in vacuo for 3–5 hr. The diisocyanate was added, stirring was continued for an additional 30 min. and the melt was poured into 4″ × 8″ × 0.075″ polyethylene lined molds and oven cured at 60–100° for 3 or 4 days. After removal from the mold, the polyurethane sheet was cut into 4″ × 0.5″ × 0.075″ strips for physical testing. The results are summarized in Table II.

Acknowledgment. The authors wish to thank Mr. R. F. Adams for the catalytic hydrogenation data and Dr. C. A. Neros and Mr. A. A. Klann for the mechanical testing data.

PAINESVILLE, OHIO

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT OF THE GIVAUDAN CORP.]

A New Synthesis of Irones. II. The Synthesis of 4-(2-*p*-Cymyl)-2-butanone

H. E. ESCHINAZI

Received January 26, 1961

In the synthesis of irones by the acid rearrangement of 2-(2,2,3-trimethylcyclobutyl)-hepta-2,4-dien-6-one a substantial amount of 4-(2-*p*-cymyl)-2-butanone is formed as a result of a hydrogen transfer reaction.

In a previous paper[1] describing a new synthesis of irones from α-pinene involving five steps we also reported the formation of a high boiling isomer in 16% yield, 4-phenylsemicarbazone, m.p. 144°.[2]

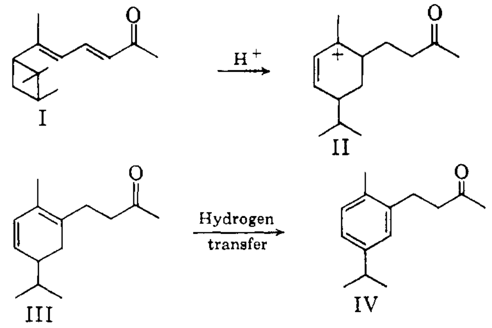
We wish to report the isolation of 4-(2-*p*-cymyl)-2-butanone (IV) as the presumed isomer from the irone-containing mixture resulting from the acid treatment of 2-(2,2,3-trimethylcyclobutyl)-hepta 2,4-dien-6-one.

The unknown ketone reacts readily in the cold with an aqueous alcoholic solution of semicarbazide acetate and gives an immediate precipitate of semicarbazone, m.p. 158–159°, from which the pure ketone is obtained: b.p. 105–106° at 1.5 mm. pressure, n_D^{20} 1.5077, α_D^{25} 0°, 2,4-dinitrophenylhydrazone, m.p. 122°.

The NMR spectrum[3] of the new ketone taken in carbon tetrachloride solution, with tetramethylsilane added as an internal standard, showed six peaks (A to F) in the spectra which corresponded well with the following groups: (A) aromatic; (B) methylene adjacent to aromatic ring, methylene adjacent to ketone and methine (—$\overset{|}{\underset{|}{C}}$—H) adjacent to an aromatic ring; (C) an isopropyl group on an aromatic ring; (D) methyl ketone; (E and F) methyls of an isopropyl group on an aromatic ring. The interpretation of these data in terms of an aromatic ring substituted by methyl and isopropyl groups and a butanone side chain was furthermore confirmed by the absence of optical rotation, and, by chemical and spectroscopic evidence. In contradistinction with irone which was smoothly hydrogenated to tetrahydroirone in the presence of palladium catalyst, the ketone was unaffected by this treatment thus pointing to the absence of alkene linkages and the possible presence of an aromatic ring. The summation of the above evidence and the Wolff-Kishner reduction of the ketone to 2-butyl-*p*-cymene confirm its structure as that of 4-(2-*p*-cymyl)-2-butanone (IV).

The synthesis of 2-butyl-*p*-cymene was achieved in a single step through the Grignard reaction between carvone and butyl magnesium bromide.[4] The infrared and ultraviolet spectra of the two hydrocarbons were identical in every respect.

The formation of 4-(2-*p*-cymyl)-2-butanone (IV) may be rationalized by assuming that a protonated form of 2-(2,2,3-trimethylcyclobutyl)-hepta-2,4-dien-6-one (I) would first undergo a cyclization accompanied by the splitting of the cyclobutane ring as in II; then the *p*-menthadiene conjugated derivative III obtained from II would, through dis-



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[1] H. E. Eschinazi, *J. Am. Chem. Soc.*, **81**, 2905 (1959).

[2] The elementary analysis gave: C, 74.03; H, 8.18. Calcd. for irone 4-phenylsemicarbazone, $C_{21}H_{29}N_3O$, mol. wt., 339.45: C, 74.29; H, 8.61; N, 12.38. Calcd. for 4-(2-*p*-cymyl)-2-butanone, 4-phenylsemicarbazone, $C_{21}H_{27}N_3O$, mol. wt., 337.42: C, 74.74; H, 8.07; N, 12.45.

