Preparation of Some Furan β-Diketones and their Reactions with Hydrazine

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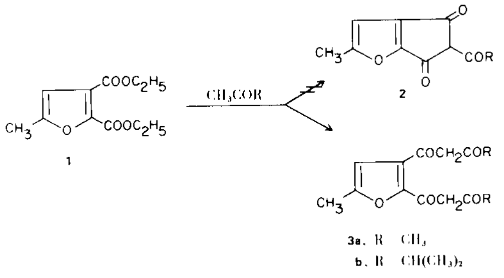
Attempts to prepare 5-acyl-5,6-dihydro-2-methyl-4*H*-cyclopenta[*b*]furan-4,6-diones (**2**) from the diethyl ester of 5-methyl-2,3-furandicarboxylic acid (**1**) and methyl ketones, following the method used to prepare the structurally related 2-acyl-1,3-indandiones (1), failed. Instead, when compound **1** was condensed with acetone or with methyl isopropyl ketone in the presence of an alkoxide the corresponding 2,3-bis(acylacetyl)-5-methylfurans (**3a** and **3b**) were isolated from the reaction mixture.

SCHEME I

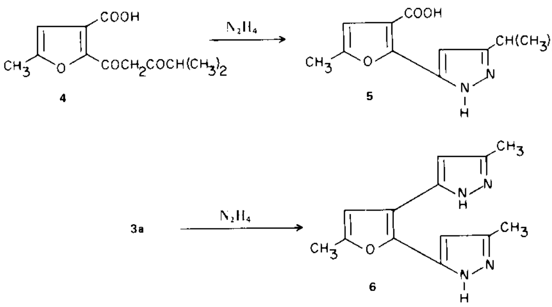


In the condensation of **1** with methyl isopropyl ketone, in refluxing benzene, when potassium *t*-butoxide was used as the catalyst, a relatively large amount of 5-methyl-2-(4-methyl-3-oxovaleryl)-3-furioc acid (**4**) was obtained in addition to compound **3b**. The assignment of the carboxyl group in position 3 was proved by the fact that this compound did not decarboxylate when treated with mercuric chloride. It had been shown by Gilman (2) that the carboxyl group in the 3 position of ring-substituted 2,3-furandicarboxylic acids is not removed when these compounds are heated in the presence of mercuric chloride, decarboxylation taking place only in the 2 position.

When sodium methoxide was used in the above condensation of compound **1** with methyl isopropyl ketone and the reaction was carried out at room temperatures, we failed to obtain compound **3b**, instead a mixture of two isomers was formed, the above reported compound **4** and 5-methyl-3-(4-methyl-3-oxovaleryl)-2-furoic acid. The structure of the latter isomer is based on the elemental analyses, spectral data and on the fact that decarboxylation took place when this compound was treated with mercuric chloride as in the method reported by Gilman (2).

Treatment of compounds **4** and **3a** with hydrazine in alcoholic or aqueous-alcoholic solutions gave 2-[3(5)-isopropyl-5(3)-pyrazolyl)]-5-methyl-3-furoic acid (**5**) and 2,3-bis[3(5)-methyl-5(3)-pyrazolyl)]-5-methylfuran (**6**), respectively. These reactions appear to proceed fairly rapidly to form the pyrazole ring, the intermediate hydrazones never having been isolated.

SCHEME II



EXPERIMENTAL (3)

2,3-Bis(acetoacetyl)-5-methylfuran (**3a**).

A mixture of diethyl ester of 5-methyl-2,3-furandicarboxylic acid (**1**) (25 g., 0.111 mole) and acetone (14 g., 0.24 mole) in ether (100 ml.) was added over a 45 minute period to a stirred, ice cold suspension in ether (400 ml.) of sodium ethoxide, prepared from sodium (7.7 g., 0.33 mole) and ethanol. The mixture was stirred in the ice bath for an additional 8 hours and left to warm to room temperature overnight. Cold water was added. The ether layer upon evaporation *in vacuo* yielded 8.8 g. of **3a**, as a yellow solid, m.p. 94.5-95°; ir (nujol) 2700 (OH), 1600 (conj. C=O) and 1540 cm^{-1} (conj. C=O in chelation); nmr (carbon tetrachloride) 6.7 (s, 1H), 6.51 (d, 1H), 6.11 (s, 1H), 2.32 (d, 3H), 2.1 and 2.05 (s, 6H). The enol proton was unobserved (4).

