Synthesis of 3-Amino(alkoxy)-2,4-dioxo-1,3-oxazolidine-5-carboxylates from Tartronic Esters

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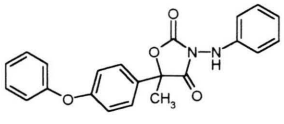
Tartronic Esters, 1,1′-Carbonyl-di-(1,2,4-triazole), 3-Amino-2,4-dioxo-1,3-oxazolidine-5-carboxylates, 3-Alkoxy-2,4-dioxo-1,3-oxazolidine-5-carboxylates

The reaction of tartronic esters (**1a-d**) with 1,1′-carbonyl-di-(1,2,4-triazole), hydrazines or hydroxylamines produces 3-amino/3-alkoxy(aralkoxy)-2,4-dioxo-1,3-oxazolidine-5-carboxylic esters (**5**,**6**) which are structurally related to the fungicides *Famoxadone* (**I**) and *Chlozolinate* (**II**). Under suitable conditions the carboxylic ester of **6** can be converted to a carboxamide (**7**), carbohydrazide (**8**) or carbohydroxamic acid (**9**).

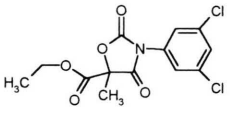
Introduction

3-Amino-oxazolidin-2,4-diones, which were described by Geffken [1] in 1981 have attracted considerable interest in agricultural chemistry due to their potent activity against phytopathogenic fungi. Recently, Famoxadone (Famoxate®) (**I**) [2], a member of this class of compounds was introduced to the market as a broad spectrum fungicide for control of infectious diseases of cereals, grapes and legumes.

In continuation of our studies directed to structural analogues of **I** we now became interested in synthesizing 3-heterosubstituted 2,4-dioxooxazolidine-5-carboxylic esters (**5**,**6**), which can be understood as a formal compromise between **I** and the small spectrum fungicide Chlozolinate (**II**) [3].



Famoxadone (I)



Chlozolinate (II)

Scheme 1.

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Chemistry

According to previous studies on atrolactic acid esters [4] we envisioned the tartronic esters **1a-d** [5,6] as suitable starting materials, which upon successive treatment with either 1,1′-carbonyldiimidazole or 1,1′-carbonyl-di-(1,2,4-triazole), hydroxylamines or hydrazines should give the desired heterocycles **5**,**6** *via* the open-chain intermediates **3**,**4**.

After several nonsatisfactory attempts to get access to **5**,**6** by means of 1,1′-carbonyldiimidazole, we found that 1,1′-carbonyl-di-(1,2,4-triazole) [7] reacted smoothly with **1a**,**c** in anhydrous methylene chloride at ambient temperature to give the intermediate triazolides **2** [i.r.: 1755–1765 cm^{-1}, (C=O)] which in turn underwent the expected hydrazinolysis or hydroxylaminolysis to **3** and **4**. Finally, subsequent treatment of **3**,**4** with triethylamine furnished the heterocycles **5**,**6** in overall yields of 30–63%.

It should be noted, that in contrast to the smooth reaction of **1a**,**c** with CDT to give the intermediates **2**, the corresponding reaction of **1b**,**d** required the presence of a base (*e.g.* triethylamine), reflecting the lower reactivity of the tertiary alcoholic group. In all cases the cyclization step could be clearly monitored by running i.r. spectra from the reaction mixture, demonstrating the gradual emergence of a (C=O)-band at 1820–1840 cm^{-1} besides a strong (C=O)-absorption at 1750–1780 cm^{-1}, typical for 2,4-dioxooxazolidines [8].

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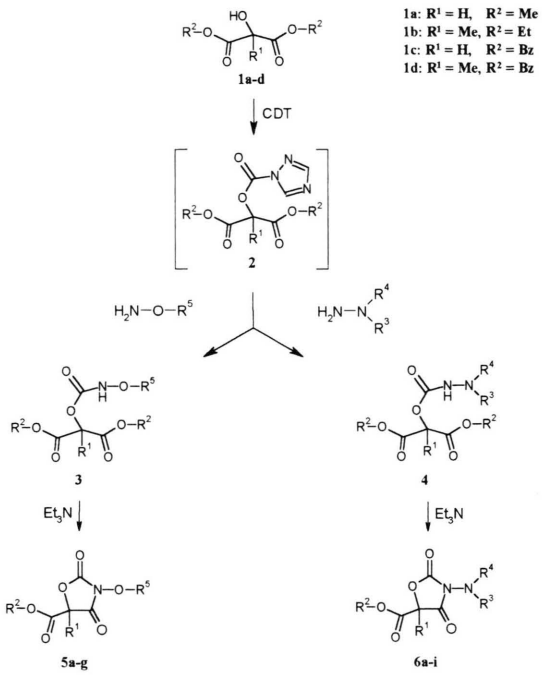


