Oxidation with Other Agents.—2,2'-Dichloroazobenzene (0.50 g.) was suspended in glacial acetic acid (10 ml.), chromic oxide (0.7 g.) dissolved in glacial acetic acid containing a few drops of water (5 ml.) added in portions with shaking, and the mixture warmed for 5 min. On cooling and dilution with water, unchanged 2,2'-dichloroazobenzene separated, 0.30 g., 60%, m.p. 137–138° (lit. m.p. 136°).[22]

2,2'-Dichloroazobenzene (0.30 g.) in glacial acetic acid (50 ml.) was treated with 100 ml. of nitric acid (50 ml. of water and 50 ml. of concentrated acid), and the mixture refluxed for 5.5 hr. On cooling, 2,2'-dichloroazobenzene was recovered in quantitative yield.

2,2',5,5'-Tetrachloroazobenzene (1.0 g.) was suspended in a solution of sodium dichromate (3.5 g.) in water (5 ml.)

and concentrated sulfuric acid (5 ml.) added. The mixture was shaken and cooled in water and finally heated on a steam bath for 2.5 hr. Extraction of the residue with benzene and evaporation of the extract gave recovered 2,2',5,5'-tetrachloroazobenzene, 0.6 g., 60%, m.p. 188–189° (lit. m.p. 189°).[24]

Spectra.—Infrared absorption spectra were determined in Nujol on a Perkin–Elmer Model 137 Infracord spectrophotometer and the ultraviolet spectra were recorded on a Beckman Model DK-2 ratio recording spectrophotometer using absolute ethanol as solvent.

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The Pyrolysis of Alkyl Hydrogen Phthalates and Related Esters[2]

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The pyrolysis of alkyl hydrogen phthalates to alcohols and phthalic anhydride proceeds with retention of configuration. Primary alkyl and cycloalkyl groups are eliminated almost exclusively as alcohols, in contrast to secondary alkyl groups, which form olefin–alcohol mixtures. Alkyl hydrogen maleates and tetrachlorophthalates react similarly to form alcohols and anhydrides. The pyrolyses of dicyclohexyl phthalate and dibutyl phthalate give approximately equal mixtures of olefin and alcohol, consistent with a mechanism involving initial normal ester pyrolysis of dialkyl phthalate to olefin and alkyl hydrogen phthate, followed by displacement of alcohol by internal attack of the carboxyl group. Dibutyl maleate reacts more slowly to a mixture of alcohol and olefin.

In a previous paper[4] the pyrolysis of sec-alkyl hydrogen phthalates to olefins was reported. An appreciable amount of 4-heptanol was formed during the pyrolysis of 4-heptyl hydrogen phthalate. This investigation was initiated in order to survey the scope of the abnormal elimination reaction, both with respect to the nature of the alkyl group and the type of dicarboxylic acid employed, and to elucidate the mechanism of the reaction.

Methyl alkyl phthalates undergo pyrolytic decomposition to the appropriate alkene, methanol, and phthalic anhydride.[5] It appears certain that an intermediate stage in this reaction is the formation of methyl hydrogen phthalate and an alkene, followed by decomposition of the acid ester to methanol and phthalic anhydride. Otherwise higher alcohols would have been formed. Furthermore, dimethyl phthalate does not decompose under identical conditions, indicating that formation of methanol takes place from methyl hydrogen phthalate.

Dialkyl phthalates and maleates react similarly to the methyl alkyl phthalates, producing one mole of alcohol and one mole of olefin. The distillate from dicyclohexyl phthalate at atmospheric pressure consisted of 42% cyclohexanol and 56% cyclohexene. A predominance of cyclohexene, as a result of dehydration of cyclohexanol is to be expected. In a larger scale experiment, with longer contact time of acid (alkyl hydrogen phthalate) and pyrolytically formed alcohol, the extent of dehydration was greater, with a 28:72 ratio being observed. Similar distillation of dibutyl phthalate gives 63% of the theoretical yield of butanol, 54% of butene, or a 54:46 ratio. Dibutyl maleate decomposition proceeded relatively slowly, but led to a 56:44 ratio of butanol–butene.

