

Reactions of dipivaloylketene and its dimer with C-nucleophiles

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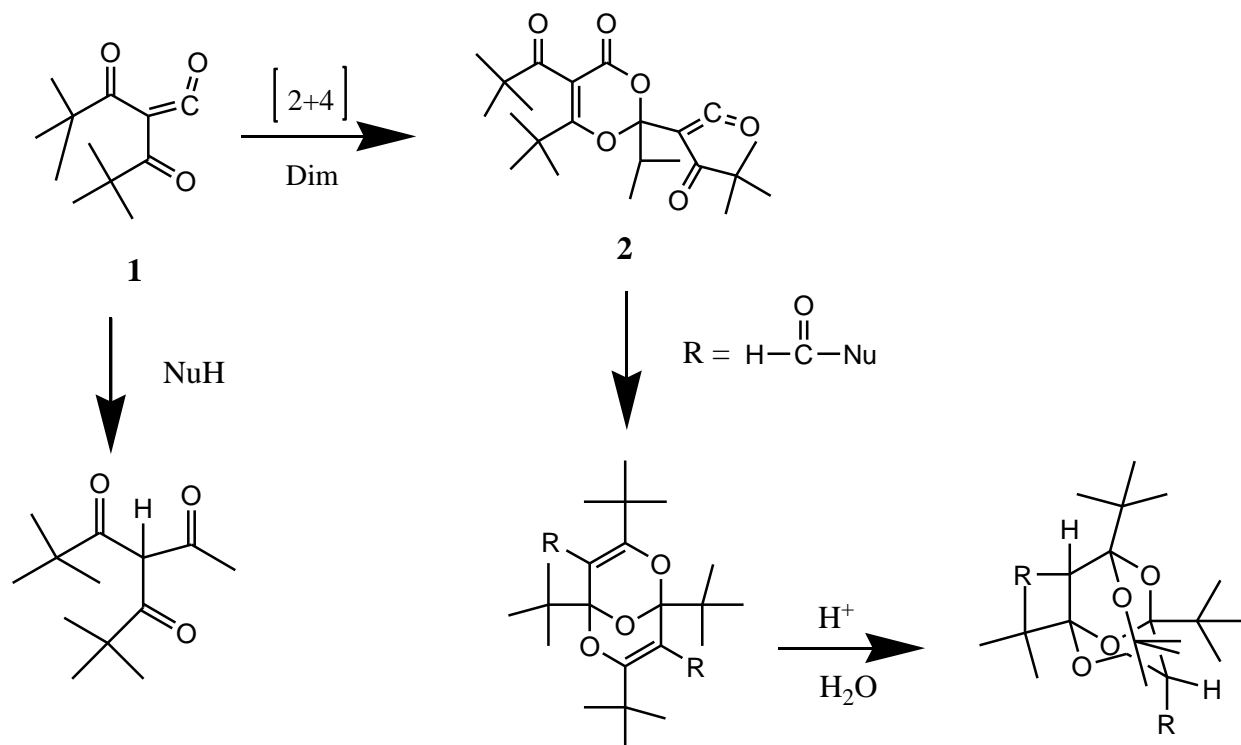
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Abstract

Dipivaloylketene **1** as well as its dimer **2** add 1,3-diketones as C-nucleophiles in strongly basic medium affording the open-chain tetracarbonyl compounds **3**. The dibenzoylmethane adduct **3a** undergoes acid induced cyclocondensation, and under concomitant loss of one pivaloyl group the 4-pyrone derivative **4** is formed. Employing diethyl malonate as C-nucleophile provides the 2-pyrone **5**.

Keywords: Dipivaloylketene, tetracarbonyl compounds, cyclocondensation

Dipivaloylketene **1** is obtained from preparative flash vacuum pyrolysis (FVP) of the corresponding furan-2,3-dione in excellent yield.¹ It slowly dimerizes to afford the 4*H*-[1,3]-dioxin-4-one derivative **2** possessing also an α -oxoketene moiety^{1,2}. Both compounds are remarkably stable and have been found to smoothly add N- as well as O-nucleophiles under very mild reaction conditions³. The reaction of **1** with nucleophiles provides the corresponding dipivaloyl acetic acid derivatives in excellent yields. On the other hand, the products obtained from the reaction of dimer **2** with nucleophiles are 2,9-dioxabicyclo[3.3.1]nona-3,7-dienes featuring the rather rare molecular skeleton of a concave, bridged bisdioxine exhibiting axial chirality³. Furthermore, these compounds can be easily transferred by acid hydrolysis into functionalized 2,4,6, 8-tetraoxatricyclo[3.3.1.1^{3,7}]decanes (2,4,6, 8-tetraoxadamantanes) (Scheme 1).⁴



