Intramolecular Nitrene Insertions into Aromatic and Heteroaromatic Systems. Part 5.[1,2] Synthesis of Diethyl 2-Alkylfuro[3,2-*c*]carbazol-5-ylphosphonates and of 9-(*N*-methylpyrrol-2-yl)pyrrolo[3,2-*b*]quinoline by Deoxygenation of *o*-Nitrophenyldi-(2-furyl)- or *o*-Nitrophenylbis-(*N*-methylpyrrol-2-yl)-methanes

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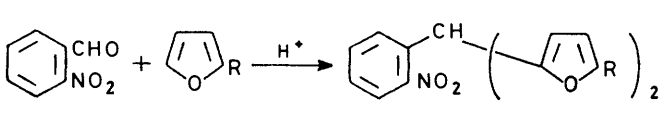
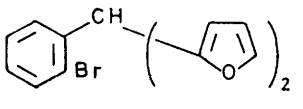
Deoxygenation of *o*-nitrophenylbis-(2-alkyl-5-furyl)methanes (2)—(4), using triethyl phosphite, gives diethyl 2-alkylfuro[3,2-*c*]carbazol-5-ylphosphonates (6)—(8). The mechanism of the reaction is discussed. Similar deoxygenation of *o*-nitrophenylbis-(*N*-methylpyrrol-2-yl)methane (12) gives 1-methyl-9-(*N*-methylpyrrol-2-yl)-pyrrolo[3,2-*b*]quinoline (13).

We have reported[3,4] that intramolecular attack by a nitrene derived from *o*-azidobenzylthiophens leads to products in which considerable rearrangement of the thiophen ring has occurred. We wished to extend this investigation to determine the mode of intramolecular nitrene attack on furan rings; however, all attempts to obtain a suitable *o*-azidobenzylfuran were foiled by the instability of furan rings to diazotisation conditions. The appropriate *o*-aminobenzylfurans can be prepared but formed tars on addition of sodium nitrite to their solutions in acid. We have been able to prepare a series of *o*-nitrophenyldi-(2-furyl)methanes (1)—(4), and deoxygenation of these has provided several examples of a new heterocyclic system.

The difurylmethanes (1)—(4) were prepared by condensation of *o*-nitrobenzaldehyde with the appropriate furan in glacial acetic acid–sulphuric acid at 0—5 °C. By a similar route *o*-bromophenyldi-(2-furyl)methane(5) was obtained; attempts to prepare the azide *via* the Grignard reagent failed. Deoxygenation of the parent compound (1), using triethyl phosphite in boiling cumene, gave many products, none of which could be characterised even after column or preparative layer chromatography. However, similar deoxygenation of the substituted compounds (2)—(4) gave, after chromatography, crystalline solids in moderate yields (28, 13, and

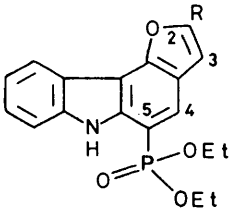


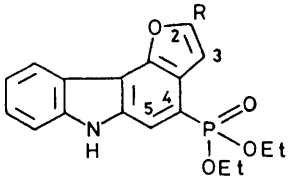


(5)

(1) R = H
(2) R = Me
(3) R = Et
(4) R = Bu^t

12% respectively); the three products were closely related, having molecular formulae $C_{18}H_{17}NO_4P{\cdot}R$ where R was Me, Et, or Bu. The evidence for the structures is spectral and is discussed in detail for the methyl derivative from compound (2). The 2-alkylfuro[3,2-*c*]carbazol-5-ylphosphonates (6), (7), and (8) are the first reported examples of a furo[3,2-*c*]carbazole system.





