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THE FREE RADICAL ADDITION OF ALDEHYDES TO α,β-UNSATURATED KETONES

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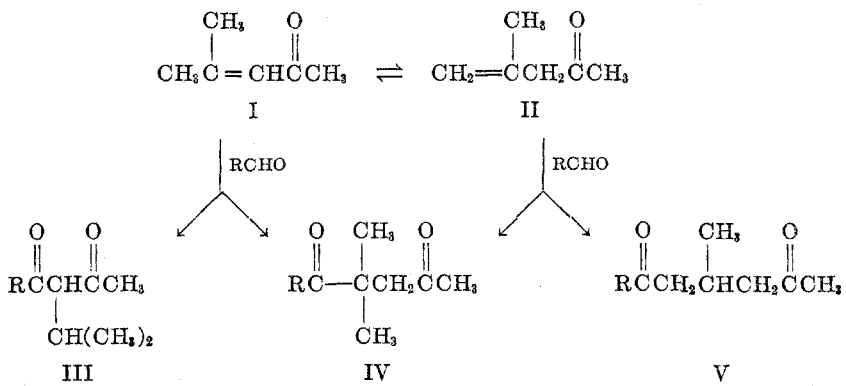
The success achieved in the free radical addition of aldehydes to unsaturated polycarboxylic esters to form acyl derivatives (1), led to an investigation of the possibility of preparing diketones by the addition of aldehydes to α,β-unsaturated ketones.

It was found that a mixture of C_{10} diketones is obtained upon refluxing mesityl oxide with an excess of butyraldehyde in the presence of a catalytic amount of benzoyl peroxide. Although the reaction rate was much slower than in the case of the unsaturated esters, the yields were uniformly good. Conversions of 40–50% were obtained after a reaction time of about 50 hours. The addition reaction was catalyzed by irradiation with ultraviolet light as well as by peroxides.

Stross, Monger, and Finch (2) have shown that mesityl oxide (I) ordinarily exists in tautomeric equilibrium with isomesityl oxide (II), and it becomes apparent that three C_{10} diketones are possible aldehyde-addition products therefrom:



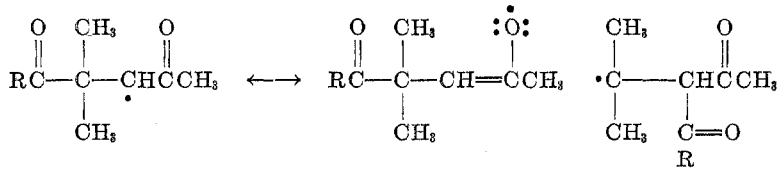
Careful fractionation of the butyraldehyde-mesityl oxide product afforded separation into two diketones, both having the molecular formula $C_{10}H_{18}O_2$. They were obtained in a 10:1 ratio, the higher-boiling component predominating. Nitric acid oxidation of the latter gave α,α-dimethylsuccinic acid, proving the major product to be 4,4-dimethyl-2,5-octanedione (IV, R is C_3H_7). The minor product was shown to be 3-isopropyl-2,4-heptanedione (III, R is C_3H_7) by alkaline cleavage to butyric acid, acetic acid, isobutyl propyl ketone, and isobutyl methyl ketone.

Since III is not derivable from II and V was not observed, structure II participates very little in the addition reaction.

It seemed that a limiting conversion of about 50% was being approached in

the reaction of butyraldehyde with mesityl oxide, and it was of interest to determine the cause. Logically, some material in the reaction mixture was reaching a critical concentration and reaction chains were being terminated nearly as fast as they were initiated. That III might have been at least partially responsible was shown by incorporating a small amount of it in an experiment otherwise identical to one which gave a 41% conversion to diketones. In the latter case the conversion reached only 24%. It will be noted that III has two tertiary hydrogen atoms easily removable by free radicals. The resulting free radicals would be relatively stable and more likely to terminate chains than to propagate them.

The fact that an acyl radical adds preferentially to the carbon atom of the double bond more remote from the carbonyl group in mesityl oxide, is in accord with the observation of Henne and Nager (3) that free radical additions do not necessarily occur at the carbon of higher electron density. As these authors point out, more important factors in the direction of addition are steric considerations and the stability of the intermediate free radical. In mesityl oxide it is difficult to judge, either from observation of its conventionally-written structure or by inspection of a Fisher-Hirschfelder-Taylor model, which of the two doubly-bonded carbon atoms is more sterically hindered. However, it would seem that greater resonance stabilization exists in radical VI than in VII, and this is perhaps



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support for the hypothesis that free radical additions occur to give the intermediate radical of less free energy (4).

