Acetylation of cyclic 1,3-diketones with isopropenyl acetate

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Dedicated to Professor RNDr. V. Sutoris, CSc., in honour of his 60th birthday

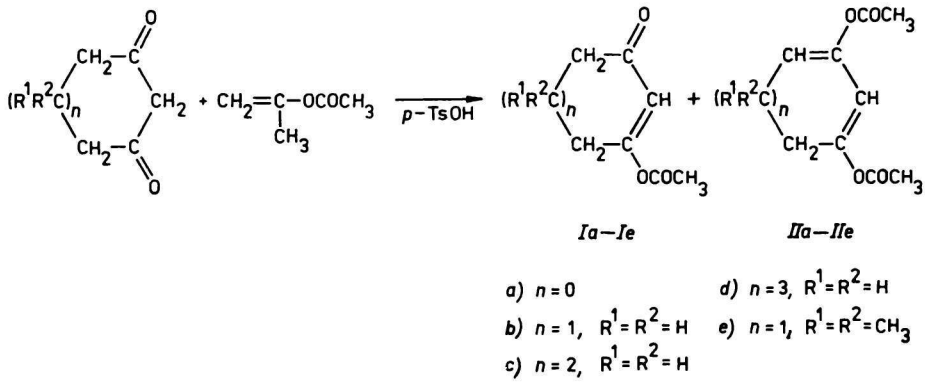
Reaction of 1,3-cyclopentanedione, 1,3-cyclohexanedione, 1,3-cycloheptanedione, 1,3-cyclooctanedione, 5,5-dimethyl-1,3-cyclohexanedione, and 1,3-indanedione with isopropenyl acetate afforded corresponding 3-acetoxy-2-cycloalken-1-ones in good yields. 1,3-Indanedione upon treatment with a slight excess of the acetylating reagent did not react in the expected way. Bindone was the only product of the reaction. A large excess of isopropenyl acetate had a beneficial effect on the course of the reaction. 3-Acetoxy-2-inden-1-one was the main product, accompanied with a small amount of *O*-acetylated bindone.

Реакцией 1,3-циклопентандиона, 1,3-циклогександиона, 1,3-циклогептандиона, 1,3-циклооктандиона, 5,5-диметил-1,3-циклогександиона и 1,3-индандиона с изопропенилацетатом были получены с хорошими выходами соответствующие 3-ацетокси-2-циклоалкен-1-оны. 1,3-Индандион при реакции с небольшим избытком ацетилирующего агента не реагировал ожидаемым образом. Единственным продуктом реакции был биндон. Большой избыток изопропенилацетата положительно влиял на ход реакции. Основным продуктом в этом случае являлся 3-ацетокси-2-инден-1-он, сопровождаемый небольшим количеством *O*-ацетилированного биндона.

The choice of an electrophilic reagent is one of the most important ways to control the direction of an electrophilic attack on the ambident 1,3-dicarbonyl grouping [1]. The conditions for selective either *C*- or *O*-alkylations of monocyclic 1,3-diketones have been described [2]. After having studied alkylations of these compounds under variety of conditions [2, 3], we turned our attention to the analogous acylation reactions.

Alike the alkylations, acylations of 1,3-diketones can also be carried out selectively with the formation of just one of the four possible isomers. Products of *C*-acylations were prepared either by treatment of 1,3-diketones salts with anhydrides of carboxylic acids at elevated temperatures [4], or by acetylation of β-dicarbonyl compounds with ketene [5]. On the other hand, acylations of 1,3-cyclohexanedione with carboxylic acid chlorides in pyridine, or with anhydrides under acidic conditions took place exclusively on the oxygen atom [4, 6, 7].

Isopropenyl acetate has been used chiefly in synthesis of acetyl enol ethers of ketones [8, 9], though its utilization in the preparation of 3-acetoxy-2-cyclopentadecen-1-one — an intermediate in the synthesis of racemic muscone — is also known [10]. The reaction of isopropenyl acetate with dimedone was described in more details [11]. Long-lasted heating of the dione in an excess of isopropenyl acetate gave rise to two compounds: the product of mono-*O*-acetylation (*Ie*) and the product of di-*O*-acetylation (*IIe*) (Scheme 1). The latter was used as a diene in the subsequent Diels—Alder reaction [11].

