

Reactions of dipivaloylketene and its dimer with NH₂-nucleophiles. Formation of amides, hydrazides, ureides and pyrimidine-2,4-diones

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Dedicated to Dr. Rudolph A. Abramovitch on the occasion of his 70th birthday

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Abstract

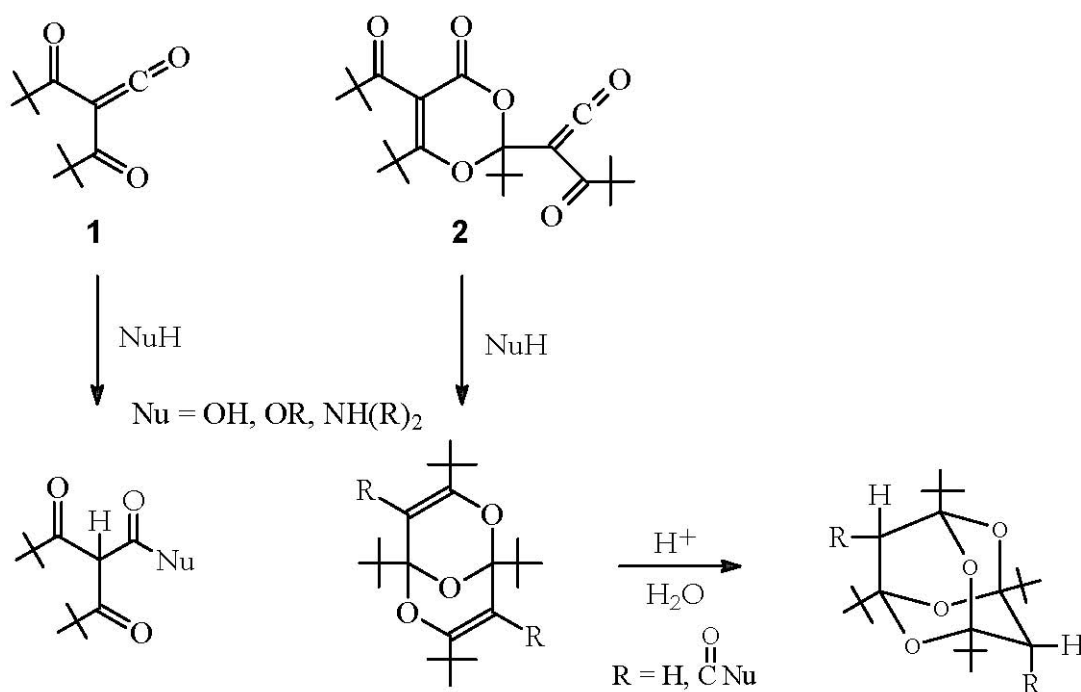
Dipivaloylketene **1** and its dimer **2** add several NH₂-nucleophiles affording the open-chain dipivaloylacetic acid derivatives **3**, **5**, **6**, **9** and **10**. With methylhydrazine as well as 2,6-dimethylaniline the 2:1 products **8** and **11**, respectively, are formed. The tetracarbonyl compounds **3a-c** only undergo PPA-induced cyclocondensation, and with concomitant loss of one pivaloyl group the pyrimidine-2,4-diones **4a-c** are obtained.

Keywords: Dipivaloylketene, NH₂ nucleophiles, amides, hydrazides, ureides, pyrimidine-2,4-diones, cyclocondensation

Introduction

Dipivaloylketene **1** is obtained in excellent yield by preparative flash vacuum pyrolysis (FVP) of the corresponding furan-2,3-dione.¹ It slowly dimerizes to afford the dioxinone derivative **2**, still possessing an α -oxoketene moiety.^{1,2} Both compounds are remarkably stable and have been found to smoothly add OH-nucleophiles as well as aryl and alkyl amines under very mild reaction conditions.³ Furthermore, in strongly basic medium 1,3-diketones also add as C-nucleophiles.⁴ As expected, from **1** and nucleophilic species the corresponding dipivaloylacetic acid derivatives are obtained in excellent yields, but the reaction products derived from dimer **2** and alcohols, water or primary electron rich arylamines represent the rather rare molecular skeleton of a concave, bridged bis-dioxine exhibiting axial chirality.³ In addition, these molecules

can be easily transformed into functionalized 2,4,6,8-tetraoxadamantanes by acidic hydrolysis (Scheme 1).⁵