Reagents: CDT: 1,1′-carbonyl-di-(1,2,4-triazole), Et_3N: triethylamine

Alkyl(aralkyl) 3-amino-2,4-dioxo-1,3-oxazolidine-5-carboxylates (**6**)

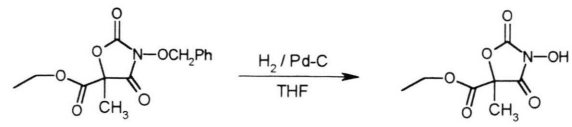
6	R^1	R^2	R^3	R^4
a	H	CH_3	H	Ph
b	H	CH_3	$-(CH_2)_5-$	
c	H	CH_3	CH_3	CH_3
d	H	CH_2Ph	H	Ph
e	H	CH_2Ph	$-(CH_2)_5-$	
f	H	CH_2Ph	CH_3	CH_3
g	H	CH_2Ph	H	H
h	CH_3	C_2H_5	H	Ph
i	CH_3	CH_2Ph	H	Ph

Alkyl(aralkyl) 3-alkoxy-2,4-dioxo-1,3-oxazolidine-5-carboxylates (**5**)

5	R^1	R^2	R^5
a	H	CH_3	CH_2Ph
b	H	CH_2Ph	CH_2Ph
c	H	CH_2Ph	CH_2OCH_3
d	H	CH_2Ph	CH_3
e	CH_3	C_2H_5	CH_2Ph
f	CH_3	C_2H_5	CH_2-2,4-Cl-Ph
g	CH_3	CH_2Ph	CH_2-2,4-Cl-Ph

Scheme 2.

5a was converted by hydrogenolysis to the cyclic N-hydroxy imide (**5h**), which is characterized by a red colored reaction with ferric chloride.



Scheme 3.

As exemplified by the reactions of **6h** with benzylamine, N,N′-dimethylhydrazine or hydroxylamine, the exocyclic ester group is attacked selectively providing 2,4-dioxooxazolidine derivatives with a carboxamide (**7**), carbohydrazide (**8**) or carbohydroxamic acid (**9**) group at C-5.

In contrast to **7**, **8**, and **9** which are stable compounds, the 5-carboxylated 2,4-dioxooxazolidine derivative **10** could not be isolated: The alkaline hydrolysis of **6h** (i) with potassium hydroxide in ethanol followed by acidification as well as the hydrogenolysis of the benzylic ester **6i** (ii) only produced the 2,4-oxazolidindione **11,** that obviously arose from the spontaneous decarboxylation of **10**.

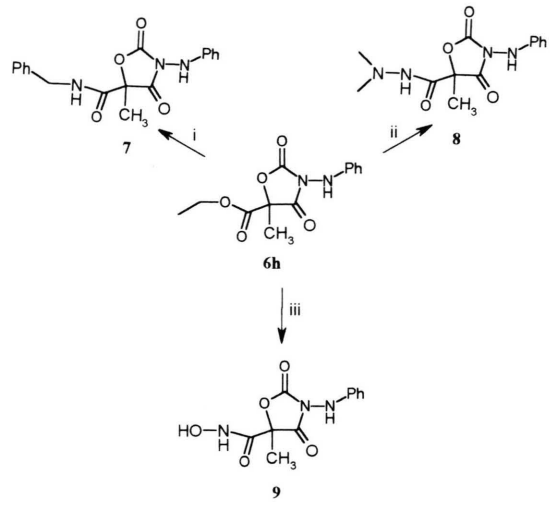
Experimental

Melting points (uncorrected) were determined on a Mettler FP 62. Elemental analysis were performed on a Heraeus CHN-O-Rapid. The IR spectra were recorded on a Perkin Elmer 1600 FTIR spectrophotometer. The ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100,62 MHz) spectra were recorded on a Bruker AMX 400 spectrometer using tetramethylsilane as an internal standard and DMSO-d_6 and $CDCl_3$ as solvents.

Dimethyl tartronate (**1a**) and *diethyl methyltartronate* (**1b**) were prepared according to literature [5,6].

