Short communication

The Synthesis of 7-Substituted-2,3-dihydropyrido [4,3-*d*]pyridazine-1,4-diones and 1,4-Dioxo-7-substituted-1,2,3,4-tetrahydropyrido[4,3-*d*]pyridazine 6-Oxides from Methyl Ketones

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Dedicated to Professor Emeritus Miha Tišler, University of Ljubljana, on the occasion of his 90th birthday.

Abstract

A general four-step transformation of alkyl, cycloalkyl, aryl, and heteroaryl methyl ketones *via* 3-(dimethylamino)-1-substituted-prop-2-en-1-ones, followed by microwave [2+2] cycloaddition of dimethyl acetylenedicarboxylate, cyclization of (2*E*,3*E*)-2-[(dimethylamino)methylene]-3-(2-substituted)succinates with ammonia or hydroxylamine hydrochloride into 2-substituted-pyridine-4,5-dicarboxylates and their *N*-oxides and final cyclization with hydrazine hydrate into of 7-substituted-2,3-dihydropyrido[3,4-*d*]pyridazine-1,4-diones and 1,4-dioxo-7-substituted-1,2,3,4-tetrahydropyrido[4,3-*d*]pyridazine 6-oxides is shown.

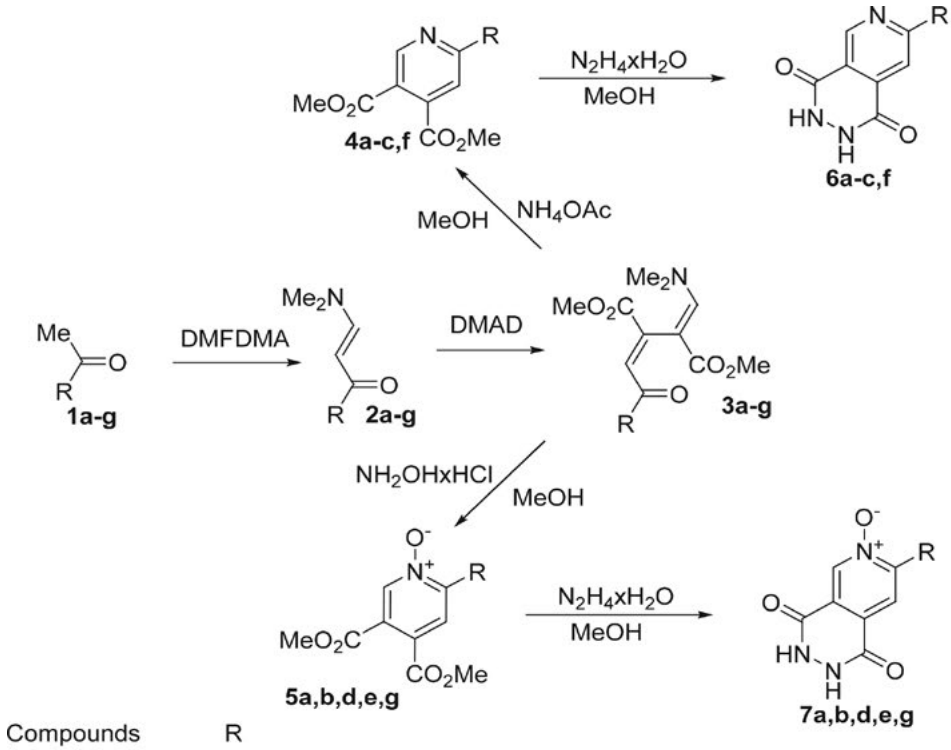
Keywords: methyl ketones, 7-substituted-2,3-dihydropyrido[4,3-*d*]pyridazine-1,4-diones, 1,4-dioxo-7-substituted-1,2,3,4-tetrahydropyrido[4,3-*d*]pyridazine 6-oxides

