°), n.m.r. (CCl$_4$) and i.r. (Nujol) spectra identical with those of an authentic sample. Quantitative examination by g.l.c. (10% Sil at 152°) with bibenzyl as internal standard gave the yield of 4-methoxybiphenyl as 3·5%. Continued elution of the column with benzene gave a red oil, which yielded orange crystals (0·19 g, 27%), m.p. 138° (from methanol) of 3-*acetyl*-1-(4-*methoxyphenyl*)-4-(4-*methoxyphenylazo*)-5-*methylpyrazole* (Found: C, 65·6; H, 5·5; N, 14·8%; *M*$^+$, 364. C$_{20}$H$_{20}$N$_4$O$_3$ requires C, 65·9; H, 5·5; N, 15·4%; *M*, 364), τ (CDCl$_3$) 7·83 (s, Ac), 7·3 (s, Me), 6·18 (s, 2 × MeO), 2—3·1 (two A$_2$B$_2$ systems superimposed, 8H, aromatic), $\nu_{max.}$ (Nujol) 1696 cm^{-1} (C=O); *oxime*, m.p. 197·5° (Found: C, 63·4; H, 5·3; N, 18·1%; *M*$^+$, 379. C$_{20}$H$_{21}$N$_5$O$_3$ requires C, 63·4; H, 5·5; N, 18·4%; *M*, 379), τ (CDCl$_3$) 7·61 (s, oxime Me), 7·23 (s, pyrazole Me), 6·07 (s, 2 × MeO), and 2—3·1 (9H, complex, phenyl and oxime protons); the i.r. (Nujol) spectrum showed no carbonyl absorption at 1696 cm^{-1}.

(iv) *3-Methoxy-N-nitrosoacetanilide.* A portion (35%) of the mixture was chromatographed on silica (50 g). Elution with petroleum gave an oil (85 mg) found to be 3-methoxybiphenyl, τ (CDCl$_3$) 6·23 (s, OMe) and 2·4—3·4 (9H, complex, aromatic). Continued elution with petroleum gave 2-(3-*methoxybenzyl*)-5-*methylfuran* as an oil (49 mg) (Found: C, 77·6; H, 7·3. C$_{13}$H$_{14}$O$_2$ requires C, 77·3; H, 6·9%), τ (CCl$_4$) 7·78 (s, Me), 6·27 (s, OMe), 6·19 (s, CH$_2$), 4·15 (s, furan 3-H and 4-H), and 2·6—3·5 (complex, C$_6$H$_4$). The aromatic absorption pattern was compared to those of 2-, 3-, and 4-methoxytoluenes. The spectrum was similar to that of 3-methoxytoluene, thus confirming the structure of the product (15% of the 1- and 4-isomers would have been detected). Continued elution of the column gave an intractable tar (0·4 g).

Quantitative examination of the reaction mixture by g.l.c. (2% NPGS at 144°) with bibenzyl as internal standard showed the presence of 3-methoxybiphenyl (6%) and 2-(3-methoxybenzyl)-5-methylfuran (19%).

(v) *4-Ethoxycarbonyl-N-nitrosoacetanilide.* A portion (72%) of the mixture was chromatographed on silica (100 g). Elution with petroleum–benzene (1 : 0—5 : 1) gave crystals (55 mg) of 4-ethoxycarbonylbiphenyl, m.p. 46° (lit.,[12] 46°), τ (CCl$_4$) 8·4 (t, Me), 5·5 (q, CH$_2$), and 1·6—2·6 (9H, complex, aromatic). Continued elution gave 2-(4-*ethoxycarbonylbenzyl*)-5-*methylfuran* as an oil (40 mg) (Found: C, 73·6; H, 7·1. C$_{15}$H$_{16}$O$_3$ requires C, 73·7; H,

