[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, DUKE UNIVERSITY]

Mechanism of Acetylation of Ketone Enol Acetates with Acetic Anhydride by Boron Trifluoride to Form β-Diketones

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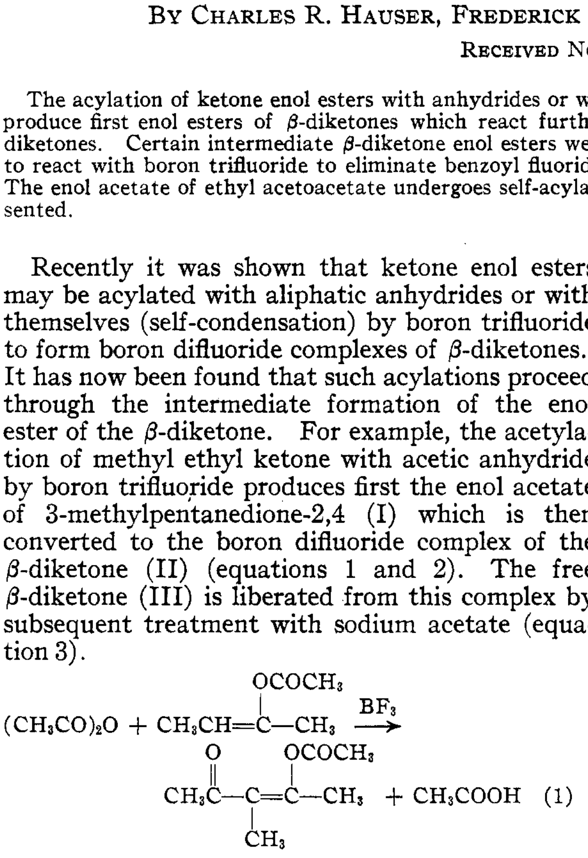
RECEIVED NOVEMBER 23, 1951

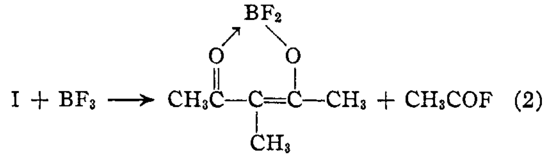
The acylation of ketone enol esters with anhydrides or with themselves by means of boron trifluoride has been shown to produce first enol esters of β-diketones which react further with the reagent to form boron difluoride complexes of β-diketones. Certain intermediate β-diketone enol esters were isolated. The enol benzoate of dibenzoylmethane was found to react with boron trifluoride to eliminate benzoyl fluoride and form the boron difluoride complex of dibenzoylmethane. The enol acetate of ethyl acetoacetate undergoes self-acylation in the presence of boron trifluoride. Mechanisms are presented.

Recently it was shown that ketone enol esters may be acylated with aliphatic anhydrides or with themselves (self-condensation) by boron trifluoride to form boron difluoride complexes of β-diketones.[3] It has now been found that such acylations proceed through the intermediate formation of the enol ester of the β-diketone. For example, the acetylation of methyl ethyl ketone with acetic anhydride by boron trifluoride produces first the enol acetate of 3-methylpentanedione-2,4 (I) which is then converted to the boron difluoride complex of the β-diketone (II) (equations 1 and 2). The free β-diketone (III) is liberated from this complex by subsequent treatment with sodium acetate (equation 3).



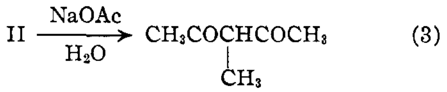
$$(CH_3CO)_2O + CH_3CH{=}\overset{OCOCH_3}{C}{-}CH_3 \xrightarrow{BF_3} CH_3\overset{O}{\overset{\|}{C}}{-}\underset{CH_3}{C}{=}\overset{OCOCH_3}{C}{-}CH_3 + CH_3COOH \quad (1)$$

I



(2)

II

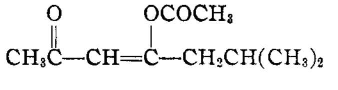


$$II \xrightarrow[H_2O]{NaOAc} CH_3CO\underset{CH_3}{C}HCOCH_3 \quad (3)$$

III

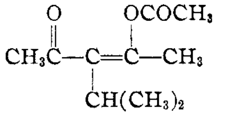
Actually β-diketone enol acetate I (12%) was isolated (along with some β-diketone III) from the reaction mixture of acetic anhydride and the enol acetate of methyl ethyl ketone, and shown to be an intermediate by being converted, on further treatment with boron trifluoride, to boron difluoride complex II. In the isolation of intermediate I, the experiment was carried out at a lower temperature than usual[3] in order to minimize the conversion of I to II. Boron difluoride complex II was obtained by treating the reaction mixture with cold sodium acetate solution; it was subsequently converted to β-diketone III by further treatment with hot sodium acetate solution.