1. Introduction

There are several methods for the preparation of 2,3-dihydro[4,3-*d*]pyridazine-1,4- dione derivatives. They have been prepared by treatment of diethyl or dimethyl pyridine-3.4-dicarboxylate with hydrate of hydrazine in refluxing ethanol, and 6-aryl- and 6-aryl-2-methyl derivatives with hydrate of hydrazine in refluxing ethanol, which allow the formation of the corresponding 7-substituted and 5,7-disubstituted-2,3-dihydropyridazine[3,4-*d*]pyridazine-1,4-diones.[1-4] Cyclization of ethyl 3-cyanoisonicotinate with hydrazine proceeds at room temperature to give 4-aminopyrido[3,4-*d*]pyridazine-1(2*H*)-one,[5,6] while pyridine-3,4-dicarbonitriles give the corresponding pyrido[3,4-*d*]pyridazine-1,4-diones.[7] Other methods include cycloamination of 4-carbofunctional-5-vinylpyridazines,[8,9] condensation of 4,5-dicarbofunctional pyridazines with amines,[9,10] condensation of 4-(iminomethyl)pyridazines with enolates,[10] intramolecular cyclization of pyridinecarbohydrazides,[1,11] intramolecular cyclization of 4-vinylpyridazine-5-carbonitriles,[12,13] by ring enlargement of furo[3,4-*c*]pyridine-1,3-diones,[2,3,5,14,15] 1*H*-pyrrolo[3,4-*c*]pyridine-1,3(2*H*) -diones with hydrazine,[1,4,16,17] by reaction of 5*H*-pyrano[3,4-*d*]pyridazines with amines,[8] intramolecular [4+2]cycloaddition of 1,2,4,5-tetrazines,[18] ring contraction of 2*H*-1,2,4-triazepines.[14] For a review see.[19]

Enaminones are well known starting compounds in the synthesis of heterocyclic systems. Their reactivity enables various transformations and functionalizations. Their synthetic value and broad applicability has also been demonstrated in the preparation of natural products and their analogues, such as aplysinopsins,[20] meridianines,[21] and dipodazines.[22] Besides the evident reactions with nucleophiles, they also exhibit reactivity with electrophiles as well, which only adds to their importance as building blocks in organic synthesis.[23] Reactions with electrophiles have been demonstrated in the synthesis of polysubstituted butadienes by microwave-assisted formal [2 + 2] cycloadditions of enaminones to electron-poor acetylenes.[24]

The functionalized buta-1,3-dienes as the basis of the synthetic route presented in this paper are prepared from simple and commercially available compounds such as alkyl, aryl, and heteroaryl methyl ketones. These are transformed by treatment with *N,N*-dimethylformamide dimethyl acetal (DMFDMA) or *tert*-butoxybis(dimethylamino)methane (Bredereck´s reagent) into the corresponding 3-(dimethylamino)-1-substituted-prop-2-enones, which are further transformed in a regiospecific microwave assisted [2 + 2] cycloaddition with dimethyl acetylenedicarboxylate (DMAD)[25] to the before mentioned 1,3-butadienes. These highly functionalized buta-1,3-dienes proved to be useful and versatile reagents in the formation of highly substituted pyridine, pyridine *N*-oxides,



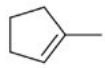
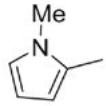
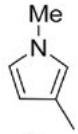
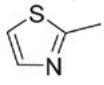
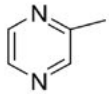
Compounds 1,2,3,4,5,6,7	R
a	Et
b	Ph
c	
d	
e	
f	
g	

Table 1.

Compound	Reaction time [h]	Yield [%]
6a	8	57
6b	24	20
6c	12	74
6f	15	44
7a	7	23
7b	12	90
7d	4	75
7e	4	89
7g	24	95

Scheme 1. Preparation of 7-substituted-2,3-dihydropyrido[3,4-*d*]pyridazine-1,4-diones **6a-c,f** and 1,4-dioxo-7-substituted-1,2,3,4-tetrahydropyrido[4,3-*d*]pyridazine 6-oxides **7a,b,d,e,g** from methyl ketones **1a-g**.

pyrrole, pyrido[3,4-*c*]pyridazine derivatives,[25b] 2-substituted pyridine-3,4-dicarboxylates and their *N*-oxides,[10g] and triazafulvalene derivatives.[25d]