Anal. Calcd. for $C_{13}H_{14}O_5$: C, 62.40; H, 5.60. Found: C, 62.25; H, 5.61.

The aqueous layer upon acidification with dilute hydrochloric acid gave 12 g. of a tarry product which could not be obtained analytically pure. The ir [(nujol) 2600 (OH), 1725 (C=O), 1600 (conj. C=O), 1550 cm^{-1} (conj. C=O in chelation)] and the nmr spectra [(DMSO) 10.4 (br, 1H), 6.63 (d, 1H), 6.25 (s, 1H), 2.38 (d, 3H) and 2.25 (s, 3H)] are similar to those of 5-methyl-2-(4-methyl-3-oxovaleryl)-3-furoic acid (**4**) suggesting that this product may be 5-methyl-2(or 3)-acetoacetyl-3(or 2)-furoic acid.

2,3-Bis(isobutyrylacetyl)-5-methylfuran (**3b**).

A mixture of 5-methyl-2,3-furandicarboxylic acid diethyl ester (**1**) (6.5 g., 0.0289 mole) and methyl isopropyl ketone (2.5 g., 0.0289 mole) in dry benzene (50 ml.) was added over a 50 minute period to a stirred suspension in benzene (150 ml.) of potassium *t*-butoxide, prepared from potassium (4 g., 0.1 mole) and an excess of *t*-butyl alcohol. The reaction mixture, which immediately turned dark brown, was stirred 1 hour at room temperature, 2 hours at 45-50°, 4 hours at reflux, then cooled and poured into ice water. The aqueous layer was acidified with dilute hydrochloric acid and extracted several times with ether. The extracts were dried over magnesium sulfate, concentrated under reduced pressure and the oily residue chromatographed on silicic acid (carbon tetrachloride and chloroform as eluent) to give (a) 2.7 g. of **3b** as an oil; ir (carbon tetrachloride) 2800-2500 (OH), 1600 (conj. C=O) and 1540 cm^{-1} (conj. C=O in chelation); nmr (deuteriochloroform) 6.9 (s, 1H), 6.57 (d, 1H), 6.17 (s, 1H), 2.54 (q, 2H), 2.38 (d, 3H), 1.22 and 1.14 (d, 12H). The enol proton was unobserved (4).

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.66; H, 7.18; O, 26.11. Found: C, 66.78; H, 7.25; O, 26.21.

(b) Three g. of 5-methyl-2-(4-methyl-3-oxovaleryl)-3-furoic acid (**4**), as light yellow crystals, m.p. 100-101°; ir (potassium bromide) 2620 (OH), 1730 (C=O), 1600 (conj. C=O), 1550 cm^{-1} (conj. C=O in chelation); nmr (deuteriochloroform) 10.4 (br, 1H), 6.62 (d, 1H), 6.21 (s, 1H), 2.54 (q, 1H), 2.42 (d, 3H) and 1.25 (d, 6H).

Anal. Calcd. for $C_{12}H_{14}O_5$: C, 60.50; H, 5.88; O, 33.61. Found: C, 60.49; H, 5.77; O, 33.81.

A mixture of compound **4** (0.11 g., 0.00047 mole), mercuric chloride (0.13 g., 0.00047 mole), water (25 ml.) and a few drops of 4*N* sodium hydroxide was heated at reflux for 45 minutes. After cooling to room temperature a small amount of 4*N* sodium hydroxide was added, some insoluble material was collected by filtration and the filtrate acidified and extracted with ether. The residue after evaporation of the ether under reduced pressure was identified as the starting material by ir and nmr spectra.

5-Methyl-3-(4-methyl-3-oxovaleryl)-2-furoic Acid and 5-Methyl-2-(4-methyl-3-oxovaleryl)-3-furoic Acid (**4**).

