The Acyloin Condensation. III. The Conjugate Addition of Some α,β-Unsaturated Esters, Followed by a Dieckmann Cyclization[1]

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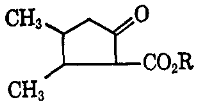
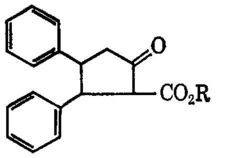
Recent work[3,4] has shown that alkyl α,β-unsaturated esters containing a β-phenyl group in the acid moiety, when refluxed with finely divided sodium in ether undergo 1,4-conjugate addition, followed by a Dieckmann cyclization, and that the reaction is general. It has been further shown that the size of the group in the alcohol moiety pronouncedly affects the yield in this reaction.[3,4] It has also been shown that positive and negative groups in the *ortho* or *para* position in the phenyl moiety cause higher and lower yields, respectively.

Table I

5-Oxo-2,3-dimethylcyclopentanecarboxylic Acid Alkyl Esters[a]



Compd	Structure	Formula	Calcd, %		Found, %		Mp, °C	% yield
			C	H	C	H		
I	R = cyclohexyl	Liquid					23, 96–100° (5 mm)	23
II	R = ethyl	Liquid					22, 79–85° (5 mm)	21
Ia	2,4-Dinitrophenylhydrazone of I	$C_{20}H_{26}N_4O_6$	57.40	6.26	57.45	6.47	139	
Ib	Oxime of I	$C_{14}H_{23}N_2O_3$	66.63	9.58	66.55	9.30	101–102	
IIa	2,4-Dinitrophenylhydrazone of II	$C_{16}H_{20}N_4O_6$	52.64	5.53	53.43	5.35	136–137	
	5-Oxo-2,3-diphenylcyclopentanecarboxylic Acid Alkyl Esters 							
III	R = 2-octyl	$C_{26}H_{32}O_3$	79.55	8.22	79.08	7.74	66–67	27
IV	R = *n*-hexyl	$C_{24}H_{28}O_3$	79.08	7.74	79.02	7.83	59–60	16
IVa	Oxime of IV	$C_{24}H_{29}NO_3$	75.96	7.70	75.81	7.71	111–112	
V	R = 2-ethoxyethyl	$C_{22}H_{24}O_4$	74.97	6.87	75.09	7.03	65–66	15
Va	2,4-Dinitrophenylhydrazone of V	$C_{28}H_{28}N_4O_7$	63.33	5.30	63.23	5.15	137–139	
Vb	Oxime of V	$C_{22}H_{25}NO_4$	71.91	6.85	71.70	6.94	88–89	
VI	R = methyl	$C_{19}H_{18}O_3$	77.53	6.16	77.74	6.16	122–123	*Ca.* 15
VIa	3,5-Dinitrobenzoate of VI	$C_{26}H_{20}N_2O_8$	63.93	4.12	63.83	4.16	151–152	
VIb	2,4-Dinitrophenylhydrazone of VI	$C_{25}H_{22}N_4O_6$	63.28	4.64	63.23	4.75	189–190	

[a] All compounds were recrystallized from 95% alcohol except III, which was recrystallized from petroleum ether (bp 30–60°).

It was interesting to observe in the work described in this article that the generality of this reaction extended to α,β-unsaturated esters with a small substituent in the β position of the acid moiety and to α,β-unsaturated esters with relatively long chains in the alcohol moiety and to methyl cinnamate.

For α,β-unsaturated esters containing small substituents in the acid moiety, ethyl acrylate, cyclohexyl crotonate, and ethyl crotonate were used. When both cyclohexyl crotonate and ethyl crotonate, respectively, were refluxed with finely divided sodium in ether, the respective conjugate addition–cyclization products I and II were produced. Ethyl acrylate gave only a viscous substance.