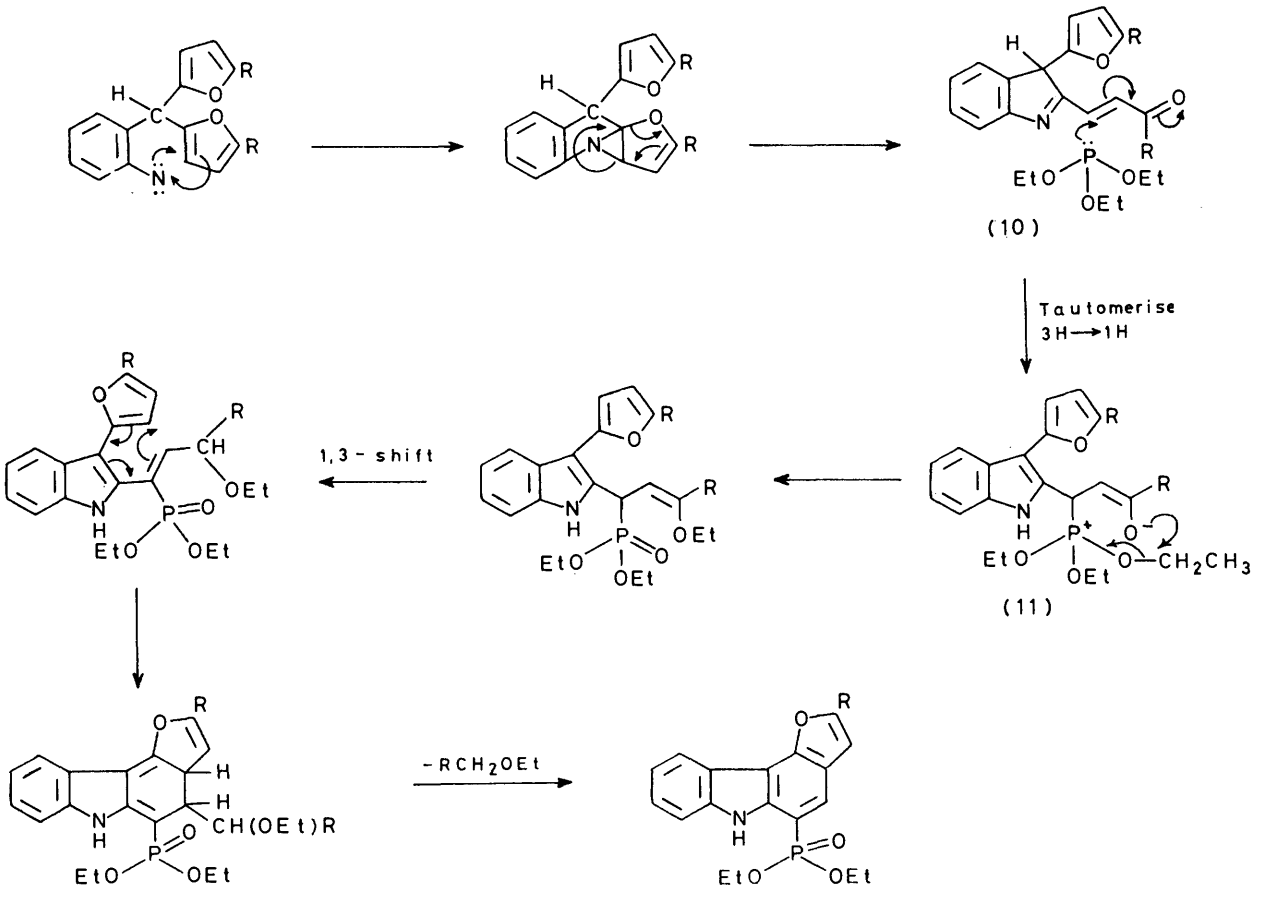
(9)