6·5%), τ (CCl$_4$) 8·65 (t, Me), 5·7 (q, CH$_2$), 7·78 (s, ring Me), 6·11 (s, CH$_2$), 4·24 (s, furan 3-H and 4-H), and 1·8—2·0 (4H, A$_2$B$_2$, aromatic). Elution of the column with diethyl ether afforded a red oil which on crystallisation from methanol–petroleum (1 : 1) yielded yellow crystals, m.p. 91—93°, of 3-*acetyl*-1-(4-*ethoxycarbonylphenyl*)-4-(4-*ethoxy-carbonylphenylazo*)-5-*methylpyrazole* (0·26 g, 15%) (Found: C, 64·2; H, 5·4; N, 12·4%; *M*$^+$, 448. C$_{24}$H$_{24}$N$_4$O$_5$ requires C, 64·3; H, 5·3; N, 12·5%; *M*, 448), τ (CDCl$_3$) 8·58 (t, 2 × Me), 5·5 (q, 2 × CH$_2$), 7·35 (s, Ac), 7·2 (s, pyrazole Me), and 1·6—2·5 (8H, complex, aromatic), $\nu_{max.}$ (Nujol) 1680—1720 cm^{-1} (C=O).

Quantitative examination of the mixture by g.l.c. (2% APL at 186°) with bibenzyl as internal standard showed the presence of 4-ethoxycarbonylbiphenyl (11·3%) and 2-(4-ethoxycarbonylbenzyl)-5-methylfuran (7·1%).

(vi) *3-Ethoxycarbonyl-N-nitrosoacetanilide.* A portion (83%) of the mixture was chromatographed on silica (100 g). Elution with petroleum–benzene (40 : 1 increasing to 10 : 1) gave an oil (0·35 g) which proved (g.l.c. on 2% APL at 190°) to be a mixture of two compounds. Further elution of the column with chloroform yielded a red oil which, on low temperature crystallisation from benzene–petroleum (1 : 10), gave low-melting crystals, melting to a red oil, of 3-*acetyl*-1-(3-*ethoxycarbonylphenyl*)-4-(3-*ethoxycarbonyl-phenylazo*)-5-*methylpyrazole* (0·78 g, 27%) (Found: C, 64·5; H, 5·4; N, 12·3. C$_{24}$H$_{24}$N$_4$O$_5$ requires C, 64·3; H, 5·4; N, 12·5%), τ (CDCl$_3$) 8·6 (t, 2 × Me), 5·55 (q, 2 × CH$_2$), 7·4 (s, Ac), 7·3 (s, pyrazole Me), and 1·5—2·7 (4H, complex, aromatic), $\nu_{max.}$ (film) 1680—1720 cm^{-1} (C=O). Preparative g.l.c. (10% Sil at 172°) of the oil obtained initially from the column afforded 3-ethoxycarbonylbiphenyl as an oil [τ (CCl$_4$) 8·6 (t, Me), 5·6 (q, CH$_2$), and 1·75—2·8 (9H, complex, aromatic)] and 2-(3-*ethoxycarbonylbenzyl*)-5-*methylfuran* as an oil (Found: C, 74·0; H, 6·75. C$_{15}$H$_{16}$O$_3$ requires C, 73·7; H, 6·5%), τ (CCl$_4$) 8·62 (t, Me), 5·65 (q, CH$_2$), 7·79 (s, furan Me), 6·1 (s, CH$_2$), 4·13 (s, furan 3-H and 4-H), and 2·0—2·3 and 2·5—2·8 (4H, complex, aromatic), $\nu_{max.}$ (film) 1720 cm^{-1} (C=O). Quantitative g.l.c. of the reaction mixture (2% APL at 206·5°) with bibenzyl as internal marker showed the presence of 3-ethoxycarbonyl-biphenyl (4%) and 2-(3-ethoxycarbonylbenzyl)-5-methyl-furan (8·6%).

(vii) *4-Methyl-N-nitrosoacetanilide.* A portion of the mixture was chromatographed on silica (90 g). Elution with petroleum gave white crystals of 4-methylbiphenyl (92 mg; m.p. and mixed m.p. 49°), i.r. (film) and n.m.r. (CCl$_4$) spectra indistinguishable from those of an authentic sample. Elution with diethyl ether gave a red oil which, on crystallisation from petroleum, gave red crystals, m.p. 105° (0·53 g, 20%), of 3-*acetyl*-1-p-*tolyl*-4-p-*tolylazo*-5-*methylpyrazole* (Found: C, 72·4; H, 6·0; N, 16·6. C$_{20}$H$_{20}$N$_4$O requires C, 72·3; H, 6·0; N, 16·9%), τ (CDCl$_3$) 7·58 (s, 2 × Me), 7·49 (s, Ac), 7·33 (s, pyrazole Me), and 2·2—3·0 (8H, complex, aromatic), $\nu_{max.}$ (Nujol) 1685 cm^{-1} (C=O). Quantitative g.l.c. (2% APL at 150°) of the reaction mixture with naphthalene as internal standard showed the presence of 4-methylbiphenyl (3·2%). 2-(4-Methylbenzyl)-5-methylfuran was not detected.

