Tetrahedron. Vol. 27, pp. 3323 to 3330. Pergamon Press 1971. Printed in Great Britain

STUDIES ON SOME ELECTROPHILIC SUBSTITUTION REACTIONS IN THE FURAN SERIES

THE SYNTHESIS OF 2,4-DISUBSTITUTED FURANS*

J. P. KUTNEY, H. W. HANSSEN and G. VIJAYAKUMARAN NAIR
Department of Chemistry, University of British Columbia, Vancouver 8, B.C.

(*Received in USA* 6 *April* 1971; *Received in the UK for publication* 14 *April* 1971)

Abstract—An investigation of several electrophilic substitution reactions on 3-methylfuran is reported. Friedel-Crafts acylation of 3-methylfuran with acetyl and propionyl chlorides yielded both 2,3- and 2,4-disubstituted furans. Vilsmeier and Gatterman formylation procedures yielded 3-methylfurfural and 4-methylfurfural while mercuration appeared to yield only the 2,3-disubstituted derivative.

IN CONNECTION with another problem it became essential to consider the synthesis of certain 2.4-disubstituted furan derivatives. A survey of the comprehensive reviews on furan chemistry[1,2] revealed that electrophilic substitution on 3-substituted furans, particularly those with electron-donating substituents had not been extensively studied and was not well understood.[3]

In summarizing the available data, Bosshard and Eugster[2] formulated a set of general rules regarding the orientation of substitution and indicated that "substituents at the 3-position which are electron-withdrawing, i.e. *meta*-directing, direct substitution to the 5-position, and those which are electron-donating, or *ortho-para* directing, direct substitution to the 2-position." Since the difference in reactivity between the 2- and 5-positions in these systems would be expected to be small, we decided to investigate more thoroughly several selected electrophilic substitution reactions of 3-methylfuran and thereby obtain a better insight into the overall reactivity of this heterocyclic system.

The starting material, 3-methylfuran (I) is available via several routes. The procedure of Cornforth[4] was found less satisfactory for general use than a sequence employing methyl 3-methyl-2-furoate[5] (II). Alkaline hydrolysis of the latter to 3-methyl-2-furoic acid (III) and subsequent decarboxylation by means of powdered copper in quinoline provided 3-methylfuran in good yield. Since this substance decomposes on standing, it was desirable to prepare it shortly before each reaction.

Our first consideration was to establish a method by which substitution patterns in furan derivatives could easily be established. The technique chosen was NMR spectroscopy. Previous data on the NMR spectra on some furans was available[6, 7] but further study was essential. Therefore a detailed investigation of the NMR spectra of 3-methyl-2-furoic acid (III) and 3-methylfuran (I) was carried out.

The NMR spectrum of III revealed two one-proton multiplets in the low field region (τ 2·48 and 3·60). These signals could readily be assigned to protons at C-5 and C-4 respectively.[8] The 3-Me protons absorbed as a multiplet at τ 7·60. A double

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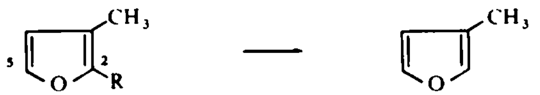
* Financial support from the National Research Council of Canada is gratefully acknowledged.



II: R = CO_2CH_3
III: R = CO_2H

I

resonance experiment in which this signal was irradiated revealed that both low field multiplets could be decoupled to give doublets, thereby establishing the coupling constant $J_{4,5}$ = 1·8 Hz for the adjacent protons on the furan ring. To establish the long range coupling constants between the ring protons and the 3-Me protons each of the low field multiplets were irradiated. Irradiation at τ 2·48 reduced the C-3 Me protons signal to a doublet, thus revealing $J_{4,\mathrm{Me}}$ = 1·0 Hz while irradiation of the C-4 proton at τ 3·60 reduced the C-3 Me signal to a doublet with $J_{5,\mathrm{Me}}$ = 0·5 Hz.

Examination of the NMR spectrum of 3-methylfuran showed that corresponding coupling constants possessed similar values to those in 3-methyl-2-furoic acid. Double irradiation studies revealed an additional coupling constant $J_{2,\mathrm{Me}}$ = 1·1 Hz. The coupling constants thus measured for the 3-methylfuran nucleus are summarized in Table 1.

