A Novel Acetonylation of Carbonucleophiles via Palladium-Catalyzed Allylation with Isopropyl 2-Methylene-3,5-dioxahexyl Carbonate

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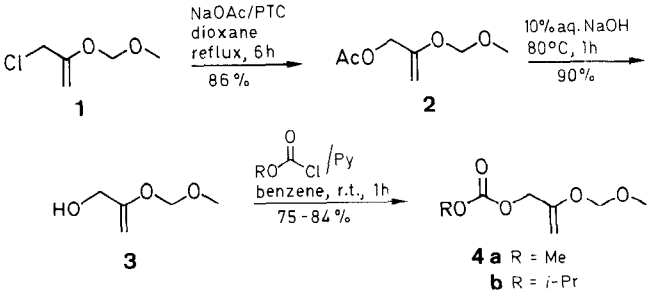
Carbonucleophiles such as malonate esters, β-keto esters, phenylacetate ester, and phenylacetonitrile were acetonylated in high yields by allylation with isopropyl (or methyl) 2-methylene-3,5-dioxahexyl carbonate (**4b** or **4a**) in the presence of palladium-phosphine catalyst under neutral conditions, followed by acidic hydrolysis. Adopting this procedure dihydrojasmone (**7**) was prepared from ethyl 3-oxononanoate (**6**) in an overall yield of 72%.

We have developed a new acetonylating reagent, 2-(chloromethyl)-3,5-dioxahex-1-ene (**1**),[1] and reported its reactivity and use, for example: a 1,3-molecular rearrangement of **1** and its derivatives,[2] acetonylation of active proton-containing compounds,[1] and catalytic acetonylation of cyclic 1,3-dicarbonyl systems.[3] During the search for a new acetonylation method under mild conditions, work concerning allyl carbonates[4] attracted our attention.

Here, we report a new method of acetonylation consisting of palladium-catalyzed allylation of carbonucleophiles with isopropyl (or methyl) 2-methylene-3,5-dioxahexyl carbonate (**4b** or **4a**) under neutral conditions followed by acidic hydrolysis. By this procedure, a high yielding synthesis of dihydrojasmone (**7**) was realized.

The reagent, isopropyl (or methyl) 2-methylene-3,5-dioxahexyl carbonate (**4b** or **4a**) was prepared from **1** by the sequence: reaction with sodium acetate under phase-transfer catalytic conditions to give 2-methylene-3,5-dioxahexyl acetate (**2**) in 86% yield, hydrolysis of **2** in 10% aqueous sodium hydroxide to afford 2-(hydroxymethyl)-3,5-dioxahex-1-ene (**3**) in 90% yield, reaction of **3** with isopropyl (or methyl) chloroformate in pyridine/benzene to give **4b** in 84% yield (**4a**, 75%) (Scheme **A**).

The acetonylation (Scheme **B**) is composed of two steps. In the first step, allylation of carbonucleophiles, was carried out by treating malonate esters, β-keto esters, phenylacetic ester, or phenylacetonitrile with 1.1 equivalent of carbonate **4** in the presence of catalytic amounts of palladium(II) acetate and triphenylphosphine in tetrahydrofuran; the subsequent step, hydrolysis of the resulting allyl compound in 1% aqueous sulfuric acid, afforded the corresponding acetonyl compounds **5** in high yield. Results of acetonylation and ^{1}H-NMR spectral data are summarized in the Table.



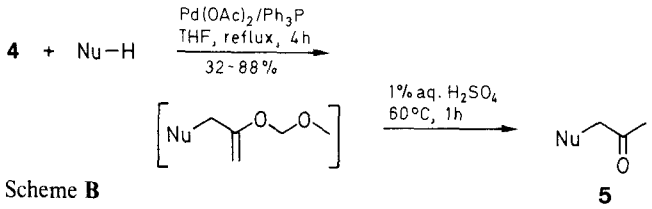
Scheme A

Table. Acetonylation of Carbonucleophiles with Methyl Carbonate **4a** and Isopropyl Carbonate **4b**