(viii) *3-Methyl-N-nitrosoacetanilide.* A portion (80%) of the mixture was chromatographed on silica (90 g). Elution with petroleum gave an oil (0·31 g) which g.l.c. (2% APL at 160°) proved to be a mixture of two components. Elution

[12] Heilbron's ' Dictionary of Organic Compounds,' Eyre and Spottiswoode, London, 1965.

with diethyl ether gave a red oil, which was washed with sodium hydrogen carbonate solution and water and dried ($MgSO_4$). The resulting red oil (1·94 g) was not identified (Found: C, 73·2; H, 6·5; N, 14·3%).

Preparative g.l.c. (10% Sil at 150°) of the colourless oil obtained initially afforded pure samples of 3-methyl-biphenyl [n.m.r. (CCl_4) and i.r. (film) spectra indistinguishable from those of an authentic sample], and 2-(3-*methyl-benzyl*)-5-*methylfuran* (Found: C, 83·9; H, 7·5. $C_{13}H_{14}O$ requires C, 84·1; H, 7·4%), τ ($CDCl_3$) 7·84 (s, furan Me), 7·75 (s, Me), 6·24 (s, CH_2), 4·3 (s, furan 3-H and 4-H), and 3·07br (C_6H_4). Comparison of the aromatic n.m.r. absorption with those of o- and m-xylenes confirmed the presence of the 3-isomer.

Quantitative g.l.c. (10% Sil at 143°) with biphenyl as internal standard showed the presence of 3-methylbiphenyl (6·5%) and 2-(3-methylbenzyl)-5-methylfuran (9%).

Reactions of Arenediazonium Chloride Solutions with 2,5-Dimethylfuran in the Presence of Potassium Acetate.— The method was that described by Eastman and Detert [13] who added in one portion the diazonium salt solution obtained from the arylamine (50 mmol), sodium nitrite (3·5 g), 10% hydrochloric acid (30 ml), and water (150 ml), to an ice-cold mixture of 2,5-dimethylfuran (4·8 g, 50 mmol), potassium acetate (15 g, 0·25 mol), and ethanol (250 ml). The mixture was kept at 0° for 3 h and then added to twice its volume of water. A red oil separated which was extracted into benzene, and the extract was dried ($MgSO_4$).

(i) *Benzenediazonium chloride (from aniline).* The benzene solution obtained was chromatographed on silica (70 g), with ether–benzene (1 : 4) as eluant. A red oil identified as 3-*acetyl*-5-*methyl*-1-*phenylpyrazole* (5·4 g; 54 mole %) was obtained, τ ($CDCl_3$) 7·71 (s, Ac), 7·42 (s, Me), 3·31 (s, pyrazole 4-H), and 2·55 (s, Ph), ν_{max} (film) 1680 cm^{-1} (C=O); *oxime*, m.p. 151°, no i.r. absorption (film) at 1680 cm^{-1}, τ ($CDCl_3$) 7·66 (s, oxime Me), 7·62 (s, pyrazole ring Me), 3·43 (s, pyrazole 4-H), 2·56 (s, Ph), and 1·94br (N·OH) (Found: C, 67·2; H, 5·9; N, 19·9%; M^+, 215. $C_{12}H_{13}N_3O$ requires C, 67·0; H, 6·05; N, 19·5%; M, 215).

G.l.c. of the original benzene extract (2% APL at 140°) showed that 2-benzyl-5-methylfuran was absent (0·2% would have been detected).