(6) R = Me
(7) R = Et
(8) R = Bu^t

The compound (6) showed $\lambda_{max.}$ 250, 275, 292, 301, and 353 nm, unaffected by acid but changed by base. The mass spectral breakdown pattern was complex, but showed major losses of 17 (OH) and 57 ($C_2H_5 + C_2H_4$). The most important evidence came from the ^{31}P, ^1H, and ^{13}C n.m.r. spectra. The ^{31}P signal was at −21 p.p.m. from phosphoric acid, in the region accepted for phosphonates. In the ^1H spectrum the presence of two ethoxy groups was shown by signals at δ 1.3 (6 H, t) and 4.1 (4 H, q of d), the latter showing coupling to ^{31}P. A signal at δ 2.55 (3 H, d, *J* 1.5 Hz) was coupled to a single proton absorption in the furan region at δ 6.42; we have observed such coupling in thiophens angularly fused to other polycyclic systems.[4] The most striking feature of the aromatic region of the spectrum was a doublet (*J* 14 Hz) at δ 7.78 which is assigned to an aromatic proton with an *ortho*-phosphorus substituent. Finally, a broad exchangeable signal at δ 10.1 agrees well with that observed for a carbazole NH. Examination of a ^{31}P decoupled ^1H n.m.r. spectrum showed simplification of the signals due to OCH_2 and collapse of the doublet (H-4) to a singlet at δ 7.78. The combined data would fit structures (6) or (9) equally well; it was possible to confirm that (6) was correct by use of the Eu(fod)$_3$ shift reagent. A large downfield shift was observed in the signals at δ 4.1 (OCH_2), 7.7 [CH = C(P)], and 10.1 (NH). The complexing power of the phosphonate is such that the shift reagent must be

adjacent to it; the pattern of downfield shifts places the phosphonate at the 5-position. The ^{13}C n.m.r. spectrum of compound (8) also agrees with that predicted. In the ^1H decoupled spectrum the aliphatic region contains peaks at δ 16.18—16.47 (d, *J* 7 Hz, CH_3CH_2OP), at 28.9 (s, CH_3C), at 33.14 (s, CH_3C) and at 62.18—62.37 (d, *J* 5 Hz, CH_3CH_2OP). In the aromatic region there are 13 resolvable signals; one, due to a CH group at δ 125.9 must represent two co-incidental absorptions due to C-4 and C-8. The other CH absorptions (from the undecoupled spectrum) are at δ 99.16 (*J* 174 Hz, C-3), 111.0, 119.0, and 122.4; carbazole shows *C*H absorptions at δ 111.5, 119.3, 120.6, and 126.1. Quaternary carbon atoms absorb in compound (8) at δ 99.1, 106.7, 119.3, 120.75, 138.9, 140.4 (d, C-5a), 152.0, and 166.55. Comparable figures for quaternary carbons in carbazole are δ 123.8 and 140.8, and for 2-methylbenzo[*b*]furan [5] δ 155.2 (C-2), 102.6 (C-3), 129.3 (C-3a), and 154.9 (C-7a).

The mechanism of formation of the furocarbazole phosphonate remains obscure. From our own experiments on the deoxygenation of *o*-nitrophenyldithienylmethanes,[6] where the pattern of products matches those from thermal decomposition of *o*-azidophenyldithienylmethanes, we believe that a nitrene intermediate is involved. It would be expected, from the work of Jones [7] and Hafner [8] that attack by nitrene on a furan leads to the αβ-unsaturated indolenyl ketone (10) which undergoes nucleophilic attack by phosphite at the β-position, to give intermediate (11), correctly sited to appear at the 5-position in the furyl carbazole. There is no evidence to indicate the method of ring closure, or the mode of elimination of the acyl group; we have found only acetaldehyde in the nitrogen effluent from the reaction, but this is obtained from compounds (3) and (4) and hence presumably comes from some phosphite decomposition. We show a possible mechanism in the Scheme but evidence for this is likely to be very difficult

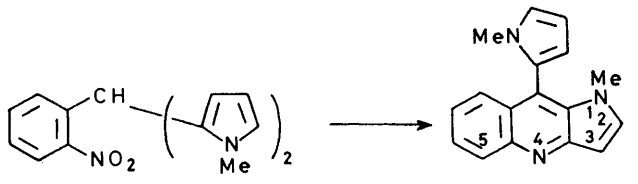


SCHEME

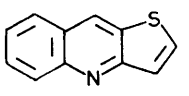
to obtain. The failure to isolate compound (6; R = H) is not surprising in view of the tendency of furylacroleins to polymerise.