[3] We wish to express our sincere thanks to Dr. Martin Saunders of Yale University, New Haven, Conn., for the NMR spectra as well as the constructive suggestions in connection with the elucidation of the structure of the ketone IV.

[4] The Grignard reaction between various alkyl halides and carvone has been described by several workers to give at first the 2-alkyl-*p*-menthatriene which rearranges to 2-alkyl-*p*-cymene under acetic-hydrochloric acid treatment, *cf.* A. Klage, *Ber.*, **39**, 2310 (1906); H. Ruppe and coworkers, *Ber.*, **39**, 1120 (1906); **47**, 3068 (1914); F. W. Semmler, K. Jonas, and P. Roenish, *Ber.*, **50**, 1835 (1917).

proportionation or intermolecular hydrogen transfer, afford 4-(2-*p*-cymyl)-2-butanone (IV).

Any dihydroirone likely to be formed as a result of this intermolecular transfer between III and irone may, under conditions similar to those reported by Büchi and co-workers,[5] cyclodehydrate to bicyclic olefins; these hydrocarbons could in turn act as hydrogen acceptors during the hydrogen transfer involving III to yield IV.

The complete proof of this hydrogen transfer reaction will have to await the final isolation of the hydrogen transfer acceptors probably present as components in the lights obtained in the reaction mixture.

EXPERIMENTAL

A mixture of 2-(2,2,3-trimethylcyclobutyl)-hepta-2,4-dien-6-one (1000 g.), benzene (5000 ml.), and 85% phosphoric acid (1500 g.) was placed in a reaction flask under a nitrogen atmosphere and stirred at room temperature for 100 hr. An equal volume of water was then added to the mixture and the stirring was continued for another 10–15 min. After separation of the bottom layer the benzene extract was neutralized with 10% sodium hydroxide, washed with water, and the solvent evaporated. The crude residue was steam distilled with overheated steam (130°) under a slight vacuum (160 mm. pressure). A yield of 590–600 g., n_D^{20} 1.5050 was obtained. The composition of the crude distillate as shown by gas-liquid chromatography[6] was:

Lights[7]	20%
Iso α-irone[a]	36.5
α-Irone[a]	6.–
β-Irone	6.–
4-(2-*p*-Cymyl)-2-butanone	31.–

[a] α-Irone and iso α-irone have also been named with the prefix neo- to designate the trans structure of their butenone side chain, *cf.* Y. R. Naves, *Helv. Chim. Acta*, **32**, 969 (1949).

The distillation of the crude product through a 4 ft.-Nickel Cannon-packed column at 0.5 mm. pressure showed the following cuts:

					Irones			
Cut	B.P.	Distillate, %	n_D^{20}	Lights	Iso α	α	β	IV
a	44–59	7.	1.4955	100[a]	—	—	—	—
b	64–69	8	1.5076	100[a]	—	—	—	—
c	68–78	8.5	1.4940	77[a]	23	—	—	-
d	80–84	43.5	1.5010	—	50	15	12	13
e	84–90	3.5	1.5093	—	—	—	16	82
f	94–96	12.5	1.5095	—	—	1	2	97
g	110–115	9.5	1.5185	—	—	—	—	81

[a] The composition of the lights consisted of about six products appearing as the main peaks; because of the small amount at hand, no attempt was made to separate and study their structure.

Cut d consisted mainly of a mixture of irones whereas cuts e, f, and g contained most of the 4-(2-*p*-cymyl)-2-butanone (IV)

When cut f (85 g.) was mixed with a cold 70% ethanol solution (400 ml.) containing semicarbazide hydrochloride 45 g.) and sodium acetate (45 g.) a rich precipitate formed almost instantly. After 15 min. the semicarbazone was filtered, washed with 500 ml. of ethanol, and dried; yield 106 g. After recrystallization from ethanol it melted at 158–159°.

Anal. Calcd. for $C_{15}H_{23}N_3O$: C, 68.94; H, 8.87; N, 16.08. Found: C, 68.70; H, 9.17; N, 16.10.

The 2,4-dinitrophenylhydrazone was prepared from a sample of semicarbazone by treatment of an acid (hydrochloric) alcoholic solution of 2,4-dinitrophenyl-hydrazine, m.p. 121–122° (ethanol).

Anal. Calcd. for $C_{20}H_{24}N_4O_4$: C, 62.5; H, 6.29; N, 14.57. Found: C, 62.79; H, 6.39; N, 14.63.

The pure ketone was recovered in almost quantitative yield when the semicarbazone, m.p. 158–159° was refluxed with 5% oxalic acid (20 volumes) for 2 hr. After extraction with benzene and neutralization with sodium carbonate, the ketone was freed from the solvent and distilled at 105° at 1.5 mm.; n_D^{25} 1.5078; α_D^{20} 0°; it gave the same semicarbazone m.p. 158–159°.

