Enol Benzoates of β-Diketones

By John Larkin, Michael G. Murray, and Derek C. Nonhebel,* Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL

Alastair D. Mitchell,* Department of Chemistry, Paisley College of Technology, Paisley

The structures of enol benzoates of substituted dibenzoylmethanes have been determined: in all cases benzoylation occurs at the carbonyl oxygen atom adjacent to the more electron-withdrawing aryl group. Benzoylacetone forms isomeric E- and Z-enol acetates and benzoates, reaction occurring at the oxygen atom of the acetyl group. A mechanism for the formation of enol benzoates of β -diketones is proposed.

ENOL esters of β -diketones are obtained by the reaction of β -diketones with acyl halides in pyridine ^{1,2} and, together with triacylmethanes, from reactions of metal chelates of β -diketones with acyl halides.^{2,3-6} Acylbenzoylmethanes invariably undergo acylation on the carbonyl oxygen atom adjacent to the alkyl group, irrespective of the size of the alkyl group in the diketone,

² H. D. Murdoch and D. C. Nonhebel, J. Chem. Soc., 1962, 2153.

or of electronic or steric effects in the acyl chloride.^{2,5-7} The product from these reactions is thus the thermodynamically less stable of the two isomeric enol esters. There are no reports of acylation at more than one of the two carbonyl oxygen atoms of unsymmetrical β-diketones, though O-methylation of certain β -diketones has given mixtures of isomeric methyl ethers as a result of attack at both carbonyl oxygens.⁸ This work was

⁶ M. G. Murray and D. C. Nonhebel, J. Chem. Soc. (C), 1970, 1172.

¹ L. Claisen, Ber., 1903, 36, 3674.

 ³³ L. Claisen, Ber., 1893, 26, 1893.
 ⁴ D. C. Nonhebel and J. Smith, J. Chem. Soc. (C), 1967, 1919.
 ⁵ H. D. Murdoch and D. C. Nonhebel, J. Chem. Soc. (C), 1968, 2298.

⁷ L. J. Roll and R. Adams, J. Amer. Chem. Soc., 1931, 53, 3469.

⁸ R. D. Campbell and H. M. Gilow, J. Amer. Chem. Soc., 1960, 82. 2389.

undertaken to see what factors controlled the position of acylation in substituted dibenzoylmethanes with a view to elucidating the mechanism of these reactions.

atom. In contrast to previous work, it was found that both acetylation and benzoylation afforded two products, the *E*- and *Z*-3-acyloxy-1-phenylbut-2-en-3-ones (4 and 5; $\mathbb{R}^1 = \mathbb{P}h$). That the two compounds were *cis-trans* isomers was established by their hydrogenation and hydrogenolysis to butyrophenone. Two enol benzoates

Benzoylation of substituted dibenzoylmethanes occurred at the carbonyl oxygen atom adjacent to the more electron-withdrawing aryl group (Table 1). The

IABLE I							
Enol benzoates of	β-diketones	R ¹ C(OBz	=CH·COF	₹2]		