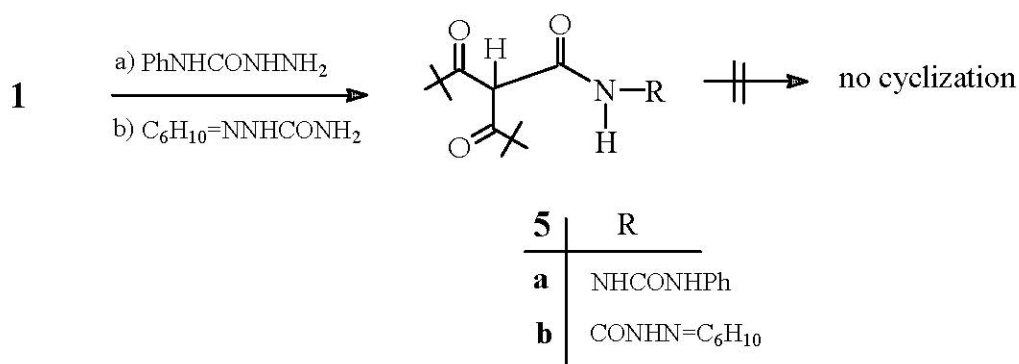
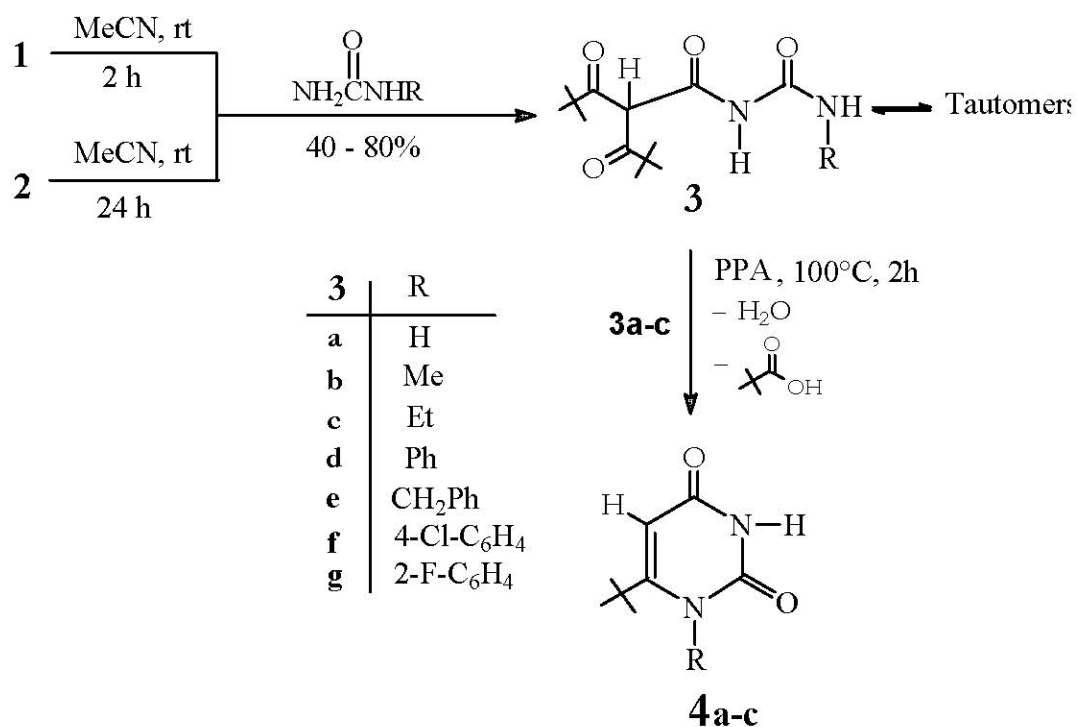
Scheme 1

These bridged bisdioxines as well as tetraoxadamantanes may serve as chiral spacer units in macrocyclic ring systems.⁶ In order to widen the scope of such molecules with respect to their application as potential host-systems in the area of host-guest chemistry, we extended our investigations to a variety of NH_2 -nucleophiles, such as ureas, primary amides, hydrazines, semicarbazides as well as further primary heteroaromatic amines.

Results and Discussion

The reaction of α -oxoketenes **1** and **2** with urea and N-alkyl/aryl ureas were performed in acetonitrile at rt to afford the disubstituted open-chain ureas **3a-g** in moderate to good yields (40-80%). Apart from correct elemental analyses and IR-spectra (for details see Experimental) by intramolecular hydrogen bridges.⁸ Furthermore, in order to establish that the primary Experimental) structural evidence for these compounds is given by their ^1H -NMR spectra which exhibit a signal at 5.65-5.95 ppm highly characteristic of the CH-proton. In the ^{13}C NMR spectrum of **3a** and **3g** as examples, the CH-signals are found at 63.5 ($^1J = 152.0$ Hz, **3a**) and

64.5 ppm ($^1J = 153.0$ Hz, **3g**). Similar results were obtained for several other closely related dipivaloylacetic acid derivatives^{3b, 7} and again make evident that these multi-carbonyl systems mostly avoid enolization in solution, although enols should be stabilized NH₂-moiety had attacked the central ketene carbon, the ¹⁵N NMR spectrum of e.g. **3b** was performed. Two antiphase doublets at - 304.4 and - 244.8 ppm confirmed the presence of two different NH-moieties, thus ruling out an attack of the NHR group.



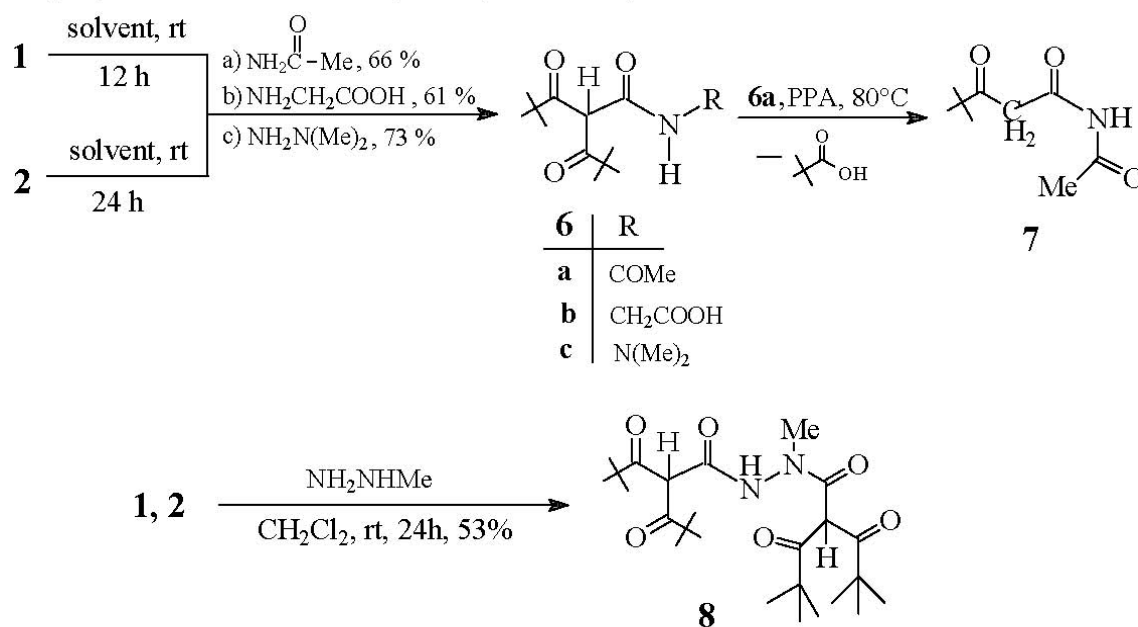
Scheme 2

Attempts to cyclize the open-chain compounds **3** with the aid of polyphosphoric acid (PPA) at 110-120°C were successful only in case of **3a-c** affording the pyrimidine-2,4-diones **4a-c**, which

represent the well-known uracil nucleus. Loss of one pivaloyl-group during the cyclization process in the strongly acidic medium is not surprising. Examples of such deacylation reactions under similar reaction conditions are well known.⁹