(ii) 4-*Methoxybenzenediazonium chloride (from p-anisidine).*—The dry benzene extract was chromatographed on silica (80 g), with benzene–ether (9 : 1) as eluant. A red oil (5·1 g) was obtained which on crystallisation from ethanol–water (20 : 1) gave dark red crystals, m.p. 84° 3-*acetyl*-1-(4-*methoxyphenyl*)-5-*methylpyrazole* (3·1 g, 27 mole %), τ ($CDCl_3$) 7·72 (s, Ac), 7·51 (s, ring Me), 6·15 (s, OMe), 3·31 (s, pyrazole 4-H), and 2·5—3·1 (A_2B_2, C_6H_4), ν_{max} (Nujol) 1675 cm^{-1} (C=O) (Found: C, 68·0; H, 5·9; N, 12·0%; M^+, 230. $C_{13}H_{14}N_2O_2$ requires C, 67·8; H, 6·1; N, 12·2%; M, 230).

Reaction of 3-Acetyl-1-(4-methoxyphenyl)-5-methylpyrazole with 4-Methoxy-N-nitrosoacetanilide.—4-Methoxy-N-nitroso-acetanilide (1 g) was added to a solution of 3-acetyl-1-(4-methoxyphenyl)-5-methylpyrazole (1 g) in benzene (10 ml) and the mixture was stirred under anhydrous conditions and in an atmosphere of oxygen-free nitrogen overnight. It was then boiled for 1 h. T.l.c. on alumina showed the presence of unchanged 3-acetyl-1-(4-methoxyphenyl)-5-

methylpyrazole (R_F 0·46), but no 3-acetyl-1-(4-methoxy-phenyl)-4-(4-methoxyphenylazo)-5-methylpyrazole(R_F 0·27) was detected.

DISCUSSION

The basic reaction involves the decomposition of NNA in a mixture of 2,5-dimethylfuran (2 mol. equiv.) and benzene (20 mol. equiv.) at room temperature to give biphenyl (0·06 mol. equiv.) and 2-benzyl-5-methyl-furan (0·27 mol. equiv.).

We tentatively propose for this reaction the mechanism outlined in Scheme 2, whereby NNA is assumed to undergo normal isomerisation to benzenediazoacetate, which is in equilibrium with the benzenediazonium acetate ion pair.[14] Biphenyl and 2-benzyl-5-methyl-furan then arise *via* two competing reactions of benzene-diazonium acetate, the first being the normal radical decomposition to give phenyl radicals and hence biphenyl,[15] by phenylation of benzene present in large excess. The second, predominant, route in this case involves, we suggest, the formation of a π-complex (1) between the electron-rich 2,5-dimethylfuran and the benzenediazonium cation. In this connection Yoshida and Osawa[16] have shown that 2,5-dimethylfuran is a strong π-base, more so than furan. The formation of the π-complex (1) would be expected to lead to increased acidity of the methyl proton, which can be removed in anhydrous conditions by the acetate counter ion, by analogy with the well substantiated removal by acetate ion of the proton *ortho* to the diazonium function in uncomplexed benzenediazonium cation leading to ben-zyne.[1,14] Removal of the side-chain proton of dimethyl-furan leads to the even more strongly complexed 5-methylfurfuryl carbanion, which then reacts with the adjacent benzenediazonium cation by nucleophilic displacement to give the observed 2-benzyl-5-methyl-furan. Evidence in support of this mechanism follows.
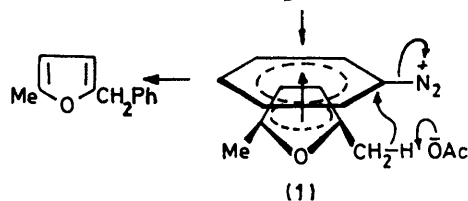
SCHEME 2