The α,β-unsaturated esters containing relatively long chains in the alcohol moiety used were 2-octyl cinnamate, *n*-hexyl cinnamate, and 2-ethoxyethyl cinnamate.

These esters ran smoothly in the above described reaction to give, respectively, modest yields of the conjugate addition–cyclization products III–V. Methyl cinnamate in this reaction gave a corresponding product VI.

The constitution of these condensation products I–VI (Table I) were demonstrated by carbon and hydrogen analyses and by their infrared spectra. Compounds I and II gave 2,4-dinitrophenylhydrazones and I also gave an oxime. These analyzed correctly. Compounds III–VI were crystalline solids. These compounds analyzed correctly. Compounds IV and V gave oximes, V and VI gave 2,4-dinitrophenylhydrazones, and VI gave a 3,5-dinitrobenzoate. Each of these derivatives analyzed correctly. Compounds I–VI absorbed strongly in the infrared at about 5.7–5.8 μ, giving a doublet. This doublet has been shown to be characteristic for the β-carbalkoxycyclopentanone group.[3,4]

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(3) E. L. Totton, R. C. Freeman, H. Powell, and T. Yarboro, *J. Org. Chem.*, **26**, 343 (1961).

(4) E. L. Totton, G. R. Kilpatrick, N. Horton, and S. Blakeney, *ibid.*, **30**, 1647 (1965).

Experimental Section[5]

The procedure described for the synthesis of IV is general and was used to prepare the condensation products described in this work.

Cyclopentanecarboxylic Acid 5-Oxo-2,3-diphenyl-*n*-hexyl Ester (IV).—In a 2-l. three-necked flask fitted with a stirrer and a reflux condenser carrying a drying tube, there was placed 23 g (1 g-atom) of sodium. After finely dividing the sodium by rapid stirring in hot xylene and decanting the xylene, the flask was half-filled with dry ether. To the flask, from a separatory funnel, there was added 116.2 g (0.50 mole) of *n*-hexylcinnamate in 100 ml of dry ether, slowly with stirring, at such a rate that gentle reflux was maintained. After the addition, the reaction mixture was refluxed for 14 hr longer. The excess sodium was destroyed by the careful addition of 100 ml of 37% sulfuric acid through the condenser, while the reaction mixture was cooled and stirred. The sodium sulfate was separated by filtration, and the water was removed from the ether layer in a separatory funnel. The sodium sulfate was triturated with two 75-ml portions of ether and the ether washings were added to the ether layer in the separatory funnel. The ether solution was washed successively with four 75-ml portions of 20% sodium carbonate followed by washing with four 75-ml portions of distilled water and dried over anhydrous sodium sulfate. The ether was removed under reduced pressure with a water pump, and the residue, a brown syrup, was placed in the freezer. A solid product formed. The product was recrystallized from petroleum ether (bp 30–60°). A pure dried sample melted at 59–60°. The product weighed 14.7 g, a yield of 16.2% of theory based on the ester.

Registry No.—I, 10498-72-3; Ia, 10498-73-4; Ib, 10498-74-5; II, 10498-75-6; IIa, 10498-76-7; III, 10498-77-8; IV, 10498-78-9; IVa, 10498-79-0; V, 10498-80-3; Va, 10498-81-4; Vb, 10498-82-5; VI, 10498-83-6; VIa, 13090-95-4; VIb, 10498-84-7.

Acknowledgment.—The authors wish to express their appreciation to Dr. R. H. Eastman of Stanford University, Stanford, Calif., for the infrared spectra in this work.

[5] (a) Melting points were taken on a Fisher-Johns apparatus. (b) Analyses were performed by Micro-Tech Laboratories, Skokie, Ill.