Compound **4a** had been prepared independently previously from 6-*t*-butyl-2-thiouracil and chloroacetic acid.^{10, 11} Structural confirmation of the pyrimidine-2,4-diones **4** is given by the singlets for the olefinic protons at 5.63 (**4a**), 5.78 (**4b**) and 5.75 ppm (**4c**) in the ¹H NMR spectra. Furthermore, in the ¹³C NMR spectrum of e.g. **4b** the carbonyls are found at 163.9 and 163.6, respectively, C-6 appeared at 153.0 and C-5 at 100.0 ppm (¹J= 135 Hz), while its ¹⁵N-NMR spectrum exhibited one antiphase doublet at -232.3 ppm (with respect to nitromethane). In order to extend this cyclization process to further compounds of type **3**, the dipivaloylacetic acid derivatives **5a,b** were prepared by simple addition of phenylsemicarbazide or cyclohexanone semicarbazone to dipivaloylketene **1**. Unfortunately, ring closure of **5** into heterocyclic systems could not be achieved.

In addition, the influence of extremely divergent basicities of NH₂-nucleophiles in reaction with α -oxoketenes **1** and **2**, e.g. acetamide, glycine as well as methyl- and 1,1-dimethylhydrazines, was investigated (Scheme 3):

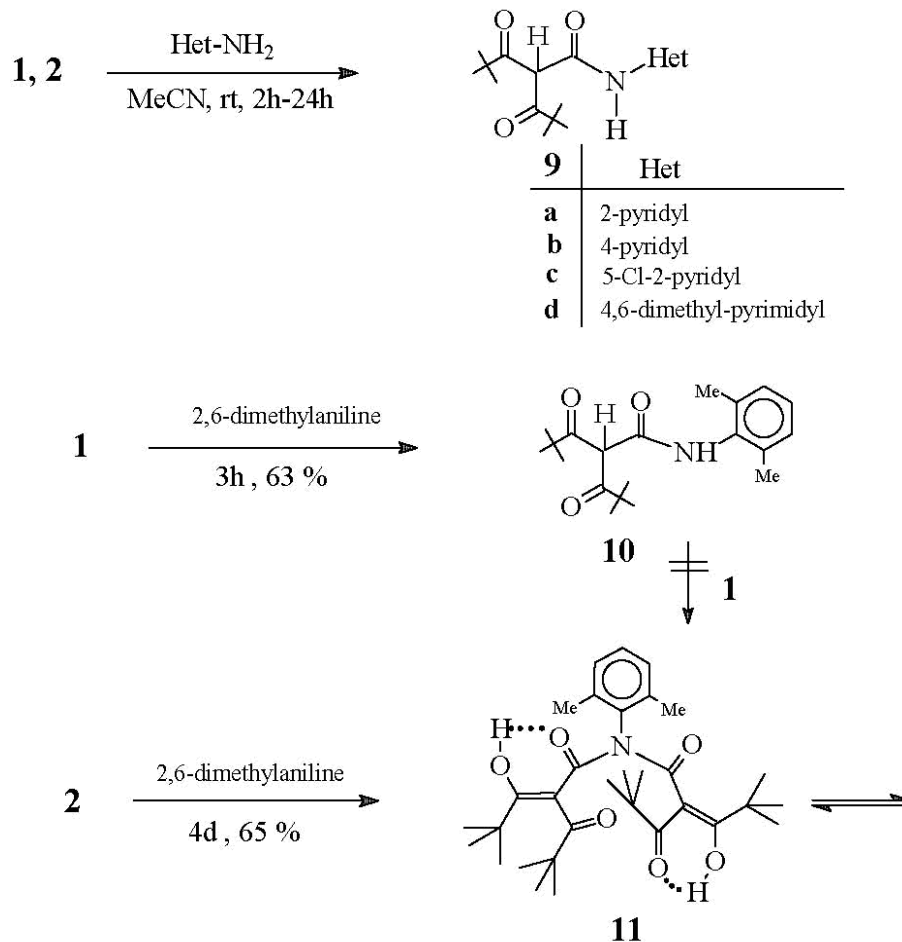


Scheme 3

Irrespective of employing α -oxoketene **1** or **2**, the primary reaction product in all cases was the corresponding open-chain derivative of dipivaloylacetic acid **6a,b,c** and **8**, the latter being a 1:2 product. Besides the expected signal pattern for the *t*-butyl and methyl groups the presence of CH-moieties in **6** and **8** was again unambiguously demonstrated by signals at 5.97 (**6a**), 5.75

(**6b**), 5.63 (**6c**) and 5.70 ppm (**8**), respectively, in the ^1H -NMR spectra. From the ^{13}C NMR spectrum of **8** an interesting structural detail became evident : while in the ^1H NMR spectrum the two slightly different CH-protons appear as one signal only (5.70 ppm), there are two signals at 62.9 ($^1J= 123.7$ Hz) and 60.7 ppm ($^1J= 123.7$ Hz) found in the ^{13}C NMR spectrum. Taking into account the different coupling constants and line-widths all carbon atoms of **8** could be clearly assigned : the CH attached to the C=O-NH-group appeared as a broad signal due to strongly hindered rotation around the C –NH bond, a phenomenon well known from dynamic NMR studies.¹² Similar line broadening is also found for the NH-C=O (164.0 ppm) as well as the adjoining pivaloyl-C=O's (206.1 ppm). In strict contrast, a distinct set of sharp signals is observed for the related carbons attached to the N-Me – moiety (62.9, 167.8 and 207.8 ppm, respectively). Attempts to cyclize the dipivaloylacetamide **6a** following the procedures successfully applied to **3a-c**, failed. The deacylated open-chain compound **7** (43%) was obtained instead; its CH_2 protons appear at 3.87 ppm.

