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FURAN DERIVATIVES—LX

A CONVENIENT NEW METHOD OF ARYLATION OF FURAN REACTION OF DIAZOAMINOBENZENES WITH FURAN AND ISOPENTYL NITRITE

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Abstract—A convenient new method for the arylation of furan with derivatives of diazoaminobenzene and isoamyl nitrite is described. Using this method the substituted 2-(X-phenyl)furan derivatives, where X is H, 4-CH_3, 4-Cl, 4-Br, 3-Cl, 3,4-diCl, 4-NO_2, 4-$COOCH_3$, 4-COOH, 4-Cl-3-CF_3 and 2-(3-pyridyl)furan were prepared. The reaction of methyl 4-aminobenzoate with furan and isopentyl nitrite gave (besides 2-(4-carbmethoxyphenyl)furan) 4,4'-dicarbmethoxydiazoaminobenzene, the structure of which was proved by mass spectrometry and by synthesis. This diazoaminobenzene derivative was unstable in the reaction medium and with isopentyl nitrite and furan at 30° gave 2-(4-carbmethoxyphenyl)furan. The mechanism of the reaction is discussed.

INTRODUCTION

It has been shown that in the reaction of a primary aromatic amine with isopentyl nitrite in benzene, nitrogen was released and the arylation of benzene occurred.[1]

$$ArNH_2 + C_5H_{11}ONO + ArH \rightarrow Ar\text{-}Ar \qquad (1)$$

Cadogan proposed that the reaction does not involve formation of diazoaminobenzenes at low temperature (b.p. of benzene) which is unsatisfactory for homolysis of the corresponding diazoaminobenzenes (130–160°).[2] Further, no products arising from reaction of radical ArNH., which should form during decomposition of diazoaminobenzene, were detected.

At present the theory is accepted that the reaction (1) is carried out via diazohydrates,[3] which by decomposition through the diazoanhydrides[4–6] give a phenyl radical and the radical ArN_2O, proved by EPR spectroscopy.[4] Previous studies[7,8] on the arylation of furan did not reveal any nitrogen derivatives in the mixture.

RESULT AND DISCUSSION

In the reaction between methyl 4-aminobenzoate with isopentyl nitrite and furan, besides of the product of arylation of furan, 2-(4-carbmethoxyphenyl)furan, we isolated another crystalline compound. The elementary analysis of this compound showed that it contains 13·70% nitrogen. The result of these experiments are in contrast with the previous ones[1,7,8] in which no nitrogen derivatives were isolated. IR spectra (KBr) revealed $\nu_{NH} = 3435\,cm^{-1}$ and $\nu_{C=O} = 1721\,cm^{-1}$. Further, the presence of aromatic skeleton $\nu = 1614\,cm^{-1}$ was also found. No absorption band corresponding to vibrations of the furan nucleus was detected.[9] The mass spectrum of the unknown compound is illustrated graphically in terms of relative intensities (Fig 1). In the spectrum only ions with a relative intensity ≥2% are recorded. The basic fragmentation of the molecular ion is the splitting of the bonds C—N and N—N (Scheme 1) and provides the most intensive ions at *m/e* 135 and 163, respectively.

An unusual fragmentation *m/e* 135 to *m/e* 103 was observed with elimination of the neutral fragment CH_3OH. This was supported by the presence of the metastable peak in a spectrum ($m^* = 78{\cdot}58$) and it was the subject of further investigation using "metastable defocusing", a technique described by Jennings.[10] The occurrence of a metastable ion was proved and its relative intensity was 3% in relation to the peak *m/e* 103.

In order to confirm our conclusion that the isolated compound is 4,4'-dicarbmethoxydiazoaminobenzene (1) this compound was prepared by the diazotisation of methyl 4-aminobenzoate. The product of this reaction was