We have performed one deoxygenation in the corresponding dipyrromethane series, [compound (12)]. Condensation of *o*-nitrobenzaldehyde with *N*-methylpyrrole using either perchloric acid or zinc chloride as catalyst gave poor yields of compound (12). Deoxygenation of compound (12) with triethyl phosphite in boiling cumene gave a mixture (t.l.c.; ethyl acetate–toluene, 20%). One spot (R_F 0.12) showed a light blue fluorescence. Column and preparative layer chromatography gave, as the only identified material, the pyrrolo[3,2-*b*]quinoline (13) (*ca.* 17%), characterised as its picrate. The pyrroloquinoline showed δ 3.0 and 3.1 (each s, 6 H,

2 × NMe), 6.2 (2 H, m, pyrryl H), 6.65 (2 H, m, pyrryl H and H-2), 7.0—7.8 (4 H, m, aromatic + H-3), and



(12) (13)



(14)

8.2br (1 H, d, H-5). Addition of $Eu(fod)_3$ simplified the spectrum; the doublet at δ 8.2 and another doublet (J 3 Hz, H-3) moved downfield, confirming the pyrrolo[3,2-*b*]quinoline structure. The spectrum of compound (13) is very similar to that of the thienoquinoline (14) [4] and to those of 9-substituted thieno[3,2-*b*]quinolines.[6] Only a few pyrrolo[3,2-*b*]quinolines have been prepared; [9,10] the yields range from 40% for the 2-phenyl derivative [9] through 20% for the unsubstituted and the 2-methyl derivatives [9] to 6% for the 1-methyl derivative,[10] so that deoxygenation, even with its low yield, provides a useful alternative approach.

EXPERIMENTAL

M.p.s were determined on a Kofler heated stage. P.l.c. was done on 40 × 20 cm plates of silica (Merck P_F 254); column chromatography on Woelm alumina (activity grade 4). U.v. spectra was measured for solutions in 95% ethanol.

General Procedure for Preparation of o-*Nitrophenyldi-(2-furyl)methanes.*—A solution of *o*-nitrobenzaldehyde (10 g, 0.066 mol) and the furan (0.22 mol) in glacial acetic acid (40 ml) was cooled to 0—5 °C, and concentrated sulphuric acid (4 ml) in glacial acetic acid (20 ml) added slowly with stirring. The flask was kept at 0—5 °C with occasional shaking and stirring for 2—3 days; the resulting solution was poured onto ice and the mixture thoroughly extracted with chloroform; the extracts were dried ($MgSO_4$) and evaporated on to alumina (30 g). The coated alumina was added to a column of alumina (200 g) prepared in petroleum (b.p. 60—80°) and eluted with benzene–petroleum (1 : 19). The first band (yellow) was the *o*-nitrophenyldifuryl-methane; yields and physical properties are reported in Table 1.

o-*Bromophenyldi(2-furyl)methane* (5).—Similarly prepared using *o*-bromobenzaldehyde; see Table 1.

o-*Aminophenyldi-(2-furyl)methane.*—A solution of the nitro-compound (1) (2 g) in 95% ethanol (100 ml) with 10% Pd–C (0.25 g) was hydrogenated at atmospheric temperature and pressure (1 h); *ca.* 500 ml of hydrogen were absorbed. The solution was filtered and evaporated and the residual oil chromatographed on alumina (100 g). Elution with petroleum (b.p. 40—60°) gave o-*amino-phenyldi-(2-furyl)methane*, b.p. 140° at 0.3 mmHg (1.3 g, 70%) (Found: C, 75.4; H, 5.55; N, 5.6. $C_{15}H_{13}NO_2$ requires C, 75.3; H, 5.45; N, 5.85%); $\nu_{max.}$ (film) 3 380 and 3 440 cm^{-1}; $\lambda_{max.}$ 226sh (4.36) and 290 (3.53); δ($CDCl_3$) 3.47 (2 H, br s, NH_2), 5.5 (1 H, s), 6.17 (4 H, m, furyl H), and 6.47—7.4 (6 H, m, C_6H_4 and furyl H).

