belief that, in some way or other, Bargellini and Melacini must have confused the two isomers, and that the literature should be corrected accordingly.

Summary

1. A series of phenylated alcohols and olefins, closely related structurally, has been prepared, including a number of new ones.

2. These alcohols and olefins have been subjected to the action of sulfuric acid (85 or 90%) and the conditions studied under which they are cyclized.

3. Evidence is presented that generally these alcohols pass first into one or more olefins, which then cyclize or polymerize, rather than the cycles being formed directly by condensation of the alcoholic OH with an ortho-H of the benzene nucleus.

4. The unsaturation in these phenylated olefins is of such a character that it can apparently occupy different locations in the side chain and still form the same cycle, although the yield varies accordingly. This shift in the location of the double bond is established by the structure of the cyclization products. Thus 1-methyltetralin is formed from 1-phenylpentanol when the OH group is in position 2, 3, 4 or 5.

5. Two alcohols have been found containing the Ph—C—C—C(C)—C—C—skeleton, each of which gives with sulfuric acid both a 5- and a 6-membered cycle.

6. Those cyclization reactions which lead to tetralins offer a convenient method for the preparation of naphthalene derivatives, for the tetralins are easily dehydrogenated by fusion with sulfur.

7. Evidence is submitted showing that the alpha- and beta-propylnaphthalenes, as recorded in the literature, have been confused.

NEW YORK, N. Y. RECEIVED OCTOBER 23, 1934

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

On the Mechanism of Reactions of Acetoacetic Ester, the Enolates and Structurally Related Compounds. I. C- and O-Alkylation

BY ARTHUR MICHAEL

According to Kekulé's[1] interpretation of intermolecular chemical change, molecules are attracted to one another by chemical affinity, forming at first a loosely-joined, double molecule. The coherence of the atoms in the approaching molecules becomes loosened, and this condition continues in the double molecule, until it separates into two, chemically different, molecules.[2]

Representing "the vibratory volumes"[3] of atoms by spheres, chemical union has been designated by their segmentation, increasing with the magnitude of the bound chemical energy holding atoms together, and polymolecular, chemical union by contact between the spheres.[4] Two atoms, A and B, of an organic molecule may enter into polymolecular union with two, directly joined atoms, X and Y, of a reagent with no or slight energetic hindrance, only when tetragon-, pentagon- and hexagon-shaped, polymolecular complexes may be formed. Projections of the polymolecular part of such graphic structures upon plane surfaces lead to the following representations of chemical and polymolecular union.[5]

Sodium acetoacetic ester consists of $CH_3C(ONa)=CHCOOEt$, with some $CH_3COCH=C(ONa)OEt$[6] and isomeric polymolecules of types

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(1) Kekulé, *Ann.*, **106**, 141 (1858); "Lehrb. org. Chem.," Vol. I, 1868, p. 142.

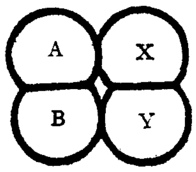
(2) These views received but little attention for many years. Armstrong [*J. Chem. Soc.*, **51**, 261 (1887)] supported them and Thiele [*Ann.*, **306**, 92 (1899)], without cognizance apparently, used partial valences in place of chemical affinity. This was criticized by Erlenmeyer, Jr. [*Ann.*, **316**, 49 (1901)], who applied Kekulé's views to explain the formation of cyclic compounds. Michael [*Ber.*, **34**, 4028 (1901); THIS JOURNAL, **32**, 991 (1910)], conceived the double or "polymolecule" as resulting from the affinities exerted between the free chemical energy of certain atoms in the respective molecules. He, therefore, concluded that they must have definite intermolecular, atomic structures and that isomeric polymolecules may be formed in accordance with the "principle of partition" [*J. prakt. Chem.*, **60**, 341, 431 (1899); *Ber.*, **39**, 2138 (1906)].

(3) Traube, "Raum der Atome," 1899, p. 70.

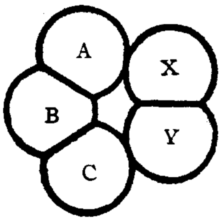
(4) Michael, THIS JOURNAL, **40**, 705 (1918). Polymolecular union in structural formulas will be indicated by asterisks between the respective atoms and unsaturation by periods over their symbols.