In continuation of our efforts to obtain compounds representing the bridged bisdioxine scaffold (see Introduction) several heteroaromatic amines were treated with oxoketenes **1** and **2**, respectively, but again the corresponding dipivaloylacetamides **9** were obtained as the only reaction products (Scheme 4). However, when the sterically hindered 2,6-dimethylaniline was employed as the nucleophile, divergent results were obtained depending on whether the monomeric oxoketene **1** or the dimeric form **2** was the substrate: while **1** underwent a simple addition reaction as usual to afford the dipivaloylacetic derivative **10** , in the case of **2** the bis-acylated amide **11** was formed. Its ^{13}C NMR spectrum made evident that **11** favours enolization (no signal above 175 ppm) due to the enolic form being stabilized by intramolecular hydrogen bonds. It is important to note that pure **10** could not be converted into **11** when treated with **1** under identical or similar reaction conditions. Obviously, compounds **10** and **11** were formed via different mechanistic pathways (see below).

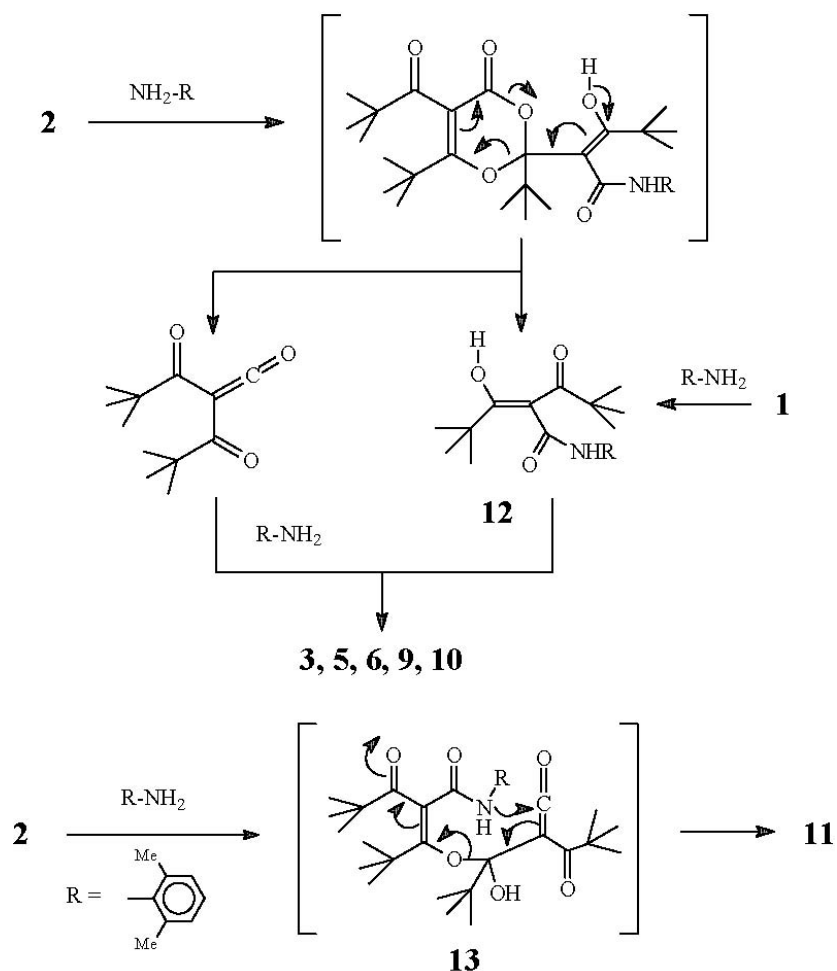


Scheme 4

Mechanistic considerations

The formation of open-chain dipivaloylactic acid derivatives **3**, **5**, **6**, **9** and **10** from dipivaloylketene **1** and the corresponding NH_2 – nucleophiles is the result of addition of the nucleophile to the ketene functionality to give **12** (Scheme 5). In case of the dimeric oxoketene **2**, the primary attack of the nucleophile at the ketene moiety must be followed by a subsequent fragmentation of the dioxinone ring. Finally, two equivalents of the corresponding dipivaloylactic acid derivatives should be formed via two consecutive elimination processes (Scheme 5)^{3b} With methylhydrazine the dipivaloylketene molecule released during this process adds to the free NH-Me group in **12** ($\text{R} = \text{NHMe}$) leading to **8**. However, the reaction of **2** with 2,6-dimethylaniline affording **11** must proceed via a somewhat different reaction pathway, since there is experimental evidence that the mono-acylated **10** cannot be converted into **11** by addition of **1** (see above). An intermediate **13** which still contains an oxoketene moiety could be formed in the initial addition of the amine (see Scheme 5). Subsequent intramolecular attack of the

amide nitrogen atom on the ketene function in **13** would lead to **11**.



Scheme 5

Experimental Section

General Procedures. Melting points were determined on a Tottoli apparatus (Buechi). IR spectra were recorded on a Perkin-Elmer 298 spectrophotometer. Elemental analyses were obtained on a Carlo Erba 1106 elemental analyzer. ^1H – and ^{13}C NMR spectra were obtained on Varian XL-200 Gemini (200 MHz), Bruker AMX 360 (360 MHz) and Bruker DRX Avance (500 MHz) spectrometers. The ^{15}N NMR spectra of **3b** and **4b** were recorded on a Bruker AMX 360 spectrometer. The mass spectrum of **11** was recorded on a Hewlett Packard LC/MSD instrument. The α -oxoketenes **1** and **2**^{1,2} and cyclohexanone semicarbazone¹³ were prepared according to the literature. All other reagents were purchased from Aldrich Chemical Co. and used without further purification. The solvents (dichloromethane, acetonitrile) were distilled and stored over

molecular sieves, the eluants used during chromatographic separations (*n*-hexane, ethyl acetate, methanol) were purchased in p.a. quality.

