Heterocycles in Organic Synthesis. Part 7.[1] Synthesis of Furfuryl Derivatives *via* 2,4,6-Trisubstituted Pyridinium Salts

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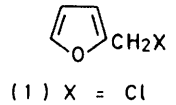
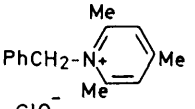
Nucleophilic displacement of the amino-group of furfurylamine by initial conversion into a 2,4,6-trisubstituted pyridinium perchlorate provides a convenient preparation of a wide variety of novel furfuryl derivatives. 2,4,6-Triphenylpyridinium derivatives are more reactive than their 2,4,6-trimethyl analogues. 2-(2,4,6-Triphenylpyridiniomethyl)furan is smoothly brominated in the 5-position, and the brominated product undergoes nucleophilic replacement of the pyridinio group with morpholine.

In Part 6 [1] we described the use of triphenylpyrylium salts for converting primary amino-functions into good leaving groups, and demonstrated several advantages of triphenylpyridine as a leaving group in nucleophilic substitution reactions. We have now applied this new synthetic method to the furfuryl series which contains many compounds of pharmaceutical interest.[2]



(1) X = Cl
(2) X = OH
(3) X = NH_2



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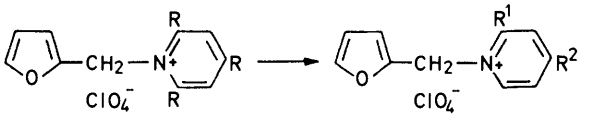
The preparation of 2-(chloromethyl)furan (1) from furfuryl alcohol (2) and thionyl chloride by Kirner [3] provided a route to many new furfuryl derivatives (particularly ethers) which were difficult or impossible to make by previously known methods. However, there are distinct disadvantages in using furfuryl chloride (1). Although it is more stable than the bromide or iodide, and can be vacuum-distilled, the chloride (1) is still relatively unstable: it polymerises upon heating and cannot be stored for long periods. In addition it has the disadvantage, intrinsic in all alkyl halides, that Menchutkin alkylation leads to a mixture of amine derivatives which are difficult to separate. Finally, 2-furfuryl chloride often gives 5-substituted products by S_N2' reaction.[4]

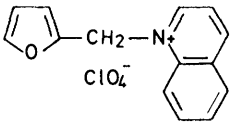
In contrast to the chloride (1), furfurylamine (3) is stable and readily available and is converted into the 2,4,6-triphenyl- and 2,4,6-trimethyl-pyridinium perchlorates (5) and (6) by the appropriate pyrylium perchlorate. Unlike the benzyl derivative (4), the 1-furfuryl-2,4,6-trimethylpyridinium perchlorate (6) was reactive towards a number of nucleophiles. Thus, pyridine and α- and γ-picoline when heated with the salt (6) at 150 °C in a sealed tube gave very good yields (75—95%) of the substitution products (7)—(9); however, the 2,4,6-triphenyl derivative (5) is still more reactive, giving a high yield (90%) of 1-furfurylpyridinium perchlorate (7) when stirred with pyridine at 20 °C. Analogously, compound (5) reacted with α- and γ-picoline giving good yields of the perchlorates (8) and (9) and with quinoline and isoquinoline at 75 °C giving 1-furfurylquinolinium perchlorate (10) (80%) and 1-furfurylisoquinolinium perchlorate (11) (92%).

Similarly the furfuryl derivatives (5) and (6) with secondary amines provide a convenient route to tertiary amines of the furfuryl series. However, whereas the trimethyl compound (6) required an elevated temperature (dimethylformamide solution under reflux), the triphenyl derivative (5) reacted satisfactorily at 20 °C, with the amine as solvent. By employing these methods, furfurylamine was converted into *N*-furfurylpiperidine (12), *N*-furfurylmorpholine (13), *N*-furfurylpyrrolidine (14), and *N*-furfuryldiethylamine (15). The pyridinium perchlorates (5) and (6) when fused with triphenyl-



(5) R = Ph
(6) R = Me

(7) R^1 = R^2 = H
(8) R^1 = Me, R^2 = H
(9) R^1 = H, R^2 = Me



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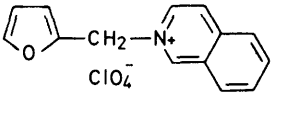