(5) When all four atoms A, B, C and D in III are unsaturated, addition may proceed at A and D, with appearance of double linkage between B and C, or at A + B and C + D according to I. Since ring-formation appears to be "a periodic function of the length of the chain" [Michael, *J. prakt. Chem.*, **49**, 28 (1894); **60**, 337 (1899)] polymolecular union may be relatively favored at the terminal atoms in certain longer chains in substances; but it is probable that this would occur with greater chemical hindrance than in the formation of penta- and hexacyclic polymolecules. These views may be applied to all chemical reactions and elucidate many now unexplained.

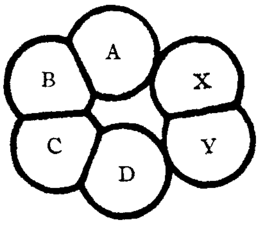
(6) Michael, *ibid.*, **37**, 488 (1888). The formation of acetylmalonic ester (less than 10%) in the chlorocarbonic ester reaction is experimental evidence of the existence of the second, car-



I



II



III

I and III may be formed primarily in the action of alkyl iodides. However, polymolecules of type I, in which alkyl is in contact with oxygen,[7] if formed, could not decompose chemically to yield O-alkyl derivatives under the experimental conditions. In all analogous reactions, the facility of O-alkylation decreases rapidly with neutralization of the positive energy of the metal;[8] the relatively weak, negative radical in sodium acetate prevents alkylation with alkyl halide under all conditions. It has been shown that sodium propylate, notwithstanding its highly energetic sodium, reacts slowly with the most reactive of alkyl iodides, and sodium lactic ester not at all,[9] under conditions that the sodium enolate ester reacts readily, although enol acetoacetic ester is decidedly more acidic than lactic ester. The replacement of the enolic hydrogen of enol acetoacetic ester by sodium greatly reduces the free negative chemical energy of the adjoined oxygen and also its affinity for alkyl. On the other hand, by largely neutralizing the influence of the two negative radicals of acetoacetic ester upon the α-carbon, that atom assumes the natural, strong affinity for alkyl, necessary for the formation of type III polymolecules, with subsequent decomposition and C-alkylation.[10] From this standpoint, O-alkylation is impossible; at a temperature at which it might begin, C-alkylation would take place instantaneously. From this standpoint, C-alkylation with all enolates depends upon the magnitude of the positive, chemical energy in the metal and the facility of the process falls off with the extent of its neutralization. With a weak positive metallic atom in the enolate, *e. g.*, silver, O-alkylation may take place with the same reagent and, with metallic atoms of intermediate polarity, mixtures of O- and C-alkyl derivatives may be formed.

Although the formation of O-ethyl acetoacetic ester from the sodium enolate is debarred energetically, it is of interest to determine whether its formation, or that of the isomeric C-alkyl derivative, would contribute more to the maximum degradation of energy. With formation of isomers, or stereomers, their heats of formation, much more than physical properties, are the major factors in determining the maximum energy degradation. As far as experimental data permit a generalization, the following "thermochemical law of structure"[11] is valid: that isomer, or stereomer, of aliphatic, or through the side chains of aromatic, compounds, has the larger heat of formation in which the positive radicals are most symmetrically grouped about a common, negative radical, or about the negative radicals in the compound. For example, the increase from primary to secondary and further to tertiary isomers; accordingly, the heats of formation of α-ethylacetoacetic, butyroacetic and β-ethoxycrotonic esters should fall off in the order named and the difference between the first two should be much less than between them and the latter. The thermochemical results with the C- and O-ethyl acetoacetic esters, given below, show that the formation of the C-ethyl derivative conduces to the possible maximum degradation of energy in the reaction between sodium enol acetoacetic ester and ethyl halide, since its heat of formation is de-

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bethoxy enolate in the reaction product, since carbethoxy enolates yield C-derivatives exclusively with all reagents (see following paper).

[7] Those in which X and Y are attached to the unsaturated α,β-carbons of the enolate are not considered owing to the far less favorable affinity relations than those that exist in type III.

