TABLE II

MIXED CONDENSATIONS OF METHYL ISOBUTYRATE AND METHYL ISOVALERATE WITH ALIPHATIC ESTERS[a]

		Mixed condensation product[b]							Self condensation product[b]						
					Analyses, %							Analyses, %			
					Carbon		Hydrogen					Carbon		Hydrogen	
Acylating methyl ester	Ester acylated	B.p., °C.	Mm.	Yield, %	Calcd.	Found	Calcd.	Found	B.p., °C.	Mm.	Yield, %	Calcd.	Found	Calcd.	Found
Isobutyrate	Et acetate	69	2.0	34.2	60.73	60.47	8.86	8.92	48	3.5	30.8	55.38	55.83	7.69	7.89
Isobutyrate	Me propionate	73–75	2.0	30.2	60.73	60.41	8.86	8.67	56	2.5	29.2	58.33	58.28	8.33	8.49
Isobutyrate	Me *n*-valerate	79–82	2.0	28.6	64.52	64.61	9.78	9.39	105–108	5.0	28.4	66.00	65.83	10.00	10.11
Isobutyrate	Me *n*-caproate	85–87	1.5	31.4	66.00	65.98	10.00	10.34	118–121	1.5	31.8	68.46	68.72	10.53	10.63
Isovalerate	Et acetate	74–75	2.0	30.2	62.79	62.83	9.30	9.52	47	2.0	28.1	55.38	55.34	7.69	7.92
Isovalerate	Me propionate	79	1.5	28.1	62.79	62.61	9.30	9.34	56	2.0	28.5	58.33	58.39	8.33	8.52
Isovalerate	Me *n*-caproate	96–98	2.0	21.2	67.29	67.32	10.28	10.69	120	2.0	17.0	68.46	68.32	10.53	10.36

[a] The ratio of reactants for each condensation was one mole of acylating ester per three moles of acylated ester and two moles of sodium ethoxide. [b] In each case the mixed and self condensation products were characterized by ketonic hydrolysis and identification of the resulting ketones through formation of known derivatives.

Experimental Procedures.—All of the condensations here reported were performed in essentially the same manner. The experiments described in detail below are illustrative of the general procedures.

Condensation of Methyl Furoate with Methyl *n*-Butyrate (Unforced).—A mixture of 63 g. (0.5 mole) of methyl furoate and 27 g. (0.5 mole) of sodium methoxide was placed in a 500-ml., three-necked flask equipped with a modified Hershberg stirrer,[6] a dropping funnel, and a reflux condenser protected by a calcium chloride tube. Fifty-one grams (0.5 mole) of methyl *n*-butyrate was added from the dropping funnel during one hour while the reaction mixture was vigorously stirred and maintained at a temperature of 100° by means of a heating mantle. Heating and stirring were continued for an additional four hours after the last of the methyl *n*-butyrate had been added. The reaction mixture was cooled to room temperature and poured onto crushed ice mixed with 60 ml. of concentrated hydrochloric acid. This mixture was stirred until all solids disappeared, and was allowed to stand until an organic layer clearly separated. The organic layer was separated, and the aqueous layer was extracted with two 100-ml. portions of ether. The organic layer and the ether extracts were combined, washed with a saturated solution of sodium bicarbonate until free of acid, then washed with water. The ether solution was dried over sodium sulfate, then over drierite. Removal of the drying agent and ether and distillation of the residue through a 61-cm. column packed with glass helices gave: (1) 12 g. of a mixture of methyl furoate and methyl α-butyryl-*n*-butyrate, b.p. 45–62° (8 mm.), (2) 7 g. of intermediate material, and (3) 38 g. (38.8%) of methyl α-furoyl-*n*-butyrate, b.p. 129–130° (6 mm.).

Other unforced condensations of methyl furoate with aliphatic esters were peformed in a similar manner. In certain cases, the reaction mixtures became quite thick, and sufficient benzene was added toward the end of the reaction period to permit pouring of the reaction mixture.

Forced Condensation of Methyl Furoate with Methyl *n*-Butyrate.—A mixture of 63 g. (0.5 mole) of methyl furoate, 54 g. (1.0 mole) of sodium methoxide, 51 g. (0.5 mole) of methyl *n*-butyrate and 100 ml. of dry benzene was placed in a 500-ml., three necked flask fitted with a modified Hershberg stirrer and dropping funnel and mounted under an 18-inch total-condensation partial-takeoff column packed with a nichrome wire spiral. Total reflux of the reaction mixture was established until the vapor temperature became constant. A solution of 102 g. (1 mole) of methyl *n*-butyrate in 200 ml. of dry benzene was added dropwise during 4.5 hours while the reaction mixture was vigorously stirred and material was taken off through the column at such a rate that the vapor temperature did not exceed 65° (preferable vapor temperature, 58–60°). The reaction was continued for 3.5 hours after the last of the methyl *n*-butyrate solution had been added. The reaction mixture was worked up by the procedure described above to give 59 g. (60.2%) of methyl α-furoyl-*n*-butyrate, b.p. 126–128° (5 mm.).