Table 1. Coupling constants of 3-methylfuran derivatives

Positions of protons	Coupling constant (Hz)
4.5	1·8
2.4	1·0
4. C-3 Me	1·0
5. C-3 Me	0·5
2. C-3 Me	1·1

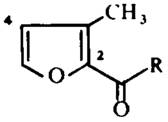
Our first step in the re-investigation of orientation in electrophilic substitution reactions of 3-alkylfurans was acylation under Friedel–Crafts conditions. 3-Methylfuran was treated with an equimolar amount of acetic anhydride at 0° and a catalytic amount of 85% orthophosphoric acid as the condensing agent. Almost immediately a brown coloration occurred due probably to facile resinification of the furan. Workup of this reaction, followed by distillation, yielded a fragrant colorless oil. Examination of this product by gas liquid chromatography (GLC) indicated that two major components were present in the ratio 6·5:3·5. These two components were then separated by preparative GLC.

The NMR spectrum of the major component showed one-proton multiplets at τ 2·55 and 3·55. These signals could readily be assigned to protons at carbons 5 and 4 respectively of a 2,3-disubstituted furan derivative. The C-3 Me protons absorbed as a multiplet at τ 7·55. Irradiation at this latter frequency reduced the low field multiplets to doublets with a coupling constant of 1·8 Hz. It could also be shown that irradiation at τ 2·55 reduced the 3-Me protons multiplet to a doublet with a J-value of 1·0 Hz while irradiation at τ 3·55 revealed another coupling to the C-3 Me protons of 0·5 Hz. These assignments were in complete agreement with those made earlier for the substitution pattern in 3-methyl-2-furoic acid and left little doubt that this product was 2-acetyl-3-methylfuran (IV).

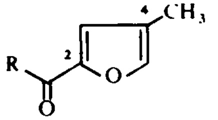
Unambiguous chemical proof was obtained when oxidation of this acylated material with sodium hypochlorite[9] yielded a colorless crystalline compound with spectroscopic properties identical with those of the previously prepared 3-methyl-2-furoic acid. It could therefore be concluded that the major component of this reaction was the expected 2.3-disubstituted derivative IV.

The second acylated component was assigned structure V. The NMR spectrum of this compound indicated one-proton multiplets at τ 2·60 and τ 2·91. These signals were assigned to protons at C-5 and C-3 respectively.* The C-4 Me group absorbed as an ill-defined quarter at τ 7·90. Irradiation at the latter frequency reduced both low field signals to doublets, with a J-value of 1·0 Hz, which further suggested that these signals must be assigned to protons at positions 3 and 5 while further double resonance experiments provided $J_{5,\,\mathrm{Me}}$ = 1·0 and $J_{3,\,\mathrm{Me}}$ = 1·1 Hz.

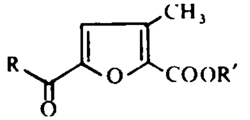
In order to substantiate the above findings we exposed 3-methylfuran to another Friedel–Crafts reaction employing propionic anhydride under the above-mentioned conditions. The resultant product was a mixture of two components in the ratio 7:3 as determined by GLC. The two compounds thus obtained were characterized as 2-propionyl-3-methylfuran (VI) and 2-propionyl-4-methylfuran (VII). Apart from extensive NMR investigations used to establish these structures, the latter substance was also prepared via an alternative and unambiguous route.



IV: R = CH_3
VI: R = CH_2CH_3
X: R = H



V: R = CH_3
VII: R = CH_2CH_3
XI: R = H



VIII: VIII: R = CH_2CH_3; R′ = CH_3
IX: R = CH_2CH_3; R′ = H

Methyl 3-methyl-2-furoate (II) was subjected to a Friedel–Crafts reaction with propionic anhydride and the expected product, VIII, was obtained in good yield. Alkaline hydrolysis of VIII provided the 2-furoic acid derivative, IX, which on decarboxylation with powdered copper in anhydrous quinoline was converted to 2-propionyl-4-methylfuran. The product obtained from this sequence was identical in all respects with that isolated from the direct substitution of the 3-methylfuran nucleus.