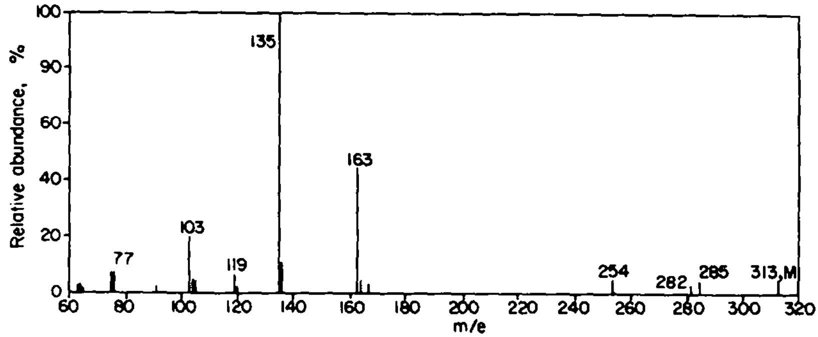
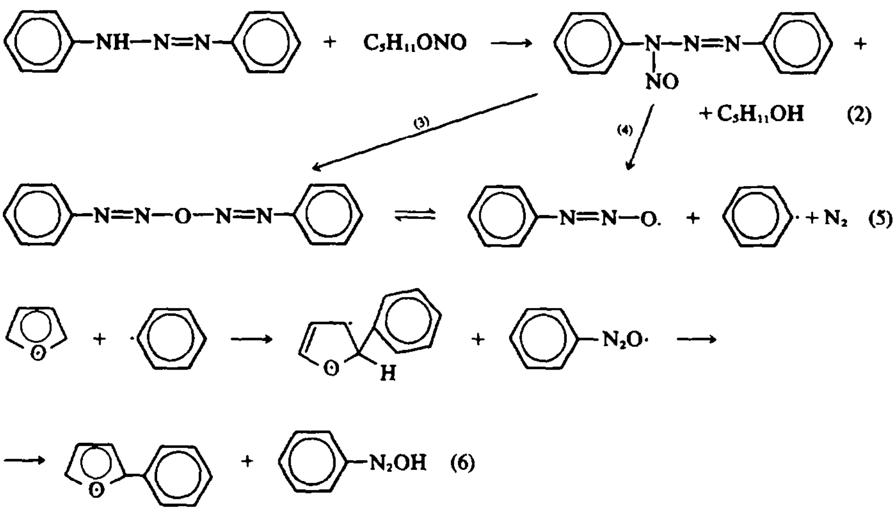


Fig 1. The mass spectrum of unknown compound.



identical with the isolated compound (Experimental).

It was of interest to know, whether the compound (1) was a by product or an intermediate in the reaction of the methyl 4-aminobenzoate with isopentyl nitrite in furan. The reaction of aromatic amines with alkyl nitrite which leads to the formation of the corresponding diazoaminobenzene derivatives has been recorded in the literature.[11-13]

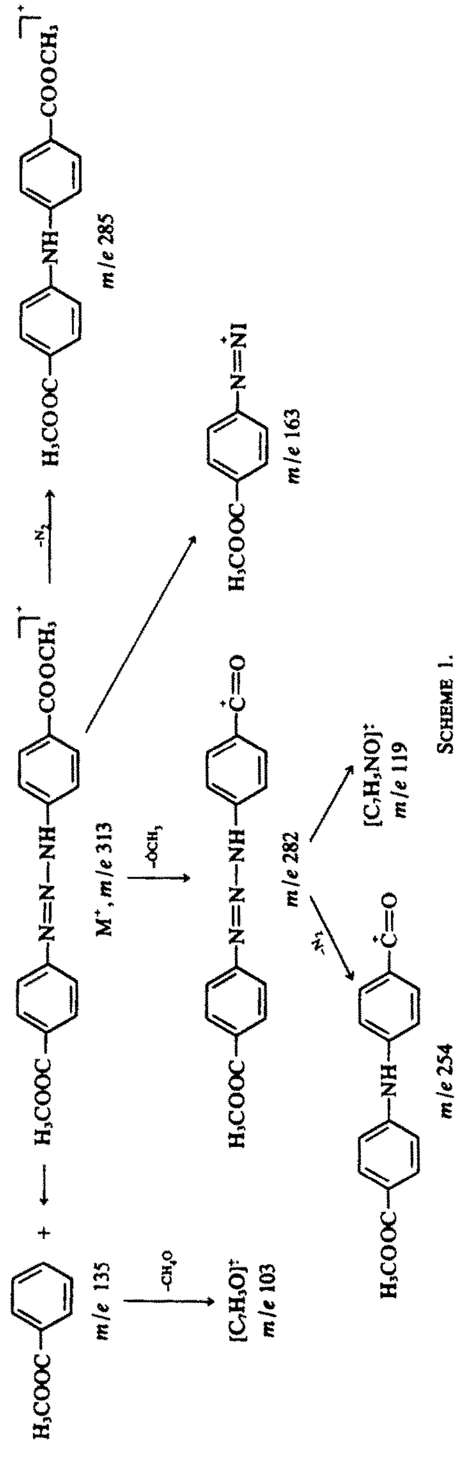
The reaction of compound 1 with isopentyl nitrite in furan at 30° (24 h) led to the formation of 2-(4(carbmethoxyphenyl)furan. The structure of this compound was confirmed by its NMR spectrum and by comparison with a standard (b.p., in mixture b.p. and GLC chromatography).

