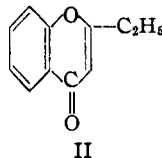
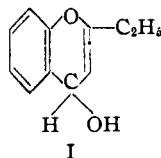


[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Reduction of Ester Vinylogs¹

BY ROBERT H. BAKER AND PATTY CAMPBELL WEISS

In an attempt to prepare 2-ethylchromen-4-ol, I, by methods more suitable than the one developed by Mozingo and Adkins,² it was observed that aluminum isopropoxide does not reduce 2-ethylchromone, II.³ The failure of this reaction

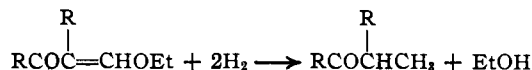


may be attributed to the fact that the ketone is a vinylog of an ester and hence has an oxidation potential which is numerically too far below that of acetone to allow it to oxidize isopropyl alcohol.⁴

It appeared that open chain vinylogs might approach more nearly the properties of esters, and hence might exhibit alkoxy exchange in the presence of aluminum alkoxides,⁵ but no reaction of this type has been unequivocally demonstrated. Both 2-ethylchromone, II, and O-ethylbenzoylacetone, IV, were recovered unchanged after re-

tar was produced. This is not surprising in light of the ease of dimerization of methyl ketones⁶ and the great instability of this compound when kept at room temperature.

The catalytic reduction of these compounds demonstrates the extraordinary lability of the alkoxy group. Over palladium catalysts Kötzt and Schaeffer⁷ found that those which are easily hydrolyzed are hydrogenated according to the equation



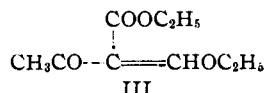
In this reaction hydrogenolysis of the ethoxy must precede the reduction of the ethylenic linkage, for there is no precedent for the reverse order which would require the hydrogenolysis of a saturated ether under mild conditions. It appeared that the hydrogenolysis reaction might be minimized and hydrogenation favored by use of catalysts less active than palladium which allow of greater selectivity. Some typical results of these experiments are shown in Table I.

TABLE I

Compound	SELECTIVE HYDROGENATION OF ESTER VINYLOGS				
	Temp., °C.	Time, min.	Cat.	Moles H ₂ per mole compd.	% Product
Ethyl α-ethoxymethyleneacetate	23	48 ^a	Ni(R)	1.6	50 Ethyl α-methylacetate
Same	150	40 ^a	CuCrO	0.8	Non-distillable tar
O-Ethylbenzoylacetone	118	40	Ni(R)	2.0	57 β-Ethoxypropylphenylcarbinol VI
Same	120	120 ^a	Ni(R)	1.0	64% Mixture of VI and β-ethoxybutyrophenone
Same	180	330	CuCrO	2.0	58 Butyrophenone, IX
Ethyl β-ethoxycrotonate	130	70	Ni(R)	0.9	86 Ethyl β-ethoxybutyrate
Same	170	120	CuCrO	0.6	45 Ethyl β-ethoxybutyrate

^a Glass liner used.

fluxing with isopropyl alcohol in the presence of aluminum isopropoxide. The latter compound was also unaffected by heating to 100° in the presence of pure aluminum s-butoxide. Ethyl α-ethoxymethyleneacetate, III, was changed



by similar treatment but the only identifiable product was a small amount of a dimer and much

Ethoxymethyleneacetate ester, III, presents a very labile ethoxy group, it being vinylogous to two carbonyl groups. Over nickel it underwent hydrogenolysis followed by hydrogenation of the carbon-to-carbon double bond under very mild conditions. Over copper-chromium oxide it is apparently polymerized before hydrogenation takes place.

In O-ethylbenzoylacetone, IV, the alkoxy is vinylogous to only one carbonyl group, and it was possible to avoid hydrogenolysis with nickel or to make it the predominating reaction over copper-chromium oxide. Of the several ways that hydrogen might attack this molecule, the more plausible are shown below.

(1) This investigation was supported in part by a grant from the Abbott Fund of Northwestern University.

(2) Mozingo and Adkins, *THIS JOURNAL*, **60**, 669 (1938).