The next type of electrophilic substitution reaction that was considered was that of formylation. The earliest method of introducing a formyl group on a furan nucleus was the Gatterman reaction. A literature survey revealed that formylation of a 3-alkylfuran under Gatterman conditions has not been published since the procedure reported by Reichstein, in 1931.[10] A more modern and preferable method of introducing a formyl group on an aromatic nucleus is the Vilsmeier formylation using dimethylformamide and phosphorus oxychloride.

3-Methylfuran was added to an equimolar mixture of dimethylformamide and phosphorus oxychloride according to the general procedure reported by Traynelis and co-workers.[11] After hydrolysis of the Schiff's base intermediate using potassium carbonate, an excellent yield of a slightly yellow oil was obtained. Analysis of this

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* It must be recognized that C_5 in the monosubstituted 3-methylfuran system becomes C_2 in the 2,4-disubstituted system.

material by GLC revealed that only two components were present, in the ratio 93·5:6·5. The major Vilsmeier product was oxidized with silver oxide in water to give a good yield of a colorless crystalline material whose spectral properties were identical with those of 3-methyl-2-furoic acid (III). This experiment established the Vilsmeier formylation provided 3-methylfurfural (X) as the major product.

The minor component in this reaction showed one-proton multiplets at τ 2·52 and 2·93 which is in accord with the expected chemical shifts of protons on C-5 and C-3 respectively, of structure XI. These assignments were further supported by double irradiation studies that revealed coupling constants consistent with the substitution pattern in 4-methylfurfural (XI).

We chose now to re-investigate the Gatterman formylation of 3-methylfuran according to Reichstein's procedure. The major component had spectral properties identical to that of 3-methylfurfural (X) while 4-methylfurfural (XI) was also believed to be present in trace amounts as determined by careful GLC examination and the NMR spectrum of the crude product. It seemed reasonable that XI was being formed in significant amounts, but being a less stable compound than the 2,3-disubstituted derivative, X, it decomposed at a faster rate. It was expected that the 4-substituted isomer is relatively less stable to the prolonged acid conditions of this reaction due to the fact that in this molecule the position most susceptible to protonation is still vacant, thus more facile resinification could occur.

In order to test this possibility, Reichstein's formylation procedure was repeated using a shorter reaction time (six hours) than had been previously specified. Indeed this experiment yielded as major components, X and XI in the ratio 93·5:6:5, respectively.

A third type of electrophilic substitution reaction that was considered for re-investigation was metalation with mercuric chloride. Mercuration, followed by replacement reactions, has been a useful method in rendering available furan derivatives which would otherwise have been inaccessible. A literature survey, however, revealed that the only mercuration reaction of a 3-alkylfuran was done by Gilman.[12] He reported the formation of the expected 3-methyl-2-furylmercuric chloride as the sole product.

3-Methylfuran was added to an aqueous solution of mercuric chloride to yield a colorless crystalline precipitate. The NMR spectrum of this material indicated one-proton multiplets at τ 2·33 and 3·58 as well as a three-proton multiplet at τ 7·86. It was therefore concluded that in this reaction only 3-methyl-2-furfurylmercuric chloride was formed, with no evidence of other isomers.

The last electrophilic substitution reaction considered was that of bromination. Gilman has reported the bromination of 3-furoic acid,[13] but there are no reports in the literature of direct halogenation of 3-methylfuran. In the present study, bromination of 3-methylfuran using dioxane dibromide was attempted. Removal of the solvent from the reaction product, however, resulted in what appeared to be a rapid polymerization to give a brown, plastic-like material. No further work was done on this reaction.

A previous study on 3-methylfuran has been reported by Finan and Fothergill.[14] These authors treated this compound with acetic anhydride and boron trifluoride and obtained, in low yield, only the 2-acetyl compound. In a similar experiment using isovaleric anhydride only the 2-substituted 3-methylfuran was obtained. Because these workers were also searching for the 2,4-disubstituted isomers, this work is of particular relevance to the present discussion.