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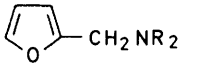
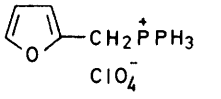


(12) NR_2 = piperidino
(13) NR_2 = morpholino
(14) NR_2 = pyrrolidino
(15) NR_2 = diethylamino



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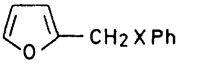


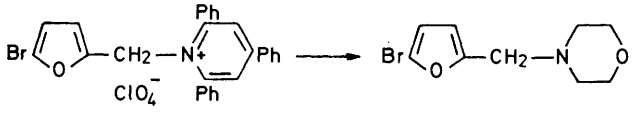
(17) X = O
(18) X = S

phosphine (80 °C) generated the triphenylphosphonium salt (16).

With pyridine 1-oxide at 120 °C the 2,4,6-trimethyl-

pyridinium perchlorate (6) gave furfural, characterised as its 2,4-dinitrophenylhydrazone.* The 2,4,6-triphenylpyridinium perchlorate (5) reacted with sodium phenoxide or sodium benzenethiolate in boiling dimethylformamide giving furfuryl phenyl ether (17) and furfuryl phenyl sulphide (18), respectively.

In addition to its utility as a leaving group, we find that the 2,4,6-triphenylpyridiniomethyl group can also protect the furan ring in electrophilic substitution reactions. Thus although many furans are destroyed by bromination,[5] we now find that 1-furfuryl-2,4,6-triphenylpyridinium perchlorate (5) is brominated to give the 5'-bromofurfuryl derivative (19) in 85% yield. The pyridiniomethyl substituent thus acts similarly to *e.g.* the CO_2Me [6] and CO_2H [7] groups in stabilising the furan ring towards electrophilic substitution.



(19) (20)

A new route is now opened to 2,5-disubstituted furans by subsequent nucleophilic displacement of the pyridiniomethyl group. As an illustration 1-(5-bromofurfuryl)-morpholine (20) was prepared in 59% yield by the reaction of (5) with morpholine.

EXPERIMENTAL

Unless otherwise stated, i.r. spectra were measured in Nujol mull and n.m.r. spectra (60 MHz) in deuteriochloroform (tetramethylsilane as internal reference). M.p.s were determined using a Kofler hot-stage apparatus. Evaporation refers to the removal of volatile material under diminished pressure. When compounds are stated to be identical, their identity has been established by comparison of m.p. and by mixed m.p., and where appropriate by comparison of i.r., n.m.r., and t.l.c. behaviour.

1-*Furfuryl*-2,4,6-*triphenylpyridinium Perchlorate* (5).—Furfurylamine (3) (0.8 ml) was added dropwise to a suspension of 2,4,6-triphenylpyrylium perchlorate (1.2 g) [8] in Et_2O (30 ml). The mixture was vigorously shaken (2 h). A red oil separated and was collected, washed with Et_2O, and dissolved in Me_2CO (5 ml). Trituration with Et_2O (10 ml) gave a solid which was recrystallised from Me_2CO–Et_2O giving *compound* (5) (0.86 g, 60%) as cream plates, m.p. 122 °C (decomp.) (Found: C, 68.8; H, 4.4; N, 2.7. $C_{28}H_{22}ClNO_5$ requires C, 69.1; H, 4.6; N, 2.7%); $\nu_{max.}$ 1 090 cm^{-1} (ClO_4^-); τ 2.0—2.65 (17 H, m, arom.), 2.75 (1 H, m, furfuryl H-5), 3.90 (1 H, m, furfuryl H-3), 4.35 (2 H, s, CH_2), and 4.61 (1 H, m, furfuryl H-4).

1-*Furfuryl*-2,4,6-*trimethylpyridinium Perchlorate* (6).—Furfurylamine (3) (1.5 g) and 2,4,6-trimethylpyrylium perchlorate [9] (2.2 g) in EtOH (30 ml) were refluxed (3 h). The mixture was cooled at 0 °C (1 h) and the solid product collected. Recrystallisation from Me_2CO–Et_2O gave *compound* (6) (2.68 g, 90%), yellow prisms, m.p. 122 °C (Found: C, 51.6; H, 5.2. $C_{13}H_{16}ClNO_5$ requires C, 51.8; H, 5.4%); $\nu_{max.}$ 1 090 cm^{-1} (ClO_4^-); τ 2.4 (2 H, s, arom.), 2.6 (1 H, m, furfuryl H-5), 3.4 (1 H, m, furfuryl H-3), 3.6 (1 H, m, furfuryl H-4), 4.25 (2 H, s, CH_2), 7.05 (6 H, s, Me), and 7.45 (3 H, s, Me).

