A Synthesis of γ-Alkylbutyrolactones from Furfural and a Lower Group of Methyl Ketones

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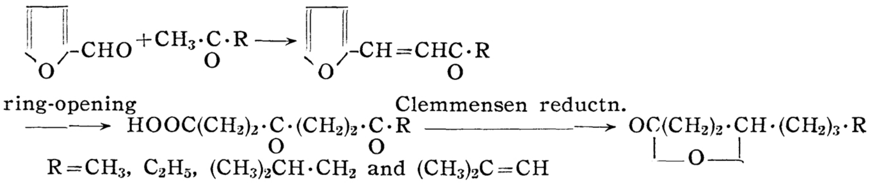
Although γ-alkylbutyrolactones are a group of the most important of all the synthetic perfumes, the lactones are used only to a limited extent by the perfume industry. It seems likely that only two compounds–namely; γ-nonalactone (commonly known as coconut aldehyde) and γ-undecalactone (peach aldehyde) are practically manufactured[2]. Their limited use is due to the lack of suitable raw materials. The authors have found that Clemmensen reduction of γ,ζ-dioxocarboxylic acid gave successfully γ-alkylbutyrolactone in excellent yield. γ,ζ-Dioxocarboxylic acid could be obtained by furan-ring opening of furfurylidene ketone, as the condensation product between furfural and methyl ketone. Thus this paper concerns a new method for preparation of γ-alkylbutyrolactones from furfural and a lower group of methyl ketones, as illustrated by the formulation described below.



$$\mathrm{HOOC(CH_2)_2\cdot\underset{O}{C}\cdot(CH_2)_2\cdot\underset{O}{C}\cdot R} \longrightarrow \mathrm{OC(CH_2)_2\cdot CH\cdot(CH_2)_3\cdot R}$$

$R=CH_3$, C_2H_5, $(CH_3)_2CH\cdot CH_2$ and $(CH_3)_2C=CH$

The condensation for furfurylidene ketone by aqueous sodium hydroxide was carried out between furfural and a series of acetone, methyl ethyl ketone, methyl isobutyl ketone and mesityl oxide by the usual procedure[3,4], and corresponding furfurylidene ketones were obtained. In the reaction of furfural with mesityl oxide, of which some different results were reported by Surmin[5], furfurylidene mesityl oxide (b. p. 128–132°/5 mm.) was distilled, accompanying furfurylidene acetone and difurfurylidene acetone as by-products. Surmin obtained exclusively amorphous furfurylidene mesityl oxide (m. p. 140–145°) without these by-products. The furfurylidene mesityl oxide gave, on furan-ring opening reaction, γ,ζ-dioxocaprylic acid which is identical with ring-cleavage product of furfurylidene acetone. This shows that the isopropylidene group in the ketone is broken down in acidic or alkali solution of an elevated temperature.

Hitherto γ,ζ-dioxocarboxylic acid has been synthesized by means of refluxing furfurylidene ketone in alcoholic hydrochloric acid for a comparatively short period with slight yield[6]. We improved Hunsdiecker's method[7] which was applied on ring-cleavage of furfurylidene acetone with good results. In our study furfurylidene ketone was added to refluxing solution of alcoholic hydrochloric acid for a period of sixty hours and corresponding γ,ζ-dioxocarboxylic acid was gained in steady and excellent yield.

Ohkawara[6] and Grundmann et al.[8] described that various reductions of ε-nitro-γ-oxocaproic acid, with an attempt to get ε-aminocaproic acid gave ε-amino-γ-oxocaproic acid, isoxazolylpropionic acid or γ-caprolactone instead of the required compounds. Taking into account these facts, we tried Clemmensen reduction on γ,ζ-dioxocarboxylic acid and, indeed, could obtain γ-alkylbutyrolactone in good yield. γ,ζ-Dioxocaprylic acid, γ,ζ-dioxopelargonic acid, and γ,ζ-dioxo-θ-methylcapric acid, were smoothly reduced to γ-octalactone, γ-nonalactone and θ-methyl-γ-

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decalactone in 76%, 73% and 66% respectively. The butyrolactones were identified by comparison of their hydrazides with those of authentic butyrolactones prepared by another method. θ-Methyl-γ-decalactone is a new compound and a liquid of strong odor, recalling that of cocos in a concentrated state and of peaches in a diluted state. It may be said to have greater odor value than γ-undecalactone.

Experimental

Condensation of Furfural with Methyl Ketones.—The condensation was carried out according to the well-established procedure of Midorikawa[3,4]. To a mixture of furfural and methyl ketone in water was at once added aqueous sodium hydroxide and the suspension was stirred for an hour as expected at a definite temperature. The reaction mixture was neutralized with acetic acid. The separated oily layer was subjected to distillation. The results are shown in Table I.