[8] Literature reference in Michael and Ross, THIS JOURNAL, **53**, 2394 (1931); **54**, 387 (1932).

[9] Michael, *Ber.*, **38**, 3222 (1905).

[10] Recently, Hückel ["Grundl. der org. Chem.," Vol. I, 1931, p. 181] again advanced the old speculation [see *Am. Chem. J.*, **43**, 339 (1910)] that C-alkylation of sodium enol acetoacetic ester proceeds through a small proportion of very reactive C–Na derivative contained in the enolate. Accordingly, chlorocarbonic ester should not yield the O- but the C-derivative. Further, the C–Na form could not exist, or be formed, in the presence of alcohol, and the assumption that it would have much greater reactivity than the O–Na form toward iodide is only a surmise; *e. g.*, sodium carbide is inert toward alkyl iodide up to 180°. For further criticism, see Scheibler, *Ber.*, **65**, 997 (1932). Although the original explanation of C-alkylation [Michael, *J. prakt. Chem.*, **37**, 487 (1888)] was given up years ago [see *J. prakt. Chem.*, **60**, 316 (1899); *Ber.*, **38**, 22, 3217 (1905); THIS JOURNAL, **32**, 1003 (1910)] the writer is frequently quoted as still supporting it. Thus, Hückel (*ibid.*, 202) criticizes it from the quite irrelevant standpoint that the reactions of alkylene halides at a high temperature are comparable to those of alkyl halides. The old interpretation of Eltekov's alkylation of alkenes, given in 1888, is not improbable today. It is energetically impossible that it should proceed with the facility of sodium acetoacetic ester alkylation, as is implied by Hückel.

[11] Michael, *J. prakt. Chem.*, **68**, 499 (1903); **79**, 418 (1909); *Ber.*, **39**, 2142 (1906); THIS JOURNAL, **32**, 1004 (1910).

cidedly greater (about 8.5% greater than the O-isomer).

According to Claisen,[12] acetoacetic and orthoformic ester condense in the presence of certain substances, to form primarily β,β-diethoxybutyric ester, which boils *in vacuo* without decomposition, but, under ordinary pressure, loses alcohol to yield β-ethoxycrotonic ester.

We found that a small amount of acetyl chloride[13] does not catalyze the reaction and that with 0.5–1 mole of the chloride there is formed besides β-ethoxycrotonic ester, approximately an equal amount of a higher boiling compound which has not been obtained pure, but the presence of β,β-diethoxybutyric ester could not be detected. In the presence of a small amount of ferric chloride an equimolecular mixture of the esters reacted to give 92% of the theoretical yield of β-ethoxycrotonic ester and practically identical results were obtained in alcoholic solution. An alcoholic solution of the esters and a small amount of ammonium chloride, after 140 hours at room temperature, yielded some β,β-diethoxybutyric ester as indicated by the elimination of some alcohol from the higher boiling fraction on distillation at ordinary pressure. It seems possible, therefore, that ammonium chloride catalyzes the formation of the diethoxy ester and, also, the elimination of alcohol from it. To restrict the second reaction, the above mixture was kept at 0–10° for sixty hours but only unchanged esters were recovered.

Claisen[14] stated that he prepared the diethoxy ester without difficulty by treating an alcoholic solution of acetoacetic ester in the cold with formimido ether hydrochloride. We found that the vacuum-distilled product when redistilled at ordinary pressure lost an amount of alcohol, which indicated the presence of 25% of the diethoxy ester.

Blaise and Maire[15] showed that concentrated sulfuric acid gives β-ethoxycrotonic ester, but, although the reaction mixture was maintained at −15° and distilled at 5–10 mm., we obtained only alcohol, formic and β-ethoxycrotonic esters.

According to Meerwein,[16] ferric chloride catalyzes the elimination of alcohol from the β,β-diethoxy ester. To study the supposed catalytic action of metallic chlorides upon that ester, we attempted to prepare the compound by addition of alcohol to β-ethoxycrotonic ester with sodium ethoxide.[17] Although the β-ethoxy ester was treated with alcoholic sodium ethoxide under various conditions and various procedures were followed in isolating the products, yet in no experiment did the vacuum-distilled, higher boiling fraction lose alcohol on distillation at ordinary pressure to indicate the formation of more than 20% of the diethoxy ester. Although Claisen repeatedly stated he had prepared the substance, no physical properties, other than that it is an oil, and no analytical data were given. Its existence seems probable, but it is doubtful if the pure ester has been isolated.