Reactions of 1-*Furfuryl*-2,4,6-*trimethylpyridinium Perchlorate* (6).—(a) *With pyridine.* Compound (6) (1.5 g) and pyridine (1.5 ml) were heated at 150 °C in an evacuated sealed tube (5 h). Ether was added to the cooled mixture and the solid product was collected and washed several times with Et_2O. Recrystallisation from Me_2CO–Et_2O (1 : 3) gave 1-*furfurylpyridinium perchlorate* (7) (1.2 g, 94%), pale brown prisms, m.p. 138 °C (Found: C, 46.3; H, 3.9; N, 5.3. $C_{10}H_{10}ClNO_5$ requires C, 46.3; H, 3.9; N, 5.4%); $\nu_{max.}$ 1 100 cm^{-1} (ClO_4^-); τ[$(CD_3)_2SO$] 0.6—1.9 (5 H, m, pyridyl), 2.13 (d, furfuryl H-5, *J* 2 Hz), 3.05 (d, furfuryl H-3, *J* 3 Hz), 3.35 (dd, furfuryl H-4, *J* 2 and 3 Hz), and 3.95 (s, CH_2).

(b) *With α-picoline.* Compound (6) (1.5 g) was treated with α-picoline (1.5 ml) in the manner described for pyridine. Recrystallisation of the product from EtOH–Et_2O (1 : 2) gave 1-*furfuryl*-2-*methylpyridinium perchlorate* (8) (1.0 g, 76%), buff plates, m.p. 151—152 °C (Found: C, 48.5; H, 4.6; N, 5.2. $C_{11}H_{12}ClNO_5$ requires C, 48.3; H, 4.4; N, 5.1%); $\nu_{max.}$ 1 090 cm^{-1} (ClO_4^-); τ[$(CD_3)_2SO$] 0.9—2.2 (4 H, m, picolyl), 2.27 (m, furfuryl H-5), 3.23 (m, furfuryl H-3), 3.50 (m, furfuryl H-4), 4.11 (s, CH_2), and 7.12 (s, Me).

(c) *With γ-picoline.* Compound (6) (1.5 g) was treated with γ-picoline (1.5 ml) in the manner described for pyridine. Recrystallisation of the product from Me_2CO gave 1-*furfuryl*-4-*methylpyridinium perchlorate* (9) (1.3 g, 97%), buff cubes, m.p. 124 °C (Found: C, 48.2; H, 4.6; N, 5.1. $C_{11}H_{12}ClNO_5$ requires C, 48.3; H, 4.4; N, 5.1%); $\nu_{max.}$ 1 090 cm^{-1} (ClO_4^-); τ[$(CD_3)_2SO$] 1.14 (d, picolyl H-2 and H-6, *J* 6 Hz), 2.05 (d, picolyl H-3 and H-5, *J* 6 Hz), 2.30 (d, furfuryl H-5, *J* 2 Hz), 3.24 (d, furfuryl H-3, *J* 4 Hz), 3.52 (dd, furfuryl H-4, *J* 2 and 4 Hz), 4.20 (s, CH_2), and 7.43 (s, Me).

(d) *With piperidine.* Compound (6) (1.5 g) and piperidine (1.5 ml) in $HCONMe_2$ (15 ml) were heated at reflux temperature (6 h). The mixture was then poured into cold water (100 ml), made alkaline (aq. NaOH), and extracted with Et_2O (3 × 20 ml). The ethereal solution after drying and evaporation gave a dark brown liquid (1.5 g) which was purified by g.l.c. Distillation of the product under diminished pressure gave *N*-furfurylpiperidine (12) (0.4 g, 55%), b.p. 98 °C at 15 mmHg (lit.,[10] 90 °C at 10 mmHg); $\nu_{max.}$ (film) 2 915 cm^{-1} (CH); τ 2.57 (d, furfuryl H-5, *J* 2 Hz), 3.65 (dd, furfuryl H-4, *J* 2 and 3 Hz), 3.76 (d, furfuryl H-3, *J* 3 Hz), 6.45 (s, CH_2), 7.55 (m, 2 × NCH_2), and 8.45 (m, 3 × CH_2CH_2), which was fully characterised as its *picrate*, m.p. 102—103 °C, yellow needles from MeOH (Found: C, 48.9; H, 4.7; N, 13.8. $C_{16}H_{18}N_4O_8$ requires C, 48.7; H, 4.6; N, 14.2%).

