[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Precision Combustion of Natural Products

BY L. F. FIESER AND R. P. JACOBSEN[1]

Baxter and Hale[2] have recently developed a technique for carrying out the combustion of organic compounds with a degree of precision comparable with that attained in other atomic weight work at the Coolidge laboratory. Both in the concordance of the individual determinations and in the agreement of the carbon and hydrogen percentages with the theoretical values (better than 0.01%), their results for the higher aromatic hydrocarbons investigated are far more accurate than those ordinarily obtainable by the most refined methods of macro-, semimicro- or microanalysis generally employed for the determination of the empirical formulas of organic compounds. Although the latter methods are sufficiently reliable and accurate for most purposes,[3] they occasionally have led to uncertain or definitely erroneous conclusions even in the case of relatively simple compounds. Thus the formula $C_{17}H_{14}$ was for a time under consideration[4] for the Diels hydrocarbon ($C_{18}H_{16}$) while fluoranthene ($C_{16}H_{10}$[5]) was long regarded as $C_{15}H_{10}$, and both problems were solved not by analysis but by synthesis. In the recent investigations of natural products of the phenanthrene group it has become abundantly clear that ordinary carbon–hydrogen determinations are not sufficiently precise to distinguish between homologs of molecular weights of the order of 350–450, where the differences in the composition of alternate formulas amount to no more than 0.06–0.5% carbon and 0.09–0.2% hydrogen. Formulas of sterols, bile acids, sex hormones, cardiac glycosides and aglycones, toad poisons and sapogenins have been subject to much uncertainty and to changing views, and in very few cases has a definite decision been reached by the combustion of the compounds themselves. Degradation studies have settled some of the problems (scillaridin A,[6] tigogenin[7] and the x-ray and crystallographic method sometimes furnishes a value for the molecular weight which is sufficiently precise to be of significance (bufagin[8]). Also of service is the determination of the neutralization equivalent of an acid degradation product,[9] or the saponification equivalent of the acetate[10] or benzoate, or of a series of homologous esters,[11] and by using sufficiently large samples (0.5–1 g.) it is possible by these methods to determine the molecular weight with an accuracy of 2–3 units.[9b,10b] Another useful expedient consists in the analysis of halogen derivatives (*e. g.*, cholesteryl acetate dibromide,[12] a sterol bromoacetate,[10c] the *p*-iodobenzoate[11]), dinitrobenzoyl derivatives[10c] or other compounds having higher percentages of oxygen, halogen, or nitrogen than the parent substances, for this gives a greater spread in the carbon values for alternate formulas differing by CH_2 (0.4–0.6% C), although the hydrogen percentages are but little affected.

Since these methods, however valuable, are all subject to some limitations with regard to generality of application, accuracy, reliability and simplicity, and since there are many problems which still await unambiguous solution, a preliminary investigation has been undertaken to determine if direct analysis by the precision method of Baxter and Hale can be used to advantage in establishing the formulas of natural products of complicated structure and high molecular weight. With the coöperation and advice of Professor G. P. Baxter, a combustion apparatus was constructed closely patterned after the original one but on a somewhat smaller scale, for it seemed likely that the size of the sample could be reduced to about 1 g. without serious sacrifice of accuracy. The filling of the quartz combustion tube[13] was modified somewhat in accordance with

(1) Du Pont Research Fellow.

(2) Baxter and Hale, THIS JOURNAL, **58**, 510 (1936).

(3) Particularly in the hands of an unusually gifted experimentalist, such as the late Dr. Samuel C. Hooker; see the analyses in the second of his posthumous papers (in press).

(4) Ruzicka and Thomann, *Helv. Chim. Acta*, **16**, 216 (1933); Cook and Hewett, *J. Chem. Soc.*, 1098 (1933).

(5) Von Braun and Anton, *Ber.*, **62**, 145 (1929).

(6) Stoll, Hofmann and Helfenstein, *Helv. Chim. Acta*, **18**, 644 (1935).

(7) Tschesche and Hagedorn, *Ber.*, **68**, 1412 (1935).

(8) Crowfoot, *Chemistry and Industry*, **54**, 568 (1935).

(9) (a) Windaus and Brunken, *Z. physiol. Chem.*, **140**, 48 (1924); (b) Stoll, Hofmann and Peyer, *Helv. Chim. Acta*, **18**, 1247 (1935).