Polysubstituted aminobutadienes, prepared by this procedure, are suitable for the preparation of polysubstituted pyridine derivatives. They also represent a group of isomeric intermediates in regard to the aminobutadienes prepared *via* the Michael addition in the Bohlmann-Rahtz synthesis of pyridine derivatives.[26] On this basis, a simple metal-free synthesis of 2-alkyl-, 2-cycloalkyl-, 2-aryl-, and 2-heteroaryl-substituted pyridine-3,4-dicarboxylates and their *N*-oxides has also been reported.[25g] Recently, we reported on a simple one-pot metal-free synthesis of 2,4,5-trisubstituted pyridine derivatives and their *N*-oxides by [2 + 2] cycloaddition of propyne iminium salts as electron-poor acetylenes to enaminones as well.[27] We also reported a simple, metal-free synthesis of electron rich 2,4,6-trisubstituted pyridine derivatives[28] and the synthesis of polysubstituted benzene derivatives, where *N*,*N*-dimethylacetamide dimethyl acetal (DMADMA) served as the reagent and building block for generating aromatic final products.[29,30] Our existing knowledge of the enaminones and 1,3-butadienes has been expanded to the synthesis of pyridines starting from Boc-protected amino acids, and the results of our research are presented in this paper.

2. Results and Discussion

In this communication we report a general and simple synthesis of 7-substituted-2,3-dihydropyrido[3,4-*d*]pyridazine-1,4-diones **6a-c,f** and 1,4-dioxo-7-substituted-1,2,3,4-tetrahydropyrido[4,3-*d*]pyridazine 6-oxides **7a,b,d,e,g** from methyl ketones **1a-g**. We have reported earlier a simple metal-free synthesis of dimethyl 2-substituted-pyridine-4,5-dicarboxylates **4a-c,f** and their *N*-oxides **5a,b,d,e,g** in the following manner: alkyl, aryl, and heteroaryl ketones **1a-g** have been converted by treatment with *N,N*-dimethylformamide dimethylacetal /DMFDMA) or *t*-butoxybis(dimethylamino)methane (Bredereck´s reagent) into the corresponding 3-(dimethylamino)-1-substituted-prop-2-en-ones **2a-g**, followed by microwave assisted [2 + 2] cycloaddition to dimethyl acetylenedicarboxylate to give dimethyl (2*E*,3*E*)-2-{(dimethylamino)methylene}-3-(2-substituted)succinates **3a-g**. Compounds **3** gave by treatment with ammonium acetate or hydroxylamine hydrochloride the corresponding dimethyl 2-substituted-pyridine-4,5-dicarboxylates **4a-c,f** and dimethyl 2-substituted-4,5-bis(methoxycarbonyl)pyridine *N*-oxides **5a,b,d,e,g**.[25e,f,g] Treatment of compounds **4** and **5** with hydrazine hydrate afforded 7-substituted-2,3-dihydropyrido[3,4-*d*]pyridazine-1,4-diones **6a-c,f** and 1,4-dioxo-7-substituted-1,2,3,4-tetrahydropyrido [4,3-*d*]pyridazine 6-oxides **7a,b,d,e,g**, respectively. (Scheme 1, Table 1).

3. Experimental

3. 1. General

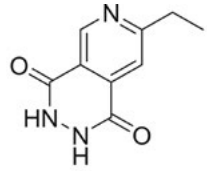
Melting points were determined on a Stanford Research Systems MPA100 OptiMelt automated melting point system. The NMR spectra were obtained on a Bruker Avance DPX 300 at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C and on a Bruker Avance III UltraShield 500 plus at 500 MHz for ^{1}H and 126 MHz for ^{13}C, using acetone-d_6, acetonitrile-d_3, $CDCl_3$, and DMSO-d_6 with Me_4Si as the internal standard, as solvents. Mass spectra were recorded on a Agilent 6224 Accurate Mass TOF LC/MS spectrometer, IR spectra on a Perkin Elmer Spectrum BX FTIR spectrophotometer. Column chromatography (CC) was performed on silica gel (Fluka, Silica gel 60, particle size 35-70 μm).