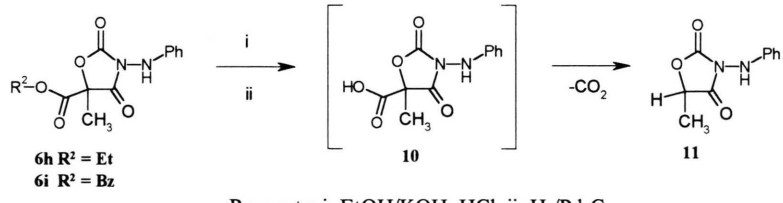
The tartronates **1c,d** *were prepared as follows*

To a stirred solution of tartronic or methyltartronic acid (10 mmol) and N-ethyl-diisopropylamine (22 mmol) in dimethyl acetamide (10 ml) benzyl bromide (22 mmol) was added dropwise at ambient temperature. After 24h the reaction mixture was diluted with 100 ml water and the precipitate dissolved in CH_2Cl_2, dried over Mg SO_4, and the solvent evaporated. The residue was purified by column chromatography on silica gel with CH_2Cl_2 as eluent.



Reagents: i: benzylamine, ii: N,N′-dimethylhydrazine, iii: $H_2NOH \cdot HCl/NaOEt$

Scheme 4.



Reagents: i: EtOH/KOH, HCl, ii: H_2/Pd-C

Scheme 5.

Dibenzyl tartronate (**1c**): Colourless crystals (80%); m.p. 73 °C (Et_2O/hexane); IR (KBr): υ = 3423 (OH), 1739, 1733 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 4.88 (d, J = 7.6 Hz, 1H, CH), 6.63 (d, J = 7.6 Hz, 1H, OH), 5.15 (d, J = 12.6 Hz, 1H, OCH_2Ph), 5.19 (d, J = 12.6 Hz, 1H, OCH_2Ph), 7.30–7.38 (m, 10H, ArH); ^{13}C-NMR (DMSO-d_6):δ (ppm) 66.4 (OCH_2Ph), 71.4 (CH), 127.8, 128.1, 128.3 (C tert., ArC), 135.4 (C quart., ArC), 168.2 (C=O).

Analysis for $C_{17}H_{16}O_5$

Calcd	C 67.99	H 5.37%,
Found	C 67.59	H 5.38%.

Dibenzyl methyltartronate (**1d**): Colourless oil (65%); IR (KBr): υ = 3488 (OH), 1740 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1,50 (s, 3H, CH_3), 5.15 (s, 2H, OCH_2Ph) 6.59 (s, 1H, OH), 7.28–7.37 (m, 10H, ArH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 22.8 (CH_3), 66.4 (OCH_2), 75.9 (C quart.), 127.7, 128.0, 128.3 (C tert., ArC), 135.5 (C quart., ArC), 170.4 (C=O).

Analysis for $C_{18}H_{18}O_5$

Calcd	C 68.78	H 5.77%,
Found	C 68.51	H 5.77%.

Alkyl(aralkyl) 3-alkoxy(aralkoxy)-2,4-dioxo-1,3-oxazolidine-5-carboxylates (**5a-5 g**) *and alkyl(aralkyl) 3-amino-2,4-dioxo-1,3-oxazolidine-5-carboxylates* (**6a-i**). General procedure.

1,1′-Carbonyl-di-(1,2,4-triazole) (10 mmol) was added portionwise to a stirred solution of **1a-d** (5 mmol) in anhydrous CH_2Cl_2 (10 ml). In the case of **1b,d** one drop of triethylamine was added to the reaction mixture. After 1h the precipitated 1,2,4-triazole was filtered off and the appropriate alkoxyamine or hydrazine (5 mmol) added to the filtrate. Stirring of the reaction mixture was continued and in the case of **1a,c** one drop of triethylamine was added after 2 h. After 40 h the reaction mixture was washed with brine (5 ml), the organic layer dried over $MgSO_4$ and concentrated. The oily residues were chromatographed on silica gel

with CH_2Cl_2 (**5a-g**) or CH_2Cl_2/Et_2O (9:1) (**6a-i**) as eluents.

Methyl 3-benzyloxy-2,4-dioxo-1,3-oxazolidine-5-carboxylate (**5a**): Colourless crystals (41%); m.p. 54 °C (Et_2O/hexane); IR (KBr): υ = 1837, 1777, 1761 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ (ppm) 3.86 (s, 3H, OCH_3), 5.15 (s, 1H, CH), 5.17 (s, 2H, $NOCH_2$), 7.38–7.48 (m, 5H, ArH); ^{13}C-NMR ($CDCl_3$): δ (ppm) 54.1 (OCH_3), 74.6 (CH), 79.8 ($NOCH_2$), 128.8, 130.0, 130.3 (C tert., ArC), 132.1 (C quart., ArC), 149.8 (C-2, C=O), 160.2, 161.9 (C=O).