		M p.	Recryst.	Fo	und (%	5)		Req	uired (%)	Method of identi-
\mathbf{R}^{1}	R²	(°C)	from *	Гс	н	N	Formula	C	н	ΝŪ	fication †
p-NO ₂ ·C ₆ H ₄	\mathbf{Ph}	155	\mathbf{PhMe}	70.8	4.05	3.56	$C_{22}H_{15}NO_5$	70.8	4.05	3.75	Α
m-BrC,H,	Ph	100	PhH-Pet	65.0	3.6		$C_{22}H_{15}BrO_3$	64.9	3.7		В
m-MeO·C ₆ H ₄	Ph	105	PhH-Pet	77.0	5.0		$C_{23}H_{18}O_4$	77.1	5.0		A
$p - MeC_{B}H_{A}$	$p-MeO \cdot C_8H_4$	130	PhH-Pet	77.2	5.6		$C_{24}H_{20}O_4$	77.4	5.4		В
Ph	<i>p</i> -MeC _e H _₄	102 - 103	PhH-Pet	81.0	5.4		$C_{23}H_{18}O_3$	80.7	5.3		A, C
\mathbf{Ph}	<i>p</i> -MeO·C ₆ H₄	9899	\mathbf{Pet}	77.3	5.1		$C_{23}H_{18}O_4$	77.1	5.1		A, C
Ph	p-BrC ₆ H ₄	122 - 123	PhH-Pet	64.6	3.9		$C_{22}H_{15}BrO_3$	64.9	3.7		A, C
Ph	p-ClC,H	98100	Et ₂ O	73.0	4.7		$C_{22}H_{15}ClO_3$	72.8	4.4		C
\mathbf{Ph}	3,4-(CH,O,)C,H,	98 - 100	Pet	74.6	4.5		$C_{23}H_{17}O_5$	74.1	4.5		\mathbf{D}
β -C ₁₀ H ₂	Ph	150 - 151	PhH	82.2	5.2		$C_{26}H_{14}O_{3}$	82.5	4.8		\mathbf{D}
Ph	2-Furyl	140	CH ₂ Cl ₂ -Hex	75.1	4.4		$C_{20}H_{14}O_4$	75.5	4.4		Α
Ph	2-Thienyl	118	CH ₂ Cl ₂ -Hex	72.3	4.5		$C_{20}H_{14}O_3S$	71.8	4.2		Α
2-Pyridyl	Ph	127	CH ₂ Cl ₂ Hex	76.9	4.9	4.5	$C_{21}H_{15}NO_3$	76.6	4.6	4.3	Α

* Pet = light petroleum; Hex = hexane. \dagger A, by comparison of u.v. spectrum with spectra of chalcones; B, by reduction and hydrogenolysis to R¹CH₂·CH₂·COR²; C, as for B but product isolated as its 2,4-dinitrophenylhydrazone; D, by hydrogenolysis to chalcone, R¹CH=CH·COR².

TABLE 2

U.v. spectra of enol benzoates and chalcones

R1	\mathbb{R}^2	R ¹ C(OBz)=CH·COR ²	$\lambda_{max./nm}$ (ε) R ¹ CH=CH·COR ²	R ¹ CO·CH=CHR ²
$p-NO_2 \cdot C_6H_4$	Ph	306 (19 000)	306 (20 700)	313 (18 500)
Ph Ph	$p-MeC_6H_4$ $p-MeO\cdotC_6H_4$	313 (20 200) 313 (22 500)	312 (21 900) 312 (25 900)	334 (21 000) 334 (26 900)
m-MeO·C ₆ H ₄	Ph 9 From 1	300 (18 000)	302 (19 000) 204 (10 700)	300 (22 000)
Ph	2-Furyl 2-Thienyl	324 (13 320) 314 (16 450)	324 (10 700) 320 (19 300)	344 (26 800) 345 (19 200)
2-Pyridyl	Ph	302 (12 160)	303 (10 500)	318 (14 500)

same pattern was true for the enol benzoates of benzoyl-2-furoylmethane, benzoyl-2-thienoylmethane, and benzoylpicolinoylmethane, benzoylation occurring at the benzoyl oxygen atom in the first two cases and at the picolinoyl oxygen atom in the last. Identities of the enol benzoates were established by hydrogenation and hydrogenolysis to give the saturated ketones (2). In were also obtained from acetylacetone. This can only be explained by *cis-trans* isomerism. During this work isomeric *cis-* and *trans*-enol acetates of acetylacetone from the reaction of acetylacetone with isopropenyl acetate were reported.⁹ Structures of our products were assigned by comparison of their n.m.r. spectra with those of the analogous E- and Z-O-acetyl derivatives of

$$R^{1}C(OBz) = CH \cdot COR^{2} \longrightarrow R^{1}CH_{2} CH_{2} \cdot COR^{2} \longrightarrow R^{1}CH = CH \cdot COR^{2}$$
(1)
(2)
(3)

some instances reduction also afforded some of the corresponding carbinol. This was reoxidised to the ketone with chromic oxide. Comparison of the reduction product with the reduction product of the appropriate chalcone (3) gave the structure of the enol benzoate. An alternative method of establishing the structures of the enol benzoates (1) was to compare the positions of their u.v. absorption maxima with those of the corresponding chalcones (3). These were significantly different from that of the isomeric chalcones, $R^2CH=CH+COR^1$ (see Table 2). In no instance was more than one enol benzoate obtained.