The preparation of 2-substituted-pyridine-4,5-dicarboxylates **4a-c,f** and dimethyl 2-substituted-4,5-*bis*(methoxycarbonyl)pyridine *N*-oxides **5a,b,d,e,g** from alkyl, cycloalkyl, aryl and heteroaryl methyl ketones has been previosly reported in our laboratory.[25e,f,g]

3. 2. General procedure for the preparation of 7-substituted-2,3-dihydropyrido [3,4-d]pyridazine-1,4-diones and 1,4-dioxo-7-substituted-1,2,3,4-tetrahydropyrido[4,3-*d*]pyridazine 6-oxides

To a solution of 0.5 mmol of the starting compound (dimethyl 6-substituted pyridine-3,4-dicarboxylate or 2-substituted-4,5-bis(methoxycarbonyl)pyridine-*N*-oxide) in 2–3 mL of methanol, 1 mmol (2 equivalents) of hydrazine monohydrate was added, followed by the addition of 2–3 drops of concentrated hydrochloric acid. The reaction mixture was stirred vigorously and heated to reflux temperature for 4–24 h.

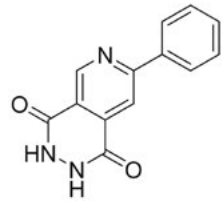
3. 2. 1. 7-Ethyl-2,3-dihydropyrido[4,3-*d*] pyridazine-1,4-dione (6a)



The product was prepared from dimethyl 6-ethylpyridine-3,4-dicarboxylate (**4a**,112 mg, 0.5 mmol), 90 °C, 8 h. The yellow product was collected by vacuum filtration and washed with Et_2O. Yield: 57% (55 mg), yellow solid; mp = higher than 350 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.30 (3H, t, J = 7.5 Hz, CH_3); 2.97 (2H, q, J = 7.6 Hz, CH_2); 7.74 (1H, s, 8-C*H*); 9.25 (1H, s, 5-C*H*). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.54, 30.77, 115.03, 148.30, 148.47, 164.77, 166.61, 166.74, 168.39. EI-HRMS: m/z = 192.0765 (MH^+) found; $C_9H_{10}N_3O_2$ calculated: m/z

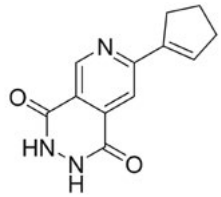
= 192.0768 (MH^+); IR (ATR): *ν* 3426, 3302, 3250, 2960, 1664, 1612, 1575, 1476, 1364, 1207, 1077, 899 cm^{-1}.

3. 2. 2. 7-Phenyl-2,3-dihydropyrido[4,3-*d*] pyridazine-1,4-dione (6b)



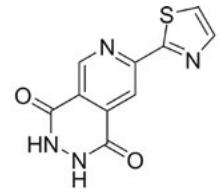
The product was prepared from dimethyl 6-phenylpyridine-3,4-dicarboxylate (**4b**, 261 mg, 096 mmol), 90 °C, 12 h. The yellow product was collected by vacuum filtration and washed by Et_2O. Yield: 74% (170 mg), yellow solid; mp = 335–339 °C. ^1H NMR (500 MHz, DMSO-d_6): *δ* 7.48–7.57 (3H, m, Ph); 8.19-8.23 (2H, m, Ph); 8.35 (1H, s, 8-C*H*); 9.36 (1H, s, 5-C*H*). ^{13}C NMR (125 MHz, DMSO-d_6): *δ* 113.8, 121.9, 126.9, 128.9, 129.6, 135.4, 137.8, 149.1, 155.7, 156.2, 157.5. EI-HRMS: *m/z* = 240.0767 (MH^+) found; $C_{13}H_{10}N_3O_2$ calculated: *m/z* = 240.0768 (MH^+); IR (ATR): *ν* 3289, 3178, 3034, 2978, 2920, 2798, 1898, 1648, 1559, 1454, 1112, 852 cm^{-1}. LC-MS; 9.1 min; *m/z*: 240.1 (MH^+).