Similarly, the intermediate β-diketone enol acetate (15%) was isolated, along with the β-diketone (43%), from the reaction mixture of acetic anhydride and the enol acetate of methyl isobutyl ketone. This experiment was carried out at about the usual temperature,[3] the intermediate apparently being more stable than intermediate I. Since the β-diketone was shown to consist of a mixture of the two possible isomers, the methyl and methylene derivatives, the intermediate β-diketone enol acetate presumably consisted of a mixture of the methyl and methylene isomers, IV and V, respectively.



$$CH_3\overset{O}{\overset{\|}{C}}{-}CH{=}\overset{OCOCH_3}{C}{-}CH_2CH(CH_3)_2$$

IV



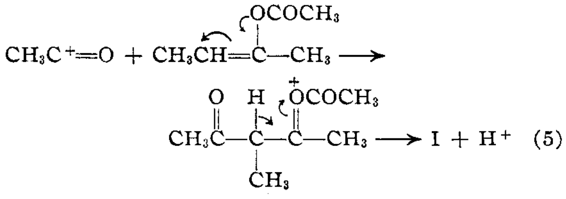
$$CH_3\overset{O}{\overset{\|}{C}}{-}\underset{CH(CH_3)_2}{C}{=}\overset{OCOCH_3}{C}{-}CH_3$$

V

The self-condensation of the ketone enol esters probably also first forms the β-diketone enol ester, although attempts to isolate such intermediates in the self-condensations of the enol acetates of acetone, methyl ethyl ketone and methyl *n*-amyl ketone were unsuccessful under various conditions. This is not surprising since these ketone enol acetates are less reactive acetylating agents than acetic anhydride, and, under the conditions required for the acetylation, the intermediate β-diketone enol acetates were presumably converted to their boron difluoride complexes.

The mechanism for the acetylation of the ketone enol acetates with acetic anhydride to form the β-diketone enol acetate (equation 1) is presumably analogous to that of the Friedel–Crafts acylation of aromatic compounds, of which it is an aliphatic analog. Thus, the anhydride is probably first converted to the acyl carbonium ion, which then condenses with the ketone enol ester, accompanied by the loss of a proton (equations 4 and 5). Similarly, the self-condensation of ketone enol esters, which is an aliphatic analog of the Fries reaction (intermolecular mechanism), would presumably

$$(CH_3CO)_2O + BF_3 \longrightarrow CH_3\overset{+}{C}{=}O + CH_3COO\overset{-}{B}F_3 \quad (4)$$



$$CH_3C^+{=}O + CH_3CH{=}\overset{OCOCH_3}{C}{-}CH_3 \longrightarrow CH_3\overset{O}{\overset{\|}{C}}{-}\underset{CH_3}{\overset{H}{C}}{-}\overset{\overset{+}{O}COCH_3}{\overset{\|}{C}}{-}CH_3 \longrightarrow I + H^+ \quad (5)$$

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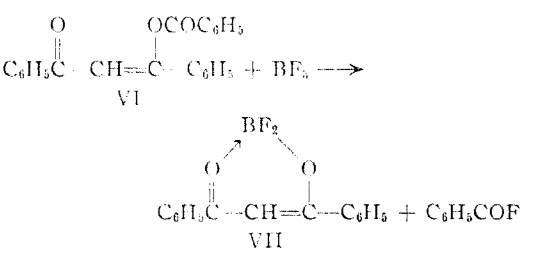
[1] Carbide and Carbon Chemicals Co. Fellow, 1949-1950.

[2] E. I. du Pont de Nemours and Co. Fellow, 1950-1951.

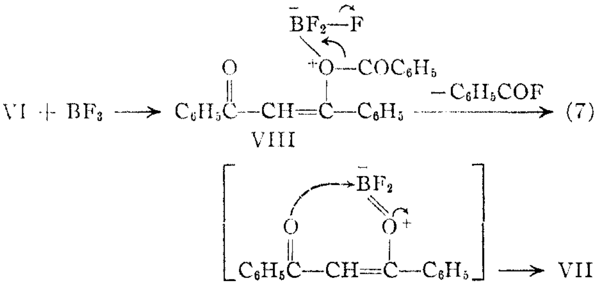
[3] F. G. Young, F. C. Frostick, J. J. Sanderson and C. R. Hauser, THIS JOURNAL, **72**, 3635 (1950).

involve the conversion of part of the ketone enol ester to the acyl carbonium ion, which then condenses with unchanged ketone enol ester to form the enol ester of the β-diketone.