Although Claisen never published any experimental evidence, he assumed that the formation of β-ethoxycrotonic ester proceeds primarily in the replacement of the keto-oxygen of acetoacetic ester by two of the ethoxy groups of orthoformic ester

$$\text{—CO—CH}_2\text{—} + (\text{EtO})_2\text{CH(OEt)} \longrightarrow \text{—C(OEt)}_2\text{—CH}_2\text{—} + \text{HCOOEt}$$

Curtiss[18] showed that β-ethoxycrotonic ester is formed by passing hydrogen chloride into alcoholic acetoacetic ester; evidently by addition of Et(OH),HCl to the keto-carbonyl group and subsequent elimination of alcohol and hydrogen chloride. Claisen, in his interpretation of the orthoformic ester reaction, overlooked that it is catalytic; in the polymolecule, HC(OEt)_3, catalyst, the chemical hindrance to the separation of an ethyl from the attached oxygen has been greatly reduced by the three negative radicals, so that, with the aid of the additional energy of the catalyst, the ester component of the polymolecule functions as an addendum to the ketocarbonyl

$$\text{CH}_3\text{COCH}_2\text{COOEt} + \text{HC(OEt)}_3\text{, catalyst} \longrightarrow$$
$$\text{CH}_3\text{C(OEt)[OCH(OEt)}_2\text{, catalyst]CH}_2\text{COOEt} \longrightarrow$$

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(12) Claisen, *Ber.*, **26**, 2731 (1893); *Ann.*, **281**, 311, footnote (1894); *Ber.*, **29**, 1006 (1896); *Ann.*, **291**, 43 footnote (1896); **297**, 3 (1897); *Ber.*, **40**, 3905 (1907).

(13) Apparently the chloride functions through the formation of hydrogen chloride, which is known to catalyze the reaction [see Claisen and Driessen, *ibid.*, **26**, 2731 (1893)].

(14) Claisen, *ibid.*, **31**, 1010 (1898).

(15) Blaise and Maire, *Ann. chim.*, [8] **15**, 567 (1908).

(16) Meerwein, Houben-Weyl, 2d ed., vol. III, p. 130. No details are given and no other references to this work could be found in the literature.

(17) Claisen, *Ber.*, **29**, 1006 (1896). Under catalytic influence, alcohol adds readily to Δ-α,β-dibasic esters [Michael and Bucher, *ibid.*, **28**, 2512 (1895); **29**, 1792 (1896)] to form ethoxy addition products. From *sym*-dibromosuccinic ester and alcoholic sodium ethoxide, through a series of additions and eliminations, *unsym*-diethoxysuccinic ester is formed as final product. Acetylene dicarboxylic ester under the same treatment gave ethoxyfumaric ester and finally the *unsym*-diethoxy ester. Later, Moureu [*Bull. soc. chim.*, [3] **31**, 493, 509 (1904)] extended the reaction to monobasic Δ-α,β-esters and with two phenyl propiolic esters obtained pure β,β-dialkoxy esters, but with aliphatic propiolic esters obtained mixtures of mono- and dialkoxy esters from which the latter were not isolated. The stability and even the course of decomposition of the β,β-diethoxy esters depends upon their structures.

(18) Curtiss, *Am. Chem. J.* **17**, 437 (1895).

$$CH_3C(OEt){=}CHCOOEt + [CH(OH)(OEt)_2] \longrightarrow HCOOEt + EtOH$$

With acetone, the course of the reaction is less equivocal; β,β-diethoxypropane is obtained almost quantitatively.[19] By replacing the negative carbethoxy group of β,β-diethoxybutyric ester by a hydrogen atom the chemical hindrance to the removal of an α-hydrogen atom from the formed acetone acetal is greatly increased. The addition product $CH_3C(OEt)[OCH(OEt)_2$, catalyst$]CH_3$ is therefore more stable toward elimination than the corresponding acetoacetic ester derivative and the reaction proceeds by substitution of $—CH(OEt)_2$, catalyst, through the alcohol present, by the more positive ethyl radical. The reaction with acetone can proceed only at the unsaturated carbonyl group; by catalytic addition of the polymolecule of orthoformic ester plus catalyst[20] and ethylation of the hydroxy group.