3. 2. 3. 7-Cyclopentenyl-2,3-dihydropyrido[4,3-*d*] pyridazine-1,4-dione (6c)



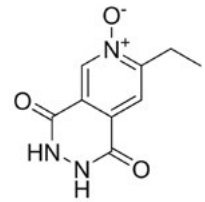
The product was prepared from dimethyl 6-cyclopentenylpyridine-3,4-dicarboxylate (**4c**,150 mg, 0.56 mmol), 90 °C, 24 h. The solid product that was formed during the reaction was a mixture of the starting dicarboxylate and the product. The solid was collected by vacuum filtration, suspended in chloroform. The insoluble product was once more collected by vacuum filtration. Yield: 20% (26 mg), brown solid; mp = higher than 330 °C. ^1H NMR (500 MHz, DMSO-d_6): *δ* 2.03 (2H, p, *J* = 7.5 Hz, 4-CH_2); 2.54–2.60 (2H, m, 3-CH_2); 2.76–2.82 (2H, m, 5-CH_2); 6.87 (1H, s, 2-C*H*); 7.81 (1H, s, 8-C*H*); 9.23 (1H, s, C*H*). ^{13}C NMR (125 MHz, DMSO-d_6): *δ* 22.8, 32.0, 33.2, 113.4, 121.0, 133.5, 134.5, 142.6, 148.6, 155.2, 155.8, 156.0. EI-HRMS: *m/z* = 230.0915 (MH^+) found; $C_{12}H_{12}N_3O_2$ calculated: *m/z* = 230.0924 (MH^+). IR (ATR): *ν* 3163, 3016, 2947, 2892, 2839, 1649, 1598, 1553, 1434, 1368, 1325, 1291, 1232, 1101, 1036, 823 cm^{-1}.

3. 2. 4. 7-(Thiazol-2-yl)-2,3-dihydropyrido[4,3-*d*] pyridazine-1,4-dione (6f)



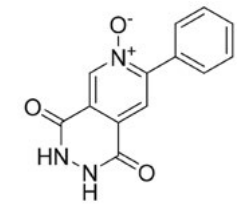
The product was prepared from dimethyl 6-(thiazol-2-yl)pyridine-3,4-dicarboxylate (**4f**, 89 mg, 0.32 mmol), 90 °C, 15 h. The yellow product was collected by vacuum filtration and washed with Et_2O. Yield: 44% (35 mg), yellow solid; mp = the product decomposes at 250 °C. ^1H NMR (500 MHz, DMSO-d_6): *δ* 7.97 (1H, d, *J* = 3.2 Hz, C*H*); 8.09 (1H, d, *J* = 3.2 Hz, C*H*); 8.54 (1H, d, *J* = 1.0 Hz, 8-C*H*); 9.29 (1H, d, *J* = 1.0 Hz, 5-C*H*). ^{13}C NMR (125 MHz, DMSO-d_6): *δ* 113.3, 117.2, 123.6, 123.8, 144.9, 149.5, 151.8, 155.9, 165.8, 167.6. EI-HRMS: *m/z* = 245.015 (MH^-) found; $C_{10}H_5N_4O_2S$ calculated: *m/z* = 245.0139 (MH^-); IR (ATR): *ν* 3420, 3260, 1741,1721, 1661, 1654, 1602, 1569, 1465, 1438, 1298, 1242, 1134, 1085, 958 cm^{-1}. LC-MS: 7.1 min; *m/z*: 247.3 (MH^+).

3. 2. 5. 7-Ethyl-1,4-dioxo-1,2,3,4-tetrahydropyrido [4,3-*d*]pyridazine 6-oxide (7a)



The product was prepared from 2-ethyl-4,5-bis(methoxycarbonyl)pyridine 1-oxide (**5a**, 156 mg, 0.65 mmol), 90 °C, 7 h. The yellow solid was collected by vacuum filtration and washed with Et_2O. Yield: 23% (31 mg), yellow solid; mp = 270–276 °C. ^1H NMR (500 MHz, DMSO-d_6): *δ* 1.26 (3H, t, *J* = 7.4 Hz, CH_3); 2.89 (2H, q, *J* = 7.4 Hz, CH_2); 7.89 (1H, s, 8-C*H*); 8.61 (1H, s, 5-C*H*). ^{13}C NMR (125 MHz, DMSO-d_6): *δ* 10.5, 23.3, 120.2, 123.5, 125.0, 134.8, 153.7, 154.3, 156.0. EI-HRMS: *m/z* = 208.0712 (MH^+) found; $C_9H_{10}N_3O_3$ calculated: *m/z* = 208.0717 (MH^+). IR (ATR): *ν* 3203, 3047, 2974, 2810, 1626, 1549, 1454, 1432, 1366, 1317, 1268, 1043, 814 cm^{-1}.