Although no attempt has been made at a thorough study of process variables in the addition of aldehydes to mesityl oxide the data in Table I allow these very general tentative conclusions on conversion:

1. At least three moles of aldehyde to one of ketone is desirable, but a higher ratio offers little advantage (Expts. 1, 4, 5).

2. An increase in reaction time from 16 to 64 hours shows a marked, but not proportional, increase in conversion (Expts. 3, 4).

3. The rate of reaction is extremely slow when ultraviolet irradiation is substituted for peroxide catalysis (Expts. 1, 6).

4. It may be slightly advantageous to maintain a completely anhydrous system (Expts. 1, 7).

5. Either weak or strong acids show a deleterious effect, whereas a weak base has little effect (Expts. 1, 8, 9, 10).

6. Oxygen does not inhibit this reaction (Expts. 1, 11).

Two other diketones — 3,3-dimethyl-2,5-hexanedione and 4,4-dimethyl-2,5-undecanedione — were prepared by the addition of acetaldehyde and enanthaldehyde, respectively, to mesityl oxide.

A number of other α,β-unsaturated ketones were evaluated as augends with butyraldehyde. Of these, phorone gave a diketone (VIII) and a triketone (IX)

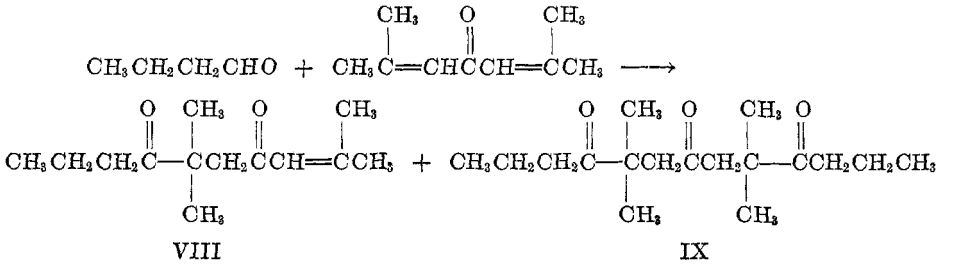

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TABLE I

ADDITIONS OF BUTYRALDEHYDE TO MESITYL OXIDE

EXPT. NO.	MOLE RATIO ALD.: KETONE	CATALYST[a] (Wt.-%)	TEMP., °C.	TIME, Hrs.	CRUDE PRODUCT[b]		REMARKS
					Conv., %	Yield, %	
1	3	1.1	83–86	50	41	97	
2	3	1.1	83–86	50	24	72	[c]
3	4	1.0	83–86	16	31	59	
4	4	1.6	81–85	64	48	75	
5	2	1.5	86–88	66	18	59	
6	3	U.V.	35–40	50	9	100	
7	3	1.9	80–86	40	48	83	[d]
8	3	1.3	80–85	50	41	77	[e]
9	3	0.6	83–90	18	14	35	[f]
10	3	1.1	83–84	49	23	59	[g]
11	3	1.6	81–90	50	50	72	[h]

[a] The catalyst was benzoyl peroxide except in the instance denoted "U.V." in which a 100-watt ultraviolet lamp (1) was used. [b] Conversions and yields are calculated on the basis of the unsaturated ketone. [c] 2% (by weight of the charge) of 3-isopropyl-2,4-heptanedione was added to the reactants. [d] A small amount of hexane was added and a Dean and Stark trap was inserted between the reaction flask and condenser in order to keep the mixture anhydrous. [e] 2% (by weight of the charge) of calcium oxide was added to the reactants. [f] 0.3% (by weight of the charge) of *p*-toluenesulfonic acid was added to the reactants. Much aldolization occurred. [g] 0.7% (by weight of the charge) of boric acid was added to the reactants. [h] A slow stream of dry air was passed through the mixture throughout the reaction period.

and 3-penten-2-one, 3-decen-2-one, and crotonophenone gave the analogous diketones. The structures of the adducts were assigned by analogy to the major butyraldehyde-mesityl oxide adduct, and no effort was made to isolate 1,3-diketones from these other reaction mixtures.