Experimental

By ARTHUR MICHAEL AND G. H. CARLSON

Preparation, Physical Properties and Heats of Combustion of α-Ethyl Acetoacetic and β-Ethoxycrotonic Esters.—These substances were prepared with every possible safeguard to ensure utmost purity.

α-Ethyl acetoacetic ester was obtained from sodium enol acetoacetic ester[21] and ethyl iodide. An ether solution of the crude product was repeatedly extracted with ammonia, fractionated and then converted into the potassium enolate, to eliminate the residual diethyl acetoacetic ester.[22] The effects of the chemical purification upon the physical constants are of interest:

	Purification	B. p., °C.	Mm.	Time after distn.	Temp., °C.	n	d_4^{16}
I	Extraction with ammonia	89	16	12 Hours	20.5	1.4185	
II	Extraction with ammonia	88.5–89	16	15 Hours	20.5	1.4185	
III	Through K derivative	(a) 87.5	15	Soon after	20.5	1.4180	
				Several days	21.0	1.4172	
		(b) 87.3	15	Soon after	20.5	1.4178	
				Several days	21.0	1.4172	
IV	(a) and (b) combined	89.3	17	15 Hours	20.5	1.4171	
				Several days	16.0	1.4189	0.9839
V	Through K derivative	89	17	Soon after	20.5	1.4192	
				Soon after	16.0	1.4210	.9847
VI	V distilled into soft glass bottle[a]			30 Hours	20.5	1.4168	
				Long after	20.5	1.4121	

[a] Pyrex glass vessels used in all other operations.

With the exception of recent observations by v. Auwers and Schmidt,[23] all previous data are not correct as they were made with preparations purified by fractionation only and, therefore, contained, besides acetoacetic ester, more or less of the diethyl derivative. The above n/D observations show the values slightly and slowly fall off on standing after distillation. The decrease on standing is more marked when the product is kept in a soft glass vessel; in VI the difference after thirty hours and about a month amounted to over 0.3%. The phenomenon is undoubtedly connected with partial enolization upon distillation and gradual reversion into balanced keto–enol equilibrium: a condition catalyzed by the alkaline material of soft glass. According to K. Meyer[24] the ester contains about 3% of the enol form, but this figure is somewhat uncertain as the preparation used probably contained some of the diethyl derivative and it is not known whether keto–enol equilibrium had been established.

β-Ethoxycrotonic ester was prepared by condensing acetoacetic with orthoformic ester in the presence of a small quantity of sulfuric acid. The product, after fractionation *in vacuo*, crystallized and was filtered from adhering oil. The crystalline ester was redistilled, crystallized, separated from adhering oil, and again redistilled. The physical constants observed were: first distillate: b. p. 86.3° at 12 mm., n_D^{37} 1.4400; second distillate: b. p. 86.2° at 12 mm., $n_D^{36.6}$ 1.4418; first crystallization: m. p. 29.8–29.9° with thermometer in melting substance, 30.5° in wide melting point tube; second crystallization: m. p. 30.5–30.7° in tube; fused crystals: $n_D^{36.5}$ 1.4420; d 42.8/4 0.9634.

Von Auwers[25] gives m. p. 31° for a preparation obtained from Claisen, and 32–33° for one prepared by himself. The latter datum is undoubtedly too high as no other observer placed it over 31°.

The heats of combustion were determined at the U. S. Bureau of Standards. "The heat of combustion is here defined as the heat liberated when one gram (weighed in air of density 0.00117 g./cc. against brass weights of density 8.4 g./cc.) of the compound is burned at the given temperature under a constant pressure of one atmosphere, the initial system consisting of the liquid compound and gaseous oxygen, and the final system consisting of gaseous carbon dioxide and liquid water."

"The observed heats of combustion of the two com-

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(19) Claisen, *Ber.*, **40**, 3908 (1907).