In order to generalize the reaction, we have studied the reaction of the unsubstituted diazoaminobenzene in furan with isopentyl nitrite at 30°. The analysis of the reaction mixture (by means GLC chromatography on column OV-17 at 160°) showed the presence of 2-phenylfuran (t_R 8·50 min) as the main product and the by-products were: isopentyl alcohol (t_R = 1·08 min), aniline 1·2% (t_R = 3·60 min), benzene 0·17% (t_R = 4·60 min), 2,2-difuryl 0·19% (t_R = 6·22 min) and 0·06% of an unknown product (t_R = 2·84 min). The remaining compounds were very difficult to identify (tars). An identical reaction mixture was formed by the reaction of aniline and isopentyl nitrite in furan.

The present and other observations could be accounted for in mechanism as shown.

The first step is the nitrosation of diazoaminobenzene. The N-nitroso compound is homolytically split to the corresponding radicals (4) or rearranges to the diazoanhydride (3) which is decomposed in a well-known way. The aryldiazoxy radical takes a hydrogen from the 2,3-dihydrofuran radicals and 2-phenylfuran is formed (6).

From the reaction mechanism clearly follows, why radicals of types ArNH can not be formed in the reaction of aromatic amines with nitrites in an aromatic solvent. This was the main reason for selecting diazoaminobenzenes as reaction intermediates. Further, this mechanism supports the existence of aryldiazoxyl radicals $ArN_2O.$, which were identified in the reaction (1) by means of EPR spectrometry,[4] and also the need for an excess of


H$_3$COOC
m/e 135
+
H$_3$COOC
N=N—NH
COOCH$_3$
M$^+$, m/e 313
-N$_2$
H$_3$COOC
NH
COOCH$_3$
m/e 285
-CH$_2$O
[C$_7$H$_3$O]$^+$
m/e 103
-OCH$_3$
H$_3$COOC
N=N—NH
C=O
m/e 282
H$_3$COOC
N=N
m/e 163
-N$_2$
H$_3$COOC
NH
C=O
m/e 254
[C$_7$H$_5$NO]$^+$
m/e 119

SCHEME 1.

isopentyl nitrite in the reaction. The formation of benzene can be understood by analogy with the formation of CH_3COOH in the decomposition of N-nitrosoacetanilide.[15,16]

EXPERIMENTAL

Gas chromatography was carried out using a Hewlett-Packard 7620 A research gas chromatograph with a dual hydrogen flame-ionisation detector A 18 × 0·2 cm steel column packed with Diatiport (80–100 mesh) and coated with 10% silicone gum UCW 98 and OV-17 were used. The flow rate of the carrier gas (nitrogen) was 33·5 ml/min. The injector port and detector temp were 220°. The column temp was 160°.

Furan was the commercial product of the highest purity grade available, and was carefully distilled before the reaction. M.ps are uncorrected. IR spectra were measured using a Zeiss (Jena) IR spectrophotometer. ^{1}H-NMR spectrum were determined in $CDCl_3$ using TMS as internal standard.

The mass spectrum of compound was measured on MS 902 S apparatus using direct inlet system. Energy of ionization was 70 eV, trap current 100/μA, temp of the ion source 110°C. The exact measurement of masses was done by usual technique of the "peak matching" using of heptacosafluorotributylamine as standard at resolving powe 20·000 (10% valley definition).

Reaction of methyl-4-aminobenzoate with isopentyl nitrite and furan. Methyl 4-aminobenzoate (4·14 g, 27·5 mMol), isopentyl nitrite (6·5 ml, 58 mMol) and furan (100 ml) were kept at 30° for 48 h. The resulting soln was washed with water and evaporated. The residue was distilled in steam. The distillate contained a solid which was filtered off; this was crude methyl-2-furylbenzoate (1·8 g, 32·3%, m.p. 121–122°) after crystallization from EtOH.

The residue of the distillation was chromatographed on silica gel with benzene as eluant afforded a yellow crystalline compound, m.p. 216–219° (Found: N, 13·70%). IR spectrum (KBr) 863, 1117, 1173, 1200, 1256, 1290, 1318, 1408, 1441, 1535, 1614, 1705, 1721, 2951, 2995, 3226 and 3435 cm^{-1}; UV spectrum (EtOH) λ_{max} 373 nm (log ϵ = 4·36); λ_{max} 294 nm (log ϵ = 4·26 and λ_{max} 259 nm (log ϵ = 4·11). M^+ 313 ($C_{16}H_{15}N_3O_4$) base peak 135.