(10) (a) Vesterberg, *Ark. Kemi, Minerol. Geol.*, **9**, No. 27, 1 (1926); (b) Sandqvist and Gorton, *Ber.*, **63**, 1935 (1930); **64**, 2167 (1931); (c) Windaus, v. Werder and Gschaider, *ibid.*, **65**, 1006 (1932).

(11) Drake and Jacobsen, THIS JOURNAL, **57**, 1570 (1935).

(12) Reinitzer, *Monatsh.*, **9**, 421 (1888).

(13) The tube (Fig. 1, Ref. 2), 19 mm. inside diameter, was 95 cm. in length to the bend and carried a No. 11 joint at this end. At the straight end it carried a male rather than a female joint (No. 25), which was found to be an improvement.

observations made by Mr. A. H. Hale in orienting experiments kindly carried out with the larger apparatus. In burning polynuclear aromatic hydrocarbons only a short layer (6 cm.) of copper oxide is required, for the substance largely volatilizes and burns at a steady rate, but in the case of sterol derivatives the sample first becomes carbonized and it was found difficult to control the combustion of the residue to such a rate that the oxygen supply would not be temporarily exhausted. Consequently a 13.5-cm. perforated platinum basket (5, Fig. 1[2]) filled with copper oxide was used in the new apparatus, and this eliminated the difficulty. The absorption tubes were reduced in size[14] and modified somewhat in construction.

Wherever possible the sample for analysis was melted under nitrogen in order to eliminate traces of solvent, and in all cases before the final weighing the sample was left for several hours in a system evacuated to a pressure less than 10^{-4} mm, and containing phosphorus pentoxide. The combustions were conducted essentially as described by Baxter and Hale[2] with such modifications as were required in individual cases. The combustion proper took about eight to nine hours, and ordinarily one analysis could be completed every other day. The weighings were made and the corrections applied as indicated.[2] Where the density of the sample was not known, an approximate value sufficiently accurate for the computation of the vacuum correction was determined by the air-displacement method of Baxter and Hilton,[15] for the entire sample is in this way conserved. In making the calculations the atomic weights 1.0078 and 12.01 were employed for hydrogen and carbon, respectively. Practice analyses (Nos. 5 and 6) of benzoic acid which had been recrystallized from water gave the following results: C, 68.859, 68.825; H, 4.940, 4.950 (calcd.: C, 68.844; H, 4.952).

The analyses given below were carried out both to test the new apparatus and to determine if substances isolated from biological material can be purified to such an extent that the results of precision combustions are of significance in drawing fine distinctions between alternate formulas. Close agreement of both the carbon and hydrogen values with those calculated for a reasonable formula affords a satisfactory criterion of purity. Thus Baxter and Hale evidently succeeded in obtaining highly pure samples of anthracene, chrysene and triphenylbenzene, but their best pyrene apparently contained elements other than carbon and hydrogen (deficiency, 0.076% carbon).

Triphenylbenzene.—A combustion was made on a sample purified by Baxter and Hale more extensively than in the work already reported.[2] Their as yet unpublished analyses, which gave the percentages recorded below with their kind permission, were obtained with 3–6 g. samples. Somewhat less than 1.4 g. of the identical material was used in our analysis (see table at the end of the paper for the data).

	C = 12.01		C = 12.00	
	C	H	C	H
Calcd. for $C_{24}H_{18}$:	94.079	5.921	94.074	5.926
Hale, analysis 60	94.081	5.920	94.024	5.920
analysis 61	94.078	5.921	94.021	5.921
Jacobsen, analysis 19	94.074	5.918	94.017	5.918

Dihydrocholesterol.—It was thought that cholesterol would afford a good test case because at least two of the formulas which in the past have been regarded as established for the compound are so close in percentage composition as to be indistinguishable by ordinary methods of direct analysis.