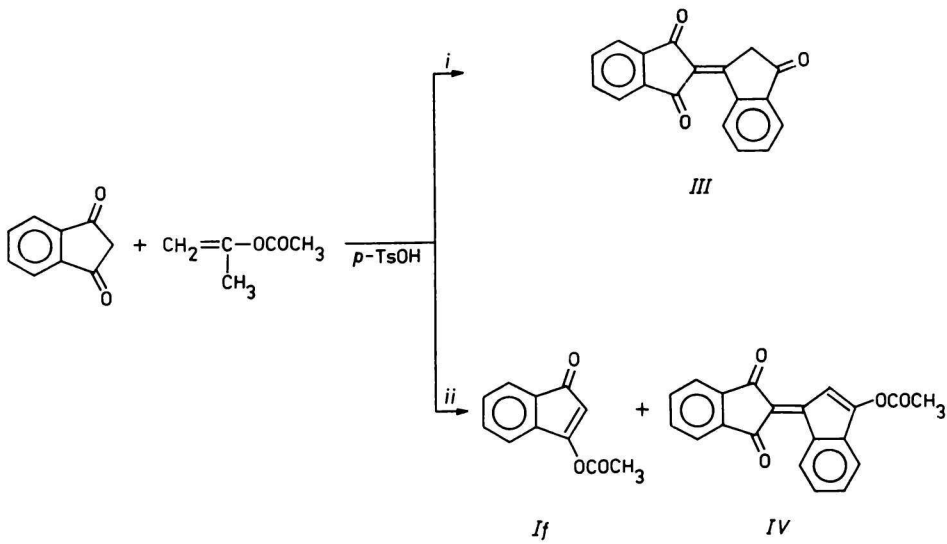


Scheme 1

The reaction of the diones with isopropenyl acetate, in our hands, was performed in two ways (see Experimental). In the first method, isopropenyl acetate was used in a slight excess (amount of substance ratio 1,5) and the reaction was shifted in the desired direction by stripping the formed acetone off. 1,3-Cyclohexanedione and dimedone gave the corresponding *O*-acetylated products (*Ib*, *Ie*) (Scheme 1) in 80 % and 78 % yields, respectively. 1,3-Indanedione resisted any acetylation under these conditions and only bindone (*III*) (Scheme 2, path i), identical in all respects with an authentic sample, was isolated after 24 h heating. 1,3-Indanedione clearly underwent an acid-catalyzed aldol-type condensation followed by elimination of water.

The second method requires large (amount of substance ratio 7) excess of the acetylating reagent. The reaction proceeds smoothly in 3 h, which is considerably reduced time in comparison with the first method. Even though our reaction period is much shorter than that recommended for the preparation of *IIe* [11], 1,3-diacetoxy-1,3-cycloalkadienes (*IIa—IIe*) (Scheme 1) were also formed. Their yields however, are poor and they only can be detected as an impurity in ^{1}H NMR spectra of crude (after distillation) products *Ia—Ie*. Rectification on a short Widmer column removes completely these by-products.

The second method enables us to prepare also compound *If* (Scheme 2, path ii) in good yields, but in this case too, the aldol condensation of 1,3-indanedione followed by *O*-acetylation of the preliminarily formed bindone took place. The structure of *O*-acetylated bindone (*IV*) (Scheme 2, path ii) was proved by ^{1}H NMR, IR, and mass spectra.



Scheme 2

Experimental

1,3-Cyclopentanedione and 1,3-cyclohexanedione were prepared by hydrogenation of corresponding unsaturated diones [12, 13]. 1,3-Cycloheptanedione and 1,3-cyclooctanedione were prepared by a three-step process from diethyl adipate and diethyl pimelate, respectively [14]. 1,3-Indanedione was synthesized from diethyl phthalate and ethyl acetate [15]. Commercially available dimedone (Labora) was purified by crystallization and isopropenyl acetate (Fluka) was used as purchased.

^{1}H NMR spectra were taken on a Tesla BS 487 instrument with 80 MHz working frequency in $CDCl_3$ solutions with TMS as an internal standard. IR spectra were recorded on a Perkin—Elmer 567 spectrometer in the region 400—4000 cm^{-1} in CCl_4. Melting points were determined on a Kofler hot-stage and are uncorrected.

Reaction of 1,3-cycloalkanediones with isopropenyl acetate

Procedure A

A mixture of 1,3-cycloalkanedione (50 mmol), isopropenyl acetate (7.5 g; 75 mmol), and *p*-toluenesulfonic acid (300 mg) is stirred and heated at 90 °C (bath temperature)

under nitrogen. The acetone formed during the reaction is continuously removed through a 20 cm spiral column. After 24 h when no more acetone distills, the mixture is cooled and worked-up as described in Procedure *B*.

Procedure B

A mixture of 1,3-cycloalkanedione (50 mmol), isopropenyl acetate (35.0 g; 350 mmol), and *p*-toluenesulfonic acid (300 mg) is stirred and heated at 110 °C (bath temperature) under nitrogen for 3 h. After cooling to the room temperature, the contents of the flask is diluted with chloroform (100 cm^3), washed successively with ice-cold saturated solutions of $NaHCO_3$ and NaCl (3×50 cm^3) and dried ($MgSO_4$). The solvent is removed and the residue distilled through a 20 cm Widmer column under reduced pressure.