TABLE 1

Physical constants of *o*-substituted phenyldi-(2-furyl)methanes

Compound	Yield	Formula	Found C	Found H	Found N	Required C	Required H	Required N	M.p./B.p. (°C)	δ
(1)	33	$C_{15}H_{11}NO_4$	67.2	4.35	4.8	66.9	4.1	5.2	120 at 0.7 mmHg	6.2 (5 H, m) [a], 7.2—8.1 (6 H, m)
(2)	50	$C_{17}H_{15}NO_4$	68.9	5.1	4.8	68.7	5.05	4.7	80 [b]	2.16 (6 H, s, CH_3), 5.86 (4 H, m), 6.2 (1 H, s), 7.1—7.9 (4 H, m)
(3)	47	$C_{19}H_{19}NO_4$	70.15	5.9	4.3	70.45	6.15	4.35	130 at 0.5 mmHg	1.1 (6 H, t, CH_3CH_2), 2.5 (4 H, q, CH_3CH_2), 5.8 (4 H, m), 6.15 (1 H, s), 7.1—7.5 (3 H, m), 7.8 (1H, d of d)
(4)	75	$C_{23}H_{27}NO_4$	M^+, 381			M^+, 381			180 at 0.3 mmHg	1.22 (18 H, s), 5.9 (4 H, m), 6.25 (1 H, s), 7.2—7.6 (3 H, m), 7.9 (1 H, d of d)
(5)	25	$C_{15}H_{11}BrO_2$	59.4	3.65		59.4	3.65			5.9 (3 H, m), 6.25 (2 H, m), 6.9—8.1 (5 H, m)

[a] Sharp signal (1 H) moved downfield by addition of $Eu(fod)_3$. [b] From petroleum (b.p. 40—60°).

o-*Aminophenylbis-(5-methyl-2-furyl)methane.*—(*a*) Prepared as described above in 53% yield. (*b*) To a solution of the nitro-compound (2) (3 g) in methanol (50 ml) with Pd–C (1 g, 10%) and ferric chloride (17 mg) was added, dropwise, hydrazine hydrate (98%; 1 ml). The mixture was heated to boiling and boiling continued for 4 h. The cooled solution was filtered, the filtrate evaoprated, and the residue chromatographed; a pure sample of o-*amino-phenylbis-(5-methyl-2-furyl)methane* (2.1 g, 80%) was obtained by elution with petroleum (b.p. 40—60°) (Found: C, 76.5; H, 6.6; N, 5.1. $C_{17}H_{17}NO_2$ requires C, 76.4; H, 6.35; N, 5.25%), $\nu_{max.}$ (film) 3 380 and 3 440 cm^{-1}; $\lambda_{max.}$ 225 (4.57) and 287 (3.28); δ($CDCl_3$) 2.17 (6 H, s, 2 × Me), 3.52 (2 H, br s, NH_2), 5.35 (1 H, s), 5.85 (4 H, m, furan H), and 6.5—7.25 (C_6H_4).

Deoxygenation Procedure for Nitro-compounds (1)—(4).—A solution of triethyl phosphite (35 ml) in cumene (50 ml) was added dropwise to a stirred solution of nitro-compound (0.05 mol) in cumene (350 ml). The mixture was boiled and stirred under nitrogen until all nitro-compound had been consumed (t.l.c.), usually in 40—45 h. The solvent

and triethyl phosphite were evaporated *in vacuo* and the residual brown oil chromatographed on alumina (400 g). Elution with petroleum (b.p. 60—80°) and low percentages of benzene in petroleum gave complex mixtures, decomposing in air. Elution with benzene–petroleum (1 : 1) gave as brown solids the phosphonates listed in Table 2.