Reaction of Methyl and Ethyl 2-Cyclopentanonecarboxylates with Amines to Give Carbinolamines, Enamines, and Adipamides

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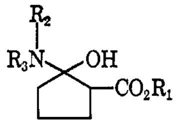
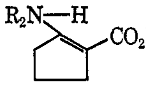
Our interest in the reaction of amines with esters of 2-cyclopentanonecarboxylic acid was stimulated by a study of the reactions of chlorophyll with amines.[1] Chlorophyll and many chlorophyll derivatives have a β-keto ester cyclopentenone ring which is readily opened by both primary and secondary amines to give ester amides.[1,2] It was desirable to study an analogous cyclic β-keto ester, to compare the relative ease of ring cleavage, and to observe what other reactions with amines might be expected.

Dieckmann was the first to study systematically the reactions of ethyl 2-cyclopentanonecarboxylate. He noted that ammonia added to the carbonyl group to give a white, crystalline solid which he suggested might be the carbinolamine or an ammonium salt.[3] More recently, Treibs, Mayer, and Madejski found that ethyl 2-cyclopentanonecarboxylate readily gave a precipitate with benzylamine and proposed that a carbinolamine (Ia) was formed.[4] These products were both relatively unstable. They decomposed in air to give back the starting ester and base, and they were dehydrated by heating or standing to give enamines. Dieckmann also reported that the predominant product on heating the ester with ammonia was adipamide.



Ia, $R_1 = CH_3CH_2$; $R_2 = H$; $R_3 = C_6H_5CH_2$
b, $R_1 = CH_3$; $R_2 = H$; $R_3 = CH_3CH_2CH_2$
c, $R_1 = CH_3$; $R_2 = H$; $R_3 = (CH_3)_2CHCH_2$
d, $R_1 = CH_3$; $R_2 = H$; $R_3 = (CH_3)_3C$
e, $R_1 = CH_3$; $R_2, R_3 = (CH_2)_5$



IIa, $R_1 = CH_3CH_2$; $R_2 = C_6H_5CH_2$
b, $R_1 = CH_3$; $R_2 = CH_3CH_2CH_2$
c, $R_1 = CH_3$; $R_2 = (CH_3)_2CHCH_2$
d, $R_1 = CH_3CH_2$; $R_2 =$ α-naphthyl
e, $R_1 = CH_3CH_2$; $R_2 =$ 8-quinolinyl
f, $R_1 = CH_3$; $R_2 = (CH_3)_2N$

We have found that many amines give comparable products with the 2-cyclopentanonecarboxylates. Our titration data clearly indicate a 1:1 complex or carbinolamine. An infrared spectrum as a mineral oil mull supports the carbinolamine structure since there is evidence of a chelated ester carbonyl. But when these products are dissolved in carbon tetrachloride, their infrared spectra exhibit a ketone carbonyl absorption and appear to be simply a mixture of ester and amine.

Mayer[5] reviewed the reactions of ethyl 2-cyclopentanonecarboxylate with amines and concluded that dehydration of the carbinolamines led to ketimines. Although Treibs, Mayer, and Madejski had earlier proposed that an enamine was formed by heating the carbinolamine Ia, Mayer assigned the ketimine structure to the product, preferring an exocyclic double bond because of steric factors.

Our data support an enamine structure rather than the ketimine structure for the dehydrated benzylamino product (IIa). We have also found that enamines (II) are readily formed at room temperature when methyl 2-cyclopentanonecarboxylate is treated with benzylamine, propylamine, isobutylamine, and *unsym*-dimethylhydrazine in solvents such as tetrahydrofuran and methanol.

Ultraviolet, infrared, and nmr spectra establish the structure of the enamines unequivocally. Our ultraviolet molar absorptivities and λ_{max} values are comparable with those reported by Hay and Caughley for

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[3] W. Dieckmann, *ibid.*, **317**, 37 (1901).

[4] W. Treibs, R. Mayer, and M. Madejski, *Ber.*, **87**, 356 (1954).

[5] R. Mayer, "Newer Methods of Preparative Organic Chemistry," Vol. II, W. Foerst, Ed., Academic Press Inc., New York, N. Y., 1963, pp 101–131.