In conclusion, our investigations have provided the first demonstration that 3-methylfuran is capable of undergoing electrophilic substitution at both α positions. These results are in agreement with those obtained with thiophene[15, 16] where both 2,3- and 2,4-disubstituted products were isolated under Friedel–Crafts conditions. On the other hand formulation of 3-methylthiophene with dimethylformamide in the presence of phosphorus oxychloride is reported[16] to give only 3-methyl-2-thenaldehyde. In summation all of these results may support the suggestion that product distribution is dependent not only on reactivities but also on such secondary effects as "relative steric bulk of the 3-alkyl group and/or the entering electrophile".[17]

EXPERIMENTAL

GLC was performed on an Aerograph Autoprep model A-700 instrument, using helium as a carrier gas at a flow rate of 80–85 ml/min. For routine analysis a column (1/4 inch × 10 feet) consisting of 20% FFAP on 60/80 mesh Chromsorb W support packing was used. A similar column (3/8 inch, 30% FFAP) was used for preparative purposes. All work was done using a column temp of 172–176°.

UV spectra were recorded in MeOH on a Cary 11 spectrophotometer. Absorption values (λ_{max}) are given in nanometers (nm). IR spectra were measured on Perkin–Elmer model 137 or 457 spectrophotometers and absorption bands (ν_{max}) are quoted in wavenumbers (cm^{-1}). NMR spectra were recorded in $CDCl_3$ on Varian T-60 and HA-100 spectrometers. The chemical shifts are recorded in the Tiers τ scale. The types of protons, integrated areas, multiplicity and the coupling constant, *J*, are indicated in parentheses. Mass spectra were recorded at 70 eV on an AEI MS9 mass spectrometer. M.ps were determined on a Kofler block and are uncorrected. Elemental analyses were performed by Mr. P. Borda of the Microanalytical Laboratory, University of British Columbia, Vancouver, B.C.

3-*Methylfuran* (I). This compound was initially prepared according to the Cornforth procedure[4] but subsequently from II[5] as shown.

3-*Methyl-2-furoic acid* (III). A soln of methyl 3-methyl-2-furoate[5] (20 g) in aqueous 1% NaOH aq (200 ml) was refluxed for 1·2 hr. This mixture was then cooled and acidified with 6N HCl. A brown granular material separated out and was collected by filtration. After washing with cold water and drying *in vacuo*, the product (13 g) was recrystallized from CH_2Cl_2 to give colourless crystals, m.p. 139–140°; (lit.[18] m.p. 136–137°), ν_{max} (chloroform): 2700–2500, 1765 cm^{-1}; NMR signals: 2·44 (m, 1H, $J_{4,5}$ = 1·8; $J_{5,Me}$ = 0·5, C-5H), 3·60 (m, 1H, $J_{4,5}$ = 1·8; $J_{4,Me}$ = 1·0, C-4H), 7·60 (m, 3H, $J_{4,Me}$ = 1·0 $J_{5,Me}$ = 0·5, C-3 Me), mass spectrum: *m/e* 126, 109, 81, 80. (Found: C, 65·44; H, 5·47. Calc. for $C_6H_6O_3$; C, 65·45; H, 5·49%).

3-*Methylfuran* (I) *via decarboxylation of* 3-*methyl-2-furoic acid*. Preceding each experiment in this investigation, 3-methylfuran was freshly prepared by the following procedure:

3-Methyl-2-furoic acid (2·3 g) was added to a mixture of powdered Cu (1·0 g) and anhyd quinoline (10 ml) in a 25 ml round-bottom flask fitted with a short-path distillation head and a cooled receiver. The system was evacuated and flushed several times with dry N_2. The mixture was then slowly heated in a sand bath to 200°, at which time the evolution of CO_2 was evident. Heating was continued to 240 until no more gas evolved and distillation of 3-methylfuran ceased (about 2 hr). The clear colorless product (1·3 g) thus obtained was found to be homogeneous by GLC; b.p. 65–66°; (lit.[4] b.p. 65–65·5°/749 mm), ν_{max} (chloroform): 1500, 1200, 890 cm^{-1}; NMR signals: 2·70 (m, 1H, $J_{4,5}$ = 1·8; $J_{2,5}$ = 1·5; $J_{5,Me}$ = 0·5, C-5H), 2·80 (m, 1H, $J_{2,Me}$ = 1·1; $J_{2,5}$ = 1·5; $J_{2,4}$ = 1·0, C-2H), 3·85 (m., 1H, $J_{4,5}$ = 1·8; $J_{4,Me}$ = 1·1; $J_{2,4}$ = 1·0, C-4H), 8·05 (m, 3H, $J_{2,Me}$ = 1·1; $J_{3,Me}$ = 1·0; $J_{5,Me}$ = 0·5, C-3Me). (Found: C, 73·10; H, 9·13. Calc. for C_5H_6O: C, 73·15; H, 9·15%).