Two mechanisms are likely for the pyrolysis of alkyl hydrogen phthalates. In the first, (mechanism I) proton transfer or hydrogen bonding leads to an intermediate species which decomposes by nucleophilic displacement at the carbonyl carbon to phthalic anhydride and an alcohol, or by carboxylate attack on the beta hydrogen to phthalic acid and olefin. In the light of Bender's work[6] on enhancement of hydrolysis rate with intra-

(1) To whom correspondence should be addressed.
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molecular catalysis in methyl hydrogen phthalate, this mechanism would account for the relatively low temperatures required. A second pathway (mechanism II) for the reaction is possible, but less likely, analogous to the carbonium ion mechanism proposed for dehydrations. To distinguish between these mechanisms, a study of the stereochemistry of the reaction was carried out.
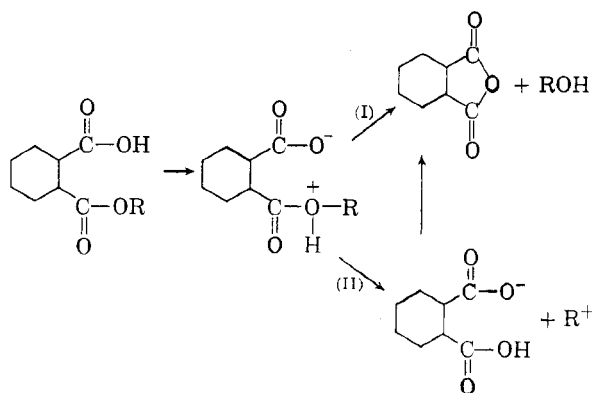
cis- and *trans*-2-methylcyclohexyl hydrogen phthalates were prepared from the corresponding alcohols, purified by recrystallization to constant melting point, and pyrolyzed. From the *cis* ester, no olefin, an 86% yield of 2-methylcyclohexanol of undetermined stereochemistry, and a quantitative yield of phthalic anhydride were obtained. The *trans* ester gave an 8% yield of olefins, 72% of apparently pure *trans*-2-methylcyclohexanol, n^{20}D 1.4620, b.p. 163°, compared to n^{20}D 1.4620, b.p. 165–165.2° for the original alcohol and n^{20}D 1.4620, b.p. 160–165° for a sample prepared by hydrolysis of the same ester. As confirmation, a sample of (—)-2-octanol, $[\alpha]^{25}$D —8.8°, was esterified with phthalic anhydride in pyridine, recrystallized, then pyrolyzed, giving (—)-2-octanol with identical rotation. The pyrolysis thus proceeds with complete retention of configuration.

Mechanism II is therefore most unlikely, since partial or total racemization is almost always found in cases of reaction by way of a carbonium ion. The first mechanism with internal acid catalysis is left as the more satisfactory of the two. In view of the stereospecificity of this reaction, it should occationally prove useful in the resolution of alcohols containing a second functional group prone to hydrolysis.

The *sec*-alkyl hydrogen phthalates gave yields of 9–41% of olefins. In contrast, the yields of olefins from primary alkyl hydrogen phthalates ranged from 0% with the methyl and butyl esters (as determined by nonreactivity of distillates with bromine) to 9% from *n*-heptyl hydrogen phthalate (determined by gas chromatography). The yield of alcohol was 86 to 92%.

Cycloalkyl hydrogen phthalates behave more like primary than secondary aliphatic esters. Thus cyclohexyl hydrogen phthalate gave only

0.4% of cyclohexene, the *cis*-2-methyl cyclohexyl ester gave none, and the *trans*, 8%. The greater constraint in the cyclic system apparently makes attack on the beta hydrogen unlikely relative to the displacement reaction.

Ethyl hydrogen tetrachlorophthalate formed ethanol as the primary product (72% yield). Some ethylene was also detected. A sample of butyl hydrogen maleate gave a 75% yield of butanol, 7% of dibutyl maleate, and some butene, but ethyl hydrogen adipate distilled with negligible (less than 2%) decomposition at 190°. A small amount of diethyl adipate was detected gas chromatographically in the distillate.

It is interesting to note that the distillation of monoethyl succinate and monoethyl sebacate leads to diethyl esters and the acid or anhydride, presumably in a bimolecular reaction, while monoalkyl maleates, phthalates, dichlorophthalates,[7] and tetrachlorophthalates, all of which contain a rigid *cis* dicarboxylate structure, form alcohol and anhydride, apparently unimolecularly. Benzhydryl succinate, relatively intermediate in flexibility forms benzhydrol and succinic anhydride.