2-Butyl-p-cymene. (a) By Wolff-Kishner reduction of 4-(2-p-cymyl)-2-butanone semicarbazone. A mixture of semicarbazone, m.p. 158–159° (5 g.), diethylene glycol (25 ml.), 85% hydrazine hydrate (2.5 ml.) and potassium hydroxide pellets (4 g.) was refluxed for 0.5 hr. at 140°; the temperature was then raised to 175° by the distillation of about 2 ml. of glycol-water mixture and the refluxing was resumed for an additional 10 hr. whereby the reaction temperature reached 190–200°. The reaction mixture was then distilled off until the pot temperature reached 260°. The distillate was shaken with a saturated sodium chloride solution, washed with 10% sulfuric acid and distilled over sodium; yield 2.4 g., b.p. 242–243° at 745 mm.; n_D^{20} 1.4930; α_D^{25} 0°. Ultraviolet absorption: λ_{max} 276 mμ, ϵ_{max} 590; λ_{max} 266.5 mμ, ϵ_{max} 580 in alcohol.

(b) *By Grignard reaction with carvone.* Freshly distilled 1-carvone (35 g.), n_D^{20} 1.4978; α_D^{25} −60° was added within 20 min. into an ether solution of *n*-butylmagnesium bromide prepared from *n*-butyl bromide (35 g.) and magnesium (6.5 g.) in ether (100 ml.). The reaction mixture was refluxed for 3 hr., left overnight and then decomposed by pouring onto 40% sulfuric acid (250 g.) at −5° under stirring. After 0.5 hr. the ether solution was separated, washed with water, and neutralized with 10% sodium hydroxide. After evaporation of the solvent the reaction product was submitted for distillation at 1.5 mm. When the pot temperature reached 80° slight gas formation (hydrogen bromide) took place. The reaction mixture was neutralized once more with 10% sodium hydroxide and distilled again at 2–4 mm. pressure. Some small amount of gas formation was again evident. The distillate, 34 g., n_D^{20} 1.4944 α_D −4°, was washed with 10% sodium hydroxide to remove any carvacrol formed, the last traces of carvone were removed by distillation over sodium and the 2-butyl-*p*-cymene (31 g.) distilled at 123–124° at 17 mm. n_D^{20} 1.4930, α_D 0°. The infrared and ultraviolet spectra were identical with the hydrocarbon obtained in (a).

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(5) G. Büchi, K. Biemann, B. Vittimberger, and H. Stoll, *J. Am. Chem. Soc.*, **78**, 2622 (1956).

(6) 30% Carbowax 20*M* polyethylene glycol compound, average mol. wt. 20,000 (Union Carbide Chemicals) with Chromosorb-W, Celite-like support (Johns-Manville). The Instrument, Perkin-Elmer model 21.

(7) The main part of the lights shown in the chromatographic curve consisted of a pair of doublet peaks, presumably due to the presence of cyclodehydration products of irone which might have also acted as hydrogen acceptors.

[Contribution from the Research Institute of Chemistry, National Taiwan University]

Synthesis of 8-Bromoflavone and Related Compounds[1]

C. T. CHANG, T. S. CHEN, and F. C. CHEN[2]

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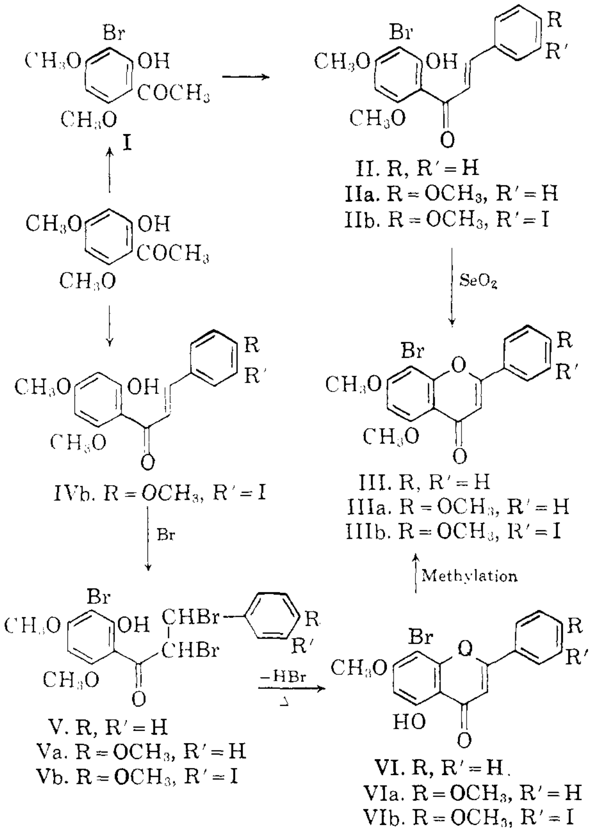
Synthesis of 8-bromo-5,7-dimethoxyflavone (III), 8-bromo-5,7,4′-trimethoxyflavone (IIIa), 8-bromo-5,7,4′-trimethoxy-3′-iodoflavone (IIIb), the corresponding chalcones (II, IIa, and IIb), their tribromides (V, Va, and Vb), and the acetophenone (I) is described. The products, m.p. 242° and 250°, formed from the dehydrobromination of the tribromochalcones, by heating above the melting point under pressure, reported earlier[3] as 6-bromo-5,7-dimethoxyflavone and 6-bromo-5,7,4′-trimethoxyflavone, are proved to be 8-bromo-5-hydroxy-7-methoxyflavone (VI) and 8-bromo-5-hydroxy-7,4′-dimethoxyflavone (VIa), respectively, showing that the 5-methoxy group is easily demethylated during the elimination of hydrogen bromide of the corresponding tribromochalcones (V and Va).