Analysis for $C_{12}H_{11}NO_6$
Calcd C 54.34 H 4.18 N 5.28%,
Found C 54.84 H 4.36 N 5.35%.

Benzyl 3-benzyloxy-2,4-dioxo-1,3-oxazolidine-5-carboxylate (**5b**): Colourless crystals (45%); m.p. 73 °C (Et_2O/hexane); IR (KBr): υ = 1835, 1772, 1750 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ (ppm) 5.14 (s, 2H, $NOCH_2$), 5.16 (s, 1H, CH), 5.26 (s, 2H, OCH_2Ph), 7.33–7.44 (m, 10H, ArH); ^{13}C-NMR ($CDCl_3$): δ (ppm) 69.1 (OCH_2Ph), 74.6 (CH), 79.8 ($NOCH_2$), 128.5, 128.7, 128.8, 129.0, 129.9, 130.3 (C tert., ArC), 132.1, 133.9 (C quart., ArC), 149.8 (C-2, C=O), 160.1, 161.4 (C=O).

Analysis for $C_{18}H_{15}NO_6$
Calcd C 63.34 H 4.43 N 4.10%,
Found C 63.35 H 4.42 N 4.17%.

Benzyl 3-methoxymethoxy-2,4-dioxo-1,3-oxazolidine-5-carboxylate (**5c**): Colourless crystals (37%); m.p. 76 °C (Et_2O/hexane); IR (KBr): υ = 1836, 1780, 1750 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 3.52 (s, 3H, OCH_3), 5.06 (s, 2H, OCH_2O), 5.27 (d, J = 12.2 Hz, 1H, OCH_2Ph), 5.31 (d, J = 12.2 Hz, 1H, OCH_2Ph), 5.93 (s, 1H, CH), 7.34–7.41 (m, 5H, ArH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 57.1 (OCH_3), 67.6 (OCH_2Ph), 74.9 (CH), 101.0 (OCH_2O), 127.9, 128.3, 128.4, (C tert., ArC), 134.8 (C quart., ArC), 150.6 (C-2, C=O), 161.0, 161.6 (C=O).

Analysis for $C_{13}H_{13}NO_7$
Calcd C 52.89 H 4.44 N 4.74%,
Found C 52.81 H 4.47 N 4.74%.

Benzyl 3-methoxy-2,4-dioxo-1,3-oxazolidine-5-carboxylate (**5d**): Colourless crystals (30%); m.p. 77 °C (Et_2O/hexane); IR (KBr): υ = 1836, 1775, 1755 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 3.90 (s, 3H, OCH_3), 5.25 (d, J = 12.3 Hz, 1H, OCH_2Ph), 5.29 (d, J = 12.3 Hz, 1H, OCH_2Ph), 5.86 (s, 1H, CH), 7.34–7.43 (m, 5H, ArH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 64.9 (OCH_3), 67.5 (OCH_2Ph), 74.9 (CH), 128.0 128.3, 128.4, (C tert., ArC), 134.8 (C quart., ArC), 150.2 (C-2, C=O), 160.5, 161.6 (C=O).

Analysis for $C_{12}H_{11}NO_6$
Calcd C 54.34 H 4.18 N 5.28%,
Found C 53.88 H 4.17 N 5.22%.

Ethyl 3-benzyloxy-5-methyl-2,4-dioxo-1,3-oxazolidine-5-carboxylate (**5e**): Colourless crystals (45%); m.p. 60 °C (Et_2O/hexane); IR (KBr): υ = 1839, 1776, 1740 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.27 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.68 (s, 3H, CH_3), 4.25 (q, 4H, J = 7.1 Hz, CH_2CH_3), 5.19 (s, 2H, $NOCH_2$), 7.38–7.49 (m, 5H, ArH); ^{13}C-NMR ($CDCl_3$): δ (ppm) 13.9 (CH_3), 18.9 (C-5, CH_3), 63.7 (OCH_2), 79.5 ($NOCH_2$), 82.3 (C-5), 128.7, 129.9, 130.3 (C tert., ArC), 132.3 (C quart., ArC), 149.9 (C-2, C=O), 163.8, 164.3 (C=O).

Analysis for $C_{14}H_{15}NO_6$
Calcd C 57.34 H 5.16 N 4.78%,
Found C 57.22 H 5.16 N 4.84%.