Acetylation of 3-*methylfuran*. 3-Methylfuran (1 g) was added to Ac_2O (1·0 g) at 0° and two drops of orthophosphoric acid (85%) were added with vigorous stirring. The resulting brown mixture was warmed to room temp and stirred for 1 hr. It was then heated briefly to 50°, cooled, and water (2 ml) was added. After further stirring (0·5 hr) a sat $NaHCO_3$ aq (8 ml) was added and the mixture was stirred overnight at room temp. The brown organic layer was taken up in ether and washed with water. After drying over Na_2SO_2, the solvent was removed *in vaco* and the brown oil so obtained was also distilled *in vacuo* (120–130°/25 mm). The resultant colorless fragrant liquid (0·5 g) was examined by GLC and found to be a mixture of two compounds in the ratio 6·5:3·5, with retention times of 9·0 and 13·5 min, respectively. These components were separated by preparative GLC. The major component (0·32 g) was characterized as IV; b.p. 64°/15 mm (lit.[15] b.p. 60°/10 mm), λ_{max}: 272, 230 nm; ν_{max} (film): 1670, 1505, 880 cm^{-1}; NMR signals: 2·55 (m, 1H, $J_{4,5}$ = 1·8; $J_{4,Me}$ = 1·0, C-2H), 3·55 (m, 1H, $J_{4,5}$ = 1·8; $J_{5,Me}$ = 0·5, C-5H), 7·52 (s, 3H, $COCH_3$), 7·60 (m, 1H, $J_{4,Me}$ = 1·0; $J_{5,Me}$ = 0·5), mass spectrum: *m/e* 124, 109, 81. (Found: C, 67·71; H, 6·50. Calc. for $C_7H_8O_2$: C, 67·73; H, 6·50%).

The second component (0·17 g) was characterized as V, b.p. 190–192°/760 mm (lit.[15] b.p. 188–192°/760 mm), λ_{max}: 273, 230 nm; ν_{max} (film): 1670, 1505, 880 cm^{-1}; NMR signals: 2·60 (m, 1H, $J_{5,Me}$ = 1·1; $J_{3,5}$ = 1·0, C-5H), 2·91 (m, 1H, $J_{3,Me}$ = $J_{3,5}$ = 1·0, C-3H), 7·54 (singlet, 3H, $COCH_3$), 7·90 (m, 3H, $J_{5,Me}$ = 1·1, $J_{3,Me}$ = 1·0, C-4Me), mass spectrum: 124, 109, 80. (Found: C, 67·70; H, 6·48. Calc. for $C_7H_8O_2$: C, 67·73; H, 6·50%).

Oxidation of 2-acetyl-3-methylfuran. The major product (0·1 g) obtained above was added drop-wise to 5% NaOCl aq (4 ml) which had been preheated to 60°. This mixture was then stirred at 60–65° for 15 min, after which time $NaHSO_3$ aq was added to destroy the unreacted hypochlorite. The mixture was then cooled to ice-bath temp, acidified with HCl, and extracted several times with ethyl ether. The organic extracts were then combined and dried over Na_2SO_4. Removal of the solvent yielded a slightly brown material (0·06 g). Recrystallization of this product from CH_2Cl_2 yielded colorless crystals, m.p. 139–140°, which had spectral properties identical to those of III.