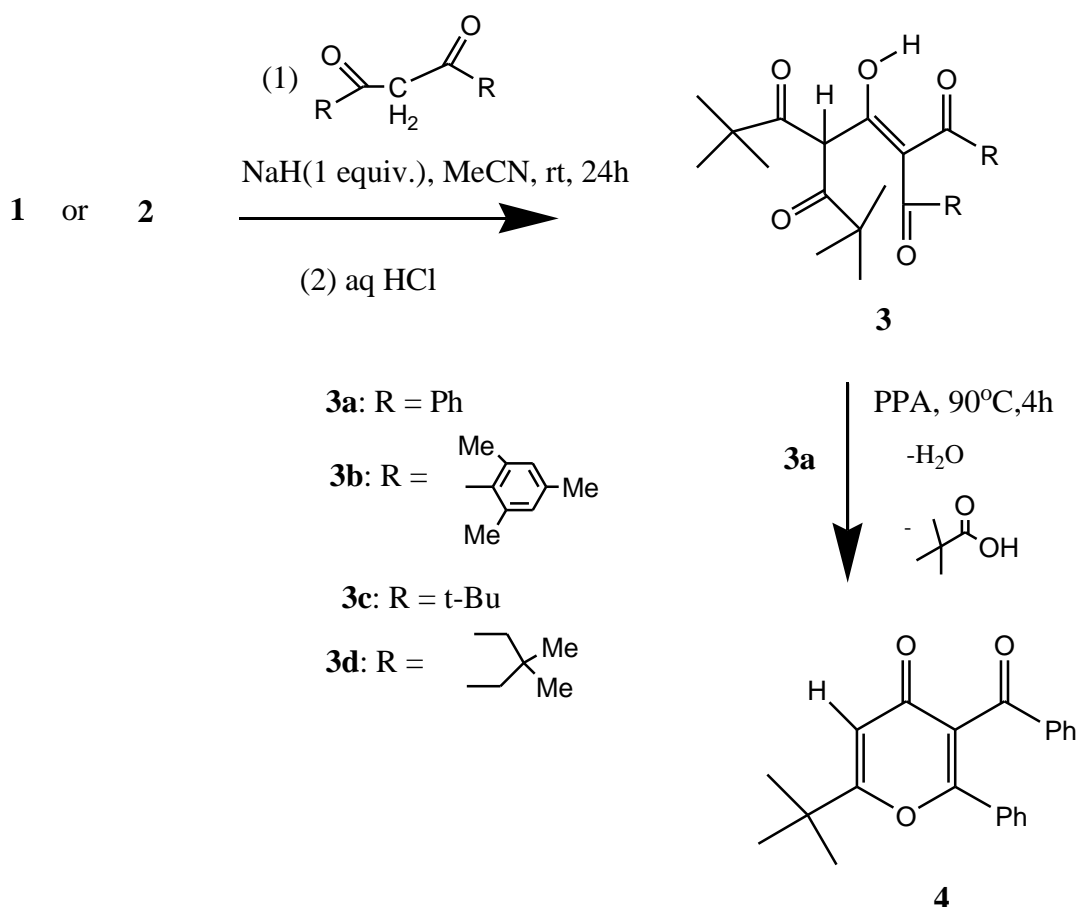
Scheme 1

These findings prompted the investigation of the reactivity of these stable α -oxoketenes **1** and **2** towards carbon-nucleophiles.