Experimental

Preparation of Alkyl Hydrogen Phthalates.—General experimental conditions are given in ref. 4. Details are given in Table I.

TABLE I
PREPARATION OF ALKYL HYDROGEN PHTHALATES

Alcohol	Reflux time, hr.	Yield of ester, %	M.p., °C.	Reported m.p., °C.
Methanol	20	44	74	82.5[a]
1-Heptanol	2[b]		Oil[c]	
4-Heptanol	6	74	56–58	60[d]
Cyclohexanol	24	21	95–97	99[e]
cis-2-Methyl-cyclohexanol	24	50	104–106	102–104[f]
trans-2-Methyl-cyclohexanol	72	20	123.5–124.5	123–124[f]
(—)-2-Octanol	1[b]	60	71–74[g]	75[h]

[a] C. D. Hodgman, ed., "Tables for Identification of Organic Compounds," Chemical Rubber Publishing Co., Cleveland, Ohio, 1960, p. 28. [b] Pyridine solvent. [c] Neut. equiv., 263. [d] M. Tuot, *Compt. rend.*, **202**, 1339 (1936). [e] M. Brunel, *Bull. soc. chim.*, [3], **33**, 274 (1905). [f] A. Skita and W. Faust, *Ber.*, **64**, 2878 (1931). [g] $[\alpha]^{25}$D 44° in absolute ethanol, J. Kenyon, *Org. Syn.*, **1**, 418 (1920). [h] (+)-2-Octyl hydrogen phthalate, $[\alpha]^{25}$D 40.3° in 95% ethanol.

Preparation of Butyl Hydrogen Maleate.—A mixture of 91 g. of maleic anhydride and 81 g. of butanol was refluxed for 16 hr., then dissolved in ether, and extracted with 1 N sodium hydroxide. Upon acidification, a semisolid sirup separated (neut. equiv. 90). The mixture was dissolved in sodium bicarbonate, washed with ether, then acidified, giving material of neut. equiv. 129. A portion was then partially dissolved in benzene. Evaporation to dryness

(7) For a review with references, see C. D. Hurd, "The Pyrolysis of Carbon Compounds," The Chemical Catalog Co., Inc.. New York, N. Y., 1929, pp. 553, 554.

TABLE II

PYROLYSIS OF ESTERS

Ester[a]	Sample size, g.	Procedure used	Yield (%) olefins	Yield (%) alcohol
Me HP	23.7	A	0[b]	92[c]
n-Bu HP	56	A	0[b]	86[c]
n-Bu HP	0.5	B	0[d]	100[d]
n-Heptyl HP[e]	6.0	A	9[d]	91[d]
4-Heptyl HP	38.5	A	13[c]	72
cis-2MC HP	8.5	A	0[d]	86[c,f]
trans-2MC HP	16.0	A	8[c]	72[c]
trans-2MC HP	0.5	C	0[d]	100[d,g]
C HP	6.0	A	0.4[d]	99.6[d] (25[c])
(−)-2-Octyl HP	16.0	A	9	67[h]
Bu₂P	101.7	A	54[c]	63[c]
C₂P	12.6	A	56[d]	44[d]
C₂P	100.5	A	72[d]	28[d]
EtHT	6.7	A	28 max[i]	72[c,j]
EtHA	21.9	A	0[b]	Trace[d,k]
BuHM	28	A	9 max[i]	39[d,l,m]
Bu₂M	50	A[m]	10[c]	13[c]

[a] A = adipate, M = maleate, P = phthalate, T = tetrachlorophthalate, C = cyclohexyl, MC = 2-methylcyclohexyl. [b] Bromine solution unaffected. [c] Weighed product. [d] Relative amounts based on gas chromatography. [e] 4% of two other peaks, probably isomeric heptene and heptyl alcohol. [f] 4.5 g. phthalic anhydride in residue. [g] trans-2-Methylcyclohexanol (no cis). [h] n^{20}D 1.4263, [α]^{20}D −8.8°, identical with original alcohol. [i] Bromine decolorized. [j] 17% of condensed distillate and the pot residue (m.p. 250–253° after recrystallization) is tetrachlorophthalic anhydride.[10] [k] Neut. equiv. 176 (theoretical for EtHA 174). Small volatile fraction of distillate is 5% ethanol, 70% probably Et₂A, 24 and 1% unknowns by gas chromatography. [l] 52% unknown, probably benzene and 9% Bu₂M in condensate distillate. Pot residue is maleic anhydride. [m] Held at reflux 8 hr.