		% C	% H
Berthelot (1856)	$C_{26}H_{44}O$	83.81	11.90
Reinitzer (1888)	$C_{27}H_{46}O$	83.87	11.99
Windaus (1903–1906), Mauthner (1909)	$C_{27}H_{44}O$	84.31	11.53

Reinitzer's formula has since been firmly established by a great body of degradative work as well as by acetyl determinations.[10c] Cholesterol from various organs is accompanied by 1–2% of dihydrocholesterol,[16] and although this can be removed by suitable purification, there is no convenient method of testing for the presence of traces of the material. Consequently it was decided to convert the sterol entirely into the dihydro compound and to submit this to analysis. Commercial cholesterol was crystallized once from alcohol and purified through the dibromide. The sterol regenerated by the sodium iodide method[17] was purified a second time through the dibromide, crystallized and hydrogenated in acetic acid solution using Adams catalyst (very rapid absorption). The product appeared to be free from any appreciable amount of cholesterol, but it was nevertheless put through the process of Anderson and Nabenhauer[18] for the removal of this impurity. After final crystallization the dihydrocholesterol, m. p. 141.8–142.5° corr. (anhydrous), developed a very faint color in the Liebermann–Burchard test only after about fifteen minutes. This material was used for analyses 7 and 12. Another sample had been prepared previously by Dr. W. F. Bruce by the same procedure, except that the cholesterol was not purified through the dibromide, and this was

(14) Over-all height of B and C, about 18 cm. The phosphorus pentoxide U-tube of B was 17 mm. o. d. The ascarite container of C was 20 mm. o. d., but this was found to be unnecessarily small.

(15) Baxter and Hilton, THIS JOURNAL, **45**, 694 (1923).

(16) Schoenheimer and co-workers, *Z. physiol. Chem.*, **192**, 73, 93 (1930).

(17) Schoenheimer, *ibid.*, **192**, 86 (1930); *J. Biol. Chem.*, **71**, 407 (1927).

(18) Anderson and Nabenhauer, THIS JOURNAL, **46**, 1957 (1924).

burned by Mr. Hale in the large apparatus. The results were as follows:

	C	H
Calcd. for $C_{26}H_{46}O$:	83.356	12.375
$C_{27}H_{48}O$:	83.436	12.447
Hale, analysis A	83.427	12.446
Jacobsen, analysis 7	83.439	12.433
Jacobsen, analysis 12	83.399	12.437
Av.	83.422	12.439

Although the difference in the carbon content of the alternate formulas amounts to only 0.08%, the average value found is so much closer to that required for the C_{27}-formula (−0.014) than to the other (0.066) that a clear distinction is possible on the basis of the carbon percentage alone. To be sure one of the values found for carbon (No. 12) is midway between the two theoretical figures, indicating that one or two analyses may not be sufficient where such a fine distinction is to be made. The hydrogen percentages appear to be somewhat more reliable, for they all agree with that for the C_{27}-formula within about 0.01%, while the average value is 0.064% higher than the percentage for the alternate formula. It is evident that the samples were reasonably pure and that it is possible from a limited number of precision analyses to determine the empirical formula of a sterol even in a very unfavorable case.

Dehydrodesoxycholic Acid.—Some doubt as to the empirical formulas generally accepted for the bile acids on the basis of analysis and degradation was expressed only recently by Stoll[6] (1935) who, however, promptly presented results of titration experiments[9b] which clearly supported the C_{24}-formulas rather than those having one more carbon atom. The analysis of a typical compound of the group was undertaken not in order to reinvestigate a problem which is already definitely settled, but to test further the possibility of achieving a sufficient purification in the case of a substance occurring in admixture with several related compounds and of a type not easily freed from contaminants and solvents. Desoxycholic acid was selected because it can be effectively separated from other bile acids through its distinctive molecular compounds, but since it is so difficultly recovered from the coördinate complexes the substance was converted into the corresponding diketo acid for purposes of analysis. The purification was carried out by Dr. M. S. Newman as follows. Commercial desoxycholic acid was first purified through the ether- and alcohol-choleic acids according to Sobotka and Goldberg[19] and then crystallized three times each as the xylene- and as the acetic acid–choleic acid. The product was oxidized with chromic anhydride in the usual manner and the dehydrodesoxycholic acid was crystallized four times from alcohol; m. p. 185.5–187.5°, corr. The sample was dried in high vacuum before being weighed, but it was not melted. The analysis was made by Mr. Hale. The results agree well with the accepted formula and indicate that a high state of purity was attained.

	C	H
Calcd. for $C_{24}H_{36}O_4$:	74.189	9.338
$C_{25}H_{38}O_4$:	74.588	9.514
Hale, analysis B	74.162	9.352

(19) Sobotka and Goldberg, *Biochem. J.*, **26**, 563 (1932).

