TABLE I

SYNTHESIS OF 2-METHYL-5-*tert*-BUTYLACYLBENZENES BY REACTION OF DI-(2-METHYL-5-*t*-BUTYLPHENYL)-CADMIUM WITH ACYL CHLORIDES

Acyl group	Yield of product[a]	B.p. °C.	B.p. Mm.	$n^{24}D$	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Acetyl[b]	40	140	18	1.5127	82.06	82.00	9.53	9.47
Propionyl[c]	37	148	18	1.5080	82.30	82.21	9.87	9.69
Isobutyryl[d]	68	103	2.4	1.5009	82.51	82.17	10.16	9.91
Pivaloyl[d]	52	122–123	3	1.4934	82.70	82.73	10.41	10.11

[a] Calcd. on the basis of acyl halide used. [b] M.p. of semicarbazone, 183°. *Anal.* Calcd. for $C_{14}H_{21}N_3O$: C, 67.98; H, 8.56; N, 16.99. Found: C, 67.91; H, 8.42; N, 17.00. [c] M.p. of semicarbazone, 146.5–147°. *Anal.* Calcd. for $C_{15}H_{23}N_3O$: N, 16.08. Found: N, 16.05. [d] These ketones failed to give crystalline semicarbazones.

90 g. of *p-t*-butylbenzyl chloride, b.p. 110–115° (6–7 mm.). Taking into account 40 g. of recovered *t*-butylbenzene, the yield of *p-t*-butylbenzyl chloride was 70%. The reaction was repeated seven times, and the combined product was carefully distilled through a 3-ft. column packed with glass helices to give pure *p-t*-butylbenzyl chloride, b.p. 88–89° (3 mm.) (reported 119–121° (16.5 mm.)[9c]), $n^{24}D$ 1.5194. Oxidation of a sample of this material with concd. nitric acid gave *p-t*-butylbenzoic acid, m.p. 164°.[10]

***p-t*-Butyltoluene** was prepared by the method of Verley[11] and the combined product of several runs was fractionally distilled through a 1.2 g. × 90 cm. Todd column packed with Podbielniak "Heli-Pak" to give pure *p-t*-butyltoluene, b.p. 106° (55 mm.), $n^{20}D$ 1.4919. Oxidation of a sample of this material with concd. nitric acid gave *p-t*-butylbenzoic acid, m.p. 164°.[10]

Acetylation of *p-t*-Butyltoluene.—This reaction was carried out essentially as described by Taylor and Watts,[2] except that a reaction temperature of −8 to −5° was used. The major product obtained was probably 2-methyl-4-*t*-butylacetophenone, b.p. 90° (1 mm.), $n^{25}D$ 1.5191, m.p. of semicarbazone, 197°.

Bromination of *p-t*-Butyltoluene.—This bromination was effected essentially as described by Taylor and Watts.[2] 2-Methyl-5-*t*-butylbromobenzene, b.p. 97–98° (4 mm.), $n^{25}D$ 1.5323, was obtained in 73% yield.

Reaction of *p-t*-Butylbenzylmagnesium Chloride with Acetic Anhydride.—*p-t*-Butylbenzyl chloride, 91 g. (0.5 mole), in 300 ml. of dry ether was added dropwise during four hours to 12.2 g. (0.5 mole) of magnesium turnings in 100 ml. of dry ether. The reaction was carried out under nitrogen. The reaction mixture was stirred for three hours under reflux, and allowed to stand overnight. The resulting Grignard solution was pumped under nitrogen to a separatory funnel and added during two hours to a stirred solution of 153 g. (1.5 moles) of acetic anhydride in 200 ml. of dry ether. Stirring was continued for four hours under reflux. The reaction mixture was treated with ice-cold dilute hydrochloric acid; the organic layer was separated, washed successively with water, 10% aqueous sodium bicarbonate, 10% aqueous sodium carbonate, water, and finally dried over anhydrous potassium sulfate. The ether was removed, and the product fractionally distilled through a Todd column with monel spiral packing. In addition to 7 g. of *p-t*-butyltoluene, two reaction products were isolated: (a) 18 g., b.p. 92–95° (2.2 mm.), $n^{24}D$ 1.5115; (b) 11 g., b.p. 97° (2.2 mm.), $n^{24}D$ 1.5048. Fraction (a) gave a semicarbazone, m.p. 183°. A mixed m.p. with the semicarbazone of 2-methyl-5-*t*-butylacetophenone was 183°, while that with the semicarbazone of 2-methyl-4-*t*-butylacetophenone was 155–160°. *Anal.* Calcd. for $C_{13}H_{21}N_3O$: C, 67.98; H, 8.56; N, 16.99. Found: C, 67.91; H, 8.42; N, 17.00.