gave a sirup of neut. equiv. 137. This was used for the pyrolysis when further attempts at purification in the same manner proved fruitless. The material reacted with concentrated ammonia. Evaporation to dryness gave ammonium maleamate (20.6% nitrogen, calcd. for C₄H₈O₃N₂, 21.2%).[8]

Pyrolysis of Esters.—Three general procedures for the thermal decomposition of esters were used. A. Distillation at atmospheric pressure (see ref. 4). B. A sample was placed in a side-arm test tube, the mouth of the tube closed with a rubber stopper containing a stopcock, and the side arm with a rubber stopper only partially bored. The tube was evacuated, then the needle of a 5-ml. hypodermic syringe was inserted through the stopper into the side arm. The tube was heated until the syringe filled, and the sample was immediately injected into a gas chromatograph. C. Heating a sealed tube containing the sample.[9]

Details are given in Table II.

Gas Chromatographic Analysis of Products.—Most of the analyses were performed using a Beckman GC-2 gas chromatograph with an 8-ft. benzyl ether on firebrick column at 160°. Peak areas were determined with a planimeter, by counting squares, or by half-width and peak height measurements. Product identification was by comparison of retention time on any given day with known samples. In general, quantitative accuracy is limited chiefly by lack of proportionality of peak area with weight for dissimilar compounds, but for olefin–alcohol mixtures, the resulting error is less than 5%. A column of 6 ft. of benzyl ether and 6 ft of nitrophenyl ether was used for the analysis of methylcyclohexenes.

(8) We wish to thank Dr. Price Truitt, Denton, Texas, for this analysis.

(9) A sample of butyl hydrogen phthalate exploded on one occasion. Caution is suggested.

(10) Reported melting point of tetrachlorophthalic anhydride 256°; ref. a (Table I) p. 147.

Steroids. CCXIV.[1] 2α-Hydroxymethylandrostane Derivatives

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Hydrogenation of 2-hydroxymethylene-3-ketoandrostanes and their methyl ethers afforded the corresponding 2α-hydroxymethyl and 2α-methoxymethyl derivatives, respectively. Reduction of 2-hydroxymethylene-3-keto-androstanes with lithium aluminum hydride also yielded the corresponding 2α-hydroxymethyl-3-keto steroids as the major products accompanied by the 2-methylene-3β-ol and 2α-hydroxymethyl-3β-ol derivatives. Several of the compounds described were found to possess a high degree of pituitary depression activity.

Condensation of ketones with ethyl formate, followed by catalytic hydrogenation of the resulting α-hydromethylene ketones in methanol over a palladium–charcoal catalyst has been found to be a convenient method for the introduction of an α-methyl substituent into a ketone,[2–4] and one that has been used frequently in these laboratories. However, no example of the hydrogenation of a hydroxymethylene ketone, unattended by hydro-

genolysis of the hydroxyl function, appears to have been recorded in the literature

We have observed that catalytic hydrogenation of 2-hydroxymethylene-3-keto-androstanes in aqueous methanol or tetrahydrofuran over a 5% palladium–charcoal catalyst affords 2α-methyl-3-keto derivatives and, in addition, the previously undescribed 2α-hydroxymethyl-3-keto derivatives. The 2α (equatorial) assignment for the latter de-
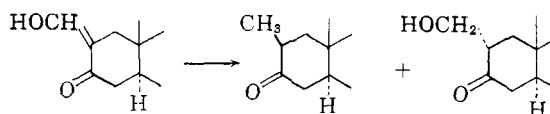
(1) Steroids. CCXIII. A. D. Cross, H. Carpio, and H. J. Ringold, in press.

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(3) H. J. Ringold, E. Batres, A. Halpern, and E. Necoechea, *ibid.*, **81**, 427 (1959).

(4) L. H. Knox, R. Villotti, F. A. Kincl, and H. J. Ringold, *J. Org. Chem.*, **26**, 501 (1961).

Figure 1