Substrate	Product	Yield (%) with **4a**	Yield (%) with **4b**	bp[a] (°C)/mbar	Molecular Formula[b] or Lit. bp (°C)/mbar	^{1}H-NMR ($CDCl_3$/TMS) δ, J (Hz)
EtO_2C CO_2Et	EtO_2C CO_2Et **5a**	84	84	80/0.15	110/7[1]	1.25 (t, 6H, J = 7), 1.51 (s, 3H), 2.16 (s, 3H), 3.08 (s, 2H), 4.18 (q, 4H, J = 7)
MeO_2C CO_2Me	MeO_2C CO_2Me **5b**	80	87	75/0.15	60/0.1[1]	2.20 (s, 3H), 3.08 (d, 2H, J = 7), 3.75 (s, 6H), 3.90 (t, 1H, J = 7)
CO_2Et	CO_2Et **5c**	80	88	80/0.15	$C_9H_{14}O_4$ (186.2)	1.27 (t, 3H, J = 7), 2.19 (s, 3H), 2.37 (s, 3H), 2.97–3.12 (m, 2H), 3.95–4.35 (m, 3H)
CO_2Et	CO_2Et **5d**	75	85	90/0.08	$C_{14}H_{24}O_4$ (256.3)	0.88 (t, 3H, J = 6), 1.16–1.76 (m, 11H), 2.10–2.26 (m, 5H), 2.60–2.80 (m, 2H), 2.96–3.12 (m, 1H), 3.96–4.30 (m, 2H)
Ph CO_2Me	Ph CO_2Me **5e**	39	72	80/0.15	$C_{12}H_{14}O_3$ (206.2)	2.15 (s, 3H), 2.70 (dd, 1H, J = 4, 18), 3.40 (dd, 1H, J = 10, 18), 3.64 (s, 3H), 4.10 (dd, 1H, J = 4, 10), 7.25 (s, 5H)
Ph CN	Ph CN **5f**	32	48	90/0.15	$C_{11}H_{11}NO$ (173.2)	2.18 (s, 3H), 2.96 (dd, 1H, J = 7, 18), 3.24 (dd, 1H, J = 7, 18), 4.36 (t, 1H, J = 7), 7.36 (s, 5H)

[a] Kugelrohr distillation.

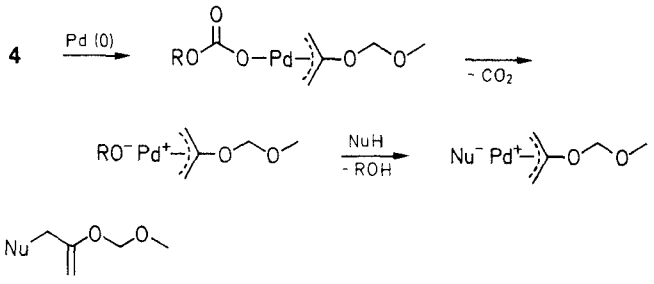
[b] Satisfactory microanalyses obtained: C ±0.38, H ±0.13.



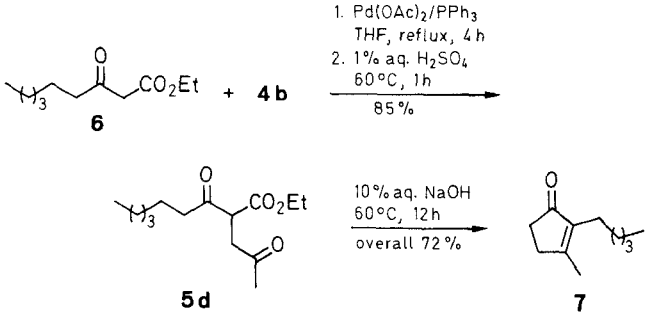
Scheme **B**

The allylation, the first step of acetonylation, can be considered to proceed through the intermediacy of the π-allyl complex of **4** with palladium as shown in Scheme **C**.[4] As the alcoholate anion that forms part of the π-allyl complex becomes more strongly basic then the substrate proton should be more easily abstracted. Therefore, isopropyl carbonate **(4b)**, which can give relatively more basic alcoholate, is more effective for the allylation of less acidic substrates, such as phenyl acetate and phenylacetonitrile, to afford better acetonylation yields than those using methyl carbonate **(4a)** (see Table).

As an example of the utilization of the present acetonylation method, dihydrojasmone **(7)** was prepared. Ethyl 3-oxononanoate **(6)** prepared in 78% yield according to Soloway's method,[5] was treated with isopropyl carbonate **(4b)** under the conditions shown in Scheme **D**, to give ethyl 2-acetonyl-3-oxononanoate **(5d)**, which was subsequently saponified, decarbonylated, and cyclized to dihydrojasmone in an overall yield of 72%.