Isophorone, benzalacetone, benzoquinone, and 4-acetoxy-3-penten-2-one failed to give adducts with butyraldehyde. Methyl vinyl ketone, a highly reactive monomer, gave a telomer or low polymer rather than a 1:1 adduct with butyraldehyde, while isopropenyl methyl ketone dimerized under the conditions employed.

TABLE II

PREPARATION OF DIKETONES

ALDEHYDE	KETONE	MOLE RATIO ALD.: KETONE	CATALYST[a] (Wt.-%)	TEMP., °C.	TIME, Hrs.	CRUDE PRODUCT[b]	
						Conv., %	Yield, %
Acetaldehyde	Mesityl oxide	5	1.5	80	91	10	31
Acetaldehyde	Mesityl oxide	3	U.V.	29–31	69	4	55
Enanthaldehyde	Mesityl oxide	1.5	2.8	80	88	37	61
Butyraldehyde	Phorone	4	1.6	82–87	69	40[c]	80[c]
						5[d]	10[d]
Butyraldehyde	3-Penten-2-one	3	2.8	81–86	144	53	64
Butyraldehyde	3-Decen-2-one	3	5.9	84–85	70	12	42
Butyraldehyde	Crotonophenone	3	3.3	84–86	49	5	24
Butyraldehyde	Methyl vinyl ketone	3	1.1	74–76	44	<5	
Butyraldehyde	Isopropenyl methyl ketone	3	1.3	77–79	71	60[e]	
Butyraldehyde	Isophorone	3	1.1	85–86	18	<5	
Butyraldehyde	Benzalacetone	3	1.7	82–86	43	[f]	
Butyraldehyde	Benzoquinone	4	1.0	83–84	22	0	
Butyraldehyde	4-Acetoxy-3-penten-2-one	4	0.7	81–85	90	[g]	

[a] The catalyst was benzoyl peroxide, except in the instance denoted "U.V." in which a 100-watt ultraviolet lamp (1) was used. [b] Conversions and yields are calculated on the basis of the unsaturated ketone. [c] 2,6,6-Trimethyl-2-decen-4,7-dione. [d] 5,5,9,9-Tetramethyl-4,7,10-tridecanetrione. [e] Dimer of isopropenyl methyl ketone, b.p. 80–81°/15 mm., n_D^{25} 1.4561. [f] An undistillable residue amounting to 14% of the starting materials was obtained. [g] A small amount of unidentified product of wide boiling range was obtained.

TABLE III

PROPERTIES OF DIKETONES

DIKETONE	B.P.		n_D^{25}	d_{25}^{25}	CALC'D		FOUND	
	°C.	MM.			C	H	C	H
3,3-Dimethyl-2,5-hexanedione	93	20	1.4363	0.9460	67.6	9.92	67.7	9.89
4,4-Dimethyl-2,5-octanedione	112–112.5	20	1.4371	.9171	70.6	10.66	70.5	10.36
3-Isopropyl-2,4-heptanedione	104–106	20	1.4350	.9078	70.6	10.66	70.5	10.45
4,4-Dimethyl-2,5-undecanedione	92–93	1	1.4447	.9050	73.5	11.40	73.5	11.21
2,6,6-Trimethyl-2-decen-4,7-dione	102.5–104	2	1.4651	.9247	74.2	10.54	73.6	10.27
5,5,9,9-Tetramethyl-4,7,10-tridecanetrione	128–136	1	1.4620	.9530	72.3	10.71	72.9	10.05
4-Methyl-2,5-octanedione	107	20	1.4303	.9219	69.2	10.33	69.3	9.99
4-Hexyl-2,5-octanedione	98–99	0.6	1.4421	.9015	74.3	11.58	73.6	11.63
3-Methyl-1-phenyl-1,4-heptanedione	125–132	1	1.5168	1.0255	77.0	8.31	76.6	8.41

Table I presents the conditions which were used for the addition of butyraldehyde to mesityl oxide and Table II gives the results which were obtained with other aldehyde-ketone combinations. Table III is a summary of the properties of the products.

EXPERIMENTAL

Preparation of diketones. The procedure used for the preparation of 4,4-dimethyl-2,5-octanedione and 3-isopropyl-2,4-heptanedione, as given below, is typical. The addition of acetaldehyde to mesityl oxide was carried out in a stainless steel rocking autoclave. Tables I and II give the conditions for each experiment and Table III gives the properties of the products.