Forced condensations of methyl isobutyrate and methyl isovalerate with other aliphatic esters were run according to this essential procedure. In those cases that the self and mixed condensation products boiled near together, separations were effected using a Todd column,[7] 90 cm. (5 mm.) with a monel spiral packing. Effectiveness of the separations was checked in each case by elemental analysis of the self and mixed condensation products and by ketonic hydrolysis of each product and identification of the resulting ketones.

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[6] E. B. Hershberg, *Ind. Eng. Chem., Anal. Ed.*, **8**, 313 (1936).

[7] Floyd Todd, *ibid.*, **17**, 175 (1945).

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NOTES

The Detection of Carbohydrate Esters and Lactones after Separation by Paper Chromatography[1]

BY M. ABDEL-AKHER[2] AND F. SMITH

In connection with investigations into carbohydrates containing lactone or ester groupings by paper partition chromatography it was necessary to develop a method for the detection of minute amounts of these substances. The hydroxamic acid test[3,4] for esters which has been shown to be useful in following the reduction of certain carbohydrate esters with lithium aluminum hydride[5] has now been modified for the location of esters and lactones on paper chromatograms.[6] After carrying out the separation of esters or lactones or ester lactones by partition chromatography in the usual manner[7,8]

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[1] Paper No. 2667, Scientific Journal Series, Minnesota Agricultural Experiment Station.

[2] M. A.-A. wishes to express his sincere thanks to the Fouad I University, Cairo, for a scholarship.

[3] F. Feigl, V. Anger and O. Frehden, *Microchemie*, **15**, 9 (1934).

[4] D. Davidson, *J. Chem. Ed.*, **17**, 81 (1940).

[5] M. Abdel-Akher and F. Smith, *Nature*, **166**, 1037 (1950).

[6] *Cf.* S. Hestrin, *J. Biol. Chem.*, **180**, 249 (1949).

[7] R. Consden, A. H. Gordon and A. J. P. Martin, *Biochem. J.*, **38**, 224 (1944).

[8] S. M. Partridge and R. C. Westhall, *ibid.*, **42**, 238 (1948).

the paper is dried and sprayed with a freshly prepared solution of alkaline hydroxylamine (made by mixing equal volumes of N methanolic hydroxylamine hydrochloride and 1.1 N methanolic potassium hydroxide). After drying in air for about 10 minutes, the paper is sprayed (wetting of the paper should be avoided) with an aqueous solution containing 1–2% ferric chloride and 1% hydrochloric acid. A blue or mauve color is quickly formed in those areas containing the esters or lactones or ester lactones.

TABLE I

R_F VALUES OF CERTAIN LACTONES AND ESTERS

Compound	R_F
(a) Using 1-butanol–ethanol-water[10]	
D-Xylono-γ-lactone	0.41
L-Rhamnono-γ-lactone	.50
D-Glucono-γ-lactone	.32
D-Galactono-γ-lactone	.35
D-Mannono-γ-lactone	.25
D-Glucoheptono-γ-lactone	.13
D-Glucono-δ-lactone	.22
Methyl β-D-glucofururonoside	.30
Mannitol hexaacetate	.85
Arabitol pentaacetate	.85
(b) Using methyl ethyl ketone–water[11]	
Mannosaccharo-1,4-3,6-dilactone	0.60
3-Methyl-D-erythrono-γ-lactone	.73
2,3,5-Trimethyl-L-rhamnono-γ-lactone	1.00
2,3,5-Trimethyl-D-galactono-γ-lactone	0.90
3,4,6-Trimethyl-D-mannono-δ-lactone	.86
2,4-Dimethyl-D-galactosaccharo-3,6-lactone methyl ester	.91
2,3,4-Trimethyl-D-glucosaccharo-1,5-lactone methyl ester	.94
2,3,5-Trimethyl-D-glucosaccharo-1,4-lactone methyl ester	1.00
(c) Using methyl ethyl ketone–petroleum ether–water[11]	
2,3,5-Trimethyl-L-rhamnono-γ-lactone	0.88
2,3,5-Trimethyl-D-galactono-γ-lactone	.58
2,3,5-Trimethyl-D-glucosaccharo-1,4-lactone methyl ester	.88
2,4-Dimethyl-D-galactosaccharo-3,6-lactone methyl ester	.59

This hydroxamic acid test can also be used for the detection of certain amides and methylamides of sugar acids and esters of amino acids.

