Catalytic Acetonylation of Cyclic 1,3-Dicarbonyl-Systems by 2-(Chloromethyl)-3,5-dioxa-1-hexene

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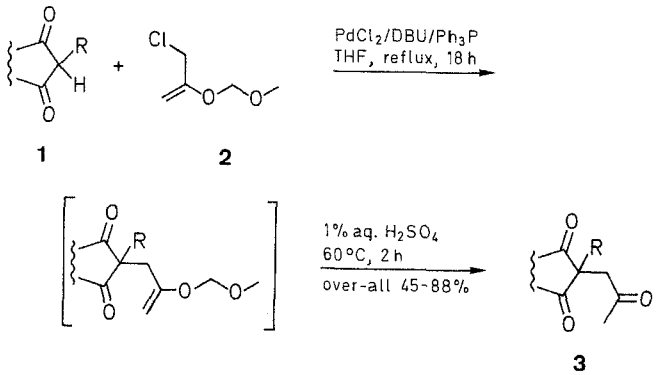
The high yield synthesis of cyclic 2-mono-(or di-)acetonyl-1,3-dicarbonyl compounds from the corresponding cyclic 1,3-dicarbonyl compounds using 2-(chloromethyl)-3,5-dioxa-1-hexene in the presence of palladium(II) catalyst is reported.

The acetonyl unit is one of the most basic functional group due to its high and versatile reactivity, and its introduction in suitable substrates is an important step in organic synthesis. Until now, a series of reagents for acetonylation of various substrates has been described. Since the review concerning the acetonylating reagents was published in 1978,[1] several new methods have been reported.[2-6] Among them, 2-(chloromethyl)-3,5-dioxa-1-hexene (**2**) developed recently[7] is very effective owing to such features as the simplicity in preparation and isolation, the stability on storage, and high reactivity. During an investigation of the reactivity of **2**, we found that **2** is also effective to introduce the acetonyl group into cyclic 1,3-dicarbonyl systems under catalytic conditions using palladium dichloride. This reaction can be considered to proceed through the intermediacy of π-allyl complex of **2** with palladium,[8,9] and to be different from S_N2 substitution reaction. For example, 2-methyl-1,3-cyclopentanedione, which could not be acetonylated by the nucleophilic displacement,[7] gave an acetonylated compound in high yield using the present catalytic method.



1 2 3

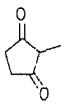
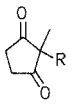
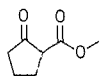
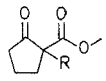
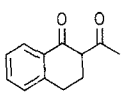
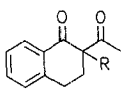
Scheme A

Here, we report the results of the catalytic acetonylation. Our experimental results suggest that the cyclic 1,3-dicarbonyl compounds with one or two active protons at a pK_a range of 4–6 are suitable to be acetonylated by this method.