4,4-Dimethyl-2,5-octanedione and 3-isopropyl-2,4-heptanedione. A mixture of 216 g. (3.0 moles) of butyraldehyde and 98.0 g. (1.0 mole) of mesityl oxide was refluxed for 50 hours, during which time 3.5 g. of benzoyl peroxide was added in 0.5- to 1.0-g. increments. The temperature rose from 83° to 86°. The mixture was fractionated to give 167.6 g. (2.33 moles) of recovered butyraldehyde, b.p. 68–74°; 56.9 g. (0.58 mole) of recovered mesityl oxide, b.p. 46–52°/50 mm., n_D^{25} 1.4398; 6.5 g. of intermediate, b.p. 59–70°/20 mm.; 69.2 g. of diketone fraction, b.p. 100–113°/20 mm., n_D^{25} 1.4378; and 5.1 g. of residue. The conversion to diketones was 41% and the yield was 97%.

The above diketone fraction was combined with 13.0 g. of a similar fraction from a previous run and fractionated through a 30-inch Lecky column. From the fractionation curve it was estimated that 3% of the distillate was forerun, 9% was 3-isopropyl-2,4-heptanedione, and 88% was 4,4-dimethyl-2,5-octanedione.

Proof of structure of 3-isopropyl-2,4-heptanedione. 3-Isopropyl-2,4-heptanedione (5 g.) was refluxed for 18 hours with 150 ml. of 2% sodium hydroxide. The alkaline hydrolysis mixture was steam-distilled, whereupon 50 ml. of ether and 5 g. of sodium bisulfite were added to the distillate with thorough shaking. The ether layer was separated and again extracted with a solution of 5 g. of sodium bisulfite in 50 ml. of water. It was then washed with a little water and the ether was evaporated. A *semicarbazone* was prepared from the residual isobutyl propyl ketone. After two crystallizations from dilute ethanol, it melted[1] at 122–123° (123–124°) (5).

Anal. Calc'd for $C_9H_{19}N_3O$: C, 58.33; H, 10.33.

Found: C, 58.11; H, 10.01.

The steam-distillation residue was acidified with sulfuric acid and 12 ml. was steam-distilled. The distillate was treated with *p*-bromophenacyl bromide to give *p-bromophenacyl butyrate*, m.p. 62–63° (63°) (6) after recrystallization from dilute ethanol.

Another 5-g. portion of 3-isopropyl-2,4-heptanedione was hydrolyzed as before. The oil was separated from the aqueous layer and the latter was extracted four times with 5-ml. portions of benzene. The combined oil and extracts were dried over Drierite and the benzene was evaporated. Several drops of distillate were then collected which gave a positive test for a methyl ketone with alcoholic sodium bisulfite solution. This was presumed to be isobutyl methyl ketone. The aqueous portion of the hydrolysis mixture was evaporated to *ca.* 25 ml. and then acidified with dilute hydrochloric acid. A small amount of sodium chloride was removed and the filtrate was extracted twice with equal volumes of ether to remove most of the butyric acid. Although attempts to prepare a *p*-bromophenacyl ester from the aqueous residue failed, this solution did give a red-brown color with ferric chloride, a test characteristic of the acetate ion (7).

Proof of structure of 4,4-dimethyl-2,5-octanedione. A stirred mixture of 0.1 g. of vanadium pentoxide and 50 ml. of 50% nitric acid was heated by a water-bath to 75°. The bath was removed and 5.0 g. of 4,4-dimethyl-2,5-octanedione was added at such a rate that the temperature remained at 68–72°. About 20 minutes was required to complete the reaction. The reaction mixture was then transferred to an evaporating dish and boiled on a hot plate until its volume was reduced by one-half. Upon cooling, the light green solution deposited white crystals. The mother liquor was decanted and the crystals were pressed between sheets of filter paper and then dried in a vacuum desiccator over potassium hydroxide. The crude α,α-dimethylsuccinic acid weighed 2.3 g. and melted at 126–127°. It was recrystallized

[1] All melting points are corrected.

three times from an ethyl acetate-hexane solution, whereupon the melting point was raised to 139–140° (140°) (8).

Anal. Calc'd for $C_6H_{10}O_4$: Neut. equiv., 73.1. Found: Neut. equiv., 73.2.