General procedure for the synthesis of dipivaloylacetic acid amide derivatives 3a-g
Equimolar amounts of the α -oxoketenes **1** (liquid) or **2** (solid), respectively, were added to a solution of the appropriate urea (1.00 mmol) in acetonitrile (2 mL), and the reaction mixture was stirred at rt for the appropriate reaction time (2 h - 24 h). After evaporation the crude solid products were recrystallized from acetonitrile or *n*-hexane / ethyl acetate (1:1).

N-(Dipivaloylacetyl)urea (3a). reaction time 3 h; yield 180 mg (67%, from **1**) as colourless crystals; mp 136-128°C (acetonitrile). IR (KBr) ν [cm^{-1}] 3440, 3320, 3120, 3020-2750, 1710, 1695, 1580, 1520, 1480; ^1H NMR (CDCl_3) δ 1.20 (s, 18H), 5.6 (br s, 1H), 5.7 (s, 1H), 7.87 (br s, 1H), 9.16 (br s, 1H). ^{13}C NMR (CDCl_3) δ 202.7 (C=O), 163.4 (NC=O), 153.5 (NCON), 63.5 (d, $J = 152.0$ Hz, CH), 46.0 (CMe₃), 26.4 (q, $J = 136$ Hz, CH₃). Anal. calcd. for C₁₃H₂₂N₂O₄ (270.33): C, 57.76; H, 8.20; N, 10.36. Found: C, 57.66; H, 8.25; N, 10.31.

1-(Dipivaloylacetyl)-3-methylurea (3b). a) From **1**: reaction time 3 h; yield 190 mg (68%) of colourless needles, mp 191-192°C (*n*-hexane/ethyl acetate 1:1). b) From **2**: reaction time 12 h; yield 170 mg (60%). IR (KBr) ν [cm^{-1}] 3340, 3220, 3110, 3020-2700, 1740, 1710, 1690, 1560, 1510, 1480; ^1H NMR (CDCl_3) δ 1.19 (s, 18H), 2.85 (d, $J = 5$ Hz, 3H), 5.65 (s, 1H), 8.04 (br s, 1H), 9.60 (br s, 1H); ^{15}N NMR (CDCl_3) δ (relative to nitromethane): -244.8 (d, $J = 85$ Hz, N-1), -306.4 (d, $J = 85$ Hz, N-3). Anal. calcd. for C₁₄H₂₄N₂O₄ (284.3): C, 59.13; H, 8.51; N, 9.85. Found: C, 59.19; H, 8.72; N, 9.68.

1-(Dipivaloylacetyl)-3-ethylurea (3c). a) From **1**: reaction time 3 h; yield 150 mg (50%) of colourless needles, mp 152-153°C (acetonitrile); b) From **2**: reaction time 12 h; yield 190 mg (63%). IR (KBr) ν [cm^{-1}] 3370, 3230, 3100, 3020-2700, 1740, 1690, 1550, 1515, 1480; ^1H NMR (CDCl_3) δ 1.17 (t, $J = 7.5$ Hz, 3H), 1.19 (s, 18H), 3.3 (q, $J = 7.5$ Hz, 2H), 5.65 (s, 1H), 8.1 (br s, 1H), 9.6 (br s, 1H). Anal. calcd. for C₁₅H₂₆N₂O₄ (298.3): C, 60.37; H, 8.80; N, 9.39. Found: C, 60.55; H, 8.90; N, 9.54.

1-(Dipivaloylacetyl)-3-phenylurea (3d). From **1**: reaction time 3 h; yield 170 mg (47%) of colourless crystals, mp 121-122°C (acetonitrile). IR (KBr) ν [cm^{-1}] 3450, 3350, 3220, 3000-2700, 1715, 1685, 1665, 1595, 1535, 1599, 1475; ^1H NMR (CDCl_3) δ 1.21 (s, 18H), 5.75 (s, 1H), 7.0-7.55 (m, 5H), 9.58 (br s, 1H), 10.17 (br s, 1H). Anal. calcd. for C₁₉H₂₆N₂O₄ (346.4): C, 65.87; H, 7.56; N, 8.09. Found: C, 65.77; H, 7.56; N, 8.19.

1-(Dipivaloylacetyl)-3-benzylurea (3e). From **1**: reaction time 3h; yield 150 mg (41%) of colourless crystals, mp 120-121°C (acetonitrile). IR (KBr) ν [cm^{-1}] 3430, 3300, 3220, 3080, 3000-2800, 1725, 1700, 1650, 1600, 1555, 1500, 1470; ^1H NMR (CDCl_3) δ 1.18 (s, 18H), 4.47 (d, $J = 5$ Hz, 2H), 5.67 (s, 1H), 7.20-7.40 (m, 5H), 8.46 (br s, 1H), 9.61 (br s, 1H). Anal. calcd. for C₂₀H₂₈N₂O₄ (360.4): C, 66.64; H, 7.83; N, 7.77. Found: C, 66.89; H, 7.91; N, 7.81.

