3-ACETOXY-2-CYCLOALKEN-1-ONES BY ACETYLATION OF CYCLIC 1,3-DIKETONES WITH KETENE

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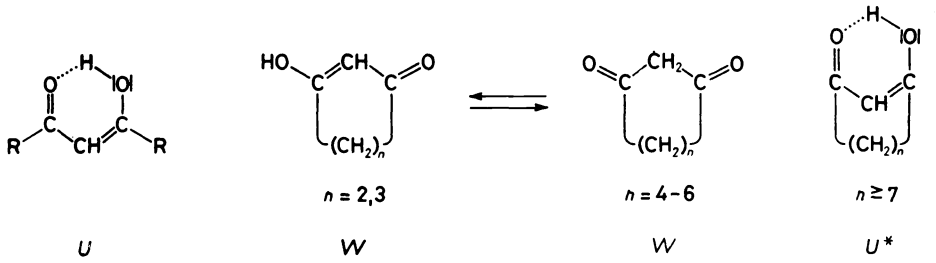
Acetylation of lower 1,3-cycloalkanediones with ketene takes place exclusively at oxygen in contrast to acyclic β-diketones. Thus, 1,3-cyclopentanedione (*I*), 1,3-cyclohexanedione (*II*) and 5,5-dimethyl-1,3-cyclohexanedione (*III*) afforded the corresponding 3-acetoxy-2-cycloalken-1-ones *VI*—*VIII* in quantitative yields. 1,3-Cycloheptanedione (*IV*) and 1,3-cyclooctanedione (*V*) differed considerably from the preceding diketones by low reactivities.

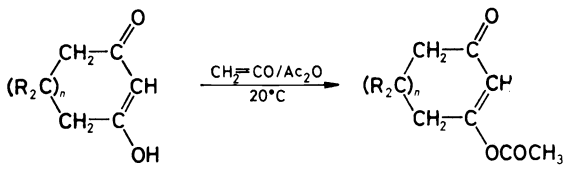
The already known reaction of acyclic β-dicarbonyl compounds with ketene[1] yielded products of C-acetylation. Recently, acetylation of cyclic β-diketones with isopropenyl acetate was described[2] to furnish products of O-acetylation of the starting 1,3-cycloalkanediones. The different way of acetylation of the acyclic and cyclic β-dicarbonyl compounds could be rationalized by diversities in their structures: acyclic β-dicarbonyl compounds can exist in an energetically more favourable intramolecularly stabilized *U*-form, whilst cyclic β-diketones with less than ten-membered rings have rigid *W*-shaped structures. Ten- and more-membered rings tend to having a *U**-shaped arrangement similar to that of β-dicarbonyl acyclic compounds[3] (Scheme 1).



SCHEME 1

Barrier to the O-acetylation of acyclic β-diketones (structure *U*) with ketene is likely a strong intramolecular hydrogen bonding and the delocalization energy of this system resulting in a partially aromatic character.

This paper investigates the reactivity and direction of acetylation of cyclic five- to eight-membered 1,3-diketones with ketene. Our experiments showed that treatment of 1,3-cycloalkanediones *I* – *V* with ketene also afforded O-acetylated products similarly as with isopropenyl acetate[2]; products of C-acetylation were not observed. Reactivity of the afore-mentioned 1,3-cycloalkanediones with ketene was strongly dependent on the readiness to passing into the enol form (cf. structure *W*, Scheme 1). Cyclic 1,3-diketones with five- and six-membered rings, i.e. 1,3-cyclopentanedione (*I*), 1,3-cyclohexanedione (*II*) and 5,5-dimethyl-1,3-cyclohexanedione (*III*) – all almost fully enolized as evidenced by their ^{1}H NMR spectra in hexadeuterodimethyl sulfoxide and by ref.[3] – reacted with ketene quite readily, even at room temperature and without a catalyst to produce 3-acetoxy-2-cycloalken-1-ones *VI* – *VIII*. The reaction rate is almost proportional to that of ketene introduced into the mixture (checked by thin-layer chromatography). Yields of these reactions are quantitative (Scheme 2).



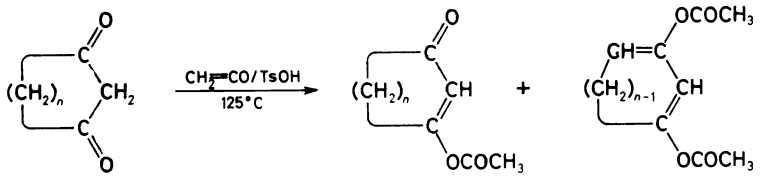
VI, $n = 0$
VII, $n = 1$; R = H
VIII, $n = 1$; R = CH_3

SCHEME 2

The situation, however, markedly changed when trying to prepare mono-O--acetylated products from the non-enolized 1,3-cycloalkanediones having seven- or eight-membered rings (evidenced by ^{1}H NMR spectral data and ref.[3]). As found, 1,3-cycloheptanedione (*IV*) and 1,3-cyclooctanedione (*V*) react with ketene in the absence of a catalyst very slowly and consequently, a long-term introduction of ketene into the mixture at elevated temperature (125°C) was needed. Compound *IV* afforded 3-acetoxy-2-cyclohepten-1-one (*IX*) in 64% yield. It is noteworthy that the di-O-acetylated product could not be detected. An addition of 4-toluenesulfonic acid as catalyst did not rise the yields of mono-O-acetyl derivatives *IX* and *X*; instead, di--O-acetyl derivatives *XI* and *XII* were the main products in the equilibrium mixture together with monoacetyl derivatives *IX*, *X* and the starting 1,3-cycloalkanedione (Scheme 3).

