555. *Some Experiments with Furans.*

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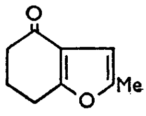
γ-(5-Methyl-2-furyl)butyric acid has been synthesised from 2-methylfuran, and cyclised to give 4,5,6,7-tetrahydro-2-methyl-4-oxobenzofuran.

THE thiophen analogue of α-tetralone has been described by Fieser and Kennelly,[1] but the related furan compound has not been prepared. This paper records the synthesis of the 2-methyl derivative (I) of this compound. In early attempts to acylate 2-methylfuran with succinic anhydride, either no reaction occurred or the furan resinified, perhaps partly owing to the insolubility of succinic anhydride.



(I)

The possibility of carrying out a Hoesch reaction on furan, mentioned by Reichstein,[2] does not seem to have been tested. Chloroacetonitrile was found to give a fair yield of 2-chloroacetyl-5-methylfuran, but this product did not react satisfactorily with diethyl malonate.

γ-2-Furylbutyric acid was made by Hofmann *et al.*[3] from 3-2′-furylpropanol by conversion into the chloride and nitrile, but the yield was not high. The alcohol was made by the catalytic reduction of 3-2′-furylacraldehyde. In our hands this reduction proved capricious. The more readily available β-2-furylacrylic acid has been reduced catalytically,

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[1] Fieser and Kennelly, *J. Amer. Chem. Soc.*, 1935, **57**, 1611.

[2] Reichstein, *Helv. Chim. Acta*, 1930, **13**, 356.

[3] Hofmann, Bridgwater, and Axelrod, *J. Amer. Chem. Soc.*, 1949, **71**, 1253.

but this reduction also proved difficult to repeat. The best method of reducing arylacrylic acids is often by means of Raney alloy in sodium hydroxide solution, which has been reported to reduce β-2-furylacrylic acid to a mixture of tetrahydrofurylpropionic acid and propylbutyrolactone.[4] By the use of milder conditions, β-2-furylpropionic acid was obtained in good yield. Reduction of this with lithium aluminium hydride in ether gave the corresponding alcohol, whose benzenesulphonate on reaction with sodium cyanide followed by hydrolysis gave γ-2-furylbutyric acid in good yield.

Attention was then turned to the 2-methyl derivative. 5-Methylfurfuraldehyde has been prepared from 2-methylfuran in 76% yield by the dimethylformamide synthesis without the use of a solvent.[5] In ethylene dichloride, the yield was 95%. With one equivalent of malonic acid in pyridine, this gave 83% of β-(5-methyl-2-furyl)acrylic acid,[6] while with 1·2 equivalents, the yield was 87%. Reduction with Raney alloy in alkaline solution then gave β-(5-methyl-2-furyl)propionic acid, which was converted into the butyric acid by the method described above. Cyclisation of this with phosphorus pentachloride and stannic chloride in benzene gave the required 4,5,6,7-tetrahydro-2-methyl-4-oxobenzofuran (I).

This ketone with methylmagnesium bromide gave only a small yield of the expected product, the residue being polymeric. This is not the case with the thiophen analogue, which reacted normally. Reduction of β-2-furylacrylic acid by lithium aluminium hydride gave a product which was probably the corresponding allyl alcohol, thus providing another case, contrary to early reports, where the double bond in an acrylic acid is not reduced by this reagent.

EXPERIMENTAL

2-Chloroacetyl-5-methylfuran.—2-Methylfuran (36 g.) and chloroacetonitrile (33 g.) were dissolved in dry ether (200 ml.) and saturated with hydrogen chloride at 0°. After storage at 0° overnight the solvent was decanted, and the deep blue crystalline deposit decomposed with water. The oil which separated was extracted with methylene chloride, dried, recovered, and crystallised from ether, to give *2-chloroacetyl-5-methylfuran* (24 g., 34%) as prisms, m. p. 70° (Found: C, 53·0; H, 4·6. $C_7H_7O_2Cl$ requires C, 53·0; H, 4·45%); this substance was a strong skin-irritant.