Results and Discussion

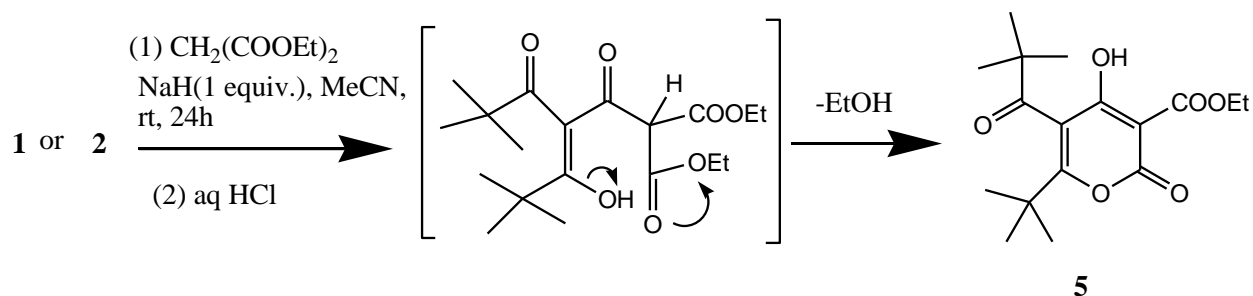
1,3-Diketones (dibenzoylmethane, dimesitylmethane, dipivaloylmethane, and dimedone) were first treated with sodium hydride (50% suspension in mineral oil)⁵ in acetonitrile to generate the corresponding carbanions. Subsequently, oxoketenes **1** or **2** were added at room temperature, and after 24 h adducts **3** were isolated. Although several tautomeric forms can be envisaged for these products, the tetracarboxyl structure **3** (as depicted in Scheme 2) is in agreement with the spectroscopic data: the dipivaloylmethyl moiety of compounds **3** is evident from the characteristic *C-H* signals in the range of δ 6.2 — 6.8; these shift values indicate a rather strong deshielding due to the anisotropic effects of vicinal carbonyl groups. Products **3** do not show any tendency to form other enol tautomers (as evidenced from the NMR spectra and within the accuracy of this method). Earlier measurements of dipivaloylacetic acid derivatives in the solid state and in solution of different solvents demonstrated a similar behaviour.⁶ Further support comes from theoretical investigations on keto-enol tautomerism of β -tricarboxyl compounds.⁶ The observation of a single *C-H* signal in structures **3** is in agreement with the corresponding¹³C

NMR signal of **3a** (δ 64.2, d, $^1J = 125$ Hz) and leads to the conclusion that only the monoenol forms **3** are present.



Scheme 2

The experimental findings that compounds **3** were also obtained from the reaction of the oxoketene **2** confirms earlier results^{3b} that strong bases (e.g. triethylamine^{3b}) catalyze the dissociation of the dioxinone ring into two monomers of ketene **1**. Attempts to cyclize the open-chain compounds **3** were successful only in case of **3a**; treatment with polyphosphoric acid at 90⁰ C afforded the 4-pyrone derivative **4**. Under the reaction conditions applied, one pivaloyl group was lost. Examples for similar deacylation reactions of polyacyl compounds in acidic media are well known.⁷ All ring carbon atoms of **4** are readily assigned from their ¹³C-NMR signals. Surprisingly, when oxoketenes **1** or **2** were treated with ethyl malonate and NaN, no open-chain adduct could be isolated, the 4-hydroxy-2-pyrone derivative **5** was the only reaction product obtained. Its structure was elucidated mainly by evaluation of its ¹³ C-NMR data. A plausible reaction mechanism for the formation of **5** is given in Scheme 3.



Scheme 3

In summary, the reaction of the stable α -oxoketenes **1** and **2** with C-nucleophiles gives rise to C-C bond formation leading to tetracarbonyl compounds **3** and / or pyrone derivatives **4** and **5** in moderate to good yields. In order to generate the required carbanions, the reactions have to be performed in the presence of a strong base, which in case of the dimer **2** also initiates a cycloreversion of the dioxinone ring^{3b}. Formation of bridged bisdioxines (see Scheme 1) was not observed in the course of this work.

Experimental Section

General Procedures. IR spectra (KBr disks) were recorded on a Perkin Elmer 298 Spectrometer, ¹H and ¹³CNMR (gated decoupling mode) spectra were recorded on a Varian XL 200 Gemini Spectrometer at 200 MHz and 50 MHz, respectively. Elemental Analyses were obtained from a CNN Elemental Analyzer Carlo Erba 1106. α -Oxoketenes **1** and **2** were prepared according to the literature.^{1,2}

General procedure for the reactions of α -oxoketenes **1** and **2** with C-nucleophiles

The monosodium salts of 1,3-diketone and diethyl malonate were prepared⁵ in situ by adding the active methylene compound (0.27 - 0.71 mmol) to a stirred suspension of NaN (equimolar in 2 mL of acetonitrile) at rt during 10-15 mm. To this suspension the α -oxoketene **1** or **2** (equimolar amount) was added at once, and stirring was continued at rt. After 24 h the mixture was diluted with H₂O (5 mL), neutralized with aqueous HCl, and extracted with dichloromethane (4 times 5 mL). The combined organic layers were dried over Na₂SO₄ for 4 h. After filtration and evaporation of the solvent the colourless crude residue was recrystallized from petroleum ether (60-80 °C) or petroleum ether / ethyl acetate.