(e) *With morpholine.* Compound (6) (1.5 g) and morpholine (1.0 ml) in $HCONMe_2$ (15 ml) were heated at reflux temperature (12 h) and the mixture was worked up as described for piperidine. The crude product was separated by column chromatography [alumina; Et_2O–light petroleum (1 : 4)]. Distillation of the oily product under diminished pressure gave *N*-furfurylmorpholine (13) (0.5 g, 67%), b.p. 102 °C at 15 mmHg (lit.,[10] 100 °C at 10 mmHg); $\nu_{max.}$ (film) 2 900—3 100 (CH), 1 585, and 1 500 cm^{-1}; τ 2.65 (d, furfuryl H-3, *J* 2 Hz), 3.70 (dd, furfuryl H-4, *J* 2 and 3 Hz), 3.85 (d, furfuryl H-5, *J* 3 Hz), 6.20 (s, CH_2), 6.35 (m, 2 × NCH_2), and 7.14 (m, 2 × OCH_2), fully characterised as its *picrate*, m.p. 133 °C, yellow plates from

* We have recently shown that heating with the sodium salt of 1-hydroxy-4,6-diphenyl-2-pyridone gives much better yields in reactions of this type (A. R. Katritzky, M. J. Cook, A. Ikizler, and G. H. Millet, unpublished work).

MeOH (Found: C, 45.3; H, 4.3; N, 13.9. $C_{15}H_{16}N_4O_9$ requires C, 45.5; H, 4.1; N, 14.0%).

(f) *With pyridine 1-oxide.* Compound (6) (4.5 g) and pyridine 1-oxide (5 g) were fused together at 120—130 °C under nitrogen (10 h). The mixture was extracted with Et_2O; distillation of the extract gave crude furfural, which was converted into its 2,4-dinitrophenylhydrazone (0.3 g, 20%), red cubes, m.p. 202—203 °C [lit.,[11] 202 °C (229 °C decomp. corr.)] (Found: C, 47.8; H, 3.3; N, 20.1. Calc. for $C_{11}H_8N_5O_5$: C, 47.8; H, 2.9; N, 20.3%).

(g) *With triphenylphosphine.* Compound (6) (1.5 g) and triphenylphosphine (2.6 g) were fused together at 80 °C under nitrogen (10 h). Trimethylpyridine was removed by ether-extraction and the oily residue was dissolved in the minimum volume of Me_2CO and precipitated with Et_2O. Recrystallisation from MeOH gave *furfuryltriphenylphosphonium perchlorate* (16) (1.5 g, 66%), light brown powder, m.p. 192 °C (Found: C, 62.2; H, 4.5. $C_{23}H_{20}ClO_5P$ requires C, 62.4; H, 4.6%); $\nu_{max.}$ 1 100 cm^{-1} (ClO_4^-); τ[$(CD_3)_2SO$] 2.1—2.7 (16 H, m, arom.), 3.75 (1 H, m, furfuryl), 3.98 (1 H, m, furfuryl), and 4.80 (d, CH_2, J_{PH} 13 Hz).

Reactions of 1-Furfuryl-2,4,6-triphenylpyridinium Perchlorate (5).—(a) *With pyridine.* Compound (3) (1.2 g) and freshly distilled pyridine (5 ml) were stirred (24 h). After dilution with ether (50 ml) and 30 min at 0 °C a solid precipitate was collected. Recrystallisation from Me_2CO–Et_2O gave 1-furfurylpyridinium perchlorate (7) (0.45 g, 90%), m.p. 137—138 °C, identical with a sample prepared from compound (4).