Fraction (b) gave a semicarbazone, m.p. 144–145°. A mixed m.p. with the semicarbazone of fraction (a) was 125–130°. This ketone has not been identified.

A solid residue from the above fractional distillation, 15 g., after two crystallizations from acetone gave 1,2-di-(*p-t*-butylphenyl)-ethane, m.p. and mixed m.p. with an authentic sample, 149°.

Preparation of 1,2-Di-(*p-t*-butylphenyl)-ethane.—This compound was prepared according to the procedure of Gardner and Borgstrom.[4] The product was obtained in 57% yield, m.p. 149°. *Anal.* Calcd. for $C_{22}H_{30}$: C, 89.73; H, 10.27. Found: C, 89.92; H, 10.11.

Reaction of 2-Methyl-5-*t*-butylphenylmagnesium Bromide with Acetic Anhydride.—A Grignard reagent was prepared in the usual manner from 113.5 g. (0.5 mole) of 2-methyl-5-*t*-butylbromobenzene and 12.2 g. (0.5 mole) of magnesium turnings in 300 ml. of dry ether. Sixty ml. of this solution was dropped over an excess of Dry Ice. Hydrolysis of the resulting complex gave 17 g. (88%) of crude 2-methyl-5-*t*-butylbenzoic acid. Two crystallizations from aqueous alcohol gave 9.6 g. of the acid melting sharply at 98°. This m.p. could not be raised by recrystallization.[5]

The remainder of the Grignard solution was caused to react with acetic anhydride according to the procedure of Newman and Booth.[6] The temperature of the reaction mixture was difficult to control, and rose from −50 to −35° before addition of the Grignard solution was complete. Distillation of the product gave 40 g. (53%) of 2-methyl-5-*t*-butylacetophenone, b.p. 110–115° (7 mm.). Redistillation through a Todd column with monel spiral packing gave 26.8 g. of the ketone, b.p. 135° (13 mm.), $n^{25}D$ 1.5124. This ketone gave a semicarbazone, m.p. 182–183°.

Synthesis of 2-Methyl-5-*t*-butylacylbenzenes by the Organocadmium Procedure.[7]—The following preparation of 2-methyl-5-*t*-butylacetophenone is typical.

To the Grignard reagent, prepared as usual from 113.5 g. (0.5 mole) of 2-methyl-5-*t*-butylbromobenzene and 12.2 g. (0.5 mole) of magnesium turnings in 260 ml. of dry ether, was added 49.6 g. (0.27 mole) of anhydrous cadmium chloride at a temperature below 13° during a period of 45 minutes. The ether was distilled off and replaced by 200 ml. of dry benzene. The temperature was slowly raised to 80°, at which time a Gilman test was faintly positive. The reaction mixture was cooled to 20°, and a solution of 36 g. (0.46 mole) of acetyl chloride in 150 ml. of dry benzene was added during 45 minutes. The reaction mixture was slowly heated to reflux and maintained at that temperature for one hour and 40 minutes. The reaction mixture was worked up as directed by DeBenneville.[7] Distillation of the product gave 34.8 g. of 2-methyl-5-*t*-butylacetophenone having the properties recorded in Table I.

The other 2-methyl-5-*t*-butylacylbenzenes reported in Table I were similarly prepared by use of the appropriate acid chloride.

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(10) Reported, K. T. Serijan, H. F. Hipsher and L. C. Gibbons, THIS JOURNAL, **71**, 873 (1949), m.p., 165.0–165.6°; m.p. of *m-t*-butylbenzoic acid, 127.0–127.6°.

(11) A. Verley, *Bull. soc. chim.*, [3] **19**, 67 (1898).

Synthesis of β-Methylcinnamaldehyde

BY E. EARL ROYALS AND E. R. COVINGTON

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The similarity of β-methylcinnamaldehyde to citral in molecular weight and certain structural features suggested that it might possibly possess a lemon-like odor. Consequently, we undertook to prepare the compound in sufficient quantity to permit purification and determination of its organoleptic properties. A synthesis of β-methylcinnamaldehyde was first reported by Rupe and Geisler[1] by Rupe rearrangement of methylphenylethy-

(1) H. Rupe and L. Geisler, *Helv. Chim. Acta*, **11**, 656 (1928).

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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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[6] 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.

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