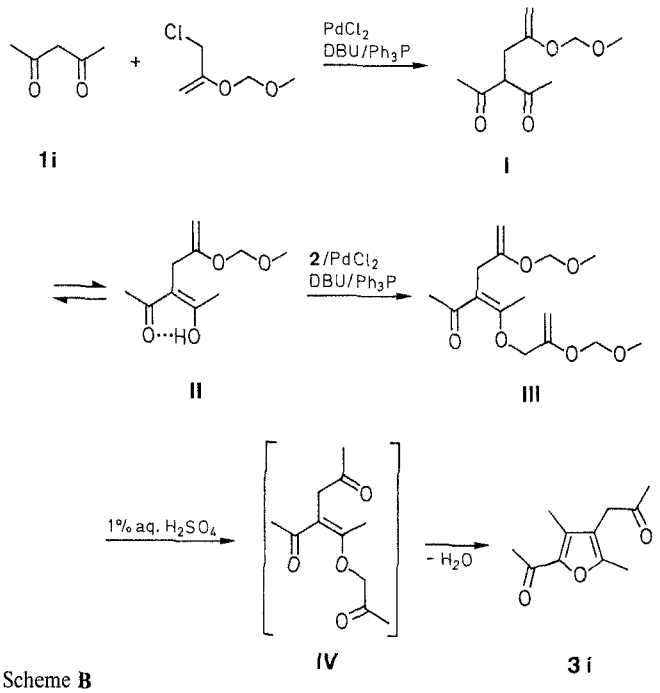
Acetonylation of cyclic 1,3-dicarbonl compounds **1** with one active proton was carried out by treating with 1.5 equivalent of **2** in the presence of palladium dichloride, triphenylphosphine, and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in tetrahydrofuran. Subsequent hydrolysis of the intermediate enol ether with 1% aqueous sulfuric acid afforded the corresponding acetonyl 1,3-dicarbonyl compounds **3** in good yields (Scheme **A**). In the case of acetonylation of 1,3-dicarbonyl compounds having two active protons, such as cyclohexane-1,3-dione (**1g**), with 1 equivalent of **2** afforded the mixture of 2-mono- and 2,2-diacetonylcyclohexane-1,3-dione (**3g**) (about 1 : 1) was obtained. However, when **1g** reacted with 2.5 equivalent **2**, diacetonyl compound **3g** was obtained in 45% yield, and only a small amount of monosubstituted compound was detected by gas-chromatography.

Different from these results, acetonylation of acetylacetone with 2.5 equivalent of **2** gave 3-acetonyl-5-acetyl-2,4-dimethylfuran (**3i**) rather than expected 3,3-diacetonylacetylacetone. The postulated formation mechanism of **3i** is shown in Scheme **B**. The intermediate **I** in the keto form generated by substitution with π-allyl complex of **2** may transform into the enol form **II** in the *Z*-conformation. The enol **II** further reacts with another molecule of π-allyl complex to afford diallylated compound **III**. Hydrolysis of **III** gives diacetonyl compound **IV**, which then cyclizes by aldol condensation to afford furan **3i**. In the enol **II**, the *Z*-conformation may predominate due to intramolecular hydrogen bonding, regulating the structure of product to the furan skeleton. It is difficult to properly account for the difference in the reactivities of 1,3-cyclohexanedione and acetylacetone. Perhaps, the monoallyl derivative of cyclohexanedione cannot transform to its enol form (corresponding to the intermediate **II** in Scheme **B**), because the intramolecular hydrogen bonding hardly forms due to its cyclic structure.

Table. Acetonylation of β-Dicarbonyl Compounds **1a–i**

Substrate	Product[a]	Yield (%)	bp[b] (°C)/mbar	Molecular Formula[c]	^{1}H-NMR ($CDCl_3$/TMS)[d] δ, J(Hz)
 **1a**	 **3a**	88	110/0.1	$C_9H_{12}O_3$ (168.2)	1.05 (s, 3H); 2.09 (s, 3H); 2.90 (s, 4H); 3.19 (s, 2H)
 **1b**	 **3b**	60	110/0.13	$C_{10}H_{14}O_3$ (182.2)	1.50–2.66 (m, 6H); 2.15 (s, 6H); 3.05 (s, 2H)
 **1c**	 **3c**	76	95/0.07	$C_{10}H_{14}O_4$ (198.2)	1.90–2.60 (m, 6H); 2.10 (s, 3H); 3.10 (d, 2H, J = 12); 3.70 (s, 3H)
 **1d**	 **3d**	79	70/0.03	$C_9H_{12}O_4$ (184.2)	2.25 (s, 6H); 2.81–3.24 (m, 4H); 4.25–4.50 (m, 2H)
 **1e**	 **3e**	69	100/0.09	$C_{10}H_{14}O_3$ (182.2)	1.23 (s, 3H); 2.10 (s, 3H); 2.00–2.40 (m, 2H); 2.685 (t, 4H, J = 8); 3.25 (s, 2H)
 **1f**	 **3f**	71	95/0.09	$C_{11}H_{16}O_3$ (196.3)	1.40–2.60 (m, 8H); 2.16 (s, 3H); 2.28 (s, 3H); 2.84 (s, 2H)
 **1g**	 **3g**	45	85/0.03	$C_{12}H_{16}O_4$ (224.3)	1.45–2.42 (m, 2H); 2.03 (s, 6H); 2.72 (t, 4H, J = 8); 3.05 (s, 4H)
 **1h**	 **3h**	49	110/0.07 (mp 97–98°C)	$C_{15}H_{16}O_3$ (244.3)	2.15 (s, 3H); 2.23 (s, 3H); 2.24–2.52 (m, 2H); 2.85–2.95 (m, 4H); 7.30–7.44 (m, 3H); 8.00–8.12 (m, 1H)
1i	**3i**	70	100/0.09	$C_{11}H_{14}O_3$ (194.2)	2.14 (s, 3H); 2.18 (s, 3H); 2.27 (s, 3H); 2.59 (s 3H); 3.66 (s, 2H)