A mixture of methyl isopropyl ketone (1.62 g., 0.0188 mole) and diethyl ester of 5-methyl-2,3-furandicarboxylic acid (**1**) (4 g., 0.0179 mole) in dry benzene (20 ml.) was added over a 45 minute period to a stirred suspension in benzene (250 ml.) of sodium methoxide, prepared from sodium (1.24 g., 0.054 mole) and absolute methanol. The mixture was stirred at room temperature for 4 days and then poured into water. The aqueous layer was acidified with dilute hydrochloric acid and the yellow-orange emulsion which formed was extracted with four 100-ml. portions of ether. The dark yellow crystalline residue, obtained after evaporation of the ether *in vacuo*, gave by fractional crystallization from an ether-hexane mixture 0.4 g. of **4** m.p. 100-101°, alone and in mixture with compound **4** above described, and 0.1 g. of 5-methyl-3-(4-methyl-3-oxovaleryl-2-furoic acid as brownish solid, m.p. 167-168°; ir (potassium bromide) 2600 (OH), 1750 (C=O), 1620 (conj. C=O) and 1550 (conj. C=O in chelation).

Anal. Calcd. for $C_{12}H_{14}O_5$: C, 60.50; H, 5.88; O, 33.61. Found: C, 60.57; H, 6.01; O, 33.83.

The latter isomer when treated with mercuric chloride under the conditions described above for compound **4** gave a product which does not show any more the C=O peak at 1750 cm^{-1} in the ir spectrum and shows in the nmr a new peak at 6.2 ppm, which appears to be the hydrogen in the 2 position of the furan ring.

2-[3(5)-Isopropyl-5(3)-pyrazolyl)]-5-methyl-3-furoic Acid (**5**).

Hydrazine hydrate 85% (0.2 g., 0.0034 mole) was added to a hot solution of compound **4** (0.6 g., 0.00252 mole) in 1-propanol (20 ml.) and water (20 ml.) and the mixture heated at reflux for 2 days. The colorless needles formed on cooling were collected by filtration and recrystallized from a water-propanol mixture to give 0.4 g. of **5**, m.p. 186-187°.

Anal. Calcd. for $C_{12}H_{14}N_2O_3$: C, 61.50; H, 5.98; N, 11.96. Found: C, 61.02; H, 5.90; N, 11.91.

2,3-Bis[3(5)-methyl-5(3)-pyrazolyl)]-5-methylfuran (**6**).

A solution of **3a** (0.9 g., 0.0036 mole) and 95% hydrazine (0.24 g., 0.0072 mole) in dry ethanol (150 ml.) was heated at reflux for 30 hours and then left at room temperature for 1 day. The solvent was evaporated *in vacuo* and the residue washed with ether and crystallized twice from an ethanol-hexane mixture to give a 90% yield of **6** as colorless crystals, m.p. 240°; ir (nujol) 3200 (NH), 1650, 1600 and 1570 cm^{-1} (C=C, C=N); nmr (DMSO) 6.51 (d, 1H), 6.40 (t, 2H), 2.32 (d, 3H), 2.29 and 2.25 (s, 6H).

Anal. Calcd. for $C_{13}H_{14}N_4O$: C, 64.50; H, 5.78; N, 23.15. Found: C, 64.46; H, 5.74; N, 23.01.

REFERENCES

(1) L. B. Kilgore, J. H. Ford and C. W. Wolfe, *Ind. Eng. Chem.*, 34, 494 (1942).

(2) H. Gilman and R. R. Burtner, *J. Am. Chem. Soc.*, 55, 2903 (1933); *ibid.*, 71, 1213 (1949).

(3) Melting points were determined with a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on Perkin Elmer Infracord Models 137 and 237 Spectrophotometers. Nuclear magnetic resonance spectra were obtained on a Varian A-60A spectrometer, using TMS as an internal standard and solvents as specified. Chemical shifts are reported as δ values (parts per million). Elemental analyses were performed by Dr. A. Bernhardt, Mikroanalytisches Laboratorium in Max Planck Institute für Kohlenforschung, Mülheim (Germany) and by Micro Analysis Inc., Marshallton, Delaware.

(4) Sadtler Standard Spectra, NMR 1032 (1971).