The conversion of the intermediate β-diketone enol acetate to the boron difluoride complex presumably forms acetyl fluoride as by-product (equation 2). Although this by-product has not been isolated, the less volatile benzoyl fluoride was isolated along with boron difluoride complex VII (90%) from the reaction mixture of the enol benzoate of dibenzoylmethane (VI) and boron trifluoride (equation 6). Benzoyl fluoride has previously been isolated, along with β-diketones, from reaction mixtures in the self-condensations of the enol benzoates of acetone and of methyl n-amyl ketone.[3] These reactions would presumably involve the intermediate formation of the corresponding enol benzoates. The mechanism for this reaction appears to involve the β-elimination of the acid fluoride (in which the acyl group functions as a proton) from the intermediate boron trifluoride complex (VIII) (equation 7). The driving force may be furnished by the formation of the resonance-stabilized boron difluoride complex (VII). The mechanism for the conversion of β-diketone enol acetate I to boron difluoride complex II would be analogous.

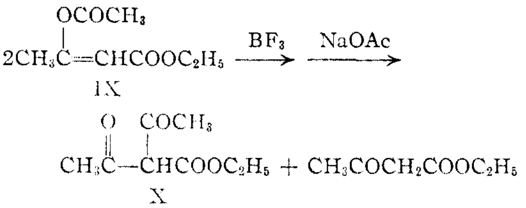


(6)



(7)

In contrast to the β-diketone enol esters, the enol acetate of ethyl acetoacetate (IX) forms with boron trifluoride triacyl product X (90%). The over-all reaction, which may be represented by equation 8, presumably involves the self-condensation of IX similar to condensations of ketone enol esters.[4] Kästner[5] has previously mentioned this reaction but he regarded it as an intramolecular rearrangement; the details have not been available.



$$2CH_3\overset{\overset{\displaystyle OCOCH_3}{|}}{C}{=}CHCOOC_2H_5 \xrightarrow{BF_3} \xrightarrow{NaOAc} CH_3\overset{\overset{\displaystyle O}{\|}}{C}{-}\overset{\overset{\displaystyle COCH_3}{|}}{C}HCOOC_2H_5 + CH_3COCH_2COOC_2H_5 \quad (8)$$

Experimental[6]

Isolation of Intermediate I and Its Conversion to II and III.—A mixture of 0.3 mole each of the enol acetate of methyl ethyl ketone[7] and acetic anhydride was saturated with boron trifluoride at −35 to −20° in 30 minutes. The resulting mixture was stirred at the same temperature for an additional 90 minutes, hydrolyzed by refluxing with sodium acetate solution, and extracted with ether. The ether extracts were washed free of acid with sodium bicarbonate solution, and dried over Drierite. On distillation, there were obtained methyl ethyl ketone (approx. 10%), recovered enol acetate (15%), a small amount of 3-methylpentanedione-2,4, and 5.5 g. (12%) of the enol acetate of 3-methylpentanedione-2,4 (I), b.p. 115–117° (30 mm.). The last product (I) gave a negative test with ferric chloride.

Anal. Calcd. for $C_8H_{12}O_3$: C, 61.52; H, 7.75. Found: C, 61.77; H, 7.49.

The enol acetate of 3-methylpentanedione-2,4 (1.1 g.) was saturated with boron trifluoride at 0°. After 30 minutes at room temperature, the mixture was shaken with a cold solution of sodium acetate, the solid collected and recrystallized from methanol to yield 0.5 g. (44%) of the boron difluoride complex of 3-methylpentanedione-2,4 (II), m.p. 94–94.5°.

Anal. Calcd. for $C_6H_9O_2BF_2$: C, 44.49; H, 5.60. Found: C, 44.78; H, 5.38.