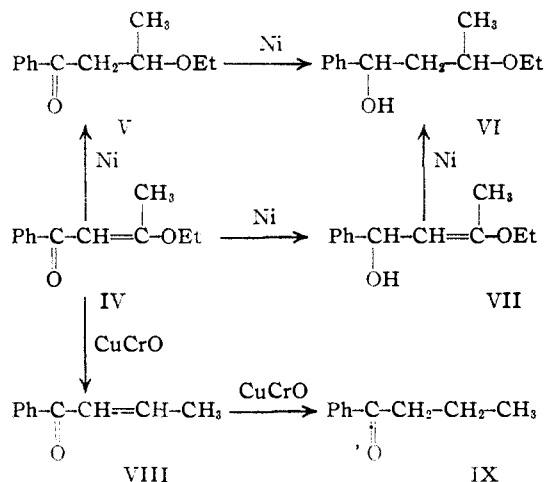
(3) This experiment was carried out by the senior author in 1939 while working under the direction of Prof. Homer Adkins.

(4) Baker and Schafer, *THIS JOURNAL*, **65**, 1675 (1943).

(5) Baker, *ibid.*, **60**, 2673 (1938).

(6) Wayne and Adkins, *ibid.*, **62**, 3401 (1940).

(7) Kötzt and Schaeffer, *J. prakt. Chem.*, **106**, 604 (1913).

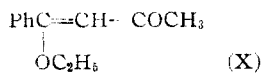


Of the two routes to the saturated ethoxycarbinol, VI, evidence that the preferred one is through the ethoxyketone, V, was obtained from experiments in which the hydrogen adding was limited to one mole. The boiling point of the ketone, V, is so near that of the alcohol, VI, that only the mixture was isolated; however, its presence was demonstrated in the mixture by polarographic and Grignard machine analysis. Evidence for the formation of the ethoxyvinyl carbinol, VII, was less conclusive, but its presence can hardly be discounted on the basis of the fact that nickel generally shows little preference for an ethylenic over a carbonyl linkage. Its presence was indicated by tests for unsaturation applied to some of the low boiling fractions resulting from various hydrogenations over nickel.

The third mode of hydrogenation leads to butyrophenone, IX, and this is brought about over copper-chromium oxide. No evidence for the formation of crotonophenone, VIII, was obtained, runs with limited quantities of hydrogen seemingly resulting only in the production of butyrophenone.

Ethyl β -ethoxycrotonate presents a still less powerful group to activate the vinylogous ethoxyl and is hydrogenated entirely to β -ethoxybutyric ester over either of the two catalysts.

The structures of the products of hydrogenation of O-ethylbenzoylacetone, IV, confirm the structure originally claimed for this enol ether by Claisen,⁸ and dispute the contention of Weygand⁹ that regardless of the method of preparation the compound is the isomeric enol ether, X.



Experimental Part

Preparation of Compounds.—Ethyl α -ethoxymethyleneacetate was prepared from one mole each of ethyl acetoacetate and acetic anhydride and two moles of ethyl orthoformate according to Claisen.¹⁰ It was found to be

desirable to distil the product rapidly from hydroquinone without the aid of a column. The product distilling at 149–151° (16 mm.) amounts to 76 g., 41%, and has n_D^{20} 1.4715–1.4720. It may be kept for a few weeks only if protected by hydroquinone at 0° and in the dark, one-half of it being destroyed by keeping under ordinary conditions at room temperature for one month.

O-Ethylbenzoylacetone was prepared by the method of Claisen.⁸ A number of preparations indicated that seven minutes of refluxing of benzoylacetone and ethyl orthoformate with strictly dry ethyl alcohol and ferric chloride gives the best yield, 53% of product n_D^{20} 1.5610–1.5615, b. p. 119° (1 mm.), when distilled through a 16-plate column.

2-Ethylchromone was a sample resulting from some research of Dr. Ralph Mazingo,² n_D^{20} 1.5820. Ethyl β -ethoxycrotonate,¹¹ n_D^{20} 1.4471–1.4478, and other compounds were made by established methods.

Aluminum Alkoxide Reactions.—The general procedure was to treat 0.05–0.10 mole of the compound with three equivalents of aluminum alkoxide dissolved in its corresponding alcohol. Aliquots were taken at the beginning and after various periods of heating and analyzed polarographically. The height of the 2-ethylchromone wave^{2,12} was not diminished after sixty hours of refluxing. The remainder of the solution after hydrolysis, isolation, and distillation through a 3-plate column yielded the major portion of unchanged 2-ethylchromone, n_D^{20} 1.5806.