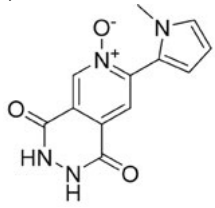
3. 2. 6. 1,4-Dioxo-7-phenyl-1,2,3,4-tetrahydropyrido [4,3-*d*]pyridazine 6-oxide (7b)



The product was prepared from 4,5-bis(methoxycarbonyl)-2-phenylpyridine 1-oxide (**5b**, 241 mg, 0.84 mmol), 90 °C, 12 h. The yellow solid was collected by vacuum filtration and washed with Et_2O. Yield: 90% (190 mg), yellow

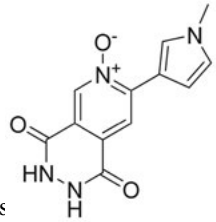
solid; mp = 275–285 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.49–7.53 (3H, m, Ph); 7.82–7.85 (2H, m, Ph); 7.95 (1H, s, 8-C*H*); 8.65 (1H, s, 5-C*H*). ^{13}C NMR (125 MHz, DMSO-d_6): δ 123.1, 124.3, 126.1, 127.9, 129.3, 129.6, 131.9, 135.9, 150.4, 153.9, 154.7. EI-HRMS: *m/z* = 256.0716 (MH^+) found; $C_{13}H_{10}N_3O_3$ calculated: *m/z* = 256.0717 (MH^+). IR (ATR): *v* 3338, 3066, 2861, 1807, 1657, 155, 1466, 1448, 1269, 1096, 813 cm^{-1}. LC-MS: 7.4 min; *m/z*: 256.1 (MH^+).

3. 2. 7. 7-(1-Methyl-1*H*-pyrrol-2-yl)-1,4-dioxo-1,2,3,4-tetrahydropyrido[4,3-*d*]pyridazine 6-oxide (7d)



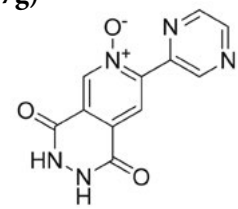
The product was prepared from 4,5-bis(methoxycarbonyl)-2-(1-methyl-1H-pyrrol-2-yl)pyridine 1-oxide (**5d**, 173 mg, 0.6 mmol), 90 °C, 4 h. The yellow product was collected by vacuum filtration and washed with Et_2O. Yield: 75% (115 mg), yellow solid; mp = 222-238 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 3.58 (3H, s, CH_3); 6.12 (1H, dd, J_1 = 3.7 Hz, J_2 = 2.6 Hz, 3'-C*H*); 6.40 (1H, dd, J_1 = 3.7 Hz, J_2 = 1.8 Hz, 5'-C*H*); 7.00 (1H, deg. dd, *J* = 2.2 Hz, 4'-C*H*); 7.85 (1H, s, 8-C*H*); 8.64 (1H, s, 5-C*H*). ^{13}C NMR (125 MHz, DMSO-d_6): δ 40.5, 112.9, 118.3, 129.6, 129.8, 130.1, 131.0, 131.7, 141.1, 149.9, 159.9, 160.6. EI-HRMS: *m/z* = 259.0822 (MH^+) found; $C_{12}H_{11}N_4O_3$ calculated: *m/z* = 259.0826 (MH^+); IR (ATR): *v* 3424, 3301, 3078, 2953, 2929, 1664, 1651, 1558, 1485, 1471, 1308, 1255, 1103, 1072, 822 cm^{-1}. LC-MS: 7.3 min; *m/z*: 259.2 (MH^+).