The boron difluoride complex (II) (0.059 mole), on refluxing 15 minutes with a slight excess of sodium acetate in 100 ml. of water, was converted in 75% yield to 3-methylpentanedione-2,4, b.p. 77–79° (30 mm.) (reported b.p. 77–79° at 30 mm.).[8] The product was further identified by its purple enol test and gray copper salt with no definite melting point.[8]

Isolation of Mixture of Intermediates IV and V.—A mixture of 42.7 g. (0.3 mole) of the enol acetate of methyl isobutyl ketone[7] and 46.0 g. (0.45 mole) of acetic anhydride was saturated in 9 minutes with boron trifluoride at −5 to 12°, the temperature being maintained by the use of a Dry Ice–acetone-bath. The resulting mixture was stirred 4 hours in an ice-bath which was gradually allowed to come to room temperature. After decomposing the complexes with hot sodium acetate solution, there were isolated a β-diketone fraction (18.0 g., 43%) and a β-diketone enol acetate fraction (8.17 g., 15%), b.p. 114–116° (20 mm.). The latter fraction was analyzed.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 65.27; H, 8.68.

The β-diketone fraction was shown by the alkali extraction method[8] to consist of 17% of 3-methylheptanedione-4,6, b.p. 72–76° (20 mm.),[8] and 83% of 3-isopropylpentanedione-2,4, b.p. 80–84° (20 mm.).[8]

Reaction of Enol Benzoate of Dibenzoylmethane (VI) with Boron Trifluoride.—A solution of 52.1 g. (0.175 mole) of this enol benzoate (m.p. 107–108°)[9] in 30 ml. of ethylene chloride was saturated with boron trifluoride at 0–10° as rapidly as possible and the reaction mixture stirred at the same temperature for one hour. After shaking with a solution of 300 ml. of water containing 20 g. (0.25 mole) of sodium acetate, the mixture was filtered. The filtrate was immediately steam distilled rapidly for 45 minutes. The distillate was extracted with ether and the ether extracts washed with saturated sodium bicarbonate solution, dried over Drierite, and the solvent distilled. The residue was distilled *in vacuo*, yielding 4.9 g. (23%) of benzoyl fluoride,

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(4) It is possible that, like a β-diketone enol ester, the enol ester of the β-ketoester (IX) might first have eliminated acetyl fluoride to form the boron difluoride complex of ethyl acetoacetate, which then was acetylated by the acetyl fluoride or by some of the original ester (IX) to form X. However, this course of reaction seems less likely, since attempts to acetylate the boron difluoride complex of benzoyl acetone with acetic anhydride under similar conditions were unsuccessful.

(5) D. Kästner, in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers Inc., New York, N. Y., 1948, p. 289.

(6) Analyses by Clark Microanalytical Laboratory, Urbana, Ill.

(7) A generous sample of this ketone enol acetate, prepared by the ketene method (ref. 3), was kindly furnished by the Carbide and Carbon Chemicals Co., South Charleston, W. Va.

(8) C. R. Hauser and J. T. Adams, THIS JOURNAL, **66**, 345 (1944).

(9) L. Claisen and E. Haase, *Ber.*, **36**, 3674 (1903).

b.p. 60–65° (30 mm.), which was identified by its strong lachrymatory properties and by its vigorous reaction with concentrated ammonium hydroxide solution to form 3.4 g. of benzamide, m.p. and mixed m.p. 126.5–127°.

The solid obtained from the sodium acetate treatment was washed with ether, combined with the residue from the steam distillation and recrystallized from benzene to give 42.6 g. (90%) of the boron difluoride complex of dibenzoylmethane (VII), m.p. and mixed m.p. 189–190°.[10] The ether wash solution was extracted with sodium bicarbonate solution to yield, on acidification, 2.5 g. of benzoic acid, m.p. 119.5–121.5°. On the basis that this acid resulted from hydrolysis of benzoyl fluoride, the total yield of the acid fluoride is 35%.

Self-condensation of the Enol Acetate of Ethyl Acetoacetate (IX) with Boron Trifluoride.—A solution of 34.4 g. (0.2 mole) of the enol acetate of ethyl acetoacetate (b.p. 102.5–104.5° at 17 mm.)[11] in 35 ml. of ethylene chloride was saturated with boron trifluoride at 0–5° in 30 minutes. The mixture was stirred for 5 hours at ice-bath temperature, then for one hour at room temperature, and decomposed by stirring with 200 ml. of 3.7 molar sodium acetate solution for 45 minutes. The aqueous mixture was extracted with ether, the extracts washed with sodium bicarbonate solution, and dried over Drierite. On distillation there were obtained ethyl acetoacetate and 15.5 g. (90%) of ethyl diacetylacetate (X), b.p. 90–93.5° (12 mm.) (reported b.p. 95–97° at 12 mm.).[12] The product was further identified by its blue copper salt, m.p. 150–152°.[13] This same result was obtained independently by two workers.