In a previous paper[4] from this laboratory, the synthesis of 8-iodo-5,7,4′-trimethoxyflavone and related compounds was described. Iodination of phloracetophenone dimethyl ether and 2′-hydroxy-4,4′,6′-trimethoxychalcone *ortho* to the hydroxyl group was accomplished with iodic acid and iodine.

The preparation of 8-bromo compounds by similar nuclear halogenation has been accomplished and is reported in this paper. The melting points of these compounds (III, 253° and IIIa 236°) are markedly different from those reported by previous investigators[3] (242° and 250°) formed by the dehydrobromination of the so-called 5′-(actually 3′)-bromochalcones (V and Va).[5]



In the present synthetic study, it has now been found that the yellowish products, obtained by the elimination of hydrogen bromide of 3-bromo-2-hydroxy-4,6-dimethoxyphenyl α,β-dibromo-β-phenyl ethyl ketone (V) and the analogues (Va and Vb), give an intense color with ferric chloride, and are insoluble in cold dilute alkaline solution, showing the presence of a free hydroxy group at position 5. By acetylation of the above yellowish products (VI, VIa, and VIb), colorless monoacetates are formed and the methylated colorless compounds are identical with the compounds III, IIIa, and IIIb, respectively. It is clear that the demethylation at position 5 occurs easily during the dehydrobromination of the corresponding tribromochalcones (V, Va, and Vb).

EXPERIMENTAL[6]

3-Bromo-2-hydroxy-4,6-dimethoxyacetophenone (I). To a stirred solution of phloroacetophenone dimethyl ether (1.6 g., m.p. 82–83°) in glacial acetic acid (30 ml.) was added dropwise a solution of bromine (1.36 g.) in glacial acetic acid (20 ml.) at room temperature. A yellow precipitate separated rapidly. On dilution with water, further precipitate was isolated. The product was recrystallized from alcohol; yield 0.96 g. of yellow needles, m.p. 186–187°.

Anal. Calcd. for $C_{10}H_{11}O_4Br$: C, 43.66; H, 4.03; Br, 29.04. Found: C, 43.54; H, 4.33; Br, 29.22.

3′-Bromo-2′-hydroxy-4′,6′-dimethoxychalcone (II). To a cooled mixture of 3-bromo-2-hydroxy-4,6-dimethoxyacetophenone (I., 0.8 g.) and benzaldehyde (0.6 g.) in alcohol (10 ml.) was added 60% potassium hydroxide (10 g.) dropwise with stirring. The reaction mixture was kept at 0° for 2 days

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(1) Presented in part before the IUPAC Symposium on the Chemistry of Natural Products, Melbourne, Australia, August, 1960: a preliminary report appeared in the "Abstracts of Papers" of the Annual Meeting of the Chinese Chemical Society, Taipei, December, 1960.

(2) To whom inquiries should be addressed.

(3) W. A. Hutchins and T. S. Wheeler, *J. Chem. Soc.*, 91 (1939), cf. Nadkarni and Wheeler, *J. Univ. Bombay*, **6**, ii, 107 (1937).

(4) A Preliminary Report: C. T. Chang, T. S. Chen, T. Ueng, S. T. Choong and F. C. Chen, *J. Formosan Sci.*, **14**, No. 1, 14 (1960).

(5) That the bromine is in the 3′ position has been proven by Donnelly. J. A. Donnelly, *Tetrahedron Letters*, No. **19**, 1 (1959).

(6) Capillary melting points were determined for all compounds and were uncorrected. We are indebted to Mr. T. Ueng for technical assistance in many of the preparations described.