Free acids are not directly detectable[9] but by hanging the chromatograms for 10 to 15 minutes in a closed jar containing a dish of ethereal diazomethane. the acids are converted into methyl esters and the latter may then be detected as described above.

With this hydroxamic acid test it has been shown that butanol–ethanol–water can be employed for the separation of certain sugar lactones. This particular solvent is not convenient for the separation of the acetates of sugar alcohols since their R_F values are very similar. The test has shown that methylated lactones and methylated ester lactones may be separated like the methyl sugars with butanol–ethanol–water,[10] with methyl ethyl ketone[11] and with methyl ethyl ketone–petroleum ether (see Table I).

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[9] *Cf.* G. Brante, *Nature*, **163**, 651 (1949).

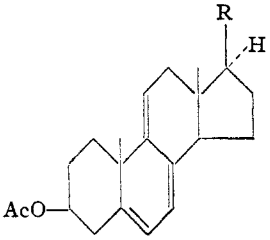
[10] L. Hough, J. K. N. Jones and W. H. Wadman, *ibid.*, **162**, 448 (1948); *J. Chem. Soc.*, 2511 (1949).

[11] L. Boggs, L. S. Cuendet, I. Ehrenthal, R. Koch and F. Smith, *Nature*, **166**, 520 (1950).

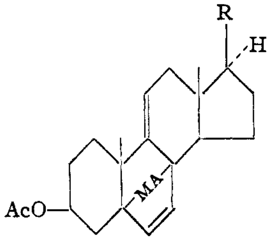
$\Delta^{5,7}$-Steroids. XI.[1] The Maleic Anhydride Adduct Products of $\Delta^{5,7,9(11)}$-Steroidal Hormones

BY ROSE ANTONUCCI, SEYMOUR BERNSTEIN, DOMINIC J. GIANCOLA AND KARL J. SAX

In Paper VII[2] of this series the preparation of $\Delta^{5,7,9(11)}$-androstatriene-3β-ol-17-one acetate (I) and $\Delta^{5,7,9(11)}$-pregnatriene-3β-ol-20-one acetate (II) was described.

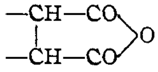


I, R(H) = O
II, R = $COCH_3$



III,ᵃ R(H) = O
IV,ᵃ R = $COCH_3$

ᵃ MA =



In this note, we wish to record the preparation of the maleic anhydride adduct products of these two trienes, and also to describe the pyrolysis of one of the adducts.[3] Compounds I and II readily reacted with maleic anhydride in xylene[4] at reflux temperature, and III and IV were obtained in good yield.

The maleic anhydride adduct (IV) of $\Delta^{5,7,9(11)}$-pregnatriene-3β-ol-20-one acetate was pyrolyzed in such a manner that the pyrolysis and evaporative distillation were carried out simultaneously (0.16 mm. pressure,[5] 200–313°). These conditions led to co-distillation of a considerable amount of IV with the desired triene (II). Compound II was easily separated from IV by treatment of the distillate with ether; the adduct product was insoluble. The triene (II) so obtained was identical with an authentic sample of II.

Experimental

Maleic Anhydride Adduct (III) of $\Delta^{5,7,9(11)}$-Androstatriene-3β-ol-17-one Acetate.—A mixture of 1 g. of $\Delta^{5,7,9(11)}$-androstatriene-3β-ol-17-one acetate (I), 0.4 g. of maleic anhydride and 50 ml. of xylene was refluxed for 18 hours. The solvent and excess maleic anhydride were removed *in*

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[1] Paper X, R. Antonucci, S. Bernstein, D. J. Giancola and K. J. Sax, *J. Org. Chem.*, in process of publication.

[2] R. Antonucci, S. Bernstein, D. J. Giancola and K. J. Sax, *ibid.*, **16**, 1159 (1951).

[3] The addition of maleic anhydride to a $\Delta^{5,7,9(11)}$-triene (dehydroergosteryl acetate), and the pyrolysis of the resulting adduct have been described previously; see Windaus and Lüttringhaus, *Ber.*, **64**, 850 (1931), and Honigmann, *Ann.*, **508**, 89 (1934).

[4] Benzene was not used in place of xylene in the reaction, but probably would be successful; see Bergmann and Stevens, *J. Org. Chem.*, **13**, 10 (1948).

[5] Subsequently, experience in this Laboratory with other similar compounds has shown that a pressure of 1–2 mm. would be preferable for this type of pyrolysis.