Reinvestigation of benzoylacetone was undertaken to confirm the absence of attack at the benzoyl oxygen acetylacetone.⁹ The chemical shift of the methine proton in the *E*-isomer is further downfield than in the *Z*-isomer and the signal appears as a quartet $(J \ 1 \ \text{Hz})$



as a result of splitting by the methyl group attached to the double bond (Table 3). This latter thus gives rise to a doublet in the spectrum of the E-isomer. The E- and Z-isomers underwent ready interconversion.

⁹ D. V. C. Awang, Canad. J. Chem., 1973, 51, 3752.

When benzoylation of benzoylacetone was carried out at various temperatures it was found that the proportion of the *E*-isomer increased from 33% at 40 °C to

TABLE 3

N.m.r. data for E- and Z-enol esters (δ values; solvent CCl₄)

Structure	\mathbf{R}^{1}	\mathbb{R}^2	н	Me	Ref.
(4)	Me	Me	5.98	2.25 (d. / 1.3 Hz)	9
(5)	Me	Me	5.72 (s)	2.13 (s)	9
(4)	Me	\mathbf{Ph}	6.26 (q, J 1 Hz)	2.38 (d, J 1 Hz)	
(5)	Me	\mathbf{Ph}	5.90 (s)	2.13 (s)	
(4)	\mathbf{Ph}	Me	6.78 (q, J 1 Hz)	2.35 (d, J 1 Hz)	
(5)	\mathbf{Ph}	Me	6.51 (s)	2.22 (s)	
(4)	\mathbf{Ph}	\mathbf{Ph}	6.90 (q, J 1 Hz)	2.46 (d, / 1 Hz)	
(5)	\mathbf{Ph}	\mathbf{Ph}	6.53 (s)	2.15 (s)	

66% at -10 °C, possibly indicating that this isomer is the kinetically preferred product.

A possible interpretation of the mechanism of the reaction is shown in the Scheme. The function of the



pyridine is to disrupt the intramolecularly hydrogenbonded enolic system giving rise to a complexed *trans*enol which then reacts with the benzoylpyridinium ion. Pyridine is an insufficiently strong base to effect the formation of an enolate anion though it clearly does interact with the β -diketone. The n.m.r. spectra of benzoylacetone and other β -diketones in pyridine showed immediate disappearance of the enolic proton signal on addition of deuterium oxide but the methine proton signal had not changed even after 5 days. When a trace of sodium deuterioxide was introduced the methine proton exchanged rapidly as the enolate ion was then present in the system.

The reaction is tentatively considered to involve the *trans*-enol, since the E-isomer appears to be the kinetically preferred product. The site of reaction is consistent with the proposed scheme in that the preferred *trans*-enol of benzoylacetone is undoubtedly that in which there is the more extended conjugated system. In substituted dibenzoylmethanes the more electronrich carbonyl group is that which is preferentially enolized, thus giving rise to attack at the more electrondeficient carbonyl oxygen atom.

EXPERIMENTAL

3-Acetoxy-1-phenylbut-2-en-1-one.—A mixture of benzoylacetone (5.1 g, 0.03 mol), anhydrous pyridine (25 ml), and acetyl chloride (3.2 g, 0.04 mol) was shaken for 1 h at 25 °C. Cold water (100 ml) was added and shaking continued for a further 2 h. The mixture was extracted with ether and the extract washed in turn with dilute hydrochloric acid, water, and sodium hydroxide solution until treatment of the organic layer with iron(III) chloride showed no trace of diketone. The ethereal extract was washed with cold water and dried (Na_2SO_4). Distillation gave the enol acetate of benzoylacetone (4 g, 65%), b.p. 125-130° at 2 mmHg (lit.,⁷ 120-122° at 2 mmHg).

T.l.c. of this enol acetate on silica gel in hexane-ether (6.5:1.5) showed the presence of two compounds in equal proportions. These were separated by t.l.c. and extracted with ether. Each solution was re-chromatographed as before. In both cases a fresh spot appeared corresponding to the other component. When the ether solutions were set aside for 3 h, 24 h, and 48 h and then re-chromatographed, increasing amounts of the other compound were found to be present. Chromatography on a column of alumina in hexane-ether (8.5:1.5) gave (E)-3-acetoxy-1-phenylbut-2-en-1-one. Further elution with the same solvent gave the (Z)-isomer.