2-Benzoyl-3-hydroxy-6,6-dimethyl-4-(2,2-dimethylpropanoyl)-1-phenylhept-2-ene-1,5d-ione (3a). a. From dibenzoylmethane (160 mg, 0.71 mmol) and **1** (150 mg, 0.71 mmol) pure **3a** (120 mg, 79%) was isolated; mp 136-137 °C (petroleum ether/ethyl acetate 3:1). b. Dibenzoylmethane (112 mg, 0.5 mmol) and **2** (210 mg, 0.5 mmol) gave **3a** (140 mg, 65%). JR

(KBr): 3000-2800, 1720, 1700, 1650, 1600, 1550 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 1.10, (s, 18H), 6.35 (s, iN), 7.03-7.65 (in, 1 iN). $^{13}\text{C-NMR}$ (CDCl_3): δ 207.47 (in, C=O pivaloyl), 196.6 (t, $^3J=3.5$ Hz, C=O benzoyl), 193.5 (dd, J 4.5 Hz, J 2.5 Hz, C-3), 185.45 (dt, 3J 3.5 Hz, C0 benzoyl), 138.6, 134.7, 133.0, 132.16, 129.46, 128.8, 128.3, 128.2 (C arom.), 113.8 (d, $^3J=4.5$ Hz, C-2), 64.3 (d, $^1J=$ Hz, C-4), 45.4 (in, $\text{C}(\text{CH}_3)_3$), 27.1, (s, $\text{C}(\text{CH}_3)_3$). Anal. Calcd. for $\text{C}_{27}\text{H}_{30}\text{O}_5$: C, 74.63; H, 6.96. Found: C, 74.68; N, 6.95.

3-Hydroxy-6,6-dimethyl-4-(2,2-dimethylpropanoyl)-2-(2,4,6-trimethylbenzoyl)-1-(2,4,6-trimethylphenyl)hept-2-ene-1,5-dione (3b). a. Dimesitylmethane (160 mg, 0.52 mmol) and **1** (110 mg, 0.52 mmol) afforded **3b** (200 mg, 77%); mp 138-139 $^\circ\text{C}$ (petroleum ether / ethyl acetate 5:1). b. Dimesitylmethane (150 mg, 0.49 mmol) and **2** (200 mg, 0.49 mmol) gave **3b** (140 mg, 57%). IR(KBr): 3060-2800, 1720, 1705, 1640, 1610, 1480 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 1.27 (s, 18N), 1.98 (s, 6N), 2.02 (s, 6N), 2.14 (s, 3N), 2.16 (s, 3N), 6.46 (s, 2H), 6.50 (s, 2N), 6.77 (s, iN). Anal. Calcd. for $\text{C}_{33}\text{N}_{42}\text{O}_5$: C, 76.41; N, 8.16. Found: C, 76.19; N, 8.10.

5-Hydroxy-4,6-di(2,2-dimethylpropanoyl)-2,2,8,8-tetramethylnon-4-ene-3,7-dione (3c). a. From dipivaloylmethane (100 mg, 0.54 mmol) and **1** (120 mg, 0.54 mmol) **3c** (80 mg, 37%) was isolated; mp 117-118 $^\circ\text{C}$ (petroleum ether). b. From dipivaloylmethane (50 mg, 0.27 mmol) and **2** (120 mg, 0.27 mmol) **3c** (40 mg, 37%) was obtained. IR (KBr): 3040-2800, 1760, 1720, 1695, 1630, 1475 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 1.13 (s, 9H), 1.18 (s, 18H), 1.30 (s, 9N), 5.55 (broad s, 1N, ON), 6.20 (s, iN). Anal. Calcd. for $\text{C}_{23}\text{N}_{38}\text{O}_5$: C, 70.02; N, 9.71. Found: C, 69.96; N, 9.45.