o-*Nitrophenylbis*-(N-*methylpyrrol*-2-*yl*)*methane* (12).—(*a*) A mixture of *o*-nitrobenzaldehyde (3 g), *N*-methylpyrrole (3.2 g), and zinc chloride (5 g), was heated and stirred on a boiling water-bath (2 h). Addition of water and extraction with methylene chloride gave, after drying and evaporation of the solvent, a residue which solidified on trituration with methanol. Recrystallized from methanol, the yellow *dipyrromethane* (12) had m.p. 156—157° (1.6 g, 28%) (Found: C, 69.4; H, 5.7; N, 14.7. $C_{17}H_{17}N_3O_2$ requires C, 69.15; H, 5.8; N, 14.25%); δ($CDCl_3$) 3.4 (6 H, s), 5.4 (2 H, m), 5.9 (2 H, t), 6.17 (2 H, s), 6.5 (2 H, m), 7.0—7.2 (1 H, m), 7.25—7.6 (2 H, m), and 7.9 (1 H, d of d).

(*b*) To a solution of *o*-nitrobenzaldehyde (1.5 g) and *N*-methylpyrrole (1.6 g) in ethanol (7 ml) was added 60% perchloric acid (1 ml) when a precipitate formed. The mixture was warmed to 65 °C and maintained at this temperature for 5 min. The mixture was poured into 10% sodium hydroxide, extracted with methylene chloride, dried, and the solvent evaporated. The residue did not crystallize, and was purified by chromatography on alumina (100 g) with petroleum–benzene (3 : 1) as eluant. The dipyrromethane was identical with and in similar yield to that obtained by procedure (*a*).

Deoxygenation of Dipyrrolylmethane (12).—Compound (12) (6.2 g) was deoxygenated as described for compounds (1)—(4), (41 h). Chromatography on alumina (300 g) of the crude products gave a number of unidentified products in small yield [eluants: petroleum (b.p. 60—80°), 1 l; benzene–petroleum (1 : 9), 2 l; benzene–petroleum (1 : 4), 1 l; benzene–petroleum (1 : 1), 1 l]. Further elution with benzene–petroleum (1 : 1) gave 1-*methyl*-9-(1-*methylpyrrol*-2-*yl*)-1H-*pyrrolo*[3,2-b]*quinoline* (13) (1 g, ~17%), converted into its *picrate*, m.p. 202—203° (from ethanol) (Found: C, 56.2; H, 3.6; N, 17.05. $C_{23}H_{18}N_6O_7$ requires C, 56.3; H, 3.7; N, 17.15%).

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TABLE 2

Diethyl 2-alkylfuro[3,2-*c*]carbazol-5-ylphosphonates

Compound	M.p. (°C)	Yield (%)	Found C	Found H	Found N	Required C	Required H	Required N	Formula	δ
(6)	154—155 [a]	28	63.75	5.6	3.95	63.85	5.6	3.9	$C_{19}H_{20}NO_4P$	1.3 (6 H, t), 2.55 (3 H, d), 4.1 (4 H, q of d), 6.42 (1 H, q), 7.1—7.6 (3 H, m), 7.7 (1 H, d), 8.4 (1 H, d of d), 10.1br (1 H, s)
(7)	124—125 [b]	13	64.5	6.1	3.8	64.7	5.95	3.75	$C_{20}H_{22}NO_4P$	1.2—1.5 (9 H, m), 2.9 (2 H, q), 4.1 (4 H, q of d), 6.45 (1 H, s), 7.2—7.5 (3 H, m), 7.7 (1 H, d), 8.5 (1 H, d of d), 10.1br (1 H, s)
(8)	142—143 [c]	12	66.15	6.8	3.65	66.15	6.55	3.5	$C_{22}H_{26}NO_4P$	1.2 (6 H, t), 1.5 (9 H, s), 4.1 (4 H, q of d), 6.4 (1 H, s), 7.2—7.5 (3 H, m), 7.7 (1 H, d), 8.25 (1 H, d of d), 10.1br (1 H, s).

[a] From CCl_4. [b] From CCl_4–petroleum (b.p. 60—80°). [c] From petroleum (b.p. 60—80°).

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