nylcarbinol. It was later shown,[2] however, that the rearrangement of such ethynylcarbinols leads essentially to ketones rather than aldehydes, and that Rupe and Geisler had in hand phenylbutenone, $CH_2{=}C(C_6H_5){-}CO{-}CH_3$ rather than β-methylcinnamaldehyde. Arens and Van Dorp have recently reported syntheses of β-methylcinnamaldehyde by two different methods.[3] In both cases, the aldehyde was prepared in only quite small quantities; it was reported to have an odor like that of cinnamaldehyde, and gave a semicarbazone, m.p. 206° (cor.). Other physical properties were not reported.

Our synthesis differs from that of Arens and Van Dorp. Ethyl β-methylcinnamate, $C_6H_5C(CH_3){=}CH{-}CO_2C_2H_5$, was prepared and reduced with a large excess of lithium aluminum hydride to β-methylcinnamyl alcohol. The latter was then oxidized to β-methylcinnamaldehyde by the use of activated manganese dioxide.[4] The semicarbazone of this aldehyde melted at 201–202° (uncor.) and probably is identical with that of Arens and Van Dorp. Our β-methylcinnamyl alcohol, however, differed from Lebedeva's compound,[5] obtained from methylphenylvinylcarbinol by acid-catalyzed rearrangement and tentatively assigned the structure, $C_6H_5C(CH_3){=}CH{-}CH_2OH$.

The odor of our aldehyde was similar to that of cinnamaldehyde and quite different from that of citral.

Experimental

Synthesis of Ethyl β-Methylcinnamate.—Ethyl β-methylcinnamate, b.p. 116–119° (4 mm.), $n^{27}D$ 1.5419–1.5434 for different fractions, was prepared in 51–68% yield by the procedure of Johnson and Kon.[6]

Synthesis of β-Methylcinnamyl Alcohol.—A solution of 19 g. (0.1 mole) of ethyl β-methylcinnamate in 50 ml. of ether was added dropwise to a solution of 7.5 g. (0.2 mole) of lithium aluminum hydride in 400 ml. of ether at a reaction temperature of −10°. After addition was complete, stirring was continued for 2 hours at −10°, and the mixture was allowed to stand overnight at room temperature. The reaction mixture was cooled in an ice–salt mixture, water was added dropwise until the initial vigorous reaction was over, and finally an additional 100 ml. of water was rapidly added. The mixture was stirred with 500 ml. of cold 10% sulfuric acid until solution of the precipitated salts was complete. The ether layer was separated, and the aqueous phase was extracted with 100 ml. of ether, saturated with sodium chloride, and again extracted with 100 ml. of ether. The ether extracts were combined with the original ether layer, washed with water, twice with 100-ml. portions of 2.5% potassium carbonate solution, thrice with 100-ml. portions of water, and dried over anhydrous sodium sulfate. The ether was removed by distillation. The residual crude products from three runs of the size described above were combined and fractionally distilled through a Todd column with monel spiral packing to give 32.16 g. (72.4%) of β-methylcinnamyl alcohol, b.p. 127–128.5° (6 mm.), $n^{25}D$ 1.5654. *Anal.* Calcd. for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.18; H, 8.27.

Synthesis of β-Methylcinnamaldehyde.—Activated manganese dioxide was prepared according to the directions of Attenburrow.[6] A solution of 5 g. of β-methylcinnamyl alcohol in 250 ml. of carbon tetrachloride was stirred for 2 hours with 50 g. of finely ground manganese dioxide. On addition of the latter, the temperature of the solution rose to 33°, then slowly dropped to room temperature during the remainder of the reaction period. The manganese dioxide was removed by filtration, washed with 100 ml. of carbon tetrachloride and the two portions of solvent were combined. Carbon tetrachloride was then removed by distillation. The crude products from three such runs (using a total of 15.5 g. of alcohol) were combined to give 11.2 g. of crude β-methylcinnamaldehyde. Fractional distillation under nitrogen through the Todd column gave 5.2 g. (34%) of β-methylcinnamaldehyde, b.p. 117–119° (6 mm.), $n^{23}D$ 1.5876, m.p. of semicarbazone, 201–202°. *Anal.* (of semicarbazone). Calcd. for $C_{11}H_{13}ON_3$: N, 20.68. Found: N, 20.40. A small forerun, 0.5 g., identified as acetophenone by formation of its semicarbazone, was obtained; 5 g. of undistillable pot residue remained.

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(2) C. D. Hurd and R. E. Christ, THIS JOURNAL, **59**, 118 (1937).

(3) J. F. Arens and D. A. Van Dorp, *Rec. trav. chim.*, **67**, 459, 973 (1948).

(4) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jensen and T. Walker, *J. Chem. Soc.*, 1094 (1852).

(5) A. I. Lebedeva, *J. Gen. Chem. (U.S.S.R.)*, **20**, 407 (1950).