O-Benzoyl Derivatives of β -Diketones.—The β -diketone (0.025 mol) and benzoyl chloride (0.0375 mol) in anhydrous pyridine (15 ml) were shaken at 25 °C for 1 h. Cold water (50 ml) was added and shaking continued for 2 h. The mixture was extracted with ether and the extract washed in turn with hydrochloric acid (1:1), water, and sodium hydroxide solution until the ether layer showed no trace of diketone (FeCl₃ test). The ether layer was washed with cold water, dried (Na₂SO₄), and passed through an alumina column (5 g) to remove tarry materials. Evaporation gave the crude enol benzoate, which was crystallised from the appropriate solvent (see Table 1).

3-Benzoyloxy-1-phenylbut-2-en-1-one.—This was prepared by the above method as a viscous oil; in order to avoid possible isomerisation it was not distilled. T.l.c. [hexaneether (8.5:1.5)] showed the presence of two compounds and the same slow interconversion as found with the enol acetate. Chromatography on an alumina column [hexaneether (8.5:1.5)] afforded (E)-3-benzoyloxy-1-phenylbut-2-en-1-one followed by the (Z)-isomer.

Hydrogenolysis of the Enol Acetate of Benzoylacetone.— Benzoylacetone enol acetate (5.0 g, 0.025 mol) in glacial acetic acid (25 ml) was hydrogenated at room temperature and atmospheric pressure over Adams catalyst (0.1 g) until absorption ceased (1 200 ml; 2.25 mol per mol of enol acetate). The catalyst was filtered off and the filtrate stirred with 8N-chromic acid (5 ml). A solution of sodium hydrogen sulphite was added and the mixture was then extracted with ether. The ether layer was washed with dilute hydrochloric acid and then dried and evaporated, leaving butyrophenone (2.5 g, 68%).

Hydrogenolyses of Enol Benzoates.—These were carried out as described above. The enol benzoate of benzoyl- β -naphthoylmethane gave β -naphthylmethyleneacetophenone, m.p. and mixed m.p. 164°, which on treatment with Brady's reagent gave β -naphthylmethyleneacetophenone 2,4-dinitrophenylhydrazone, m.p. 236° (Found: C, 68.2; H, 4.4; N, 12.3. C₂₅H₂₀N₄O₄ requires C, 68.2; H, 4.6; N, 12.7%).

Hydrogenations of Chalcones.—These were carried out in the same manner. Reduction of 4'-bromochalcone afforded β -phenyl-p-bromopropiophenone as plates (from petroleum), m.p. 101° (Found: C, 62.6; H, 4.8; Br, 27.8. C₁₅H₁₃BrO requires C, 62.3; H, 4.5; Br, 27.6%).

The 2,4-dinitrophenylhydrazone of β -(m-bromophenyl)propiophenone was obtained, by treatment of the reduction product of 3-bromochalcone with Brady's reagent, as orange needles (from benzene-petroleum), m.p. 202–203° (Found: C, 53.2; H, 3.85; N, 11.95. $C_{21}H_{16}BrN_4O_4$ requires C, 53.7; H, 3.65; N, 11.95%). Reduction of 4'-methoxy-4-methylchalcone similarly gave, after treatment with Brady's reagent, the 2,4-dinitrophenylhydrazone of β -(p-tolyl)-p-methoxypropiophenone as orange needles

(benzene), m.p. 201–202° (Found: C, 63.5; H, 5.4; N, 12.8. $C_{23}H_{22}N_4O_4$ requires C, 63.6; H, 5.1; N, 12.9%). Reduction of 4-nitrochalcone gave β -(p-aminophenyl)-propiophenone as needles (from methanol), m.p. 78.5–80° (Found: C, 80.0; H, 6.8; N, 5.8. $C_{15}H_{15}NO$ requires C, 80.0; H, 6.7; N, 6.2%).

[5/1481 Received, 28th July, 1975]