(20) Even in the action of as energetic a reagent as phosphorus pentachloride on acetone, direct replacement of O by Cl_2 cannot take place. Primarily, $(CH_3)_2CCl(OPCl_4)$ must be formed which decomposes into $CH_3CCl_2CH_3$ and $POCl_3$.

(21) Elion's [*Rec. trav. chim.*, **3**, 246 (1884)] method of purifying acetoacetic ester through the bisulfite compound is laborious, and accompanied by considerable loss; upon standing of the bisulfite mixture some reduction of the ester appears to take place. A better method is to purify it through the sparingly soluble copper enolate and check purity through melting points.

(22) Michael, *Ber.*, **38**, 2093 (1905).

(23) Von Auwers and Schmidt, *ibid.*, **46**, 505 (1913).

(24) K. Meyer, *ibid.*, **45**, 2864 (1912).

(25) Von Auwers, *ibid.*, **44**, 3530 (1911).

pounds were reduced by the method given by Washburn [*B. S. J. Res.*, **10**, 525 (1933)] to the heats of combustion under a constant pressure of one atmosphere at the final temperatures of the experiments." The mean value of four determinations with α-ethyl acetoacetic ester with the bomb at 33°, in terms of international joules/g. (air), is 28027 with ±10 mean deviation. With β-ethoxycrotonic ester and the bomb at 39.6°, the mean value of three determinations is 28456 joules/g. (air), with ±2 mean deviation. This compound froze in the bomb at 33° under the pressure of the oxygen so "it was necessary to make the combustion at the higher temperature. Assuming its specific heat is 1.9 joules per gram degree Centigrade, it is calculated that the heat of combustion at 33° is 28465 international joules per gram (weighed in air)." Calculated on these values, the heat of formation of the α-ethyl ester is 8.5% higher than that of the β-ethoxy ester.[26]

Condensation of Acetoacetic and Orthoformic Ester. (A) With Sulfuric Acid.—Twenty grams of acetoacetic and 25 g. of orthoformic ester were cooled to −15° and 4 drops of concentrated sulfuric acid added. During the next twenty-four hours the mixture was maintained at −15 to −10° and then dry potassium carbonate in excess was added. The mixture at room temperature under 5–10 mm. gave 7.8 g. of distillate. The residual oil (25.3 g.; calcd. for β-ethoxycrotonic ester, 24.3 g.; for β,β-diethoxybutyric ester, 31.5 g.) partially solidified and 12.7 g. of β-ethoxycrotonic ester (m. p. 31–31.5°) was filtered off. The filtrate at ordinary pressure gave 1 g. of low boiling material and 7.2 g. of β-ethoxycrotonic ester.

(B) With a Trace of Acetyl Chloride.—A drop of acetyl chloride was added at room temperature to 5 g. of orthoformic and 4.4 g. of acetoacetic ester. After standing for a week, the mixture gave 1.2 g. of distillate (mostly orthoformic ester) at 10 mm. and room temperature, and 7.7 g. at 60–65°, leaving a residual oil of 0.5 g. Two grams of the main distillate gave 1.1 g. of copper acetoacetic ester of m. p. 190°, showing that at least 3.4 g. (78%) of acetoacetic ester was recovered unchanged. No condensation product could be detected.

(C) With One Equivalent of Acetyl Chloride.—A mixture of 10 g. of orthoformic and 8.8 g. of acetoacetic ester was treated at −25° with 5.3 g. of acetyl chloride. After standing for three days at room temperature, 10.6 g. of an oil, containing hydrogen chloride, was distilled off at room temperature under 10 mm. The residual oil (8.3 g.) gave fractions: (1) 3.5 g. of β-ethoxycrotonic ester, b. p. 65° at 3 mm.; (2) 3.8 g., b. p. 137–138° at 2 mm. On redistillation, fraction (2) boiled at 144° at 2 mm. and melted at 12.5–13°. The distillate gave no color with alcoholic ferric chloride.

(D) With a Trace of Ferric Chloride.—Five grams of orthoformic and 4.4 g. of acetoacetic ester containing 0.1 g. of ferric chloride were kept at room temperature for twenty-four hours. The volatile products (3.3 g.) were removed, at room temperature, under 9 mm. The residual oil distilled at 21 mm., gave 4.9 g. (calcd. 5.3 g.) not quite pure β-ethoxycrotonic ester, b. p. 95–100°; m. p. 15–20°. It gave a faint red color with ferric chloride and evidently contained a trace of acetoacetic ester.

