Reactions of Ethyl β -Methoxycrotonate with some α, β -Unsaturated Carbonyl Compounds. Synthesis of 6-Aroyl-5-aryl-3-methoxycyclohex-2-enones

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3-Aryl-1-phenyl-2-propen-1-ones Ia-h and 1-aryl-3-phenyl-2-propen-1-ones Ii- ℓ reacted with ethyl β -methoxy-crotonate (II) in the presence of sodium hydride in dry THF at 0° for 10 hours to give the corresponding 6-aroyl-5-aryl-3-methoxy-2-cyclohexen-1-ones III. The structures of the products were confirmed by ir, pmr, ¹³C nmr and uv spectroscopy.

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Some reactions of ethyl β -methoxycrotonate (II) have been reported previously in the synthesis of some naturally occurring oxygen ring compounds [1-4].

In conjunction with our studies of the reaction of α,β -unsaturated compounds [5-10] we thought it might be of interest to extend this work to the synthesis of 6-aroyl-5-aryl-3-methoxycyclohex-2-enones III, since compounds of related structure were prepared from the reactions of α,β -unsaturated ketones with carbonyl compounds [11-15].

It has been shown that, in the presence of a base, ethyl β -methoxycrotonate (II) condenses with carbonyl compounds in a Stobbe like reaction [13]. This fact which indi-

Scheme I

$$H_{3}CO \xrightarrow{H} OE1 \xrightarrow{NGH} THF$$

$$H_{3}CO \xrightarrow{H} OE1 \xrightarrow{THF} CH_{3}CO \xrightarrow{H} OE1$$

$$H_{3}CO \xrightarrow{H} OE1 \xrightarrow{Ar'} O \xrightarrow{Ar'} OE1$$

$$CH_{3}O \xrightarrow{H} OE1 \xrightarrow{Ar'} O \xrightarrow{Ar'} OE1$$

$$CH_{3}O \xrightarrow{H} OE1 \xrightarrow{Ar'} O \xrightarrow{Ar'} OE1$$

Compounds I and III

a	$Ar = C_6H_5$	$Ar' = C_6H_5$
b	$Ar = C_6H_5$	$Ar' = p-ClC_6H_4$
c	$Ar = C_6H_5$	$Ar' = o-ClC_6H_4$
d	$Ar = C_6H_5$	$Ar' = p - BrC_6H_4$
e	$Ar = C_6H_5$	$Ar' = p-CH_3OC_6H_4$
f	$Ar = C_6H_5$	$Ar' = o - CH_3OC_6H_4$
g	$Ar = C_6H_5$	$Ar' = p-CH_3C_6H_4$
h	$Ar = C_6H_5$	$Ar' = o-Cl_2C_6H_3$
i	$Ar = p \cdot CH_3C_6H_4$	$Ar' = C_6H_5$
j	$Ar = p - ClC_6H_4$	$Ar' = C_6H_5$
k	$Ar = p-CH_3OC_6H_4$	$Ar' = C_6H_5$
l	$Ar = o\text{-}ClC_6H_4$	$Ar' = C_6H_5$

cates the ability of the mesomeric anions of the starting ester to react as a γ -carbanion, prompted us to study the reaction of this ester with α,β -unsaturated ketones, some nitrogen containing compounds [16], substituted carbonyl compounds [17] and substituted benzaldehydes through the synthesis of substituted dihydro-2-pyrones [18] under similar conditions.

In the present work, the reactions of chalcones with ethyl β -methoxycrotonate were investigated. These reactions afford 6-aroyl-5-aryl-3-methoxycyclohex-2-enones. It seems that these reactions proceed by a conjugate addition of the ester anions to the chalcones followed by an intramolecular Claisen condensation to give the corresponding substituted 2-cyclohexen-1-ones (Scheme 1).

The structure of products IIIa-g was deduced from the spectral data (Table II and III). The ir spectral data showed the absence of an ester group and the appearance of a band at 1695-1675 cm⁻¹ corresponds to the conjugated carbonyl while the band at 1665-1645 cm⁻¹ corresponds to the exocyclic carbonyl.

The nmr spectra were used to determine the presence of the enolic nature of the diones IV as well as to achieve an unambiguous structure assignment (Scheme II).

The absence of low field values corresponding to the exchangeable proton at δ 14-16 indicates that either the tautomers IV a and b are not present under these conditions or that they are present in a very small amount, *i.e.* mainly as a 1,3-diketone. This 1,3-diketone was proved by the reaction of one of these compounds, IIIa, with hydrazine hydrate to give a substituted dihydroindazole V as white needles mp 196-197°.

Table I

Physical and Analytical Data of Compounds III

Compound Yield		M.P.°C	Formula	Analysis Found %	Calcd./
No.	%	Solvent(s)		C	Н
a	42	141-142	$C_{20}H_{18}O_{3}$	78.43	5.88
		Benzene		78.51	5.72
b	45	149-150	$C_{20}H_{17}ClO_3$	70.58	5.00
		Ethanol		70.52	5.08
c	42	172-173	$C_{20}H_{17}ClO_3$	70.58	5.00
		Ethanol		70.43	5.12
d	34	149-150	$C_{20}H_{17}BrO_3$	62.17	4.61
		Ethylacetate		62.03	4.51
e	44	150-151	$C_{21}H_{20}O_{4}$	75.00	5.95
		Ethanol		75.10	5.89
f	45	138-140	$C_{21}H_{20}O_{4}$	75.00	5.95
		Ethanol		74.94	5.81
g	44	144-145	$C_{21}H_{20}O_3$	78.75	6.25
		Ethanol	2	78.49	6.13

The 'H nmr spectroscopic data for compounds IIIa-g in deuteriochloroform solution were carefully studied and are given in Table II. Our assignment of these structures is based upon the proton magnetic resonance studies of similar compounds [15]. These compounds show four important peaks at δ 5.32-5.46, 3.8-4.4, 4.48-4.94 and 2.64-2.92 with intensities corresponding to one hydrogen each except in some examples which correspond to two hydro-

gens. These peaks correspond to H-2, H-5, H-6 and H-4 respectively.