Chlorogenin.—This sapogenin was isolated from *chlorogalum pomeridianum* by Liang and Noller,[20] who made a thorough characterization of the substance by all of the standard analytical methods in the attempt to establish the empirical formula. They reported in all nineteen analyses (C–H, Br) of the sapogenin or its derivatives, as well as Zerewitinoff determinations, several values for the molecular weight found by different methods, and saponification equivalents of the dibenzoate. Liang and Noller commented on the difficulty often encountered in obtaining satisfactory combustion data for sapogenins and stated that six macrocombustions gave a value for carbon about 1.5% below that indicated by the results obtained by a commercial microanalyst and by a microanalyst accustomed to the combustion of sapogenins. The latter results (calculated for C = 12.00) hardly distinguish between the formulas $C_{26}H_{42}O_4$ (C, 74.58; H, 10.12) and $C_{27}H_{44}O_4$ (C, 74.94; H, 10.26), Dr. A. Schoeller obtaining the values C, 75.03, 75.23; H, 9.95, 9.97; while Dr. M. Furter found C, 74.53, 74.87; H, 10.24, 10.14. The results are typical of those generally obtained by these and other expert microanalysts,[21] and it may be said that it is possible to obtain quite closely agreeing results by following a certain standard procedure but that different procedures may give rather divergent results. It is also evident that the deviations in the analyses are of the same order of magnitude as the differences in the alternate formulas.

Leaning particularly on the results of the saponification studies, since the maximum deviation in seven determinations amounted to only 8 units in the molecular weight, Liang and Noller were led to conclude that chlorogenin has the C_{26}-formula.

Professor Noller very kindly supplied a sample of the material for precision analysis, and his description is as follows: "After reaching a constant melting point by our usual purification process, this material was extracted with boiling distilled water, crystallized three times from pure dioxane and then twice from pure methyl alcohol. Every effort was made to remove and keep out fibers and dust particles. This sample in a capillary tube begins to shrink at 272° and melts at 275–277°, corr." It seemed inadvisable to drive off adhering solvent by melting the substance because of the danger of decomposition, but fortunately the sample was in the form of microcrystals and it was dried by heating at 150° in nitrogen for thirty minutes and then left overnight in the high vacuum system. The approximate density determined with a 4-g. sample was 1.18. The results were as follows.

	C	H
Calcd. for $C_{27}H_{44}O_4$:	74.956	10.250
Analysis No. 13	74.961	10.250
No. 14	74.987	10.254

The analyses leave little doubt that the C_{27}-formula is correct, and it is interesting to note that the agreement of both the carbon and hydrogen values with the theoretical percentages indicates clearly that Liang and Noller succeeded in obtaining chlorogenin of the highest purity and, in particular, in freeing it from traces of the companion substance tigogenin ($C_{27}H_{44}O_3$).

(20) Liang and Noller, THIS JOURNAL, **57**, 525 (1935).

(21) See the analyses of bufotalin and bufotalone by Professor J. Lindner, *Ann.*, **517**, 28 (1935).

Sarsasapogenin.—The sapogenins of the type now known to be related to the sterols were for many years believed to be C_{26}-compounds but in 1935 Simpson and Jacobs,[22] working with sarsasapogenin, came to the conclusion that the preponderance of evidence from a large number of analyses of the sapogenin and its derivatives favored the revision of the hitherto accepted formula $C_{26}H_{42}O_3$ of Power and Salway[23] to $C_{27}H_{44}O_3$. Shortly afterward Tschesche and Hagedorn[7] isolated aetio*allo*-bilianic acid (C_{19}) as a degradation product of tigogenin, and this fact, coupled with the correlation[24] of tigogenin with gitogenin and the isolation[25] of C_8-ketones as products of the cleavage of the side chain of this substance, affords good evidence that tigogenin contains twenty-seven carbon atoms. In the case of sarsasapogenin the isolation of the Diels hydrocarbon[25] (C_{18}) and of a methyl hexyl ketone[26] (C_8) as dehydrogenation products is consistent with either the C_{26}- or C_{27}-formula and the substance has not been correlated with tigogenin. Consequently it was a matter of interest to investigate the question by the present method.

Dr. W. A. Jacobs kindly supplied for the purpose a highly purified sample of sarsasapogenin, described as having been crystallized from acetone, m. p. 199–200°. The approximate density, determined as above, was 1.21. Samples which had been dried by melting in nitrogen and left in the high vacuum line gave the following results.