Scheme **C**[4]



Scheme **D**

Isopropyl 2-Methylene-3,5-dioxahexyl Carbonate (4b):
A mixture of 2-(chloromethyl)-3,5-dioxahex-1-ene (**1**; 11.6 g, 85 mmol), NaOAc (7.7 g, 94 mmol), and Bu_4NHSO_4 (1.4 g, 4.3 mmol) in dioxane (50 mL) is refluxed for 6 h. After removal of

solid material by filtration and of the solvent by evaporation, 10% aq. NaOH (40 mL) is added to the residue, and the solution is stirred at 80°C for 1 h. 2-(Hydroxymethyl)-3,5-dioxahex-1-ene (**3**) formed is extracted with CH_2Cl_2 (2 × 50 mL), dried ($MgSO_4$), and the solvent evaporated. Isopropyl chloroformate (8.8 g, 70 mmol) is added dropwise to a mixture of **3**, pyridine (20 mL), and benzene (30 mL) at 0°C, and the mixture is stirred at r.t. for 1 h. After removal of solid material by filtration and of the solvent by evaporation, **4b** is isolated by Kugelrohr distillation at reduced pressure as a colorless oil; overall yield: 11.3 g (65%); bp 62°C/0.08 mbar.

$C_9H_{16}O_5$ calc. C 52.93 H 7.90
(204.2) found 53.09 7.92

IR (neat): ν = 1750 (C=O), 1650 (C=C), 1100 cm^{-1} (C–O).

^{1}H-NMR ($CDCl_3$): δ = 1.24–1.32 (d, 6 H, $(CH_3)_2C$); 3.40 (s, 3 H, OCH_3); 4.34–4.50 (m, 2 H, $C=CH_2$)); 4.53 (s, 2 H, $COOCH_2$); 4.70–4.90 (m, 1 H, CH); 4.98 (s, 2 H, OCH_2O).

MS: m/z = 204 (M^+).

Dimethyl Acetonylmalonate (5b); Typical Procedure for Acetonylation:

A mixture of dimethyl malonate (1.1 g, 8 mmol), isopropyl carbonate **4b** (1.5 g, 8.8 mmol), $Pd(OAc)_2$ (0.036 g, 0.16 mmol), and Ph_3P (0.42 g, 1.6 mmol) in THF (10 mL) is refluxed for 4 h. The mixture is cooled, treated with 1% aq. H_2SO_4 (10 mL), and stirred at 60°C for 1 h. The product is extracted with CH_2Cl_2 (2 × 50 mL) and dried ($MgSO_4$). Compound **5b** is obtained as a colorless oil by Kugelrohr distillation at reduced pressure; yield: 1.32 g (87%); bp 75°C/0.15 mbar (Lit.[1] bp 110°C/7 mbar).

Dihydrojasmone (7):

According to the typical procedure described above, 10% aq. NaOH (10 mL) is added to the acidic solution containing **5d**, and stirred at 60°C for 12 h. The product is extracted with petroleum ether bp 60–70°C (2 × 50 mL), and the organic layer is washed with water until it is neutral to pH test paper, dried ($MgSO_4$), and concentrated at reduced pressure. Product **7** is isolated by Kugelrohr distillation at reduced pressure as a colorless oil; overall yield from ethyl 3-oxononanoate (**6**; 1.6 g, 8 mmol): 0.96 g (72%); bp 70°C/0.05 mbar. The spectral data of the product is in accordance with that of previously reported **7**.[6]

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(1) Gu, X.-P.; Nishida, N.; Ikeda, I.; Okahara, M. *J. Org. Chem.* **1987**, *52*, 3192.
(2) Gu, X.-P.; Ikeda, I.; Okahara, M. *J. Org. Chem.* **1988**, *53*, 2737.
(3) Gu, X.-P.; Ikeda, I.; Okuhara, T.; Okahara, M. *Synthesis* **1988**, 535.
(4) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y.; Sugiura, T.; Takahashi, K. *J. Org. Chem.* **1985**, *50*, 1523.
(5) Soloway, S.B.; LaForge, F.B. *J. Am. Chem. Soc.* **1947**, *69*, 2677.
(6) Yamashita, M.; Matsumiya, K.; Tanabe, M. *J. Jpn. Oil Chem. Soc.* **1988**, *37*, 245; *C.A.* **1989**, *111*, 58054.