(b) *With α-picoline.* Compound (5) (1.2 g) was treated with α-picoline (5 ml) as described for pyridine. Recrystallisation of the product from Me_2CO–Et_2O gave 1-furfuryl-2-methylpyridinium perchlorate (8) (0.35 g, 70%), m.p. 151 °C, identical with a sample prepared from compound (6).

(c) *With γ-picoline.* Compound (5) (1.2 g) was treated with γ-picoline (5 ml) as described for pyridine. Recrystallisation of the product from Me_2CO–Et_2O gave 1-furfuryl-4-methylpyridinium perchlorate (9) (0.75 g, 95%), m.p. 127 °C, identical with a sample prepared from compound (6).

(d) *With quinoline.* Compound (5) (1.2 g) and quinoline (5 ml) were heated at 75 °C with stirring (6 h.) A deep red colouration developed. After cooling, the solution was diluted with Et_2O (30 ml) giving an oily red product which was dissolved in Me_2CO (5 ml) and triturated with Et_2O giving a pale red solid. Recrystallisation from EtOH–Et_2O gave *1-furfurylquinolinium perchlorate* (10) (0.6 g, 80%), as pale red plates, m.p. 118 °C (Found: C, 54.2; H, 4.1; N, 4.4. $C_{14}H_{12}ClNO_5$ requires C, 54.3; H, 3.9; N, 4.5%); $\nu_{max.}$ 1 080 cm^{-1} (ClO_4); τ[$(CD_3)_2SO$] 0.25—0.34 (d, quinoline H-2), 0.60—0.70 (d, quinoline H-3), 1.23—1.15 (dd, quinoline H-4), 1.98—1.59 (4 H, m, Ph), 2.34 (d, furfuryl H-5), 6.92 (dd, furfuryl H-4), 3.64 (dd, furfuryl H-3), and 6.54 (2 H, s, CH_2).

(e) *With isoquinoline.* Compound (5) (1.2 g) was treated with isoquinoline (5 ml) as described for pyridine. Recrystallisation from Me_2CO–Et_2O gave *N-furfurylisoquinolinium perchlorate* (11) (0.8 g, 92%), m.p. 146 °C, buff powder (Found: C, 54.7; H, 4.1; N, 4.5. $C_{14}H_{12}ClNO_5$ requires C, 54.3; H, 3.9; N, 4.5%); $\nu_{max.}$ 1 080 (ClO_4^-) and 1 645 cm^{-1} (C=N); τ[$(CD_3)_2SO$] 1.1—1.3 (dd, isoquinoline H-1), 1.41 (m, isoquinoline H-3 and H-4), 1.62—1.88 (m, isoquinoline H-5, H-6, H-7, and H-8), 2.28 (d, furfuryl H-5, J 2 Hz), 3.03 (dd, furfuryl H-4, J 2 and 3 Hz), 3.36 (d, furfuryl H-3, J 3 Hz), and 3.86 (s, CH_2).

(f) *With piperidine.* Compound (5) (1.2 g) and piperidine (5 ml) were stirred together (48 h) and the mixture was then treated with Et_2O. The semi-solid product was stirred with aqueous NaOH (10%) and extracted with Et_2O; evaporation gave an oily product. Fractional distillation under diminished pressure gave *N*-furfurylpiperidine (0.3 g, 75%), b.p. 97 °C at 15 mmHg, identical with a sample prepared from compound (6). Treatment with picric acid gave a picrate, m.p. 102 °C, identical with an authentic sample.

(g) *With morpholine.* Compound (5) (1.2 g) was treated with morpholine (5 ml) in the manner described for piperidine. Distillation of the oily product gave *N*-furfurylmorpholine (13) (0.3 g, 78%), b.p. 102 °C at 15 mmHg, which was converted into the picrate, m.p. 133 °C, identical with an authentic sample.