TABLE I

Ketone	Grams of Ketone	Furfural g.	aq. 5%	NaOH, 10%	cc. 33%	Reactn. Temp., °C	Reactn. Time hr.	Condn. Product	B. p., °C	mm	Yield[a], %
Acetone	32	25	—	—	5	10–20	4	FA and DFA	95–96 181–184	6 4	66 28
Methyl Ethyl Ketone	50	25	—	25	—	60	1	FMEK	103–104	6	77
Methyl Isobutyl Ketone	50	25	18	—	—	60	2	FMIBK	116–117	5	80
Mesityl Oxide	50	25	16	—	—	60	1	FMSO, FA and DFA	128–132 95–96 181–184	5 6 4	17 16 —

a) Yield was based on furfural. FA refers to furfurylidene acetone, DFA to difurfurylidene acetone, FMEK to furfurylidene methyl ethyl ketone, FMIBK to furfurylidene methyl isobutyl ketone and FMSO to furfurylidene mesityl oxide.

Fractionation of condensation product of furfural with mesityl oxide gave furfurylidene acetone (b. p. 95–96°/6 mm.), furfurylidene mesityl oxide (b. p. 128–132°/5 mm.) and the last distillate (b. p. 181–184°/4 mm.) whose boiling point approximately corresponds to that of difurfurylidene acetone.

Furfurylidene mesityl oxide is a viscous and slightly yellowish liquid (yellow amorphous substance of m. p. 140–145° according to Surmin[5]) and does not easily show the formation of semicarbazone, hydrazone or bisulfite-addition product. B. p. 128–132° (5 mm).

Anal. Found: C, 74.47; H, 7.05. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86%.

Ring-opening of Furfurylidene Ketones.—All runs were carried out according to the following general procedure. 30 g. of furfurylidene ketone dropped onto a refluxing mixture of 150 cc. of conc. hydrochloric acid and 300 cc. of methanol. The addition required sixty hours. After evaporating methanol and hydrochloric acid under reduced pressure, the crystallized residue was pressed on a porous plate. Once recrystallization from petrolether-ethyl acetate gave γ, ς-dioxocarboxylic acid as shown in Table II.

TABLE II

Furfurylidene Ketone	Reactn. Time, hr.	Reactn. Product	M. p., °C	Yield, %	Carbon, % Found	Carbon, % Calcd.	Hydrogen, % Found	Hydrogen, % Calcd.
FA	60	γ, ς-Dioxocaprylic acid[a]	75–76[3]	50	55.85	55.80	7.22	7.03
FMEK	60	γ, ς-Dioxopelargonic acid	85–86[4]	24	58.07	58.05	7.55	7.58
FMIBK	60	γ, ς-Dioxo-θ-methyl capric acid	80[2,3]	32	61.70	61.66	8.34	8.47
FMSO	60	γ, ς-Dioxocaprylic acid[b]	75–76	30	—	—	—	—

a, b) The mixture melting point with a) and b) was not depressed.

Clemmensen Reduction of γ, ς-Dioxocarboxylic Acids[9].—The general procedure of the reduction is illustrated as follows: A mixture of 10 g. of γ, ς-dioxocarboxylic acid, 50 g. of amalgamated zinc, 40 cc. of water, 100 cc. of conc.

TABLE III

γ, ς-Dioxocarboxylic Acid	Product	B. p., °C	mm.	Yield, %	Hydrazide M. p., °C	Hydrazide Nitrogen, % Found	Hydrazide Nitrogen, % Calcd.
γ, ς-Dioxocaprylic Acid[10]	γ-Octalactone	102–105	5.5	76	79–80	16.21	16.08
γ, ς-Dioxopelargonic Acid[10]	γ-Nonalactone	126–127	8	73	84	14.73	14.88
γ, ς-Dioxo-θ-methylcapric Acid	θ-Methyl-γ-decalactone	120–122	2	70	96–97	12.96	12.96

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9) E.L. Martin", Organic Reactions", Vol. I, John Wiley and Sons, Inc., New York, N.Y. (1942), p. 162.

10) B. Rothstein, *Bull. soc. chim. France*, (5), 2, 80 (1935); ibid., (5), 2, 1936 (1935); E.E. Blaise and A. Koehler, ibid., (4), 7, 415 (1910).

hydrochloric acid and 50 cc. of toluene, was boiled vigorously for twenty-four hours. The three 25 cc. portions of conc. hydrochloric acid were added at six-hour intervals during the refluxing period. The toluene layer and ether extracts which were obtained by shaking the water layer, were combined, washed with sodium bicarbonate solution and then subjected to distillation. The results are listed in Table III.

A mixture melting point of hydrazide of γ-nonalactone obtained by Clemmensen reduction and that of authentic lactone[10] prepared by employing *n*-heptaldehyde and malonic acid, was not depressed.

θ-Methyl-γ-decalactone.—This lactone is a transparent liquid having a strong coco odor and is easily soluble in usual organic solvents. B. p. 121° (2 mm.), d_4^{20} 0.941, n_D^{20} 1.4500.

Anal. Found: C, 71.33; H, 11.00. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94%. Saponification value, Found: 309. Calcd.: 304.

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