Propionylation of 3-methylfuran. 3-Methylfuran (1 g) and propionic anhydride (1·6 g) were mixed and a catalytic amount (2 drops) of orthophosphoric acid (85%) was added. The cooled mixture was stirred vigorously for 1 hr during which time it had acquired a dark red color. It was then heated to 60–65° and maintained at this temp for 2 hr. The mixture was then cooled and stirred with water (2 ml) for 1 hr. The dark organic layer was separated and again stirred with sat Na_2CO_3 aq (5 ml) for 24 hr. It was then washed thoroughly with water, extracted with ether (2 × 5 ml) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residual reddish brown oil obtained was distilled *in vacuo*. A colorless fragrant liquid (0·5 g) was collected, b.p. 125–130°/25 mm. Examination of this material by GLC indicated that it was a mixture of two compounds in the ratio 7:3, with retention times of 1·8 and 2·8 min, respectively. These components were then separated by preparative GLC. The major component was characterized as VI, b.p. 77–80°/5 mm, λ_{max}: 278, 230 nm; ν_{max} (film): 1670, 1505, 881 cm^{-1}; NMR signals: 8·85 (tr, 3H, $\underline{CH}_3$—CH_2—), 7·65 (s, 3H, C-3CH_3), 7·2 (q, 2H, —CO—$\underline{CH}_2$—CH_3), 3·65 (d, $J_{4,5}$ = 2·5, 1H, C-4H), 2·65 (d, $J_{4,5}$ = 2·5, C-5H), mass spectrum: *m/e* 138, 109. (Found: C, 69·71; H, 7·27. Calc. for $C_8H_{10}O_2$: C, 69·56; H, 7·24%).

The minor component was characterized as VII, b.p. 78–82°/5 mm, λ_{max}: 280, 230 nm; ν_{max} (film): 1675, 1505, 880 cm^{-1}; NMR signals: 8·85 (tr, 3H, $\underline{CH}_3CH_2$—), 7·9 (s, 3H, C-4 CH_3), 7·2 (qu, 2H, —CO—$\underline{CH}_2$—CH_3), 3·05 (s, 1H, C-3H), 2·75 (broad s, 1H, C-5H), mass spectrum: *m/e* 138, 109. (Found: C, 69·68; H, 7·26. Calc. for $C_8H_{10}O_2$: C, 69·56; H, 7·24%).

Methyl-3-methyl-5-propionyl-2-furate (VIII). Methyl 3-methyl-2-furoate (25·6 g, 0·2 mole) was dissolved in propionic anhydride (75 ml) and orthophosphoric acid (7·0 g) was added to it with vigorous stirring. The cooled mixture was allowed to come to room temp and then stirred at 65–70° for 48 hr. After this time the mixture was cooled and treated with water. The dark brown organic layer was extracted with chloroform, the chloroform extract washed with $NaHCO_3$ aq and dried over Na_2SO_4. The solvent was removed *in vacuo* and the semi-solid residue was distilled at 120°/0·3–4 mm. A pale yellow crystalline material was collected in the receiver (23·5 g), m.p. 109–111°. It was recrystallized from aqueous EtOH (70%), colorless shining needles, m.p. 113–114°, λ_{max} 280, 285 (sh), 212 nm; ν_{max} (chloroform): 1745, 1700 cm^{-1}; NMR signals: 8·8 (tr, 3H, —CH_2—$\underline{CH}_3$), 7·65 (s, 3H, C-3CH_3), 7·2 (q, 2H, —CO—CH_2—), 6·1 (s, 3H, —$COOCH_3$), 3·0 (s, 1H, C-5H), mass spectrum: *m/e* 196, 167, 138, 123, 109. (Found: C, 61·01; H, 5·97. Calc. for $C_{10}H_{12}O_4$: C, 61·22; H, 6·12%).

3-Methyl-5-propionyl-2-furoic acid (IX). A soln VIII (9·8 g) in 10% NaOH aq (100 ml) was heated under reflux for 1·5 hr. The soln was then cooled and acidified with HCl and stirred for a few min. The product which separated as a brown granular solid was collected by filtration. It was washed with a little ice-cold water and dried *in vacuo*. Crystallization from MeOH afforded the pure acid as pale yellow shining prisms (7·6 g), m.p. 179–181°, λ_{max}: 282, 212 nm; ν_{max} (chloroform): 2700–2500, 1765, 1700 cm^{-1}; NMR signals: 8·8 (tr, 3H, $\underline{CH}_3$—CH_2—), 7·6 (s, 3H, C-3CH_3), 7·0 (q, 2H, —CH_2—CO—), 2·85 (s, 1H, C-4H), − 0·2 (s, 1H, —COOH); mass spectrum: *m/e* 182, 137. (Found: C, 59·21; H, 5·50. Calc. for $C_9H_{10}O_4$: C, 59·33; H, 5·49%).