Ethyl 3-(2,4-dichlorobenzyloxy)-5-methyl-2,4-dioxo-1,3-oxazolidine-5-carboxylate (**5f**): Colourless crystals (48%); m.p. 83 °C (Et_2O/hexane); IR (KBr): υ = 1841, 1764, 1744 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.21 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.75 (s, 3H, CH_3), 4.28 (q, 2H, J = 7.1 Hz CH_2CH_3), 5.28 (s, 2H, $NOCH_2$), 7.29–7.50 (m, 3H, ArH); ^{13}C-NMR ($CDCl_3$): δ (ppm) 13.9 (CH_3), 18.9 (C-5, CH_3), 63.9 (OCH_2), 75.5 ($NOCH_2$), 82.5 (C-5), 127.5, 129.7, 133.1(C tert., ArC), 129.3, 136.0, 136.6 (C quart., ArC), 149.7 (C-2, C=O), 163.7, 164.2 (C=O).

Analysis for $C_{14}H_{13}Cl_2NO_6$
Calcd C 46.43 H 3.62 N 3.87 Cl 19.58%,
Found C 46.24 H 3.65 N 3.97 Cl 19.63%.

Benzyl 3-(2,4-dichlorobenzyloxy)-5-methyl-2,4-dioxo-1,3-oxazolidine-5-carboxylate (**5 g**): Colourless crystals (52%); m.p. 99 °C (Et_2O/hexane); IR (KBr): υ = 1836, 1772, 1745 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.78 (s, 3H, CH_3), 5.19 (s, 2H, $NOCH_2$), 5.21 (d, J = 12.2 Hz, 1H, OCH_2Ph), 5.26 (d, J = 12.2 Hz, 1H, OCH_2Ph), 7.20–7.40 (m, 8H, ArH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 18.9 (C-5, CH_3), 69.2 (OCH_2Ph), 75.6 ($NOCH_2$), 82.5 (C-5), 127.5, 128.2, 128.9, 129.0 129.7, 133.0 (C tert., ArC), 134.0, 136.0, 136.6 (C

quart., ArC), 149.5 (C-2, C=O), 163.6, 164.0 (C=O).

Analysis for $C_{19}H_{15}Cl_2NO_6$
Calcd C 53.79 H 3.56 N 3.30 Cl 16.71%,
Found C 53.71 H 3.55 N 3.42 Cl 16.70%.

Methyl 2,4-dioxo-3-phenylamino-1,3-oxazolidine-5-carboxylate (**6a**): Colourless crystals (60%); m.p. 138 °C (Et_2O/hexane); IR (KBr): υ = 3316 (NH), 1836, 1766, 1751 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 3.84 (s, 3H, OCH_3), 6.01 (s, 1H, CH), 6.77–7.22 (m, 5H, ArH), 8.73 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 53.5 (OCH_3), 75.8 (CH), 112.3, 120.5, 129.0 (C tert., ArC), 145.1 (C quart., ArC), 153.1 (C-2, C=O), 162.9, 164.8 (C=O).

Analysis for $C_{11}H_{10}N_2O_5$
Calcd C 52.80 H 4.03 N 11.20%,
Found C 52.84 H 4.06 N 11.24%.

Methyl 2,4-dioxo-3-(piperidinoamino)-1,3-oxazolidine-5-carboxylate (**6b**): Colourless crystals (54%); m.p. 93 °C (Et_2O/hexane); IR (KBr): υ = 1825, 1776, 1755 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.47 (dt, J = 6.1/5.6 Hz, 2H, CH_2), 1.74 (dt, J = 6.1/5.6 Hz, 4H, 2 CH_2), 3.23 (t, J = 5.6 Hz, 4H, CH_2NCH_2), 3.90 (s, 3H, OCH_3) 5.18 (s, 1H, CH); ^{13}C-NMR ($CDCl_3$): δ (ppm) 22.8, 25.8 (3 CH_2), 52.6 (CH_2NCH_2), 54.0 (OCH_3), 75.0 (CH), 152.1 (C-2, C=O), 162.7, 164.2 (C=O).

Analysis for $C_{10}H_{14}N_2O_5$
Calcd C 49.59 H 5.83 N 11.57%,
Found C 49.16 H 5.78 N 11.50%.