	C	H
Calcd. for $C_{26}H_{42}O_3$:	77.563	10.514
$C_{27}H_{44}O_3$:	77.835	10.644
Analysis No. 16	77.827	10.644
No. 18	77.822	10.641

The results leave no doubt as to the correctness of the C_{27}-formula of Simpson and Jacobs. A third analysis was made in which the sample was heated at 140° in a nitrogen atmosphere for thirty minutes and dried further in high vacuum at room temperature. The sapogenin was in the form of thick, heavy needles and the results of analysis indicate that some solvent probably was retained; found: C, 77.570; H, 10.643.

Fichtelite.—Summarizing the analyses of this fossil resin hydrocarbon by various workers (averages: 86.9, 13.1), Bamberger[27] in 1889 remarked: "To add to so many closely agreeing figures by new analyses seems purposeless. A decision can be expected only from molecular weight determinations and from degradation products." Results by the former method favored the formula $C_{18}H_{32}$, but did not settle the problem, and the substance has resisted most attempted degradations. Eventually Ruzicka[28] obtained retene ($C_{18}H_{18}$) as a product of dehydrogenation, and finally[29] he identified also methane. From the recent observation, Ruzicka has concluded that fichtelite is almost without doubt $C_{19}H_{34}$.

A small sample of the crude fichtelite remaining from Bamberger's original investigation was kindly placed at our disposal by the late Dr. Samuel C. Hooker. The material was distilled in vacuum and the colorless distillate taken up in purified ligroin and shaken with successive portions of concentrated sulfuric acid to remove traces of retene. After several crystallizations from alcohol the hydrocarbon was obtained as lustrous, flat needles, m. p. 44.6–45.7°, corr. The sample sufficed for but one analysis and this was made by Mr. Hale before the new apparatus had been constructed. Unfortunately the substance carbonized in the boat and the rapid combustion of the residue probably overtaxed the short layer of copper oxide, as the total deficiency in the percentages is beyond the limit of experimental error.

	C	H
Calcd. for $C_{18}H_{32}$:	87.018	12.981
$C_{19}H_{34}$:	86.945	13.056
Hale, analysis C	86.875	13.062

While the value found for carbon deviates from the C_{19}-theory by an amount comparable with the difference between the two theoretical figures, the value for hydrogen, which is certainly more reliable, agrees so well with that calculated for $C_{19}H_{34}$ that the result can be regarded as definitely supporting Ruzicka's formula.

ANALYTICAL DATA

Analysis	Sample, g.	CO_2, g.	H_2O, g.	Deviations from calcd. % C	% H
		Benzoic acid			
5	0.94968	2.39632	0.41931	+0.015	−0.012
6	0.93110	2.34829	0.41186	−0.019	−0.002
		Triphenylbenzene			
19	1.37886	4.75332	0.72933	−0.005	−0.003
		Dihydrocholesterol			
Hale, A	2.04122	6.24036	2.27099	−0.009	−0.001
7	0.90640	2.77139	1.00729	+0.003	−0.014
12	0.92558	2.82869	1.02894	−0.037	−0.010
		Dehydrodesoxycholic acid			
Hale, B	2.02094	5.49218	1.68933	−0.027	+0.014
		Chlorogenin			
13	0.99942	2.74533	0.91563	+0.005	0.000
14	0.88244	2.42483	0.80876	+0.031	+0.004
		Sarsasapogenin			
16	0.86195	2.45824	0.82002	−0.008	0.000
18	1.03485	2.95114	0.98427	−0.013	−0.003
		Fichtelite			
Hale, C	0.98579	3.13825	1.15094	(−0.070)	+0.006
			Average	±0.016	±0.006

Summary

It is shown that substances of high molecular weight and of both plant and animal origin can be obtained by the usual methods of purification in a condition satisfactory for precision analysis. The analytical results for the most part agree with

(22) Simpson and Jacobs, *J. Biol. Chem.*, **109**, 573 (1935).
(23) Power and Salway, *J. Chem. Soc.*, **105**, 201 (1914).
(24) Tschesche, *Ber.*, **68**, 1090 (1935).
(25) Jacobs and Simpson, *J. Biol. Chem.*, **108**, 501 (1934); THIS JOURNAL, **56**, 1424 (1934).
(26) Ruzicka and van Veen, *Z. physiol. Chem.*, **184**, 69 (1929).
(27) Bamberger and Strasser, *Ber.*, **22**, 3361 (1889).
(28) Ruzicka, Balas and Schinz, *Helv. Chim. Acta*, **6**, 692 (1923).
(29) Ruzicka and Waldmann, *ibid.*, **18**, 611 (1935).

the theoretical values within about 0.02% for carbon and 0.01% for hydrogen (see table), a degree of accuracy quite adequate for distinguishing between alternate formulas even in difficult cases.