In the case of 1,3-indanedione the reaction period is 10 h. After work-up as described above, the solid residue is extracted with petroleum ether (b.p. = 30—50 °C, 200 cm^3) in a Soxhlet apparatus. The extract is allowed to crystallize at −20 °C to give *If*. *O*-Acetylated bindone (*IV*) remains in a thimble of a Soxhlet apparatus.

3-Acetoxy-2 cyclopenten-1-one (Ia)

Yield: 82 % (*B*), b.p.(1.3 kPa) = 84—85 °C, $n(\lambda_D, 20\ °C) = 1.4947$.

^{1}H NMR, δ/ppm: 2.30 (s, 3H, CH_3CO), 2.30—2.50 (m, 2H, $—CH_2—$), 2.60—2.75 (m, 2H, $—CH_2—$), 6.16 (t, $J = 1.5$ Hz, 1H, −CH=).

For $C_7H_8O_3$ ($M_r = 140.1$) w_i(calc.): 60.00 % C, 5.75 % H; w_i(found): 59.15 % C, 5.76 % H.

3-Acetoxy-2-cyclohexen-1-one (Ib)

Yield: 80 % (*A*), 85 % (*B*), b.p.(1.3 kPa) = 104—106 °C, $n(\lambda_D, 20\ °C) = 1.4936$.

^{1}H NMR, δ/ppm: 1.75—2.63 (m, 6H, $—(CH_2)_3—$), 2.16 (s, 3H, CH_3CO), 5.70 (t, $J = 1.5$ Hz, −CH=), in accord with the literature [7].

3-Acetoxy-2-cyclohepten-1-one (Ic)

Yield: 80 % (*B*), b.p.(1.3 kPa) = 111—113 °C, $n(\lambda_D, 20\ °C) = 1.4919$.

^{1}H NMR, δ/ppm: 1.75—2.63 (m, 8H, $—(CH_2)_4—$), 2.18 (s, 3H, CH_3CO), 5.80 (s, 1H, −CH=).

For $C_9H_{12}O_3$ ($M_r = 168.2$) w_i(calc.): 64.27 % C, 7.19 % H; w_i(found): 63.84 % C, 7.22 % H.

3-Acetoxy-2-cycloocten-1-one (Id)

Yield: 81 % (*B*), b.p.(53 Pa) = 97—99 °C, $n(\lambda_D, 20\ °C) = 1.4920$.

^{1}H NMR, δ/ppm: 1.35—2.50 (m, 10H, $—(CH_2)_5—$), 2.14 (s, 3H, CH_3CO), 5.25 (s, 1H, −CH=).

For $C_{10}H_{14}O_3$ ($M_r = 182.2$) w_i(calc.): 65.91 % C, 7.74 % H; w_i(found): 65.02 % C, 7.70 % H.

3-Acetoxy-5,5-dimethyl-2-cyclohexen-1-one (Ie)

Yield: 78 % (*A*), 86 % (*B*), b.p.(1.3 kPa) = 106—108 °C, $n(\lambda_D, 20\ °C) = 1.4793$.

^{1}H NMR, δ/ppm: 1.10 (s, 6H, $(CH_3)_2$), 2.18 (s, 5H, CH_3CO—, —CH_2—), 2.36 (s, 2H, —CH_2—), 5.74 (s, 1H, −CH=), in accord with the data given in Ref. [11].

3-Acetoxy-2-inden-1-one (If)

Yield: 75 % (*B*), m.p. = 70—72 °C.

^{1}H NMR, δ/ppm: 2.40 (s, 3H, CH_3CO), 5.98 (s, 1H, −CH=), 7.05—7.53 (m, 4H, C_6H_4).

IR, $\tilde{\nu}$/cm^{-1}: 1745, 1713, 1685.

For $C_{11}H_8O_3$ (M_r = 188.2) w_i(calc.): 70.21 % C, 4.29 % H; w_i(found): 69.92 % C, 4.32 % H.

O-Acetylated bindone (IV)

Yield: 15 % (*B*), m.p. 184—186 °C (decomp.), $M^+ = 316$.

^{1}H NMR, δ/ppm: 2.37 (s, 3H, CH_3CO), 7.00—7.42 (m, 4H, C_6H_4), 7.58—8.09 (m, 5H, C_6H_4, −CH=).

IR, $\tilde{\nu}$/cm^{-1}: 1775, 1715, 1675, 1650.

For $C_{20}H_{12}O_4$ (M_r = 316.3) w_i(calc.): 75.94 % C, 3.82 % H; w_i(found): 76.00 % C, 3.86 % H.

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