Effect of changing the solvent. An alternative route to 2-benzyl-5-methylfuran is given in Scheme 3 (X = H), whereby phenyl radicals phenylate the solvent, benzene, and also abstract a hydrogen atom from a methyl group of 2,5-dimethylfuran to give the 5-methylfurfuryl radical (2). This, in turn, is oxidised by the unchanged benzenediazonium cation to give the 5-methylfurfuryl carbonium ion, which then attacks the solvent to give
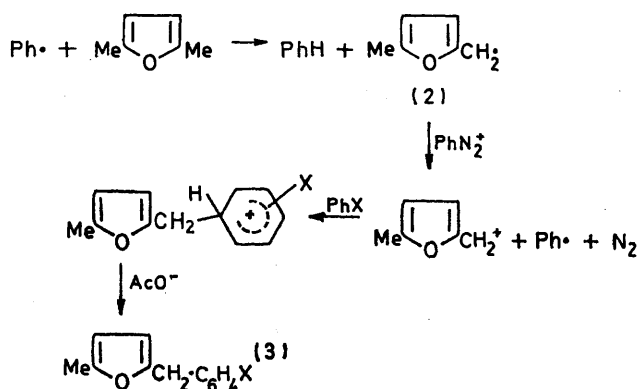
[13] R. H. Eastman and F. L. Detert, *J. Amer. Chem. Soc.*, 1948, **70**, 962.

[14] J. I. G. Cadogan, *Accounts Chem. Res.*, 1971, **4**, 186; *Chem. Soc. Special Publ. No.* 24, 1970, 71.

[15] J. I. G. Cadogan, R. M. Paton, and C. Thomson, *J. Chem. Soc. (B)*, 1971, 583.

[16] Z. Yoshida and E. Osawa, *J. Amer. Chem. Soc.*, 1966, **88**, 4019.

the observed product. This process regenerates a phenyl radical in the chain reaction and there are precedents.[15,17]

$$Ph\cdot + Me\overset{\ \ }{\underset{O}{\bigcirc}}Me \longrightarrow PhH + Me\overset{\ \ }{\underset{O}{\bigcirc}}CH_2^\cdot$$

(2)

$$\downarrow PhN_2^+$$

(3)

SCHEME 3

This Scheme, and the far less likely one involving the corresponding direct furfurylation of benzene by the radical (2), can be discounted by the observation that decomposition of NNA in a mixture of 2,5-dimethyl-furan (2 mol. equiv.) and t-butylbenzene (20 mol. equiv.) gave no 2-(t-butylbenzyl)-5-methylfuran (3; X = Bu^t), predicted by Scheme 3, the main product being, again, 2-benzyl-5-methylfuran (0·17 mol. equiv.), showing that the side-chain phenylating system originates in the NNA, as required by the proposed mechanism (Scheme 2). Also in accord with Scheme 2 is the formation, as a minor product, of a mixture of isomeric t-butylbi-phenyls (0·06 mol. equiv.) of composition 2-, 25%; 3-, 51%; 4-, 24%, identical, within experimental error, with that found for the reaction of authentic phenyl radicals with t-butylbenzene (2-, 24; 3-, 49; 4-, 27%).[18]

Effect of adding water to the system. It has already been established in connection with our studies of aryne formation from acylarylnitrosamines [1,14] and *in situ* diazotisation of anilines,[19] that, whereas acetate ion is sufficiently basic in anhydrous benzene to remove an *ortho*-proton in the benzenediazonium cation, addition of water to the system suppresses the reaction, by solvation of the acetate ion leading to a reduced basicity, and possibly by scavenging of the intermediate zwitterion
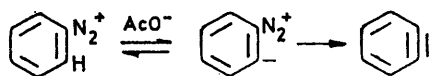
Reaction suppressed by H$_2$O

SCHEME 4

by water (Scheme 4). As an extension of this it has been shown more recently [20] that the formation of indazole from *o*-methylbenzenediazonium acetate, which proceeds *via* removal of a methyl proton by acetate ion, is also suppressed by added water. In accord with the

foregoing and Scheme 2 in which removal of a proton by acetate ion is a key step, addition of water (1 mol. equiv.) to the reaction of NNA in 2,5-dimethylfuran–benzene led to the almost complete suppression of the formation of 2-benzyl-5-methylfuran (0·3%).

Effect of changing the aryl substituent: formation of pyrazoles. The results of these experiments are summarised in the Table. In general, the accountance for

Reaction of substituted NNA in 2,5-dimethylfuran (2 mol. equiv.) and benzene (20 mol. equiv.) at room temp.