1-(Dipivaloylacetyl)-3-(4-chlorophenyl)urea (3f). From **1**: reaction time 3 h; this product had

to be purified by column chromatography (silicagel (70-230 mesh), eluant dichloromethane/methanol 100:2) to give 290 mg (76%) of a colourless solid, mp 139-140°C (acetonitrile). IR(KBr) ν [cm^{-1}] 3440, 3340, 3000-2800, 1715, 1690, 1590, 1535, 1475; ^1H NMR (DMSO- d_6) δ 1.15 (s, 18H), 5.95 (s, 1H), 7.40 (d, $J=8.6$ Hz, 2H), 7.60 (d, $J=8.6$ Hz, 2H), 10.07 (br s, 1H), 10.80 (br s, 1H). Anal. calcd. for $\text{C}_{19}\text{H}_{25}\text{N}_2\text{O}_4\text{Cl}$ (379.8): C, 59.92; H, 6.62; N, 7.35. Found: C, 60.29; H, 6.70; N, 7.13.

1-(Dipivaloylacetyl)-3-(2-fluorophenyl)urea (3g). From **1**: reaction time 3 h; this product had to be purified by column chromatography (silicagel 70-230 mesh, eluant dichloromethane/methanol 100:2) to give 220 mg (67%) of a colourless solid, mp 119-120°C (*n*-hexane/ethyl acetate 1:1). IR(KBr) ν [cm^{-1}] 3330, 3220, 3120, 3000-2800, 1725, 1700, 1620, 1600, 1550, 1455; ^1H NMR (CDCl_3) δ 1.23 (s, 18H), 5.78 (s, 1H), 7.09 (m, 3H), 8.19 (t, $J=7.5$ Hz, 1H), 9.12 (br s, 1H), 10.38 (br s, 1H); ^{13}C NMR (DMSO- d_6) δ 206.4 (C=O), 167.5 (NCO), 156.0 (NCON), 150.8, 127.5 (d, $J=330$ Hz), 125.1, 124.8, 123.5, 116.2, 64.5 (d, $J=153.0$ Hz), 45.2, 26.9 (q, $J=135.1$ Hz). Anal. calcd. for $\text{C}_{19}\text{H}_{25}\text{N}_2\text{O}_4\text{F}$ (364.4): C, 62.61; H, 6.91; N, 7.68. Found: C, 62.55; H, 6.96; N, 7.62.

Conversion of urea derivatives **3a-c** into pyrimidine-2,4-diones **4a-c** – General procedure .

A mixture of polyphosphoric acid (PPA, 2g) and the appropriate urea derivative **3a-c** (0.5 mmol) was heated to 100-120°C with frequent stirring for 2 h. After cooling to rt, the reaction mixture was diluted with water (5 mL) and extracted with dichloromethane (4x 5 mL). The combined organic layers were dried over sodium sulfate, the solvent was evaporated, and the crude solid products were recrystallized from acetonitrile or ethyl acetate.

6-*t*-Butyl-pyrimidine-2,4(1*H*,3*H*)dione (4a). ¹⁰ Yield 80 mg (80%) of colourless crystals; mp 229-230°C (acetonitrile) (lit.¹⁰ mp 227-228°C). IR(KBr) ν [cm^{-1}] 3350-3100, 3060-2700, 1710, 1665, 1535, 1490; ^1H NMR (CDCl_3) δ 1.32 (s, 9H), 5.63 (s, 1H), 9.36 (br s, 1H), 9.85 (br s, 1H).

6-*t*-Butyl-1-methylpyrimidine-2,4(1*H*,3*H*)-dione (4b). Yield 70 mg (50%) of colourless crystals; mp 162-163°C (ethyl acetate). IR(KBr) ν [cm^{-1}] 3310-3100, 3000-2700, 1705, 1665, 1585, 1480; ^1H NMR (CDCl_3) δ 1.4 (s, 9H), 3.54 (s, 3H), 5.78 (s, 1H), 9.84 (br s, 1H); ^{13}C NMR(CDCl_3): δ 163.9, 163.6 (C=O), 153.0 (C-6), 100.0 (C-5), 35.9 (C(Me)₃), 34.3 (NCH₃), 29.6 (CH₃). ^{15}N NMR (CDCl_3) δ - 232.3 (NH). Anal. calcd. for $\text{C}_9\text{H}_{14}\text{N}_2\text{O}_2$ (182.2): C, 59.32; H, 7.74; N, 15.37. Found: C, 59.11; H, 7.79; N, 15.30.

6-*t*-Butyl-1-ethylpyrimidine-2,4(1*H*,3*H*)-dione (4c). Yield 70 mg (53%) of colourless crystals; mp 140-142°C (acetonitrile). IR(KBr) ν [cm^{-1}] 3280-3120, 3050-2800, 1705, 1660, 1590, 1490; ^1H NMR (CDCl_3) δ 1.3 (t, $J=7$ Hz, 3H), 1.4 (s, 9H), 4.1 (q, $J=7$ Hz, 2H), 5.75 (s, 1H), 9.12 (br s, 1H). Anal. calcd. for $\text{C}_{10}\text{H}_{16}\text{N}_2\text{O}_2$ (196.2): C, 61.22; H, 8.22; N, 14.27. Found: C, 61.72; H, 8.56; N, 14.42.

Synthesis of the dipivaloylacetic acid amide derivatives **5**, **6**, **8**, **9**, **10** and **11**.

These experiments followed the preparative procedure described for the synthesis of compounds **3** exactly: Equimolar amounts of the oxoketenes **1** or **2** and the appropriate reagent were

dissolved in dichloromethane or acetonitrile and stirred at rt for 2 – 24 h. The workup was identical to that given for **3**.

1-Dipivaloylacetyl-4-phenylsemicarbazide (5a). Reaction time 2 h, yield 110 mg (56%) of colourless needles; mp 164-166°C (acetonitrile). IR(KBr) ν [cm^{-1}] 3360, 3220, 3000-2800, 1720, 1705, 1670, 1650, 1600, 1550, 1500; ^1H NMR (CDCl_3) δ 1.13 (s, 18H); 5.66 (s, 1H), 6.95-7.47 (m, 5H), 8.33 (s, 1H), 8.57(s, 1H), 9.91 (s, 1H). Anal. calcd. for $\text{C}_{19}\text{H}_{27}\text{N}_3\text{O}_4$ (347.2): C, 64.84; H, 8.16; N, 12.60. Found: C, 64.86; H, 8.09; N, 12.47.