4-[(4,4-Dimethyl-2,6-dioxocyclohexylidene)(hydroxymethyl)-2,2,6,6-tetramethylheptane-3,5-dione (3d). a. Dimedone (70 mg, 0.5 mmol) and **1** (105 mg, 0.5 mmol) gave **3d** (120 mg, 65%); mp 71-72 $^\circ\text{C}$ (petroleum ether). b. Dimedone (70 mg, 0.5 mmol) and **2** (210 mg, 0.5 mmol) yielded **3d** (130 mg, 70%). IR (KBr): 3040-2800, 1720, 1700, 1665, 1570, 1490, 1475 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 1.06 (s, 6H), 1.16 (s, 18H), 2.32 (s, 2N), 2.57 (s, 2N), 6.86 (s, 1N). Anal. Calcd. for $\text{C}_{20}\text{H}_{30}\text{O}_5$: C, 68.55; H, 8.63. Found: C, 68.02; H, 8.62.

3-Benzoyl-6-*t*-butyl-2-phenyl-4H-pyran-4-one (4). A mixture of **3a** (170 mg, 0.39 mmol) and polyphosphoric acid (2g, excess) was heated at 85-90 $^\circ\text{C}$ with occasional stirring for 4 h. After cooling to 20 $^\circ\text{C}$ N_2O (5 mL) was added, and the reaction mixture was stirred for 2 mm. Further dilution with H_2O (20 mL) was followed by extraction with dichloromethane (3 x 10 mL). The combined organic layers were dried over Na_2SO_4 . After the solvent was removed on a rotary evaporator the colourless solid obtained crystallized from petroleum ether / ethyl acetate (4:1) to give **4** (90 mg, 65%); mp 186-187 $^\circ\text{C}$. IR(KBr): 3000-2800, 1670, 1645, 1610, 1600, 1580, 1490, 1450 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 1.40 (s, 9H), 6.4 (s, 1N), 7.28, 8.0 (in, 1ON). $^{13}\text{C-NMR}$ (CDCl_3): δ 193.8 (t, $^3J=4.5$ Hz, benzoyl C=O), 178.6 (s, C-4), 175.9 (in, C-6), 161.8 (t, $^3J=5.5$ Hz, C-2), 137.0, 134.5, 131.5, 130.0, 129.2, 128.0 (arom. C), 125.5 (d, $^3J=3.5$ Hz, C-3), 110.5 (d, $^1J=162.5$ Hz, C-5), 36.5 (m, $\text{C}(\text{CH}_3)_3$), 28.0 (q, $^1J=125.0$ Hz, $\text{C}(\text{CH}_3)_3$). Anal. Calcd. for $\text{C}_{22}\text{N}_{20}\text{O}_3$: C, 79.50; N, 6.06. Found: C, 79.74; H, 6.07.

Ethyl 6-(*t*-butyl)-4-hydroxy-5-(2,2-dimethylpropanoyl)-2-oxo-2H-pyran-3-carboxylate (5) a. Diethyl malonate (120 mg, 0.73 mmol) and **1** (150 mg, 0.71 mmol) gave **5** (130 mg, 54%); mp 55-56 $^\circ\text{C}$ (petroleum ether). b. Diethyl malonate (80 mg, 0.5 mmol) and **2** (200 mg, 0.475 mmol)

afforded **5** (80 mg, 9%). IR(KBr): 3040-2800, 1750, 1700, 1640, 1610, 1545 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 1.28 (s, 18H), 1.42 (t, $J=7.5$ Hz, 3H), 4.47 (q, $J=7.5$ Hz, 2H). $^{13}\text{C-NMR}$ (CDCl_3): δ 209.6 (m, C=O pivaloyl), 177.2 (d, $^2J=4.5$ Hz, C-4), 172.9 (m, C-6), 171.7 (t, $J=3$ Hz, C=O ethoxycarbonyl), 157.1 (s, C-2), 114.2 (d, $^3J=7$ Hz, C-5), 91.0 (d, $^3J=4.5$ Hz, C-3), 62.8 (t, $^1J=150$ Hz, OCN_2), 45.5, 38.7 (m, $\text{C}(\text{CH}_3)_3$), 29.0, 28.6 (q, $^1J=125$ Hz, $\text{C}(\text{CN}_3)_3$), 14.2 (q, $^1J=125$ Hz, CH_3). Anal. Calcd. for $\text{C}_{17}\text{H}_{24}\text{O}_6$: C, 62.95; N, 7.46. Found: C, 63.00; N, 7.41.

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