		$Me\overset{\ \ }{\underset{O}{\bigcirc}}CH_2Ar$	$ArN_2\overset{\ \ }{\underset{Me\ N\ N}{\bigcirc}}COMe$, Ar
Ar in ArN(NO)Ac	ArPh (%)	(%)	(%)
Ph	6	27	Trace
p-MeO·C$_6$H$_4$	3·5	0	27
m-MeO·C$_6$H$_4$	6	19	
p-CO$_2$Et	11	7	15
m-CO$_2$Et	4	9	27
m-Me	6·5	9	
p-Me	3	0	20

starting material in these reactions was low, but the benzylfurans isolated all retained the integrity of the aryl system; *e.g.* 3-methoxy-*N*-nitrosoacetanilide gave 2-(3-methoxybenzyl)-5-methylfuran. This, as required by Scheme 2, rules out attack *via* a bidentate species, *e.g.* an aryne, or by the furfuryl system at a nuclear position other than that attached to the diazonium function.

In the cases of *p*-methoxy-, *p*-ethoxycarbonyl-, and *m*-ethoxycarbonyl-*N*-nitrosoacetanilides, however, additional products, 1-aryl-3-acetyl-4-arylazo-5-methyl-pyrazoles (4), were formed in appreciable yields. These
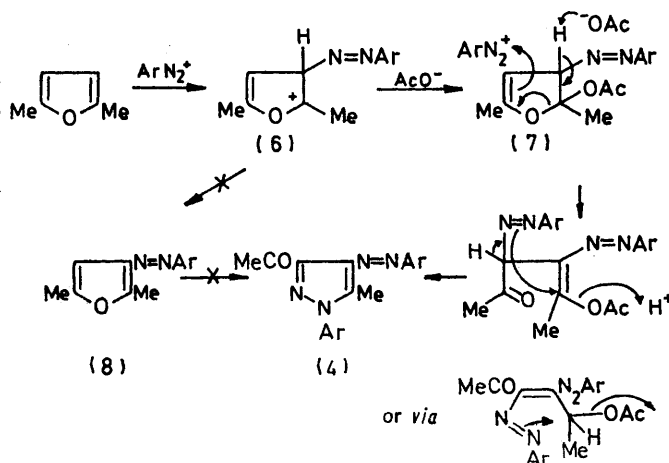
SCHEME 5

can be accounted for by assuming, in these cases, a third possible reaction of the intermediate diazonium cation (Scheme 5), whereby electrophilic azo-coupling at the

[17] C. Rüchardt and R. Werner, *Tetrahedron Letters*, 1969, 2407; J. I. G. Cadogan, R. M. Paton, and C. Thomson, *Chem. Comm.*, 1970, 229.

[18] J. I. G. Cadogan, D. H. Hey, and G. H. Williams, *J. Chem. Soc.*, 1954, 3352.

[19] J. I. G. Cadogan, J. R. Mitchell, and J. T. Sharp, *Chem. Comm.*, 1971, 1.

[20] B. H. Klanderman, D. P. Maier, G. W. Clark, and J. A. Kampmeier, *Chem. Comm.*, 1971, 1003.

free 3-position in 2,5-dimethylfuran occurs to give the intermediate (6) and hence (7), the latter then undergoing consecutive ring opening and further azo-coupling by reaction with the diazonium acetate ion pair, followed by ring closure to give the observed 3-acetyl-1-aryl-4-arylazo-5-methylpyrazole (4).

An alternative scheme whereby 2,5-dimethylfuran undergoes azo-coupling at position 3 to give 3-arylazo-2,5-dimethylfuran (8) (Scheme 5), followed by further coupling at position 4, is discounted on the grounds of deactivation of the intermediate azo-compound towards further coupling.