The heights of the O-ethylbenzoylacetone wave¹³ also showed that no reduction of this compound had occurred. After treatment with water and fractionation, the compound corresponded in boiling point and refractive index to starting material. As a further test to see if alkoxyl exchange is possible, this compound was heated with pure aluminum *s*-butoxide for two hours at 100°. Then just sufficient water was added to hydrolyze the alkoxide and the oil was isolated. This was distilled through a 3-plate micro column yielding fractions which appeared to be unchanged material. A small tail fraction was analyzed as follows:¹⁴ Calcd. for O-ethylbenzoylacetone, C₁₂H₁₄O₂: C, 75.76; H, 7.41. Calcd. for O-*s*-butylbenzoylacetone, C₁₄H₁₈O₂: C, 77.03; H, 8.31. Found: C, 76.05; H, 7.67. Since the tail fraction represented 15% of the starting weight and the carbon analysis cannot admit of more than 25% of *s*-butyl derivative, the exchange in the whole fraction cannot have been greater than 4%, if any.

Ethyl α -ethoxymethyleneacetate, when thus treated with aluminum isopropoxide in isopropyl alcohol, turned quite yellow after ten minutes at 60°. There was a sharp drop in the height of the polarographic wave which remained approximately equivalent to one-half of the original concentration after three hours. After treatment with water and isolation, there was obtained a viscous yellow oil 50% of which was distillable at 200–218° (1 mm.). This was an amber colored plastic mass which did not crystallize after standing a year. Its molecular weight, Rast, was 370, while that calculated for the starting material is 186.

Hydrogenations.—The catalysts, apparatus and procedures were similar to those which are particularly adapted to selective hydrogenations.^{15,16} No solvents were used, and glass liners for the bombs appeared to be of no benefit except possibly in the case of ethyl α -ethoxymethyleneacetate which reacted with metals to such an extent that much of the nickel catalyst was destroyed. The products were fractionated through either a 10- or 16-plate column and the recorded boiling points are subject to the usual errors attending slow fractionation through electrically heated, total condensation apparatus.

Identification of Hydrogenation Products.—Ethyl α -methylacetate, n_D^{20} 1.5215, was converted into the

(11) Wislicenus and Schollkopf, *J. prakt. Chem.*, **203**, 269 (1917).

(12) Adkins and Cox, *This Journal*, **60**, 1151 (1938).

(13) $\pi = -1.67$ volts, empirical in lithium chloride solution.

(14) Analysis by Dr. T. S. Ma, University of Chicago.

(15) Adkins, "Reactions of Hydrogen," University of Wisconsin Press, Madison, Wisconsin, 1937.

(16) Sprague and Adkins, *This Journal*, **56**, 2669 (1934).

(8) Claisen, *Ber.*, **40**, 3903 (1907); **59**, 144 (1926).

(9) Weygand, *ibid.*, **58**, 1473 (1925).

(10) Claisen, *Ann.*, **297**, 1 (1897).

2,4-dinitrophenylhydrazone, m. p. 59°, and into ethyl methyl ketone the semicarbazone of which melted at 136°.¹⁷

β -Ethoxypropylphenylcarbinol has not been previously described. It has the following constants: b. p., 82.5° (1 mm.); n_D^{20} 1.4995; d_4^{20} 0.994; M_D , found, 56.8; M_D , calcd., 52.0; mol. wt., cryoscopic in benzene 202, cryoscopic in camphor 198; mol. wt. calcd., 194; % hydroxyl, found, 8.76, 8.75¹⁸; calcd., 8.76. The Baeyer and iodoform tests are negative. We are unable to explain the anomaly in molecular refractivity except on the basis that this product is in all probability a mixture of two racemic forms.

β -Ethoxybutyrophenone was thought to be present in the reaction mixture resulting from limited hydrogenation of O-ethylbenzoylacetone over nickel. Nine fractions boiling 94–110° (1 mm.) were collected from a 3-plate distillation. The first six of these, 94–100°, showed a gradual drop in refractive index, n_D^{20} 1.5137–1.5075 and represented 64% of the weight of starting material. The last two fractions n_D^{20} 1.5645 represented 11% recovery of crude starting material. Fraction number three gave negative tests with bromine and with permanganate, and the presence of an aryl ketone in approximately 50% concentration was demonstrated by the polarograph, $\pi = -1.68$. Assuming the mixture to be pure alcohol and ketone the Grignard machine analysis indicated 56% of alcohol of molecular weight 195 and 44% ketone of molecular weight 194. The calculated molecular weights of the

expected ketone and alcohol, V and VI, are 194 and 196, respectively.