(6) J. D. A. Johnson and G. A. R. Kon, *J. Chem. Soc.*, 2748 (1926).

The Synthesis of β,β-Dimethylacrylic Acid in Rat Liver Homogenates[1]

BY HARRY RUDNEY

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β,β-Dimethylacrylic acid (senecioic acid, methylcrotonic acid), a postulated intermediate in the biosynthesis of cholesterol[2] and rubber,[3] has been found to be synthesized from acetate in rat liver preparations.[4,5] In this note the details are presented of the isolation and degradation of DMA[6] following its biosynthesis from $C^{14}H_3COOH$ in a rat liver homogenate system. The results shown in Table I are in agreement with the hypothesis that DMA is a precursor of cholesterol since the pattern of labeling is similar to that found in the isoöctyl side-chain of cholesterol.[7] A similar distribution has been observed in HMG[8] suggesting that DMA arises from HMG *via* decarboxylation and dehydration.[8]

Experimental Part

Ten μmoles of $C^{14}H_3COONa$ (specific activity = 1.5×10^5 c.p.m./μM. acetate) and 40 μmoles, of DMA were incubated with the homogenate as previously described.[8] At the end of the incubation, the mixture was made alkaline with KOH (final concn. 0.17 *N*) and 0.4 mmole of DMA was added as carrier. After standing ½ hour at room temp., the mixture was acidified with H_2SO_4, mixed with Celite (2 g./ml.) and continuously extracted with ether for eight hours.

The ether extract was neutralized, and evaporated to dryness. The residue was taken up in 0.7 ml. of 2 *M* phosphate buffer *p*H 7.6, 1.2 g. of Celite was added and the mixture was placed on a buffered Celite column (20 g., *p*H 7.6) and separated with butanol and chloroform according to the procedure of Bueding and Yale[9] with some minor modifications. Elution with 200 ml. of 100% chloroform removed C_6 and higher fatty acids. DMA was obtained immediately afterward when the solvent was changed to 5% butanol–

(1) Aided by grants from the Life Insurance Medical Research Fund and the Elizabeth Severance Prentiss Fund of Western Reserve University.

(2) K. Bloch, L. C. Clarke and I. Harary, THIS JOURNAL, **76**, 3859 (1954).

(3) J. Bonner, M. W. Parker and J. C. Montermoso, *Science*, **120**, 549 (1954).

(4) H. Rudney, *Federation Proc.*, **13**, 286 (1954).

(5) J. L. Rabinowitz, THIS JOURNAL, **76**, 3037 (1954).

(6) The following abbreviations are used DMA = β,β-dimethylacrylic acid, HMG-β-hydroxy-β-methylglutaric acid.

(7) J. Wursch, R. L. Huang and K. Bloch, *J. Biol. Chem.*, **195**, 439 (1952).

(8) H. Rudney, THIS JOURNAL, **76**, 2595 (1954).

(9) E. Bueding and H. W. Yale, *J. Biol. Chem.*, **193**, 411 (1951).

95% chloroform. It was rechromatogramed on another column (48 g., *p*H 7.8) with 1% butanol, 99% $CHCl_3$, as eluent. The DMA contained considerable radioactivity, and its purity was established by the following criteria. The radioactivity and titratable acidity curves coincided as the compound was eluted from the column; the *p*-bromophenacyl ester gave the correct m.p., with no depression on admixture with a sample of authentic derivative; the specific activity of the derivative did not change upon recrystallization. The percentage of total counts added, incorporated in the DMA equalled 0.28%. DMA was degraded as follows. A Schmidt reaction gave carbon 1 as CO_2.[10] Oxidation of DMA with acid permanganate gave acetone representing carbons 3, 4 and 4′ and CO_2 representing carbons 1 and 2. The activity of carbon 2 was calculated by difference. Acetone was trapped in bisulfite and identified as the 2,4-dinitrophenylhydrazone. Degradation of acetone with NaOI provided carbon 4 and 4′ as iodoform, which was oxidized to CO_2.[11] The radioactivity in carbon 3 was obtained by subtracting the specific activity of carbons 4 and 4′ from that observed when the acetone moiety was totally oxidized. All CO_2 samples were counted as finitely thick plates of $BaCO_3$ in a gas flow counter, with appropriate corrections for self absorption.

TABLE I

	C.p.m./mmole carbon	% Isotope distribution
CH_3 CH_3 4 + 4′	3350	63.8
$_3C$	trace	..
$_2CH$	3712	35.3
$_1COOH$	168	1.6
Total oxidation calcd.	2120	
found	2100	

(10) E. F. Phares, *Arch. Biochem.*, **33**, 173 (1951).

(11) W. W. Shreeve, F. Leaver and I. Siegel, THIS JOURNAL, **74**, 2404 (1952).