2-Propionyl-4-methylfuran (VII). A mixture of 3-methyl-5-propionyl-2-furoic acid (9·1 g, 0·05 mole), anhyd. quinoline (20 ml) and powdered Cu (2·0 g) was heated at 200–210° under N_2 for 3 hr. The evolution ceased by this time and the mixture was extracted with chloroform (50 ml). The chloroform extract was filtered to remove the Cu powder and washed successively with 1N HCl (3 × 50 ml) and water (100 ml) and finally with $NaHCO_3$ aq until neutral to litmus. It was then dried over $NaSO_4$ and the solvent was removed *in vacuo*. The residual dark oil was distilled using a short fractionating column. The fraction boiling at 78–82°/5 mm was collected as a colorless fragrant liquid (5·4 g). The physical and spectral data of this compound were identical with those of the product obtained by the propionylation of 3-methylfuran.

Vilsmeier formulation of 3-*methylfuran.* Phosphorus oxychloride (2·1 g, 0·014 moles) was added with constant stirring to dimethylformamide (1·0 g, 0·014 moles) in a round-bottom flask fitted with a condenser, dropping funnel and a source of dry N_2. The addition, carried out at ice-bath temp. required 30 min and the mixture was then kept cold for a further 30 min. 3-Methylfuran (1·1 g, 0·015 moles) was then added to the mixture over a 15 min period. Stirring was maintained for 1 hr at 0° and a further hour at room temp. The mixture was then poured into ice-water, neutralized with K_2CO_3, and allowed to stir overnight. The organic layer was separated and the aqueous layer was extracted several times with ethyl ether. The organic layer and extracts were combined and dried over Na_2SO_4. Removal of the ether yielded a slightly yellow oil (1·2 g) which was examined by GLC and found to contain two components in the ratio 93·5 :6·5, having retention times of 8 and 10 minutes, respectively.

The major component (1·1 g) was characterized as X. b.p. 62–64°/15 mm (lit.[11] b.p. 60–61°/12 mm). ν_{max} (film): 1680, 890 cm^{-1}; NMR signals; 0·24 (s, 1H, CHO), 2·43 (m, 1H, $J_{4,5}$ = 1·8; $J_{5,Me}$ = 0·5, C-5H), 3·58 (m, 1H, $J_{4,5}$ = 1·8; $J_{4,Me}$ = 1·0, C-4H), 7·60 (m, 3H, $J_{4,Me}$ = 0·5, C-3 Me), mass spectrum: *m/e* 110, 109, 81. (Found: C, 65·34; H, 5·55. Calc. for C_6H_6O: C, 65·45; H, 5·49%).

The minor component (0·1 g) was characterized as XI, ν_{max} 1675, 888 cm^{-1}; NMR signals: 0·40 (s, 1H, CHO), 2·52 (m, 1H, $J_{5,Me}$ = 1·1; $J_{3,5}$ = 1·0, C-5H), 2·93 (m, 1H, $J_{3,5}$ = J_{Me} = 1·0), 7·88 (m, 3H, $J_{5,Me}$ = 1·1; $J_{3,Me}$ = 1·0, C-4 Me), mass spectrum: *m/e* 110, 109, 81. (Found: C, 65·67; H, 5·75. Calc. for C_6H_6O: C, 65·45; H, 5·49%).

Gatterman formulation of 3-*methylfuran.* Anhyd HCN was generated, in a dropping funnel, from zinc cyanide (2·7 g, 0·03 moles) in ether (20 ml) by bubbling anhyd HCl through the mixture for 2 hr. The light brown 2-phase system was then added with vigorous stirring to a cooled (− 10°) soln of 3-methylfuran (1·1 g, 0·015 moles) in ether (20 ml). After stirring for 1 hr, the mixture was allowed to come to room temp and then stirred overnight. The ethereal layer was then decanted and the residue was washed with a small amount of ether. Water (50 ml) was then added to the residue, and the mixture was steam distilled. The aqueous distillate was extracted several times with ether and the combined organic extracts were dried over Na_2SO_4. Removal of the solvent yielded a small amount of yellow oil (0·06 g). Examination of this material by GLC revealed the presence of several components. The major component (retention time 8 min) was isolated by preparative GLC and was found to have spectral properties identical to those of X.