3-Penten-2-one. To 300 ml. of saturated sodium chloride solution there was added 35 g. of sodium hydroxide pellets. When the base had dissolved, the precipitated sodium chloride was removed by filtration. This filtrate, 600 ml. of ether, and 580 g. (10 moles) of acetone were placed in a 3-l., three-necked flask fitted with a stirrer and a thermometer. The stirred mixture was cooled by an ice-bath and a solution of 454 g. (*ca.* 10.3 moles) of acetaldehyde in 580 g. (10 moles) of acetone was added dropwise at a rate designed to maintain the temperature at 10–12°. The addition required two hours. The mixture was stirred for 15 minutes longer, the ice-bath was then removed, and stirring was continued for an additional 15 minutes. The aqueous (lower) layer containing suspended sodium chloride was separated, and the organic layer was neutralized carefully with 85% phosphoric acid. The color changed from amber to yellow and more salt precipitated. The solution was dried over Drierite, filtered, and left in the refrigerator overnight. The low-boiling components were removed by distilling up to 60° at slightly reduced pressure. Then 1 ml. of concentrated sulfuric acid was added to the yellow residue causing it to turn dark amber. Distillation was continued collecting water and product up to 105°/200 mm. Potassium carbonate was added to the distillate until the latter was saturated. The organic layer was separated, dried over potassium carbonate, and then fractionated through a Lecky column. The distillate, b.p. 54–122°/atm., evidently contained water. It was refluxed with 100 ml. of hexane under a Dean and Stark trap until the water was removed. (During this operation the mixture bumped severely causing loss of 20–30% of the product through the condenser.) Fractionation through the Lecky column gave 132.4 g. (15% yield) of 3-penten-2-one, b.p. 119–121°, n_D^{25} 1.4341 (b.p. 122–123°, n_D^{20} 1.4350) (9).

3-Decen-2-one. Enanthaldehyde was condensed with acetone by the method of Rupe and Hinterlach (10) to give a 39% conversion to crude product. A fraction, b.p. 117–126°/10.5 mm., n_D^{25} 1.4426, was used. Rupe and Hinterlach reported b.p. 125–126°/12 mm.

Crotonophenone. The Friedel-Crafts condensation of crotonyl chloride with benzene as reported by Fuson, Christ, and Whitman (11) was followed. However, it was found that the reaction did not proceed at 5° in the presence of ultraviolet light as these authors reported, but that at 15–20° in the absence of illumination the condensation occurred smoothly to give 69% of product, b.p. 114°/11.5 mm.–115°/11 mm., n_D^{25} 1.5582 (b.p. 111–112°/9 mm., n_D^{18} 1.5626 (12).

4-Acetoxy-3-penten-2-one. A 500-ml. flask was charged with 200 g. (2.0 moles) of isopropenyl acetate, 100 g. (1.0 mole) of acetylacetone, and 2 g. of conc'd sulfuric acid. An 8-inch Vigreux head with adjustable take-off was attached to the flask. The mixture was heated to gentle reflux and acetone was removed by distillation as formed. After 2½ hours 76 ml. (*ca.* 1 mole) of acetone, b.p. 56–59°, had been removed, and the pot temperature had risen from 85° to 110°. The balance of the material was then distilled rapidly, and the distillate was collected in several portions at successively lower pressures. The distillate, b.p. 30°/100 mm.–119°/14 mm., was fractionated through a Lecky column to give 76.9 g. (54% yield) of 4-acetoxy-3-penten-2-one, b.p. 91–94°/18 mm. n_D^{25} 1.4494 (b.p. 92°/18 mm., n_D^{25} 1.4507) (13). Its *2,4-dinitrophenylhydrazone* melted at 122° (122°) (14).

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SUMMARY

A mixture of 1,4- and 1,3-diketones has been obtained in 10:1 ratio by the free radical addition of butyraldehyde to mesityl oxide. Acetaldehyde and enanthaldehyde also have given diketones with mesityl oxide.

Butyraldehyde has been added successfully to phorone, 3-penten-2-one, 3-

decen-2-one, and crotonophenone, respectively, but the addition has failed with methyl vinyl ketone, isopropenyl methyl ketone, isophorone, benzalacetone, benzoquinone, and 4-acetoxy-3-penten-2-one.

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