Methyl 3-dimethylamino-2,4-dioxo-1,3-oxazolidine-5-carboxylate (**6c**): Colourless crystals (45%); m.p. 92 °C (Et_2O/hexane); IR (KBr): υ = 1819, 1777, 1750 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 2.77 (s, 6H, $(CH_3)_2N$), 3.78 (s, 3H, OCH_3), 5.64 (s, 1H, CH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 43.1 ($N(CH_3)_2$), 53.2 (OCH_3), 75.0 (CH), 152.2 (C-2, C=O), 162.8, 164.1 (C=O).

Analysis for $C_7H_{10}N_2O_5$
Calcd C 41.59 H 4.99 N 13.86%,
Found C 41.37 H 4.91 N 14.01%.

Benzyl 2,4-dioxo-3-phenylamino-1,3-oxazolidine-5-carboxylate (**6d**): Colourless crystals (61%); m.p. 126 °C (Et_2O/hexane); IR (KBr): υ = 3327 (NH), 1836, 1771, 1754 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 5.34 (s, 2H, OCH_2Ph), 6.07 (s, 1H, CH), 6.72–7.20 (m, 5H, ArH), 7.36–7.44 (m, 5H, ArH), 8.74 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ (ppm) ^{13}C-NMR (DMSO-d_6): δ (ppm) 67.9 (OCH_2Ph), 75.9 (CH), 112.3, 120.5, 128.1, 128.4, 128.5, 129.0 (C tert., ArC), 134.7, 145.1 (C quart., ArC), 153.1 (C-2, C=O), 162.3, 164.7 (C=O).

Analysis for $C_{17}H_{14}N_2O_5$
Calcd C 62.58 H 4.32 N 8.59%,
Found C 62.43 H 4.34 N 8.56%.

Benzyl 2,4-dioxo-3-(piperidinoamino)-1,3-oxazolidine-5-carboxylate (**6e**): Colourless crystals (57%); m.p. 91 °C (Et_2O/hexane); IR (KBr): υ = 1825, 1761, 1734 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.46 (dt, J = 6.1/5.6 Hz, 2H, CH_2), 1.73 (dt, J = 6.1/5.6 Hz, 4H, 2 CH_2), 3.19 (t, J = 5.6 Hz, 4H, CH_2NCH_2), 5.18 (s, 1H, CH), 5.26 (d, J = 12.2 Hz, 1H, OCH_2Ph), 5.33 (d, J = 12.2 Hz, 1H, OCH_2Ph), 7.37 (s, 5H, ArH); ^{13}C-NMR ($CDCl_3$): δ (ppm) 22.8, 25.8 (3 CH_2), 52.6 (CH_2NCH_2), 68.9 (OCH_2Ph), 75.1 (CH), 128.4, 128.8, 129.0 (C tert., ArC), 134.0 (C quart.,ArC), 152.1 (C-2, C=O), 162.1, 164.1 (C=O).

Analysis for $C_{16}H_{18}N_2O_5$
Calcd C 60.37 H 5.70 N 8.80%,
Found C 60.10 H 5.68 N 8.77%.

Benzyl 3-dimethylamino-2,4-dioxo-1,3-oxazolidine-5-carboxylate (**6f**): Colourless crystals (48%); m.p. 93 °C (Et_2O/hexane); IR (KBr): υ = 1825, 1782, 1753 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 2.77 (s, 6H, $(CH_3)_2N$), 5.28 (s, 2H, OCH_2Ph), 5.72 (s, 1H, CH), 7.34–7.41 (m, 5H, ArH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 43.1 ($N(CH_3)_2$), 67.5 (OCH_2Ph), 75.1 (CH), 127.9, 128.3, 128.4 (C tert., ArC), 134.9 (C quart., ArC), 152.2 (C-2, C=O), 162.2, 164.1 (C=O).

Analysis for $C_{13}H_{14}N_2O_5$
Calcd C 56.11 H 5.07 N 10.07%,
Found C 55.90 H 5.04 N 10.02%.

Benzyl 3-amino-2,4-dioxo-1,3-oxazolidine-5-carboxylate (**6 g**): Colourless crystals (58%); m.p. 103 °C (Et_2O/hexane); IR (KBr): υ = 3348, 3263 (NH_2), 1820, 1739 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 5.17 (s, 2H, NH_2), 5.25 (d, J = 12.2 Hz, 1H, OCH_2Ph), 5.30 (d, J = 12.2 Hz, 1H, OCH_2Ph), 5.87 (s, 1H, CH), 7.34–7.41 (m, 5H, ArH); ^{13}C-NMR (DMSO-d_6): 67.6 (OCH_2Ph), 75.3 (CH), 127.9, 128.3, 128.4 (C tert., ArC), 134.8 (C quart., ArC), 154.3 (C-2, C=O), 162.5, 165.1 (C=O).