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[10] G. T. Morgan and R. B. Tunstall, *J. Chem. Soc.*, **125**, 1963 (1924).

[11] L. Claisen and E. Haase, *Ber.*, **33**, 1244 (1900).

[12] A. Spassow, in "Organic Syntheses," **21**, 46 (1941).

[13] H. Böhme and H. Fischer, *Ber.*, **76B**, 106 (1943).

DURHAM, N. C.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE PENNSYLVANIA STATE COLLEGE]

The Diels–Alder Reaction between Sorbic Acid and Substituted Styrenes

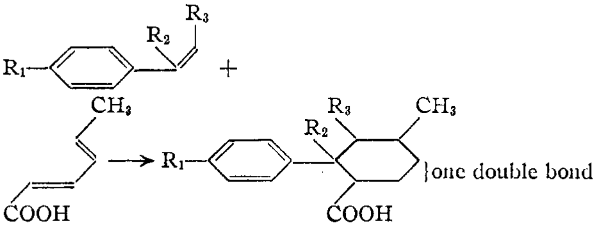
BY N. C. DENO AND JAMES D. JOHNSTON

RECEIVED DECEMBER 6, 1951

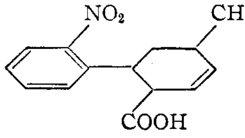
The Diels–Alder reactions of sorbic acid with styrene and nine substituted styrenes have been studied. All adducts were proven to have structures in which the carboxyl and phenyl groups are ortho to each other. Difficulties with both the polar and biradical mechanisms for the Diels–Alder reaction are presented.

To further test polar mechanisms of the Diels–Alder reaction,[1–5] the reaction between sorbic acid and a series of styrenes has been studied. The yield and properties of the adducts are summarized in Table I. In general the reaction product consisted of approximately equal amounts of a single crystalline isomer and a non-crystalline mixture of isomers. In all cases the carboxyl group in the crystalline product was proved to be ortho to the phenyl group as illustrated in equation (1). A comparison of the yields of crystalline product to total adduct, as given in Table I, shows that the major portion of most of the adducts have the carbon skeleton indicated. In several cases the non-crystalline adduct was also shown to contain at least in part adducts of the same carbon skeleton. It is probable that structures other than I-X are present in only minor amounts.

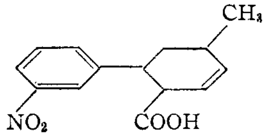
The adducts from sorbic acid with *o*- and *m*-nitrostyrene were also studied and found to possess structures IX and X. All adducts can be correlated with polar mechanisms except VIII and IX, which are clearly exceptional. These two closely resemble the exception to polar mechanisms reported by Ropp and Coyner,[6] who found that 1-(*p*-nitrophenyl)-butadiene and acrylic acid yielded XI.



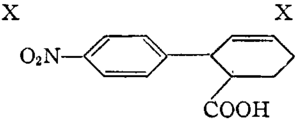
	R_1	R_2	R_3
Ia and Ib	H	H	H
II	H	CH_3	H
III	*i*-C_3H_7	CH_3	H
IV	Cl	H	H
V	Cl	CH_3	H
VI	OCH_3	CH_3	H
VII	OCH_3	H	CH_3
VIII	NO_2	H	H



IX



X



XI

Position of double bond unproven in IX and X

Proofs of Structures.—The adduct (II) from α-methylstyrene was dehydrogenated with sulfur to give 2-phenyl-4-methylbenzoic acid as previously described.[7] The 145° adduct (Ia) from styrene plus sorbic acid was similarly converted to 2-phenyl-4-methylbenzoic acid.

The *p*-isopropyl-α-methylstyrene adduct (III) was dehydrogenated with sulfur accompanied by loss of the angular methyl group. The resulting acid was cyclized to the corresponding fluorenone,

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[1] B. J. F. Hudson and R. Robinson, *J. Chem. Soc.*, 715 (1941).

[2] R. Robinson and H. N. Rydon, *ibid.*, 1398 (1939).

[3] M. J. S. Dewar, "Electronic Theory of Organic Chemistry," Oxford University Press, London, 1949, pp. 150–156.

[4] A. E. Remick, "Electronic Interpretations of Organic Chemistry," 2nd edition, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 447.

[5] W. E. Bachmann and N. C. Deno, THIS JOURNAL, **71**, 3062 (1949).

[6] G. A. Ropp and E. C. Coyner, *ibid.*, **72**, 3960 (1950).

[7] N. C. Deno, *ibid.*, **72**, 4057 (1950).