The unknown compound (13·7% N found) (1 g), isopentyl nitrite (2 ml) and furan (50 ml) were kept at 30° for 24 h. The resulting soln was washed with water, dried (Na_2SO_4) and evaporated. Chromatography on alumina of the residue with benzene as eluant afforded white crystalline compound (0·5 g) m.p. 121°, which was shown by GLC on a 10% UCW 98 160° to be methyl-2-furylbenzoate. τ ($CDCl_3$) 2·14 (center of AABB' 4H);[18] 2·52 (dd, 5H); 3·22 (dd, 3H); 3·51 (dd, 4H); 6·09 (s, $COOCH_3$); $I_{3,4}$ = 3 Hz, $I_{3,5}$ < 1 Hz, $I_{4,5}$ = 1·8 Hz.

4,4'-Dicarbmethoxydiazoaminobenzene was prepared from diazotised methyl 4-aminobenzoate and NaOAc, m.p. and mixed m.p. 218–219° (EtOH). (Found: C, 61·25, H, 5·00 and N, 13·62. $C_{16}H_{15}N_3O_4$ (313·61) requires: C, 61·34, H, 4·83, N, 13·41%); IR spectrum (KBr) 865, 1117, 1173, 1200, 1257, 1291, 1318, 1410, 1440, 1535, 1612, 1705, 1719, 2950, 2995, 3225 and 3435 cm^{-1}; UV (EtOH) λ_{max} = 373 nm (log ϵ = 4·30), λ_{max} = 293 (log ϵ = 4·25), λ_{max} = 259 nm (log ϵ = 4·12). M^+ 313 ($C_{16}H_{15}N_3O_4$) base peak 135.

Reaction of diazoaminobenzene and substituted diazoaminobenzenes with isopentyl nitrite and furan. Diazoaminobenzene (1·97 g, 10 mMol), isopentyl nitrite (2 ml, 11 mMol) and furan (50 ml) were kept at 30° for 24 h. The soln was washed with water, dried (Na_2SO_4) and evaporated. The residue was analysed by GLC with column reported above, gave 2-phenylfuran (t_R 8·50 min 10% OV-17 160°) and isopentyl alcohol (t_R 1·06 min), 1·2% aniline (t_R 3·60 min), 0·17% benzene (t_R 4·60 min), 0·19% 2,2-bifuryl (t_R 6·22 min) and 0·06% unknown product (t_R 2·84 min). The soln was distilled (89–92°/7 mmHg) to give 1·1 g (34·5%) 2-phenylfuran. 2-Phenylfuran as standard was prepared from aniline, isopentyl nitrite and furan.[4]

The following reactions of substituted diazoaminobenzenes and isopentyl nitrite with furan were similarly carried out: 4,4'-Dichlorodiazoaminobenzene gave 2-(4-chlorophenyl)furan, t_R 7·17 min on UCW 98–160° and all following derivatives, m.p. and mixed m.p. 65–66°, lit[18] 66°; 52·3%; 3,3'-dichlorodiazoaminobenzene gave 2-(3-chlorophenyl)furan, t_R 6·78 min, (b.p. 75°C/2 mm Hg lit[8] b.p. unknown 43·2%); 3,3'4,4'-tetrachlorodiazoaminobenzene gave 2-(3,4-dichlorophenyl)furan, t_R 14·17 min), m.p. 51–2°, 31·2%. (Found: Cl, 33·01, C, 56·52 and H, 2·85. $C_{10}H_{16}Cl_2O$ (213·06) requires: Cl, 33·29, C, 56·36, H, 2·83%); IR spectrum (CCl_4) ν_{max} 888 (furyl ring), 1615 (phenyl ring); UV spectrum λ_{max} (EtOH) 289 nm (log ϵ = 4·47); λ_{max} = 235 nm (log ϵ = 4·05); λ_{max} = 228 nm (log ϵ = 4·14).