Analysis for $C_{11}H_{10}N_2O_5$
Calcd C 52.80 H 4.03 N 11.20%,
Found C 52.49 H 4.02 N 11.27%.

Ethyl 5-methyl-2,4-dioxo-3-phenylamino-1,3-oxazolidine-5-carboxylate (**6h**): Colourless crystals (61%); m.p. 99 °C (Et_2O/hexane); IR (KBr): υ = 3306 (NH), 1836, 1767, 1739 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.26 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.86 (s, 3H, CH_3), 4.26–4.38 (m, 2H, CH_2CH_3), 6.75–7.26 (m, 5H, ArH), 8.77 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 13.6 (CH_3), 18.1 (C-5, CH_3), 63.5 (OCH_2), 82.8 (C-5), 112.2, 120.7, 129.1 (C tert., ArC), 145.2 (C quart., ArC), 152.6 (C-2, C=O), 164.4, 168.2 (C=O).

Analysis for $C_{13}H_{14}N_2O_5$
Calcd C 56.11 H 5.07 N 10.07%,
Found C 56.02 H 5.10 N 10.03%.

Benzyl 5-methyl-2,4-dioxo-3-phenylamino-1,3-oxazolidine-5-carboxylate (**6i**): Colourless crystals (63%); m.p. 109 °C (Et_2O/hexane); IR (KBr): υ = 3295 (NH), 1836, 1768, 1739 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.89 (s, 3H, CH_3), 5.33 (d, J = 12.2 Hz, 1H, OCH_2Ph), 5.36 (d, J = 12.2 Hz, 1H, OCH_2Ph), 6.65–7.11 (m, 5H, ArH), 7.36–7.44 (m, 5H, ArH), 8.71 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 18.3 (C-5, CH_3), 68.5 (OCH_2Ph), 82.8 (C quart.), 112.2, 120.5, 128.3, 128.6, 129.0 (C tert., ArC) 134.5, 145.1 (C quart., ArC), 152.5 (C-2, C=O), 164.3, 168.0 (C=O).

Analysis for $C_{18}H_{16}N_2O_5$
Calcd C 63.52 H 4.74 N 8.23%,
Found C 63.55 H 4.79 N 8.23%.

Ethyl 3-hydroxy-5-methyl-2,4-dioxo-1,3-oxazolidine-5-carboxylate (**5h**):

5a (1,5 mmol) was hydrogenated in THF using catalytic amounts of 10% Pd/C. The reaction mixture was stirred at ambient temperature for 1h, filtrated and rotoevaporated. The oily residue was crystallized from CH_2Cl_2/hexane (1:1).

5h: Colourless crystals (91%); m.p. 91 °C (Et_2O/hexane); IR (KBr): υ = 3216 (OH), 1837, 1770, 1707 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.21 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.77 (s, 3H, CH_3), 4.24 (q, 2H, J = 7.1 Hz CH_2CH_3), 11.67 (s, 1H, OH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 13.6 (CH_3), 18.3 (C-5,CH_3), 63.2 (OCH_2), 81.9 (C-5), 151.4 (C-2, C=O), 164.5, 165.0 (C=O).

Analysis for $C_7H_9NO_6$
Calcd C 41.39 H 4.47 N 6.89%,
Found C 41.38 H 4.48 N 6.89%.

N-Benzyl-5-methyl-2,4-dioxo-3-phenylamino-1,3-oxazolidine-5-carboxamide (**7**):

A solution of **6h** (5 mmol) and benzylamine (5 mmol) in CH_2Cl_2 (5 ml) was allowed to stand for 20 h at ambient temperature. After removal of the solvent the residue was chromatographed with Et_2O/CH_2Cl_2(3:7) as eluent.

7: Colourless crystals (28%); m.p. 149 °C (CH_2Cl_2/hexane); IR (KBr): υ = 3306, 3221 (NH), 1819, 1741, 1697 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.84 (s, 3H, CH_3), 4.63 (d, J = 15.8 Hz, 1H, NCH_2Ph), 4.69 (d, J = 15.8 Hz, 1H, NCH_2Ph), 6.62–7.13 (m, 5H, ArH), 7.24–7.37 (m, 5H, ArH), 7.93 (s, 1H, NNH), 10.46 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 18.8 (C-5, CH_3), 43.2 (NCH_2Ph), 84.4 (C-5), 112.0, 112.2, 118.9, 127.0, 127.2, 127.7, 128.2, 128.5, 128.6, 129.0 (C tert., ArC), 134.8, 148.4 (C quart., ArC), 153.9 (C-2, C=O), 163.8, 170.3 (C=O).