5-Methylfurfuraldehyde.—Phosphorus oxychloride (250 ml.) was added to dimethylformamide (200 g.) with stirring and ice-cooling during 10 min. The mixture was diluted with ethylene dichloride, and 2-methylfuran (187 g.) in ethylene chloride (250 ml.) added with stirring in 1 hr. below 20°. After 2 hr. at room temperature the solution was brought to reflux, then cooled, and added to a solution of sodium acetate (1800 g. hydrated) in water (2·5 l.), refluxed for 15 min., and cooled. The organic layer was washed with sodium carbonate solution and with water, then evaporated, and the residue distilled. 5-Methylfurfuraldehyde (239 g., 96%) was collected at 64°/7 mm. as a pale yellow oil, n_D^{30} 1·5237.

β-(*5-Methyl-2-furyl*)*acrylic Acid.*—5-Methylfurfuraldehyde (239 g.), malonic acid (258 g.), and pyridine (125 ml.) were heated on the steam-bath for 3 hr. After cooling, the crystalline mass was diluted with aqueous hydrochloric acid, and the product (287 g., 87%) filtered off and dried in a desiccator. A specimen formed colourless needles, m. p. 152—153°, from aqueous methanol. Kuhn *et al.*[6] give m. p. 153—154°.

β-(*5-Methyl-2-furyl*)*propionic Acid.*—The above acid (146 g.) was dissolved in water (1 l.) containing sodium hydroxide (40 g.), and Raney alloy (100 g.) was added. The suspension was stirred in an ice-bath, and a solution of sodium hydroxide (80 g.) in water (300 ml.) was added, the temperature being kept below 20°. The solution was then stirred at 30° for 2 hr. After filtration, the solution was acidified with tartaric acid (250 g.) in water (500 ml.) and concentrated hydrochloric acid (150 ml.) and extracted with ethyl acetate (2 × 500 ml.). The extract was washed, dried, and evaporated. The residue crystallised from light petroleum (b. p. 40—60°) to give β-(5-methyl-2-furyl)propionic acid (114 g., 78%) as needles, m. p. 55—58°.

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[4] Papa, Schwenk, and Ginsberg, *J. Org. Chem.*, 1951, **16**, 253; *Org. Synth.*, Coll. Vol. III, p. 742.

[5] Traynelis, Miskel, and Sowa, *J. Org. Chem.*, 1957, **22**, 1269.

[6] Kuhn, Köhler, and Köhler, *Z. physiol. Chem.*, 1937, **247**, 197.

Recrystallisation from n-pentane raised the m. p. to 57—57·5° (Robinson and Todd [7] give m. p. 54—55°, Wichterle gives m. p. 61—62°) (Found: C, 62·25; H, 6·65. Calc. for $C_8H_{10}O_3$: C, 62·3; H, 6·5%). The p-*bromophenacyl ester* formed laths, m. p. 103—104°, from methanol (Found; C, 55·9; H, 4·6. $C_{15}H_{15}O_3Br$ requires C, 55·75; H, 4·6%).

β-2-Furylpropionic acid, obtained similarly, had m. p. 58°.

3-(5-*Methyl*-2-*furyl*)*propan*-1-*ol*.—The above acid (130 g.) in ether (500 ml.) was added gradually to lithium aluminium hydride (40 g.) in ether (1 l.). The solution was decomposed with water, and a solution of sodium tartrate (500 g.) and concentrated hydrochloric acid (150 ml.) in water was added. The ether layer was separated, the aqueous layer extracted again with ether, and the combined ether layers washed and evaporated. Distillation of the residue gave 3-(5-methyl-2-furyl)propan-1-ol (112 g., 95%), b. p. 94°/3 mm., n_D^{30} 1·4775. The α-*naphthylurethane* formed needles, m. p. 94—95°, from light petroleum (b. p. 100—120°) (Found: C, 73·8; H, 6·3. $C_{19}H_{19}O_3N$ requires C, 73·8; H, 6·2%).

3-2′-Furylpropan-1-ol, prepared similarly, had b. p. 96°/8 mm., n_D^{30} 1·4719. Reduction of β-2-furylacrylic acid gave an oil, b. p. 110°/7 mm., n_D^{27} 1·5311.