3. 2. 8. 7-(1-Methyl-1*H*-pyrrol-3-yl)-1,4-dioxo-1,2,3,4-tetrahydropyrido[4,3-*d*]pyridazine 6-oxide (7e)



The product was prepared from 4,5-bis(methoxycarbonyl)-2-(1-methyl-1H-pyrrol-3-yl)pyridine 1-oxide (**5e**, 340 mg, 1.17 mmol), 90 °C, 4 h. The yellow product was collected by vacuum filtration and washed with Et_2O. Yield: 89% (269 mg), yellow solid; mp = decomposes at 292 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 3.72 (3H, s, CH_3); 6.84 (1H, deg. dd, *J* = 1.2, 4'-C*H*); 6.91 (1H, deg. dd, *J* = 2.6 Hz, 5'-C*H*); 8.18 (1H, s, 8-C*H*); 8.32 (1H, deg. dd, *J* = 2.0 Hz, 2'-C*H*); 8.62 (1H, s, 5-C*H*). ^{13}C NMR (125 MHz, DMSO-d_6): δ 36.1, 108.0, 113.8, 117.5, 122.0, 123.3, 123.9, 126.8, 136.2, 146.8, 153.9, 154.7. EI-HRMS: *m/z* = 259.0823 (MH^+) found; $C_{12}H_{11}N_4O_3$ calculated: m/z = 259.0826 (MH^+); IR (ATR): *v* 3416, 3295, 3199, 2992, 1653, 1614, 1571, 1535, 1487, 1442, 1366, 1250, 1171, 1091, 831 cm^{-1}. LC-MS: 6.6 min; *m/z*: 259.2 (MH^+).

3. 2. 9. 1,4-Dioxo-7-(pyrazin-2-yl)-1,2,3,4-tetrahydropyrido[4,3-*d*]pyridazine 6-oxide (7g)



The product was prepared from 4,5-bis(methoxycarbonyl)-2-(pyrazin-2-yl)pyridine 1-oxide (**5g**,144 mg, 0.5 mmol), 90 °C, 24 h. The yellow product was collected by vacuum filtration and washed with Et_2O. Yield: 95% (125 mg), yellow solid; mp = higher than 350 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.56 (1H, s, C*H*); 8.72 (s, 1H, C*H*); 8.78 (1H, d, *J* = 2.5 Hz, C*H*); 8.87–8.91 (1H, m, C*H*); 9.87 (1H, d, *J* = 1.5 Hz, C*H*). ^{13}C NMR (125 MHz, DMSO-d_6): δ 124.1, 136.5, 144.6, 144.9, 145.26, 145.29, 145.6, 146.9, 157.0, 158.1. EI-HRMS: *m/z* = 258.0624 (MH^+) found; $C_{11}H_8N_5O_3$ calculated: *m/z* = 258.0622 (MH^+); IR (ATR): *v* 3447, 3033, 2981, 1667, 1635, 1563, 1498, 1404, 1273, 1242, 1119, 827 cm^{-1}. LC-MS: 5.9 min; *m/z*: 255.7 [$(M-2H)^-$].

4. Conclusion

A general four-step metal-free synthesis of a series of 7-substituted-2,3-dihydropyrido[3,4-*d*]pyridazine-1,4-diones and 1,4-dioxo-7-substituted-1,2,3,4-tetrahydropyrido[4,3-*d*]pyridazine 6-oxides was designed starting from alkyl, cycloalkyl, aryl or heteroaryl methyl ketones in good to excellent yields.

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Povzetek

V tem članku je opisana štiristopenjska pretvorba alkil, cikloalkil, aril in heteroaril metil ketonov, ki jih preko 3-(dimetilamino)-1-substituiranih-prop-2-en-1-onov z [2+2] cickloadicijo na dimetil acetilendikarboksilat pretvorimo v (2*E*,3*E*)-2-[(dimetilamino)metilen]-3-(2-substituirane)sukcinate in naprej z amoniakom ali hidroksilaminom v 2-substituirane piridin-4,5-dikarboksilate in njihove *N*-okside. Iz teh nastanejo pri cilizaciji s hidrazinovim hidratom 7-substituirani 2,3-dihidropirido[3,4-*d*]piridazin-1,4-dioni in 1,4-diokso-7-substituirani 1,2,3,4-tetrahidropirido[4,3-*d*]piridazin 6-oksidi.