The variation in the observed product ratio (benzylfuran to pyrazole) is in accord with the competitive operation of Schemes 2 and 5. Thus, with p-methoxy-N-nitrosoacetanilide, the strongly electron-repelling p-methoxy-group represses the tendency to π-complex formation to such an extent that azo-coupling at position 3 leading to the pyrazole (4; Ar = p-MeO·C$_6$H$_4$) becomes dominant. In the unsubstituted case, π-complexing leading to the 2-methyl-5-benzylfuran is more important, as it is in the case of the 3-methoxyphenyl derivative, where the strong conjugative electron release of the methoxy-group cannot come into play as in the case of the 4-methoxy-isomer. A similar situation exists in the case of the 4- and 3-methylphenyl derivatives. In the former the strongly conjugative electron release leads to depression of the π-complexing ability and hence to competitive attack *via* azo-coupling. In the case of the *m*-tolyl derivative this is not so strong and the situation is more like that for the unsubstituted case. In both the 3- and 4-ethoxycarbonylphenyl derivatives, on the other hand, the strongly electron-withdrawing nature of the carboxylate groups can, in theory, lead to an increase in π-complexing, and hence side chain benzylation and/or to electrophilic azo-coupling at position 3 leading to pyrazole, the relative likelihood of the occurrence of these processes being unpredictable. In practice both processes occur.

The literature contains one report of a closely related but different reaction. Eastman and Detert [13] noted the formation of 3-acetyl-5-methyl-1-(p-nitrophenyl)pyrazole
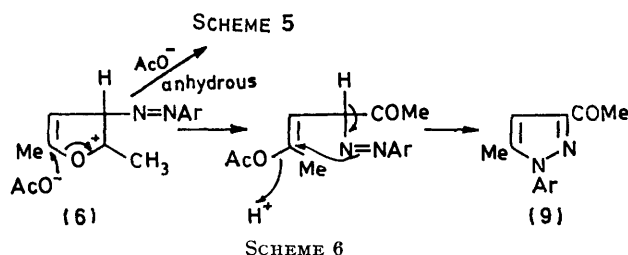
SCHEME 5

SCHEME 6

(9; Ar = p-O$_2$N·C$_6$H$_4$) from the reaction of ice-cold aqueous ethanolic p-nitrobenzenediazonium chloride with 2,5-dimethylfuran in the presence of sodium acetate

[21] L. Benati, N. La Barba, M. Tiecco, and A. Tundo, *J. Chem. Soc.* (*B*), 1969, 1253.

buffer. We can accommodate this observation by an extension (Scheme 6) of Scheme 5 whereby the intermediate (6) formed by azo-coupling at position 3 of 2,5-dimethylfuran undergoes attack by acetate ion at position 5 with ring opening and subsequent cyclisation. The reason that compound (9) is formed under Eastmann and Detert's aqueous conditions, whereas 3-acetyl-4-arylazo-5-methyl derivatives are formed under ours, is that the acetate ion acts as a strong base under our anhydrous conditions (step i, Scheme 5) but not in aqueous solution. In agreement with these observations we find that the reaction of aqueous benzene- and p-methoxybenzene-diazonium chlorides with 2,5-dimethylfuran in the presence of acetate ion gives high yields of the corresponding 3-acetyl-1-aryl-5-methylpyrazoles (9: Ar = Ph or p-MeC$_6$H$_4$). Further, the corresponding 2-benzylfurans were absent, as a result of the suppression of acetate basicity by water as required by Scheme 2.

The formation of the pyrazoles (9) raises the possibility that they might be intermediates in the formation of our 3-acetyl-1-aryl-4-arylazo-5-methylpyrazoles (4) (Scheme 5). This can be discounted because we have shown that 3-acetyl-1-(p-methoxyphenyl)-5-methyl-pyrazole (9; Ar = p-MeO·C$_6$H$_4$) is recovered unchanged from treatment with p-methoxy-N-nitrosoacetanilide in benzene under our conditions, and that none of the 3-acetyl-1-(p-methoxyphenyl)-4-(p-methoxyphenylazo)-5-methylpyrazole (4; p-MeO·C$_6$H$_4$) is formed.