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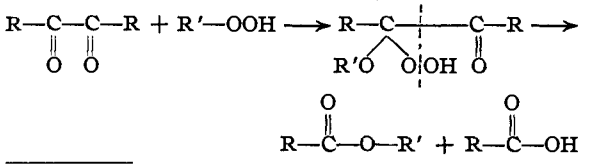
The Action of Ethylhydroperoxide on Alpha Diketones—Mechanism

BY R. P. BARNES AND ROSCOE E. LEWIS

In connection with our work on alpha diketones we have had many occasions to use the alkaline hydrogen peroxide cleavage reaction of Weitz and Scheffer.[1] This reagent which is a specific cleavage reagent for all alpha diketones seems particularly interesting in view of the fact that the most highly hindered alpha diketones cleave with ease when subjected to it.

Mesitylbenzylglyoxal[2] resists all reagents which involve a 1,2-addition to the carbonyl adjacent to the mesityl group, yet it is cleaved quantitatively by this reagent. Dimesityl diketone[3] resists all reagents which involve addition to carbonyl except strongly alkaline hydroxylamine, zinc in alcoholic potassium hydroxide, and alkaline hydrogen peroxide. The explantion of the fact that dimesityl diketone yields to these drastic treatments is that one of the twinned carbonyls activates the other and hence reduction is effected, presumably by way of 1,2-addition.

To test the mechanism of this cleavage reaction as proposed by Weitz and Scheffer,[1] which according to them involves a 1,4-addition of OH groups to the ends of the system of twinned carbonyls, the use of an unsymmetrical reagent occurred to the authors. If this reaction goes according to the mechanism proposed by its authors, either a symmetrical or an unsymmetrical reagent would yield two molecules of acid; if, on the other hand, it should go by way of a 1,2-addition to a carbonyl, it would yield one molecule of an acid and one molecule of an ester



(1) Weitz and Scheffer, *Ber.*, **54**, 2327 (1921).
(2) R. P. Barnes, THIS JOURNAL, **57**, 937 (1935).
(3) Kohler and Baltzly, *ibid.*, **54**, 4015 (1932).

Ethylhydroperoxide was made according to Baeyer and Villiger[4] and the following compounds were subjected to treatment with this reagent in alkaline solution with the indicated results.

	Substance	Cleavage products
I	$C_6H_5COCOC_6H_5$	Benzoic acid and ethyl benzoate
II	p-$CH_3OC_6H_4COCOC_6H_4OCH_3$-$p$	Anisic acid and ethyl anisoate
III	$C_6H_5COCOC_6H_4OCH_3$-p	Anisic and benzoic acids; ethyl benzoate and anisoate
IV	$C_6H_5CH_2COCOC_6H_5$	Benzoic and phenylacetic acids
V	$C_6H_5CH_2COCOC_6H_2(CH_3)_3$	Benzoic and trimethylbenzoic acids

(I) and (II) cleave cleanly and rapidly yielding the corresponding acid and ester; (III) cleaves less rapidly producing a mixture of benzoic and anisic acids and a mixture of ethyl benzoate and anisoate. The latter is explained by the fact that neither carbonyl is hindered and hence addition takes place to either carbonyl with the corresponding cleavage products. (IV) and (V) (in enolic modification) cleave still more slowly with the result that exposure of the esters to the hot alkaline solution effects complete hydrolysis.

Experimental Part

Treatment of the Alpha Diketone with Alkaline Ethylhydroperoxide.—In each case 1.0 g. of the alpha diketone was dissolved in methyl alcohol to which 20 cc. of approximately 15% ethylhydroperoxide was subsequently added. The solution was made slightly alkaline with 20% sodium hydroxide and warmed on the water-bath. When the color of the solution faded it was poured into 100 cc. of cold water to check further hydrolysis. The solution was extracted with ether. The alkaline solution was acidified with hydrochloric acid, yielding acid; the ethereal solution was evaporated and the residual ester refluxed for thirty minutes with hydrochloric acid, whereupon the ester was

(4) Baeyer and Villiger, *Ber.*, **34**, 738 (1901).