Since the carbon-13 spectra are more sensitive to changes in structures, an examination of the carbon-13 spectra of compounds IIIb and IIIg was undertaken. The results of this investigation are summarized in Table III.

The non-aromatic regions are characterized by the presence of eight signals. The shifts of the O- and C-methyl groups and the carbonyl function are derived from chemical shift theory [13]. The quaternary carbons C-1, C-3 and the Ar-C=O resonance at ca. 198, 177 and 195 ppm are distinguished from other signals by its multiplicaty in the off-resonance experiments. In the case of the remaining carbons, C-2 resonates at 102.2, C-4, C-5, C-6 and CH₃O resonates at 35.8, 41.4, 56.0 and 59.2 ppm respectively for IIIb and resonates at 36.0, 41.7, 56.0 and 59.5 ppm respectively for compounds IIIg. The above assignments were made on the basis of model compounds [19] and single-frequecy off-resonace decoupling.

EXPERIMENTAL

The ir spectra were obtained in Nujol mulls on a Beckman Acculab T-M spectrophotometer. The uv absorption spectra were recorded in methanol or chloroform on a Pye Unicam SP 8-200 spectrophotometer. The nmr spectra were taken on a Bruker WH 90 Ds spectrometer equipped with ASPECT 2000, 32 K Computer, operating at 22.63 MHz. Melting points are uncorrected. Elemental analysis were performed by Alfred Bernhardt Laboratories, Ruhr, Germany.

Preparation of Ethyl β -Methoxycrotonate II [20].

Ethyl acetoacetate (130 g) was mixed with redistilled trimethylorthoformate (106 g) and dry methanol (100 ml), and then concentrated hydro-

Table II
Spectral Data of Compounds III

Compound	Infrared	Bands (Nujol) [h]		Nucle	ar Magnetic Re	esonance Value	es [a] δ	
No.	(cm ⁻¹)	Assignments	H-2 [b]	H-4 [c]	H-5 [d]	H-6 [e]	OMe [f]	Ar-H [g]
a	1695 1658	conjugated C=0 exocyclic C=0	5.44	2.76	3.92	4.62	3.68	7.2-7.72
ь	1687 1665	conjugated $C = 0$ exocyclic $C = 0$	5.44	2.72	3.9	4.6	3.7	7.1-7.76
c	1675 1645	conjugated $C = 0$ exocyclic $C = 0$	5.46	2.92	4.4	4.84	3.72	7.75-7.88
d	1685 1650	conjugated $C = 0$ exocyclic $C = 0$	5.4	2.7	3.88	4.56	3.68	6.86-7.77
e [i]	1675 1645	conjugated C=0 exocyclic C=0	5.32	2.64	3.8	4.48	3.6	6.52-7.66
f [j]	1685 1655	conjugated $C = 0$ exocyclic $C = 0$	5.4	2.86	4.08	4.96	3.68	6.56-7.8
g [k]	1690 1660	conjugated $C = 0$ exocyclic $C = 0$	5.44	2.75	3.9	4.9	3.7	6.82-7.8

[[]a] Deuteriochloroform was used as a solvent: [b] s, 1H. [c] s, 2H. [d] Sextet, 1H. [e] d, 1H, $J_{5,6} = 11$ -13.5 Hz. [f] s, 3H. [g] m, 10H for compound a and 9H for compounds b-g. [h] Only absorption bands in the more significant range 1800-1500 cm⁻¹ were reported. [i] 3.56, s, 3H, OCH₃. [j] 3.7, s, 3H, OCH₃. [k] 2.2, s, 3H, CH₃.

Table III

Carbon-13 Chemical Shifts (δ) for Compounds III

	IIIb	IIIg [b]
C-1	198.155	198.480
C-2	102.229	102.229
C-3	177.098	177.488
C-4	35.875	36.070
C-5	41.464	41.724
C-6	56.086	56.021
Ar-C=0	195.100	195.555
CH ₃ O	59.271	59.596
Aromatic	139.859, 137.974	138.364, 136.804
Carbons	133.165, 129.785	132.905, 129.466
	128.680, 127.511	128.680, 127.966, 127.121

[a] Deuteriochloroform was used as a solvent. [b] 20.992, CH₃.

chloric acid (0.5 ml) was added. The mixture was distilled immediately to give ethyl β -methoxycrotonate (144 g, 100 %), bp 188-194°.

6-Aroyl-5-aryl-3-methoxy-2-cyclohexenones III. General Procedure.

A mixture of 1,3-diaryl-2-propen-1-ones I (0.05 mole), 75 ml of dry THF and ethyl β -methoxycrotonate (II) (0.05 mole) was added to a suspension of sodium hydride (0.05 mole) in 75 ml of dry THF at 0°. The mixture was stirred for 10 hours at 0°, quenched with water (15 ml) and acidified with dilute hydrochloric acid to pH 7. The water layer is extracted with ethyl acetate (3 \times 100 ml). The combined ethyl acetate solutions were dried with magnesium sulfate. After evaporation of the solvent under vacuum, crystallisation of the residue from the appropriate solvent, the presponding products were obtained (Table I).

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