4,4'-Dinitrodiazoaminobenzene gave 2-(4-nitrophenyl)furan, t_R 6·75 min (m.p. and mixed m.p. 134–135°, lit[20,21] 133–135°, 30·8%); 4,4'-dibromodiazoaminobenzene gave 2-(4-bromophenyl)furan, t_R 11·05 min (m.p. 83–84°, 35·2%) (Found: Br, 36·01, C, 54·02 and H, 3·15. $C_{10}H_7BrO$ (223·05) requires: Br, 35·83, C, 53·86, H, 3·16%); IR spectrum (CCl_4) ν_{max} 889 (furyl ring), 1617 (phenyl ring), λ_{max} (EtOH) = 287 nm (log ϵ = 4·39); λ_{max} = 229 nm (log ϵ = 3·87); λ_{max} = 222 nm (log ϵ = 3·92). 4,4'-Dimethyldiazoaminobenzene gave 2-(4-tolyl)furan (b.p. 67°/2 mmHg, lit[19] 56°/0·5 mmHg, 41·2%); 4,4'-dicarboxydiazoaminobenzene gave 2-furyl-4-benzoic acid (m.p. and m.p. mixed 226°, lit[22] 226°, 42·3%); 4,4'-dicarbmethoxydiazoaminobenzene gave methyl-2-furyl-4-benzoate, t_R 19·70 min (m.p. and m.p. mixed 121–2°, lit[17] 121°, 70%); 3,3'-ditrifluoromethyl-4,4'-dichlorodiazoamino-benzene gave 2-(3-trifluoromethyl-4-chlorophenyl)-furan, t_R 7·04 min (b.p. 86–90°/4 mmHg, 42·8%. (Found: Cl, 13·96, C, 53·55, H, 2·32. $C_{11}H_6ClF_3O$ (246·62) requires: Cl, 14·37, C, 53·50, H, 2·04%); IR spectrum (CCl_4) ν_{max} 890 (furyl ring), 1617 (phenyl ring); λ_{max} (EtOH) = 290 nm (log ϵ = 4·13), λ_{max} = 227 nm (log ϵ = 3·69). Bis 1,3 pyridyl(3)-triazene gave 2-(3-pyridyl)furan (b.p. 78–80°/4 mmHg,[23] t_R = 7·69 min, 28·2%).

Table 1. Composition of some ions in the mass spectrum

	Mass		
m/e	Measures	Calculated	Composition
77	77·0379	77·0391	C_6H_5
103	103·0182	103·0184	C_7H_3O
119	119·0365	119·0371	C_7H_5NO
163	163·0495	163·0507	$C_8H_7N_2O_2$
254	254·0829	254·0817	$C_{15}H_{12}NO_3$
282	282·0863	282·0879	$C_{15}H_{12}N_3O_3$
313	313·1072	313·1062	$C_{16}H_{15}N_3O_4$

REFERENCES

[1] J. I. G. Cadogan, *J. Chem. Soc.* 4257 (1962)

[2] R. L. Hardie and R. H. Thompson, *Ibid.* 1286 (1958)

[3] I. P. Gračerov and A. F. Levit, *Zh. Org. Khim.* **4**, 10 (1968)

[4] A. F. Levit and I. P. Gračerov, *Ibid.* **5**, 310 (1969)

[5] C. Rüchardt and E. Merz, *Tetrahedron Letters* 2431 (1964)

[6] C. Rüchardt and B. Freudenberg, *Ibid.* 3623 (1964)

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

[8] L. Benati, C. M. Camaggi, M. Tiecco and A. Tundo, *J. Hetěroc. Chem.* **9**, 919 (1972)

[9] K. Nakanishi, *Infrared Absorption Spectroscopy* p. 52. Holden-Day San Francisco (1962)

[10] K. R. Jennings, *J. Chem. Phys.* **43**, 4176 (1965)

[11] J. Griess, **18**, 298 (1865)

[12] Meyer and Ambuhl, *Ber. Dtsch. Chem. ber* **8**, 1074 (1875)

[13] Ger. Pat. 905,014 Feb. 25, 1954 (Cl. 120,27); *Chem. Abstr.* **50**, 12111b (1956)

[14] W. A. Waters, *Free Radical Reactions*, p. 151. Butterworths London (1973)

[15] J. I. G. Cadogan, *Accounts Chem. Res.* **4**, 186 (1971)

[16] J. I. G. Cadogan, *Essays on Free-Radical Fractions*, Special Publication No. 24, p. 71. The Chemical Society London (1970)

[17] Ľ. Fišera, J. Kováč, M. Lucký and J. Surá, *Chem. Zvesti* **28**, 386 (1974)

[18] R. Grigg, J. A. Knight and M. V. Sargent, *J. Chem. Soc.* (C) 976 (1966)

[19] D. C. Ayres and J. R. Smith, *Ibid.* (C) 2737 (1968)

[20] H. H. Hodgson and R. R. Davies, *Ibid.* 1013 (1939)

[21] J. Kováč, R. Frimm and A. Krutošíková, *Zborník prác Chemickotechnologickej fakulty SVŠT*, Bratislava p. 37

[22] Ľ. Fišera, J. Surá, J. Kováč and M. Lucký, *Collection Czech. Chem. Commun.* **39**, 1711 (1974)

[23] H. S. Rayang and H. Sakura, *J. Chem. Soc. Commun.* 594 (1972)