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The Kostanecki–Robinson Acylation of 5-Hydroxy-6-Acetyl-4-methylcoumarin

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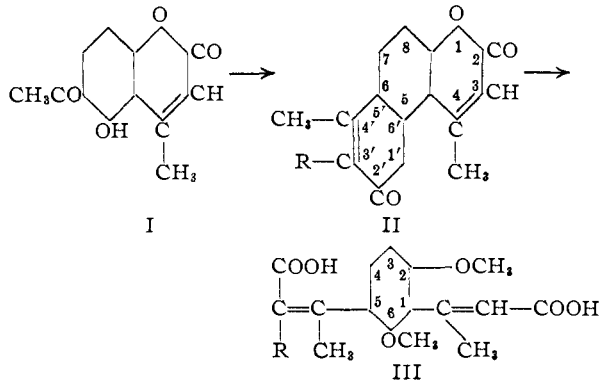
5-Hydroxy-6-acetyl-4-methylcoumarin, now easily available by the condensation of resacetophenone with ethyl acetoacetate in the presence of anhydrous aluminum chloride, is a useful substance for synthetic work. Sethna, Shah and Shah[1] carried out its Kostanecki–Robinson acetylation and benzoylation, obtaining chromono- and flavono-α-pyrones. This study now has been extended to its propionylation and butyrylation under the conditions of the Kostanecki–Robinson reaction and the results are described in this paper.

On heating 5-hydroxy-6-acetyl-4-methylcoumarin (I) with propionic anhydride in presence of its sodium salt, the product obtained was found to be insoluble in cold alkali and did not give any color with alcoholic ferric chloride. It did not give any styryl derivative with benzaldehyde. Further on treating the product with sodium ethoxide or hydroxide, the unchanged product was recovered. Hence the product has been assigned the constitution, 4,3′,4′-trimethylcoumarino-5′,6′-(6,5)-α-pyrone (II, R = CH_3).



I II

III

On treating the coumarin (I) with butyric anhydride in the presence of sodium butyrate, the product obtained has been assigned the structure, 4,4′-dimethyl-3′-ethylcoumarino-5′,6′-(6,5)-α-pyrone (II, R = Et) on similar grounds.

The above structures were confirmed by converting the coumarino-α-pyrones into the corresponding methoxycinnamic acid derivatives, *viz.*, 2,6-dimethoxy-5-(α-carboxy-α,β-dimethylvinyl)-β-methylcinnamic acid (III, R = CH_3) and 2,6-dimethoxy-5-(α-carboxy-α-ethyl-β-methylvinyl)-β-methylcinnamic acid (III, R = Et), using the modified method of Shah and Shah.[2]

5-Hydroxy-6-acetyl-4-methylcoumarin (I) also was treated with acetic anhydride in presence of fused sodium phenyl acetate; the product obtained has been assigned the structure, 4,4′-dimethyl-3′-phenyl-5′,6′ (6,5)-α-pyrone (II, R = Ph) on grounds similar to those mentioned above. However, its methoxycinnamic acid derivative could not be prepared satisfactorily.

The above results show that α-pyrone ring does not affect the course of the Kostanecki–Robinson reaction, as the results are in line with those of the observations of the previous investigators.[3]

Experimental

4,3′,4′-Trimethylcoumarino-5′,6′(6,5)-α-pyrone.—5-Hydroxy-6-acetyl-4-methylcoumarin (5 g.), freshly fused sodium propionate (4 g., 2 molar equivalents) and propionic anhydride (10 ml., 4 molar equivalents) were refluxed at 160–170° for 12 hours. The cooled mixture was then decomposed with ice-water. The pasty mass that separated was washed with cold dilute alkali and then with water. The solid obtained was crystallized from acetic acid, lustrous short needles, m.p. 225°, yield 2.0 g.

Anal. Calcd. for $C_{15}H_{12}O_4$: C, 70.32; H, 4.7. Found: C, 70.02; H, 4.6.

Action of Alkali.—The product dissolved in alcohol (10 ml.) was treated with potassium hydroxide (20 ml., 10%) on steam-bath for 3 hours. It was acidified and the solid obtained was crystallized from acetic acid; m.p. 225° undepressed in mixture with the original product. It also was treated similarly with sodium ethoxide with the same result.

2,6-Dimethoxy-5-(α-carboxy-α,β-dimethylvinyl)-β-methylcinnamic Acid.—To the product (1 g.) dissolved in minimum acetone, potassium hydroxide (10 ml., 3 *N*) was added and refluxed on hot water-bath for some time. Dimethyl sulfate (10 ml.) was added, keeping the mixture alkaline; 5 ml. of dimethyl sulfate and 10 ml. of alkali were added every half-hour. Heating was continued for four hours, the

(1) S. M Sethna, N. M. Shah and R. C. Shah, *J. Chem. Soc.*, 228 (1938).

(2) N. M. Shah and R. C. Shah, *J. Univ. Bombay*, **7**, 213 (1938).

(3) I. M. Heilbron, D. H. Hey and B. Lythgoe, *J. Chem. Soc.*, 1581 (1934).