This reaction was repeated under the conditions described above using a shorter reaction time of 6 hr. In this case, the product (0·13 g) obtained was found to contain an additional minor component with a retention time of 10 min in the GLC separation. Subsequent isolation and characterization of this material proved that it had spectroscopic properties identical with those of XI. The two furfural isomers occurred in this reaction in the ratio 93·5 :6·5.

Oxidation of 3-*methylfurfural.* 3-Methylfurfural (0·1 g) was added a mixture of Aq_2O (0·3 g) in 10% NaOH (2 ml) and stirred for 30 min at room temp. The mixture was then filtered, cooled to ice-bath temp. and neutralized with dil HCl. This mixture was then extracted several times with ethyl ether. The extracts were dried over Na_2SO_4 and the solvent was removed to yield colorless crystalline material (0·09 g), m.p. 139–140°. Characterization of this product revealed that it had spectral properties identical to those of III obtained previously.

3-*Methyl*-2-*mercurylfuran chloride.* 3-Methylfuran (1·6 g, 0·02 moles) in MeOH (1 ml) was added to a stirring soln of mercuric chloride (5·0 g, 0·02 moles) in water (20 ml) at room temp. Almost immediately a white material precipitated. After stirring for 2 hr the mixture was filtered. The ppt was washed with water and air dried (6·1 g), m.p. 138–139° (lit.[13] m.p. 142°), λ_{max} 237 nm; ν_{max} (nujol): 1400, 1060, 885 cm^{-1}; NMR signals: 2·33 (m, 1H, $J_{4,5}$ = 1·8; $J_{5,Me}$ = 0·5, C-5H), 3·58 (m, 1H, $J_{4,5}$ = 1·8; $J_{4,Me}$ = 1·0, C-4H), 7·86 (m, 3H, $J_{4,Me}$ = 1·0; $J_{5,Me}$ = 0·5, C-3 Me).

REFERENCES

[1] A. P. Dunlop and F. N. Peters, *The Furans*, Reinhold, New York (1953)

[2] P. Bosshard and C. H. Eugster, *Advances in Heterocyclic Chemistry* (Edited by A. R. Katritzky and A. J. Boulton), Vol. 7, p. 377. Academic Press, New York (1966)

[3] See also. L. A. Paquette. *Principles of Modern Heterocyclic Chemistry* p. 124. Benjamin. New York (1968)

[4] J. W. Cornforth. *J. Chem. Soc.* 1310 (1958)

[5] D. M. Burness, *Organic Syntheses* (Edited by M. Tishler) Vol. 39, p. 49. Wiley, New York (1959)

[6] L. M. Jackman and S. Sternhell, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry* (Second Edition), p. 173, 207–214, Pergamon Press, London (1969)

[7] S. Rodmar. S. Forsen, B. Gestblom, S. Gronowitz and R. A. Hoffman, *Acta Chem. Scand.* **19**, 485 (1965)

[8] R. J. Abraham and H. J. Bernstein, *Canad. J. Chem.* **39**, 905 (1961)

[9] M. W. Farrar and R. Levine, *J. Am. Chem. Soc.* **71**, 1496 (1949)

[10] T. Reichstein, H. Zschokke and A. Goerg, *Helv. Chim. Acta* **14**, 1277 (1931)

[11] V. J. Traynelis, J. J. Miskel and J. R. Sowd, *J. Org. Chem.* **22**, 1269 (1957)

[12] H. Gilman and R. Burtner, *J. Am. Chem. Soc.* **55**, 559 (1933)

[13] H. Gilman and R. Burtner, *Ibid.* **55**, 2903 (1933)

[14] P. A. Finan and G. A. Fothergill, *J. Chem. Soc.* 2723 (1963)

[15] H. D. Hartough and A. I. Kosak, *J. Am. Chem. Soc.* **69**, 3093 (1947)

[16] J. Lamy, D. Lavit and Ng.Ph. Bun-Hoï, *J. Chem. Soc.* 4202 (1958)

[17] Ref. 3. p. 125

[18] Ref. 1, p. 548.