[a] $R = CH_2COCH_3$.
[b] Kugelrohr distillation, bath temperature is given.
[c] Satisfactory microanalyses obtained: C ±0.25, H ±0.22.
[d] Recorded on a JEOL-PS-100 NMR spectrometer.



Scheme **B**

Results of acetonylation and ^{1}H-NMR spectral data are summarized in the Table. The acetonylation method of cyclic 1,3-dicarbonyl compounds developed in this study has the following advantages comparing with the reported method: high yield and easy hydrolysis with 1% aqueous sulfuric acid.

2-Acetonyl-2-methyl-1,3-cyclopentanedione (3a); Typical Procedure for Acetonylation:

A mixture of 2-methyl-1,3-cyclopentanedione **1a** (1.0 g, 8.9 mmol), **2** (1.8 g, 13.0 mmol), triphenylphosphine (2.3 g, 8.9 mmol), DBU (2.0 g, 13.0 mmol), and $PdCl_2$ (0.08 g, 0.45 mmol) in THF (100 mL) is heated to reflux for 18 h. After removal of solid material by filtration and of the solvent by evaporation, 1% aq. H_2SO_4 (2 mL) and dioxane (2 mL) are added to the residue, and the solution is stirred at 60°C for 2 h. The product is extracted with CH_2Cl_2 and dried ($MgSO_4$). The acetonyled product is isolated as a colorless oil by Kugelrohr distillation at reduced pressure; yield: 1.32 g (88%); bp 110°C/0.1 mbar.

3-Acetonyl-5-acetyl-2,4-dimethylfuran (**3i**) is isolated by silica gel chromatography with acetone/hexane (30:70, v/v) as eluent.

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(1) Nakai, T. *J. Synth. Org. Chem. Jpn.* **1978**, *36*, 49; C.A. **1978**, *89*, 41560.
(2) Jouhari, R., Maillard, B., Filliatre, C., Villenave, J. *Synthesis* **1982**, 760.
(3) Kjonaas, R.A., Patel, D.D. *Tetrahedron Lett.* **1984**, *25*, 5467.
(4) Schuda, P.F., Bernstein, B. *Synth. Comm.* **1984**, *14*, 293.
(5) Maruyama, K., Tai, S. *Chem. Lett.* **1985**, 681.
(6) Gu, X.-P., Ikeda, I., Komada, S., Masuyama, A., Okahara, M. *J. Org. Chem.* **1986**, *51*, 5425.
(7) Gu, X.-P., Nishida, N., Ikeda, I., Okahara, M. *J. Org. Chem.* **1987**, *52*, 3192.
(8) Baker, R. *Chem. Rev.* **1973**, *73*, 487.
(9) Trost, B.M., Curran, D.P. *J. Am. Chem. Soc.* **1980**, *102*, 5699.