Analysis for $C_{18}H_{17}N_3O_4$
Calcd C 63.71 H 5.05 N 12.38%,
Found C 63.31 H 5.08 N 12.33%.

N^2-Dimethyl-5-methyl-2,4-dioxo-3-phenylamino-1,3-oxazolidine-5-carbohydrazide (**8**): *From* **6h** (5 mmol) and N,N-dimethylhydrazine (5 mmol) according to the procedure for **7**.

8: Colourless crystals (24%); m.p. 179 °C (CH_2Cl_2/hexane); IR (KBr): υ = 3370, 3177 (NH), 1830, 1755, 1681 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.80 (s, 3H, CH_3), 2.81 (s, 6H, $(CH_3)_2N$), 6.65–7.20 (m, 5H, ArH), 7.93 (s, 1H, NNH), 10.44 (s, 1H, CONH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 18.6 (C-5, CH_3), 43.3 ($N(CH_3)_2$), 82.6 (C-5), 112.1, 118.9, 128.6 (C tert., ArC), 148.5 (C quart., ArC), 151.6 (C-2, C=O), 163.7, 168.6 (C=O).

Analysis for $C_{13}H_{16}N_4O_4$
Calcd C 53.42 H 5.52 N 19.17%,
Found C 53.42 H 5.58 N 18.73%.

5-Methyl-2,4-dioxo-3-phenylamino-1,3-oxazolidine-5-carbohydroxamic acid (**9**):

5bh (2 mmol) and H_2NOH·HCl (2.2 mmol) were dissolved in anhydrous EtOH (10 ml) and dropwise treated with a freshly prepared solution of NaOEt (4 mmol Na in 10 ml EtOH). After 36 h the reaction mixture was adjusted to pH 3 with HCl and extracted with EtOAc. The combined or-

ganic layers were dried over $MgSO_4$, rotoevaporated and the resulting oil crystallized from CH_2Cl_2.

9: Colourless crystals (38%); m.p. 161 °C (CH_2Cl_2); IR (KBr): υ = 3324 (OH), 3262 (NH), 1836, 1754, 1699 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.84 (s, 3H, CH_3), 6.66–7.17 (m, 5H, ArH), 7.93 (s, 1H, NNH), 10.47 (s, 1H, NH), 11.60 (s, 1H, OH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 18.8 (C-5, CH_3), 82.5 (C-5), 112.1, 118.9, 128.7 (C tert., ArC), 148.4 (C quart., ArC), 151.4 (C-2, C=O), 163.6, 165,9 (C=O).

Analysis for $C_{11}H_{11}N_3O_5$

Calcd	C 49.81	H 4.18	N 15.84%,
Found	C 49.40	H 4.15	N 15.76%.

5-Methyl-3-phenylamino-1,3-oxazolidin-2,4-dione (**11**):

a) KOH (3 mmol) in 10 ml EtOH was added dropwise to a stirred solution of **6h** (3 mmol) in EtOH (10 ml) within 60 min. After 24 h the reaction mixture was adjusted with HCl (5%) under ice cooling to pH 1 and extracted with EtOAc (5 x 10 ml). The combined organic layers were dried over $MgSO_4$ and rotoevaporated. The solid residue was recrystallized from Et_2O/hexane (65%).

b) **6i** (1.5 mmol) was hydrogenated in THF using catalytic amounts of 10% Pd/C. The reaction mixture was stirred at ambient temerature for 1h, filtrated and the oily residue crystallized from Et_2O/hexane (85%).

(**11**): Colourless crystals; m.p. 109 °C (Et_2O/hexane); IR (KBr): υ = 3305, (NH), 1825, 1752, (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.56 (d , J = 7.1 Hz, 3H, CH_3), 5.34 (q, J = 7.1 Hz 1H, CH) 6.77–7.23 (m, 5H, ArH), 8.57 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ (ppm) 16.0 (C-5, CH_3), 75.1 (CH), 112.3, 120.2, 129.0 (C tert., ArC), 145.5 (C quart., ArC), 153.8 (C-2, C=O), 172.1 (C-4, C=O).

Analysis for $C_{10}H_{10}N_2O_3$

Calcd	C 58.25	H 4.89	N 13.59%,
Found	C 58.13	H 5.01	N 13.43%.

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