1-Dipivaloylacetyl-3-cyclohexylidenaminourea (5b). Reaction time 24 h, yield 90 mg (52%) of a colourless solid; mp 146-147°C (acetonitrile). IR(KBr) ν [cm^{-1}] 3500, 3000-2800, 1700, 1670, 1660, 1600, 1485; ^1H NMR (CDCl_3) δ 1.25 (s, 18H), 1.44-2.44 (m, 10H), 5.85 (s, 1H), 8.38 (s, 1H). Anal. calcd. for $\text{C}_{19}\text{H}_{31}\text{N}_3\text{O}_4$ (365.3): C, 62.46; H, 8.49; N, 11.51. Found: C, 62.47; H, 8.59; N, 11.55.

N-Acetyl-2,2-dipivaloylacetylacetamide (6a). (a) From **1**: yield 100 mg (74%) of colourless crystals; mp 70-71°C; b) from **2**: yield 90 mg (66%); mp 70-71°C (n-hexane/ethyl acetate 1:1). IR(KBr) ν [cm^{-1}] 3460, 3340, 3040-2800, 1735, 1715, 1675, 1615, 1550, 1480; ^1H NMR (CDCl_3) δ 1.2 (s, 18H), 2.26 (s, 3H), 5.97 (s, 1H), 9.47 (s, 1H). Anal. calcd. for $\text{C}_{14}\text{H}_{23}\text{NO}_4$ (269.3): C, 62.43; H, 8.60; N, 5.20. Found: C, 62.55; H, 8.52; N, 5.19.

2,2-Dipivaloyl-N-carboxymethylacetamide (6b). From **1** (the glycine was suspended in acetonitrile), reaction time 24 h : yield 70 mg (61%) of colourless crystals; mp 180-181°C (n-hexane/ethyl acetate 1:1). IR(KBr) ν [cm^{-1}] 3300, 3020-2800, 1750, 1720, 1660, 1540, 1490; ^1H NMR (CDCl_3) δ 1.20 (s, 18H), 4.01 (d, $J = 5$ Hz, 2H), 5.75 (s, 1H), 7.2 (s, 1H). Anal. calcd. for $\text{C}_{14}\text{H}_{23}\text{NO}_5$ (285.3): C, 58.93; H, 8.13; N, 4.91. Found: C, 58.96; H, 8.06; N, 5.00.

1-Dipivaloylacetyl-2,2-dimethylhydrazine (6c). (a) From **1** (solvent dichloromethane), reaction time 12 h: yield 140 mg (73%) of a pale-yellow solid; mp 170-172°C (n-hexane/ethyl acetate 1:1); b) from **2**, reaction time 24 h: yield 60g (40%). IR(KBr) ν [cm^{-1}] 3180, 3080, 3020-2800, 1715, 1700, 1675, 1480, 1470; ^1H NMR(CDCl_3) δ 1.2 (s, 18H), 2.55 (s, 6H), 5.63(s, 1H), 7.22 (s, 1H). Anal. calcd. for $\text{C}_{14}\text{H}_{26}\text{N}_2\text{O}_3$ (270.3): C, 62.22; H, 9.63; N, 10.37. Found: C, 62.38; H, 9.82; N, 10.39.

N-Methyl-N,N'-di(dipivaloylacetyl)hydrazine (8). (a) From **1** (solvent dichloromethane), reaction time 12 h: yield 80 mg (53%) of colourless needles; mp 186-187°C (n-hexane/ ethyl acetate 1:1); b) from **2** , reaction time 24 h: yield 60 mg (40%). IR(KBr) ν [cm^{-1}] 3270, 3050-2800, 1720, 1700, 1645, 1520, 1480; ^1H NMR (CDCl_3) δ 1.18 (s, 18H), 1.21 (s, 18H), 3.1 (s, 3H), 5.7 (s, 2H), 8.75 (s, 1H); ^{13}C NMR (CDCl_3) δ 207.8 (s, C=O), 206.1 (br s, C=O), 167.8 (s, NCO), 164.0 (br s, NCO), 62.9 (d, $J = 123.7$ Hz, CH), 60.7 (br d, $J = 123.7$ Hz, CH), 45.7 (s, CMe_3), 45.5 (s, CMe_3), 35.3 (q, $J = 135$ Hz, NCH_3), 27.1, 26.9 (q, $J = 135$ Hz, CH_3). Anal. calcd. for $\text{C}_{25}\text{H}_{42}\text{N}_2\text{O}_6$ (466.6): C, 64.35; H, 9.07; N, 6.05. Found: C, 64.37; H, 9.13; N, 5.92.

2,2-Dipivaloyl-N-(2-pyridyl)acetamide (9a). (a) From **1** (solvent acetonitrile), reaction time 2 h: yield 120 mg (39%) of pale-yellow needles; mp 93-94°C (acetonitrile); from **2**, reaction time

24 h: yield 200 mg (59%). IR(KBr) ν [cm^{-1}] 3210, 3020-2700, 1720, 1700, 1660, 1600, 1585, 1550, 1480; ^1H NMR(CDCl_3) δ 1.23 (s, 18H), 5.77 (s, 1H), 7.01-8.31 (m, 4H). Anal. calcd. for $\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_3$ (304.4): C, 67.08; H, 7.95; N, 9.20. Found: C, 67.21; H, 8.13; N, 9.16.

2,2-Dipivaloyl-N-(4-pyridyl)acetamide (9b). (a) From **1** (solvent acetonitrile), reaction time 2 h: yield 190 mg (66%) of a pale-yellow solid; mp 156-158°C (acetonitrile); b) from **2**: reaction time 24 h: yield 210 mg (75%); IR(KBr) ν [cm^{-1}] 3240, 3180, 3020-3600, 1720, 1700, 1680, 1600, 1520, 1475; ^1H NMR (CDCl_3) δ 1.21 (s, 18H), 5.81(s, 1H), 7.44 (d, $J = 6.5$ Hz, 2H), 8.49 (d, $J = 6.5$ Hz, 2H), 8.93 (s, 1H). Anal. calcd. for $\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_3$ (304.4): C, 67.08; H, 7.95; N, 9.20. Found: C, 67.41; H, 8.18; N, 9.30.