Butyrophenone, n_D^{20} 1.5127, showed a polarographic wave in lithium chloride solution at -1.68 volts (empirical). It gave a semicarbazone, m. p. 189–190°, and a 2,4-dinitrophenylhydrazone, m. p. 190°, in agreement with the literature.¹⁷

Ethyl β -ethoxybutyrate, n_D^{20} 1.4076; d_4^{20} 0.925; M_D found, 42.6, calcd., 42.4; had the correct boiling point at 745 mm., 173°.¹⁹

Summary

1. Compounds which are open-chain vinyls of esters are too much like esters to be reduced by aluminum alkoxides. They, however, are not sufficiently ester-like to undergo alkoxyl exchange with these reagents.

2. When the alkoxyl group is in a vinylous position to both a keto-carbonyl and a carbethoxyl, it undergoes hydrogenolysis over nickel under very mild conditions. When the alkoxyl is vinylous to only a keto-carbonyl it is more resistant to hydrogenolysis and the nature of the hydrogenation products may be controlled by selection of catalysts. The carbethoxyl group does not labilize such groups sufficiently to allow of hydrogenolysis prior to hydrogenation of the ethylenic linkage.

(19) Purdie and Marshall, *J. Chem. Soc.*, 59, 478 (1891).

(17) Huntress and Mulliken, "Identification of Pure Organic Compounds." Order I, John Wiley and Sons, Inc., New York, N. Y., 1941.

(18) Adkins, Frank and Bloom, *THIS JOURNAL*, 63, 554 (1941).

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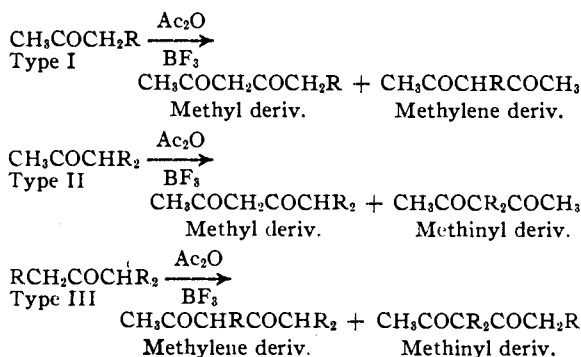
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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

The Acetylation of Certain Unsymmetrical Aliphatic Ketones with Acetic Anhydride in the Presence of Boron Trifluoride^{1,2}

BY CHARLES R. HAUSER AND JOE T. ADAMS

The acetylation of ketones with acetic anhydride in the presence of boron trifluoride to form 1,3-diketones has been carried out previously apparently only with ketones such as acetone,^{3,4} diethyl ketone³ or acetophenone,^{3,5} each of which can yield but a single monoacetyl derivative. The purpose of this investigation has been to determine the products of acetylation, in the presence of boron trifluoride, of certain unsymmetrical aliphatic ketones each of which might form two different monoacetyl derivatives. Three types of unsymmetrical ketones have been studied, types I, II and III, represented below, with which it is possible to form, respectively, the methyl and methylene derivatives, the methyl and methinyl derivatives, and the methylene and methinyl derivatives, thus



Seven ketones have been acetylated, five of type I, methyl ethyl, methyl *n*-propyl, methyl isobutyl, methyl *n*-amyl and methyl *n*-hexyl ketones, and one each of types II and III, methyl isopropyl ketone and 2-methylcyclohexanone,⁶ respectively. The yields of acetylation products isolated from these ketones were 28–59%, the

(1) Paper XXIII of series on "Condensations;" for paper XXII, see *THIS JOURNAL*, 66, 309 (1944).

(2) This investigation was supported in part by a grant from the Duke University Research Council.

(3) Meerwein and Vossen, *J. prakt. Chem.*, 141, 149 (1934).

(4) "Organic Syntheses," Vol. 20, 6 (1940).

(5) Breslow and Hauser, *THIS JOURNAL*, 62, 2385 (1940).

(6) Although this ketone has a cyclic, instead of the linear structure represented by the general formula above, it should react as a typical type III ketone.