(h) *With pyrrolidine.* Compound (5) (5.0 g) and pyrrolidine (5 ml) were stirred at room temperature (24 h). The mixture was worked up as described for piperidine and the crude product was purified by column chromatography [alumina; light petroleum (b.p. 40—60 °C)–Et_2O (4 : 1)]. Distillation of the product under diminished pressure gave *N*-furfurylpyrrolidine (14) (0.85 g, 55%), b.p. 96—97 °C at 15 mmHg (lit.,[12] 82—84 °C at 8 mmHg); $\nu_{max.}$ (film) 2 920 cm^{-1} (CH); τ 2.45 (d, furfuryl H-5, J 2 Hz), 3.5 (dd, furfuryl H-4, J 2 and 3 Hz), 3.65 (d, furfuryl H-3, J 3 Hz), 6.0 (s, CH_2), 6.95 (m, 2 × NCH_2), and 8.08 (m, 2 × CH_2). This amine was fully characterised as its picrate, yellow needles, m.p. 137 °C (lit.,[12] 135—136 °C) (Found: C, 47.5; H, 4.7; N, 14.6. Calc. for $C_{15}H_{16}NO_8$: C, 47.4; H, 4.2; N, 14.7%).

(i) *With diethylamine.* Compound (5) (1.2 g) was treated with Et_2NH (15 ml) in the manner described for piperidine. The mixture was separated by column chromatography [light petroleum (b.p. 40—60 °C)–Et_2O (4 : 1)] and distillation of the pale yellow oil under reduced pressure gave N-*furfuryldiethylamine* (15) (0.25 g, 63%), b.p. 127 °C at 15 mmHg; $\nu_{max.}$ (film) 2 985 cm^{-1} (CH); τ 2.60 (d, furfuryl H-5, J 2 Hz), 3.65 (dd, furfuryl H-4, J 2 and 3 Hz), 3.82 (d, furfuryl H-3, J 3 Hz), 6.16 (s, CH_2), 7.30 (q, CH_2CH_3, J 6 Hz), and 8.8 (t, Me). The *N*-furfuryldiethylamine was fully characterised as its *picrate*, m.p. 132 °C, yellow plates (EtOH) (Found: C, 47.5; H, 4.9; N, 14.8. $C_{15}H_{18}N_4O_8$ requires C, 47.1; H, 4.8; N, 14.7%).

(j) *With triphenylphosphine.* Compound (5) (1.2 g) and triphenylphosphine (1.5 g) were fused together at 80—85 °C (15 min) under nitrogen. The glassy product was washed with Et_2O (3 × 25 ml) and recrystallisation from Me_2CO–Et_2O gave furfuryltriphenylphosphonium perchlorate (16) (1.1 g, 98%), m.p. 192 °C, identical with a sample prepared from compound (6).

(k) *With sodium phenoxide.* Compound (5) (1.2 g) and sodium phenoxide (1.0 g) in $HCONMe_2$ (10 ml) were heated at reflux temperature (6 h). The solution was cooled, poured into water (100 ml), and extracted with Et_2O (3 × 25 ml). The extract was purified by t.l.c. (silica gel; Et_2O–light petroleum) giving a yellow oil. Distillation under diminished pressure gave furfuryl phenyl ether (17) (0.25 g, 53%), b.p. 110 °C at 15 mmHg (lit.,[13] 139—140 °C at 20 mmHg); $\nu_{max.}$ (film) 3 300, 1 610, and 1 600 cm^{-1}; τ 2.0—3.2 (m, Ph and furfuryl H-5), 3.70 (dd, furfuryl H-4, J 2 and 3 Hz), 3.88 (d, furfuryl H-3, J 3 Hz), and 5.12 (s, CH_2); n_D^{20} 1,563 4.

(l) *With sodium benzenethiolate.* Compound (5) (1.2 g) was treated with sodium benzenethiolate (1.0 g) in $HCONMe_2$ (15 ml) as described for sodium phenoxide. After t.l.c., distillation of the yellow oil gave furfuryl phenyl sulphide (18) (0.25 g, 55%), b.p. 133 °C at 15 mmHg (lit.,[14] 138—140 °C at 8 mmHg); $\nu_{max.}$ (film) 2 960 and 1 590 cm^{-1}; τ 2.1—3.2 (m, Ph and furfuryl H-5), 3.72 (dd, furfuryl H-4, *J* 2 and 3 Hz), 3.90 (d, furfuryl H-3, *J* 3 Hz), and 5.53 (s, CH_2).