(E) With Ferric Chloride in Alcohol Solution.—A solution of 10 g. of orthoformic, 8.8 g. of acetoacetic ester, 0.2 g. of ferric chloride and 10 g. of alcohol stood for twenty-four hours at room temperature. On fractionation at 12 mm., 14.2 g. of oil distilled over at room temperature. The residual oil (11.1 g.) gave 9.3 g. (calcd. 10.7 g.) of β-ethoxycrotonic ester, b. p. 84–86° at 20 mm.; m. p. 24–25°. The distillate gave a faint red color with ferric chloride, but no copper acetoacetic ester with copper acetate solution.

(F) With Ammonium Chloride.—A solution of 10 g. of orthoformic and 8.8 g. of acetoacetic ester in 10 g. of alcohol with 0.5 g. of ammonium chloride stood for 140 hours at room temperature. At room temperature under 10 mm., 13.3 g. of liquid distilled over. The residual oil gave fractions: (1) 2.7 g., b. p. up to 70° at 12 mm.; (2) 9.0 g. b. p. 70–90° at 12 mm. The fractions gave a color with ferric chloride and did not solidify at all at −20°. They were dissolved in ether and the solution extracted with a cold solution of 10% sodium hydroxide. On fractionating the dry ether solution, there were obtained fractions: (3) 2.3 g., b. p. up to 90° at 12 mm.; (4) 6.1 g., b. p. 90–91° at 12 mm. Fraction (4) gave no color with ferric chloride and at −20° deposited 0.2 g. of a solid. Six grams of (4) distilled at ordinary pressure gave 0.5 g. of alcohol and 5.2 g. of β-ethoxycrotonic ester which solidified immediately on cooling.

(G) With Ammonium Chloride in the Cold.—A solution of 10 g. of orthoformic, 8.8 g. of acetoacetic ester in 10 g. of alcohol, containing 0.5 g. of ammonium chloride, was kept for sixty hours at 0 ± 5°. The residual oil remaining after heating to 70° at 10 mm. gave 5.8 g. of oil, b. p. 60–70° at 2 mm. On fractionation at ordinary pressure it gave: (1) 1.9 g., b. p. 175–180°; (2) 3.1 g., b. p. 180–190°. On shaking 1.5 g. of (2) with copper acetate, 1.1 g. of copper acetoacetic ester was obtained. A condensation product could not be isolated.

Action of Formimido Ether Hydrochloride on Acetoacetic Ester.—Thirty grams of the hydrochloride was added slowly at 0° to a solution of 35.6 g. of acetoacetic ester in 75 g. of alcohol. After standing for six days at 0 ± 2°, 14.5 g. (calcd. 14.65 g.) of ammonium chloride was filtered off and the alcohol distilled from the filtrate at 60° under 10 mm. The residual oil gave fractions: (1) 2.6 g., b. p. up to 91° at 8 mm.; (2) 42.2 g., b. p. 91–98° at 8 mm. (almost entirely at 97–98°). The distillate partially solidified when cooled. The decanted oil (21 g.) at ordinary pressure gave 2.4 g. (corresponding to 10.7 g. of diethoxybutyric ester) of alcohol and 18.2 g. of β-ethoxycrotonic ester, b. p. 193–198°, which solidified completely when cooled.

Addition of Alcohol to β-Ethoxycrotonic Ester. With One Equivalent of Sodium Ethoxide. (A) Catalyst Removed by Acetic Acid.—A solution of 10 g. of β-ethoxycrotonic ester in 15 cc. of alcohol was added at 0° to an

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(26) After this work was completed, we found a statement in Landolt–Börnstein's tables (1st supplement, p. 877 (1927)) giving data by Roth, v. Auwers and Wrede unpublished elsewhere, on the heats of combustion of α-ethyl acetoacetic and α-ethoxycrotonic esters. Herr Roth, in reply to an inquiry regarding the second compound, was unable to give further information, except that it was probably a Claisen preparation. Since there is no record in the literature of an α-ethoxycrotonic ester, it is very probable that the compound in question was the β-ethoxy derivative. The combustion values are somewhat higher than those given above, the α-ethyl acetoacetic ester used undoubtedly contained some diethyl ester.