γ-(5-*Methyl*-2-*furyl*)*butyric Acid*.—3-(5-Methyl-2-furyl)propan-1-ol (104 g.) and pyridine (200 ml.) were stirred, and benzenesulphonyl chloride (150 g.) was added in 2 hr. so that the temperature remained below 20°. After a further 2 hr. ice was added, and the whole poured into ice-water (1 l.) and ether, the ether extract was dried and evaporated, and the residue in methanol (250 ml.) refluxed with sodium cyanide (46 g.) in water (100 ml.) for 12 hr. After cooling, water and ether were added, and the extract was washed, dried, and evaporated. Distillation gave 4-(5-*methyl*-2-*furyl*)*butyronitrile* (69 g., 61%), b. p. 91°/2 mm., n_D^{20} 1·4710. The distillation residue was mostly the acid, and it was combined with the nitrile and the whole refluxed for 12 hr. with sodium hydroxide (42 g.) in water (120 ml.). After acidification, the product was extracted with ether, crystallisation from n-pentane then gave γ-(5-*methyl*-2-*furyl*)*butyric acid* (87 g., 70%) as rhombs, m. p. 57—58° (Found: C, 64·5; H, 7·2. $C_9H_{12}O_3$ requires C, 64·3; H, 7·2%). γ-2-Furylbutyric acid was obtained similarly; the nitrile had b. p. 110°/8 mm., n_D^{20} 1·4695.

4,5,6,7-*Tetrahydro*-2-*methyl*-4-*oxobenzofuran*.—γ-(5-Methyl-2-furyl)butyric acid (73 g.) in benzene (600 ml.) was treated with phosphorus pentachloride (91 g.) with stirring at 0°. After ¼ hr. stannic chloride (53 ml.) in benzene (100 ml.) was added with stirring below 5°. An orange solid began to separate at once. The whole was stirred for ½ hr. and added to ice-water and toluene. The organic layer was washed with cold dilute hydrochloric acid, with potassium carbonate solution, and with water, dried, and evaporated. Distillation gave 4,5,6,7-*tetrahydro*-2-*methyl*-4-*oxobenzofuran* (51 g., 77%), b. p. 104°/2 mm., n_D^{24} 1·5235 (Found: C, 71·2; H, 6·8; O, 22·1. $C_9H_{10}O_2$ requires C, 72·0; H, 6·7; O, 21·3%). The *dinitrophenylhydrazone* formed dark red prisms, m. p. 255—257°, from chloroform–ethanol (Found: C, 54·5; H, 4·2; O, 24·4; N, 17·1. $C_{15}H_{14}O_5N_4$ requires C, 54·5; H, 4·3; O, 24·2; N, 17·0%).

Grignard Reaction with 4,5,6,7-*Tetrahydro*-2-*methyl*-4-*oxobenzofuran*.—A Grignard solution was prepared from magnesium (14 g.) and methyl bromide in ether (500 ml.). To this was added the above ketone (71 g.) in ether (200 ml.). After the addition was complete, the complex was decomposed with aqueous ammonium chloride, and the ether layer dried and evaporated. Distillation of the residue gave a product, either 6,7-dihydro-2,4-dimethylbenzofuran or the exocyclic isomer (27 g., 39%), b. p. 72°/2·5 mm., $\lambda_{max.}$ 242 mμ (log ε 3·76 in cyclohexane) (Inflection only, with strong end-absorption). No OH group was detectable by the infrared spectrum. The residue was a water-clear gum that did not distil below 200°/2·5 mm.

Grignard Reaction with 4,5,6,7-*Tetrahydro*-4-*oxobenzothiophen*.—To a Grignard solution from magnesium (6 g.) and methyl bromide in ether (250 ml.) the above ketone (25 g.) was added in ether. The complex was decomposed with aqueous ammonium chloride, and the ether layer dried and evaporated. Distillation of the residue gave 6,7-dihydro-4-methylbenzothiophen (or the double-bond isomer) (21 g.), b. p. 130°/14 mm., $\lambda_{max.}$ 229 mμ (log ε 4·3 in cyclohexane) (no OH band in the infrared spectrum).

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[*Received, April* 6*th*, 1959.]

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[7] Robinson and Todd, *J.*, 1939, 1743.

[8] Wichterle, *Coll. Czech. Chem. Comm.*, 1939, **11**, 171.