Significant differences in the reactivity between the five- and six-membered and the seven- and eight-membered 1,3-cycloalkanediones can be rationalized by the

readiness of the first two to forms enol form under the given reaction conditions; enol is an intermediate in O-acetylation and its formation is likely the rate-determining crucial reaction step. Seven- and eight-membered cyclic β-diketones could be O-acetylated only at elevated temperatures; the seven-membered diketone reacted selectively without a catalyst to afford 3-acetoxy-2-cyclohepten-1-one (*IX*), i.e. only mono acetylation took place. This was, however, not the case with the eight-membered homologue *X*.



n = 4 :	(*IV*) 32%	(*IX*) 18%	(*XI*) 50%
n = 5 :	(*V*) 35%	(*X*) 8%	(*XII*) 57%

SCHEME 3

The presented reactions constitute a suitable method for preparing 3-acetoxy-2--cycloalken-1-ones by reaction of ketene with 1,3-cycloalkanediones as far as they undergo enolization. This method makes it possible to obtain the required products in quantitative yields in a quite short time at room temperature without catalyst, absolutization of solvents and without an inert atmosphere.

The structure of all the synthesized compounds was corroborated by spectral (IR and ^{1}H NMR) methods (see Table I).

EXPERIMENTAL

Diketones *I* and *II* were obtained by hydrogenation of the corresponding unsaturated diones[4,5] and diketones *IV* and *V* by a three-step synthesis starting from diethyl adipate and diethyl pimelate[6], respectively. The commercially available dimedone (*III*) was purified by crystallization from acetone.

The ^{1}H NMR spectra were measured with a Tesla BS 487 apparatus operating at 80 MHz and the IR spectra with a Perkin–Elmer, model 567 spectrophotometer (range 400–4 000 cm^{-1}). Ketene was produced by pyrolysis of acetone vapors over the red-hot resistance wire in the ketene lamp[7] (rate 0·45 mol ketene per hour, determined by the reaction of ketene with aniline[8]). Impurities accompanying ketene were freezed out at −40°C prior to the reaction. The products and the time course of reactions were monitored both by capillary gas chromatography (phase OV-1) and thin-layer chromatography (on Silufol UV-254 sheets, Kavalier, Czechoslovakia, detection by UV_{254} light). Characteristic data for products prepared are presented in Table I.

Acetylation of 1,3-Cycloalkanediones with Ketene

Method A: Ketene was introduced into a suspension of the respective 1,3-cycloalkanedione (50 mmol) in acetic anhydride (50 ml) at room temperature. The solid phase disappeared during the reaction; the solvent was then distilled off at 60°C/2 kPa and the crude product was purified by vacuum distillation at 13 Pa.

Method B: Ketene was introduced into a solution of 1,3-cycloalkanedione (8 mmol) in dibutyl ether (50 ml) in a vessel equipped with a reflux condenser at 125°C for 5 h. The solvent was distilled off at 30°C/13 Pa and the crude product was chromatographed on silica gel (40 to 100 mesh, ref.[9]) ethyl acetate–petroleum ether (1 : 2) being the elution solvent.

TABLE I

Synthesis and properties of 3-acetoxy-2-cycloalken-1-ones and 1,3-diacetoxy-1,3-cycloalkadienes

Compound	Method (Time[a] min)	Yield %	B.p. °C/13 Pa	R_F[b] n_D^{20}	IR[c] cm^{-1}	^1H NMR[d] (δ, ppm) CH_3—	—CH_2—	—CH=
				3-Acetoxy-2-cycloalken-1-ones				
VI	*A* (7)	100	93–95	0·40 1·4950	1 790, 1 710, 1 600	2·27 s	2·10–2·52 m, 2·52–2·86 m	6·16 t[e]
VII	*A* (8)	100	93–96	0·52 1·4928	1 768, 1 668	2·21 s	1·80–2·65 m[f]	5·87 t[e]
VIII	*A* (15)	100	99–102	0·65 1·4805	1 764, 1 667	2·23 s, 1·13 s[f]	2·29 s[g], 2·45 d[e,h]	5·92 t[e]
IX	*B* (300) *C* (600)	64 18	110–113	0·70 1·4921	—	2·18 s	1·47–2·40 m[f], 2·40–2·82 m	5·84 s
X	*C* (600)	8	—	0·65[j] 1·4922	—	2·14 s	1·37–2·55 m[i]	5·28 s
				1,3-Diacetoxy-1,3-cycloalkadienes				
XI	*C* (600)	50	—	0·85 1·4899	1 750, 1 672	2·11 s[f]	1·67–2·80 m[f]	5·41 s, 5·56 t[k]
XII	*C* (600)	57	—	0·70[j] 1·4880	1 756, 1 666	2·10 s, 2·13 s	1·35–1·90 m[l], 1·90–2·55 m[l,h]	5·38 t[m] 5·45 s

[a] Time during which ketene was introduced; [b] TLC on SiO_2 (petroleum ether–ethyl acetate 1 : 1); [c] in $CHCl_3$; [d] in $CDCl_3$; [e] J = 1·5 Hz; [f] 6 H; [g] CH_2CO; [h] CH_2C=; [i] 10 H; [j] petroleum ether–ethyl acetate 2 : 1; [k] J = 6 Hz; [l] 4 H; [m] J = 8 Hz.

Method C: Ketene was introduced into a solution of 1,3-cycloalkanedione (7 mmol) and 4-toluenesulfonic acid (0·1 g) for 10 h, under the same conditions and work-out as specified with method *B*.

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