ethylate solution prepared from 1.46 g. of sodium and 20 cc. of alcohol. The mixture became semi-solid after twenty-four hours and was treated in the cold with 4 g. (1 equiv.) of acetic acid. The alcohol was removed, the semi-solid residue suspended in ether, washed with cold water, and the solvent removed from the dried solution. The residual oil gave 8.1 g. of β-ethoxycrotonic ester, b. p. 76–79° at 3 mm. A residue of 0.05 g. of solid remained in the flask, m. p. 140–142°, which apparently was isodehydracetic acid.

(B) **Catalyst Removed by Water.**—Ten grams of β-ethoxycrotonic ester was added to a cold solution of 1.46 g. of sodium in alcohol. After twenty-four hours the alcohol was removed under reduced pressure, the semi-solid suspended in ether and washed with ice water. From the dried ether solution 9.1 g. of oil, b. p. 73–77° at 2 mm., was obtained. The distillate gave no color with ferric chloride and solidified when cooled. Nine grams distilled at ordinary pressure gave 0.5 g. of alcohol, corresponding to 2.2 g. of β,β-diethoxybutyric ester, and 8.5 g. of β-ethoxycrotonic ester, which solidified at room temperature.

(C) **One-Tenth Equivalent of Sodium Ethoxide at Boiling Point of Mixture.**—Ten grams of β-ethoxycrotonic ester was added to a cold solution of 0.15 g. of sodium in 10 cc. of alcohol. The solution was heated on a water-bath for twenty-two hours and dry carbon dioxide then bubbled through for two hours. The alcohol was removed at reduced pressure, the residue suspended in ether and washed with cold water. The dried ether solution gave 9.1 g. of oil, b. p. 75–77° at 3 mm. On distillation at ordinary pressure 8.7 g. of β-ethoxycrotonic ester, b. p. 200°, but no alcohol was obtained.

(D) **Products Distilled Directly from Catalyst.**—Ten grams of β-ethoxycrotonic ester was added to a solution of 0.15 g. of sodium in 10 cc. of alcohol and the mixture warmed on a water-bath for two hours. The alcohol was removed at reduced pressure and the semi-solid residue at 4 mm. gave 8.6 g. of unchanged β-ethoxycrotonic ester.

(E) **Products Distilled from Catalyst after Six Days.**—The last experiment was repeated, but the solution stood at room temperature for six days. The alcohol was removed at reduced pressure, and 9.5 g. of oil distilled from the semi-solid residue at 2 mm. by heating in a water-bath at 100°. Redistilled at ordinary pressure 9.3 g. of the oil gave 0.3 g. of alcohol (corresponding to 1.3 g. of β,β-diethoxybutyric ester) and 8.5 g. of β-ethoxycrotonic ester.

Summary

1. The theory of polymolecular formation, as antecedent to chemical change, has been extended to explain the appearance of isomers in organic reactions. The formation of O- and C-derivatives of acetoacetic ester has been interpreted from that viewpoint.

2. In agreement with the "thermochemical rule of structure," it has been proved that C-ethyl has a larger heat of formation than O-ethyl acetoacetic ester. The formation of the C-product, therefore, contributes more than the O-derivative would to the maximum degradation of energy.

3. The formation of β-ethoxycrotonic ester from acetoacetic and orthoformic esters has been reinvestigated. Contrary to Claisen, β,β-diethoxybutyric ester could not be isolated from the reaction products, and the amount formed was small. No experimental evidence could be found to support Claisen's conclusion that it is the primary reaction product; his view that the reaction proceeds by direct substitution of the carbonyl oxygen by two ethoxy groups cannot be upheld.

4. The following general rule is maintained: an organic compound, with a group of unsaturated atoms, and a reactant, with addendum components manifesting a developed affinity for the unsaturated atoms, invariably react primarily through addition. When, seemingly, substitution has occurred, this is due to a subsequent elimination from the addition product. The ketone-orthoformic ester reaction has been interpreted from this point of view.

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