1-(5-*Bromofurfuryl*)-2,4,6-*triphenylpyridinium Perchlorate* (19).—Dichloromethane (15 ml) containing bromine (2.4 g, 0.015 mol) was added dropwise to compound (5) (4.9 g, 0.01 mol) in dichloromethane (30 ml) at −20 °C. Stirring was continued at −20 °C for 15 min and at room temperature for 1 h. After addition of ether (60 ml), the perchlorate salt was filtered off and washed with ether (2 × 25 ml). The solid was triturated with ether (25 ml) and recrystallised from Me_2CO–Et_2O giving *compound* (19) (2.4 g, 85%) as needles, m.p. 123 °C (decomp.) (Found: C, 59.0; H, 3.6; N, 2.7. $C_{28}H_{21}BrClNO_5$ requires C, 59.3; H, 3.7; N, 2.5%); $\nu_{max.}$ 1 080 cm^{-1} (ClO_4^-); τ[$(CD_3)_2SO$] 1.5—2.5 (17 H, m, arom.), 3.65 (1 H, d, furfuryl H-3), and 4.20—4.40 (3 H, m, furfuryl H-4 and CH_2).

1-(5-*Bromofurfuryl*)*morpholine* (20).—Compound (19) (2.8 g, 0.005 mol) and morpholine (10 ml) were stirred for 12 h at 20 °C. After addition of ether (40 ml), the mixture was cooled until morpholine perchlorate (checked by n.m.r.) crystallised and was filtered off. Ether and the rest of the morpholine were removed at 60 °C and 15 mmHg. The residue was basified (aq. NaOH) and then dilute HCl was added (to pH 1). 2,4,6-Triphenylpyridine was filtered off. The solution was made alkaline (aq. NaOH to pH 7—8) and extracted with ether (4 × 30 ml). The ethereal solution after drying and evaporation gave a brown oil which when distilled *in vacuo* gave 1-(5-*bromofurfuryl*)-*morpholine* (20) (0.56 g, 59%), b.p. 80 °C at 0.4 mmHg (Found: C, 44.2; H, 5.1; N, 5.7. $C_9H_{12}BrNO_2$ requires C, 43.9; H, 4.9; N, 5.7%); $\nu_{max.}$ 1 120 cm^{-1}; τ 3.60—3.85 (2 H, m, furfuryl H-3 and H-4), 6.10—6.40 (4 H, m, ring O–CH_2), 6.45 (2 H, s, CH_2), and 7.35—7.70 (4 H, m, ring N–CH_2).

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REFERENCES

[1] Part 6, A. R. Katritzky, J. B. Bapat, R. J. Blade, B. P. Leddy, P.-L. Nie, C. A. Ramsden, and S. S. Thind, preceding paper.
[2] D. R. Shridhar, C. V. R. Sastry, S. R. Moorty, N. K. Vaidya, P. G. Reddy, G. S. Reddi, and G. S. Thapar, *J. Medicin. Chem.*, 1977, **20**, 149.
[3] W. R. Kirner, *J. Amer. Chem. Soc.*, 1928, **50**, 1955.
[4] S. Divald, M. C. Chun, and M. M. Joullié, *J. Org. Chem.*, 1976, **41**, 2835.
[5] P. Bosshard and C. H. Engster, *Adv. Heterocyclic Chem.*, 1966, **7**, 398.
[6] P. Linda and G. Marino, *J. Chem. Soc.* (*B*), 1968, 392.
[7] A. F. Shepard, N. R. Winslow, and J. R. Johnson, *J. Amer. Chem. Soc.*, 1930, **52**, 2083.
[8] A. T. Balaban and C. Toma, *Tetrahedron*, Suppl. 7, 1966, 1.
[9] A. T. Balaban and C. D. Nenitzescu, *Org. Synth.*, Coll. Vol. V, 1973, p. 1106.
[10] H. Böhme and A. Müller, *Arch. Pharm.*, 1963, **296**, 65.
[11] ' Dictionary of Organic Compounds,' 4th edn., Eyre and Spottiswoode, London, 1965, vol. 3, p. 1478.
[12] F. Haglid and I. Wellings, *Acta Chem. Scand.*, 1963, **17**, 1727.
[13] H. Normant, *Ann. Chim.* (*France*), 1942, **17**, 335 (*Chem. Abs.*, 1944, **38**, 3282[6]).
[14] I. I. Lapkin, N. V. Bogoslovskii, and F. G. Saitkulova, *Zhur. org. Khim.*, 1966, **2**, 156 (*Chem. Abs.*, 1966, **64**, 14155*b*).