Effect of changing the furan system. The results of reactions of NNA with 2-methylfuran, 2,5-di-t-butylfuran, 2,5-dimethylthiophen, and 2,3,4,5-tetramethylfuran are all accommodated by Scheme 2. 2-Methylfuran, which is not as electron-rich as 2,5-dimethylfuran, does not give 2-benzylfuran, but gives 2-phenyl-5-methylfuran, the expected product of radical phenylation.[2, 21] For the same reason 2,5-dimethylthiophen similarly gives 2,5-dimethyl-3-phenylthiophen, while 2,5-di-t-butylfuran, having no α-hydrogen atoms, also reacts by nuclear phenylation to give the 3-phenyl derivative. Tetramethylfuran gives a mixture (28%) of 2-benzyl-3,4,5-trimethylfuran (8·6 parts) and 3-benzyl-2,4,5-trimethylfuran (1 part), in accord with the relatively greater acidity of the 2-methyl protons as required by Scheme 2. This result also excludes the possibility of an electrocyclic mechanism involving the prior formation of the intermediates (10) and (11) (Scheme 7), which otherwise would have been attractive in view of the implication of the related (6) in Schemes 5 and 6. Electrophilic attack by the diazonium cation on tetramethylfuran would be expected to take place largely at the 2-position, however, which would lead by Scheme 7 to mainly the 3-benzyl derivative rather than the reverse, which is observed.

The question of aryne participation in the reaction of NNA with 2,5-dimethylfuran. A competing pathway for the decomposition of NNA and the concomitant benzene-diazonium acetate involves the formation of benzyne;[14, 22]

[22] C. Rüchardt and C. C. Tan, *Angew. Chem. Internat. Edn.*, 1970, **9**, 522.

indeed a small amount (2%) of the benzyne–dimethyl-furan adduct was formed in the reaction of 4'-chloro-*N*-nitrosobenzanilide. 2-Benzyl-5-methylfuran (30%) was also produced. Involvement of a bidentate inter-mediate, such as benzyne, in the formation of the latter has already been ruled out (see before). The complex equilibria involved in the decomposition of NNA are


(10)   (11)
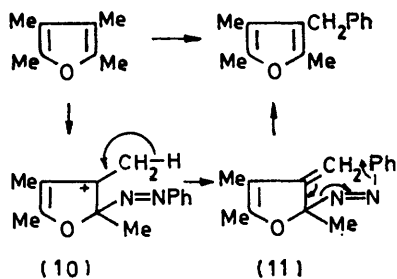
SCHEME 7

markedly affected by temperature,[14,23] and unpublished experiments[24] show that the decomposition in 2,5-dimethylfuran is no exception. Thus it is particularly noteworthy that the experiments reported in this paper refer to the decomposition at room temperature only.

Conclusion. The novel formation of 2-benzyl-5-methylfurans and 3-acetyl-1-aryl-4-arylazo-5-methyl-pyrazoles from reactions of acylarylnitrosamines in anhydrous 2,5-dimethylfuran in benzene and the previously recorded formation of 3-acetyl-5-methyl-1-

(*p*-nitrophenyl)pyrazole from aqueous *p*-nitrobenzene-diazonium acetate and 2,5-dimethylfuran, can therefore be accommodated by Scheme 8. The key role in this is
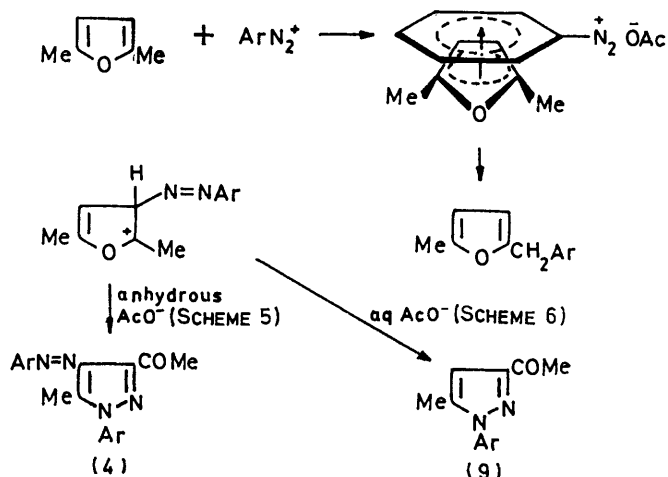
SCHEME 8

played by the diazonium acetate ion pair, and these reactions provide a further example of the recently recognised high basicity of the acetate ion in non-aqueous systems.[1,14]

[23] V. Hassmann, C. Rüchardt, and C. C. Tan, *Tetrahedron Letters,* 1971, 3885.

[24] J. I. G. Cadogan, J. R. Mitchell, and J. T. Sharp, unpub-lished observations.