2,2-Dipivaloyl-N-(5-chloro-2-pyridyl)acetamide (9c). The equimolar mixture (0.46 mmol) of oxoketene **2** and 2-amino-5-chloropyridine in acetonitrile was refluxed for 12 h: yield 140 mg (44%) of colourless crystals; mp 131-132°C (acetonitrile); IR(KBr) ν [cm^{-1}] 3370, 3020-2800, 1730, 1700, 1575, 1515; ^1H NMR (CDCl_3) δ 1.24 (s, 18H), 5.77 (s, 1H), 7.63 (d, $J = 10$ Hz, 1H), 8.0 (d, $J = 10$ Hz, 1H), 8.26 (s, 1H), 9.20 (s, 1H). Anal. calcd. for $\text{C}_{17}\text{H}_{23}\text{N}_2\text{O}_3\text{Cl}$ (338.88): C, 60.25; H, 6.84; N, 8.26. Found: C, 60.29; H, 6.87; N, 8.16.

2,2-Dipivaloyl-N-(4,6-dimethylpyrimidyl)-acetamide (9d). As described for **9c**, from equimolar mixtures (0.4 mmol) of **2** and 2-amino-4,6-dimethylpyrimidine after 24 h at 80°C 70 mg (52%) of **9d** were obtained as colourless crystals; mp 133-135°C (*n*-hexane/ ethyl acetate 1:2). IR(KBr) ν [cm^{-1}] 3220, 3000-2800, 1725, 1700, 1680, 1610, 1545, 1480. ^1H NMR(CDCl_3) δ 1.25 (s, 18H), 2.43 (s, 6H), 6.18 (br s, 1H), 6.75 (s, 1H), 8.95 (br s, 1H); ^{13}C NMR(CDCl_3) δ 203.0 (C=O), 168.1 (NCO), 167.9 (NCN), 156.7 (NCMe), 110.6 (=CH), 65.1 (CH), 46.1 (CCH₃), 27.3, 26.3 (CCH₃), 23.9 (CH₃). Anal. calcd. for $\text{C}_{18}\text{H}_{27}\text{N}_3\text{O}_3$ (333.4): C, 64.84; H, 8.16; N, 12.60. Found: C, 64.86; H, 8.09; N, 12.47.

N-Dipivaloylacetyl-2,6-dimethylaniline (10). Reaction time 3 h, yield 70 mg (63%) of a colourless solid; mp 136-137°C (ethyl acetate); IR(KBr) ν [cm^{-1}] 3320, 3080-2800, 1720, 1700, 1650, 1595, 1500, 1480; ^1H NMR(CDCl_3) δ 1.27 (s, 18H), 2.14 (s, 6H), 5.93 (s, 1H) 7.05 (s, 3H), 8.37 (s, 1H). Anal. calcd. for $\text{C}_{20}\text{H}_{29}\text{NO}_3$ (331.45): C, 72.77; H, 8.82; N, 4.22. Found: C, 72.73; H, 8.99; N, 4.18.

N,N-Di-(dipivaloylacetyl)-2,6-dimethylaniline (11). From **2**, reaction time 4 d; yield: 130 mg (56%) of colourless plates; mp 184-185°C (ethyl acetate). IR(KBr) ν [cm^{-1}] 3440, 3150, 3000-2850, 1730, 1690, 1665, 1610, 1480, 1450; ^1H NMR(CDCl_3) δ 1.149 (s, 9H), 1.22, 1.236, 1.256 (br s, 27H), 2.29 (s, 6H), 6.75 (s, 1H), 7.05 (s, 2H); ^{13}C NMR(CDCl_3) δ 175.0 (s, NCO), 164.8 (s, NCO), 163.5 (m, CCO), 162.5 (m, CCO), 133.9, 132.7, 128.9 (d, $J = 156$ Hz), 126.0 (d, $J = 156$ Hz), 105.5, 103.2, 100.5, 97.8 (s, C=CO, *E/Z*-isomers, rotamers), 40.1, 38.6, 38.3 (CMe₃), 29.1, 28.4, 25.5 (qs, $J = 118$ Hz, CCH₃), 20.1 (q, $J = 118$ Hz, CH₃); MS (APCI) : 540.5 (M-H⁺), 542.6 (M+H⁺). Anal. calcd. for $\text{C}_{32}\text{H}_{47}\text{NO}_6$ (541.7): C, 70.95; H, 8.74; N, 2.58. Found: C, 70.79; H, 8.82; N, 2.55.

1-Acetylamino-4,4-dimethylpentane-1,3-dione (7). A mixture of 160 mg (0.6 mmol) of **6a** and PPA (1.5 g) was heated at 70–80°C for 3 h with frequent stirring. After cooling to rt and dilution with water (10 mL) the reaction mixture was extracted by dichloromethane (4 x 5 mL). The combined extracts were dried over anhydrous sodium sulfate, the solvent was evaporated, and the crude product was recrystallized from *n*-hexane. Yield 80 mg (43%) of a colourless solid; mp 81°C (*n*-hexane). IR(KBr) ν [cm⁻¹] 3280, 3180, 3040-2840, 1740, 1720, 1700, 1610, 1535, 1505; ¹H NMR (CDCl₃) δ 1.20 (s, 9H), 2.26 (s, 3H), 3.87 (s, 2H), 9.1 (br s, 1H). Anal. calcd. for C₉H₁₅NO₃ (185.2): C, 58.36; H, 8.16; N, 7.56. Found: C, 58.40; H, 8.03; N, 7.46.

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