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The unusual thermal transformations of the dimethyl 2,2,3,3-tetramethyl-7a-R-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate derivatives

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ABSTRACT

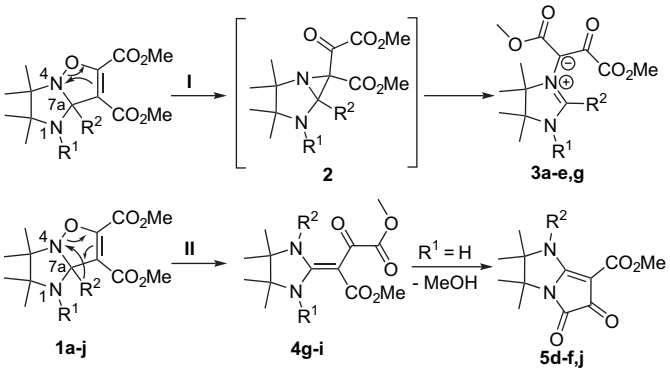
Dimethyl 2,2,3,3-tetramethyl-7a-R-1,2,3,7a-tetrahydroimidazo[1,2-*b*]-isoxazole-6,7-dicarboxylate derivatives were shown to undergo thermal rearrangement along two competing routes giving rise to dimethyl 2-(2-R-4,5-dihydro-1*H*-3λ-5-imidazol-3-ylidene)-3-oxosuccinate derivatives and (or) dimethyl-2-oxo-3-(1-R-imidazolidin-2-ylidene)succinates. The latter undergoes intramolecular cyclization producing, in case of *N*-unsubstituted derivatives, methyl 5,6-dioxo-1-R-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-7-carboxylates.

1. Introduction

One of the most common approaches to the synthesis of 2,3-dihydroisoxazole derivatives is a 1,3-dipolar cycloaddition reaction of alkynes with nitrones. 2,3-Dihydroisoxazoles formed this way, as a rule, undergo further thermal transformations. The most typical route for these rearrangements is the initial cleavage of the N–O bond with further cyclization to the corresponding acylaziridines.[1] Sometimes, the cleavage of the N–O bond is accompanied by the migration of the substituent from position 3 of the isoxazoline ring to the nitrogen atom.[2–5] Thus, the goal of this paper is to study the thermal rearrangements of dimethyl 2,2,3,3-tetramethyl-7a-R-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate derivatives **1**,[6] that are, in turn, the annelated derivatives of 2,3-dihydroisoxazole.

2. Results and discussion

It was shown that dimethyl 2,2,3,3-tetramethyl-7a-R-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate derivatives **1** undergo a rearrangement by at least two competing ways upon heating (Scheme 1). One way is the formation of ylides **3** and another one is the migration of the substituent R^2 to the nitrogen N-4, leading to enaminones **4**. In the absence of the substituent at the nitrogen N-1 (R^1=H) enaminones **4** undergo further cyclization with the formation of methyl 2,2,3,3-tetramethyl-5,6-dioxo-1-aryl-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-7-carboxylate derivatives **5**.



Scheme 1.

The structures of compounds **3**, **4** and **5** were proved by ^{1}H and ^{13}C NMR, IR and UV spectroscopy as well as X-ray analysis (Fig. 1).

The reaction conditions and the ratio of the products **3** and **4** or **5**, which are formed as the result of two competing rearrangements are presented in Table 1.

The direction of the rearrangement is shown to depend on the nature of the substituent R^2. If R^2 is alkyl (**1a**, **1b**), the only pathway **I** is present. It probably includes the initial formation of

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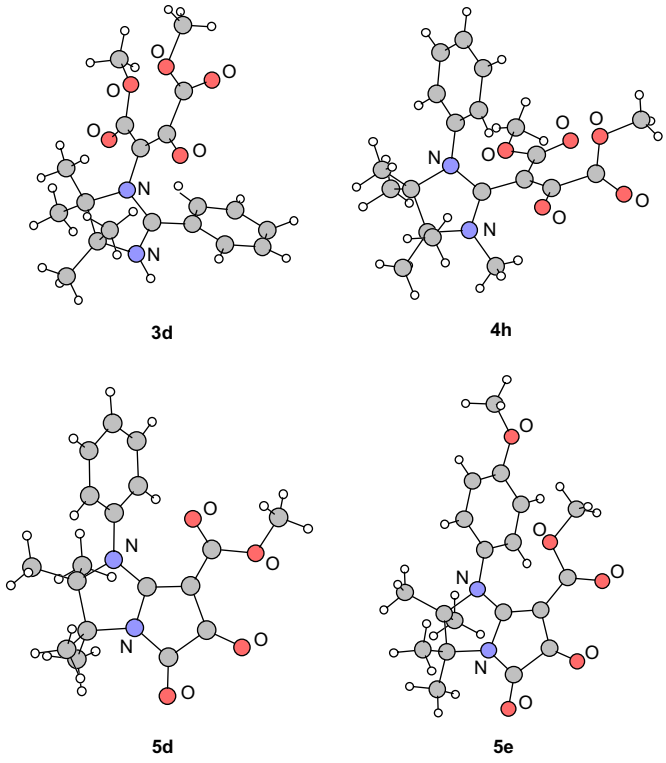


Figure 1. Crystal structure of dimethyl 2-(2-phenyl-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-3λ-5-imidazol-3-ylidene)-3-oxosuccinate **3d** (CCDC 628084), dimethyl-2-oxo-3-(3,4,4,5,5-pentamethyl-1-phenylimidazolidin-2-ylidene)succinate **4h** (CCDC 628083), methyl 2,2,3,3-tetramethyl-5,6-dioxo-1-phenyl-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]-imidazol-7-carboxylate **5d** (CCDC 628086) and methyl 2,2,3,3-tetramethyl-5,6-dioxo-1-(4-metoxyphenyl)-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-7-carboxylate **5e** (CCDC 628085).

acylaziridine **2**[7,8] with subsequent cleavage of the azyridine ring leading to ylide **3** formation.[9] The other way (**II**) is predominant in the case of substituents bearing conjugated π-system (R^2=Ar, –CH=CH–Ph), being sometimes the only path observed (cf. Table 1). It should be noted that the migration occurs only to nitrogen N-4, but not to N-1. The evidence for this is the formation of enaminones **4g–i** from cycloadducts **1g–i**, where methyl group is attached to N-1 (R^1=Me).

The data presented in Table 1 demonstrate that the relative content of R^2 migration product **4** or **5** substantially increases with the enhance of π-donor character of substituent R^2. Thus, in the case of compound **1c** (R^2=4-NO_2–C_6H_4) product **4** or **5** is not observed, whereas the reaction of **1d** (R^2=C_6H_5) and especially **1e** (R^2=4-OMe-C_6H_4) results in formation of appreciable amount of aryl migration product **5**. For the **1f** (R^2=4-NMe_2–C_6H_4) rearrangement leads exclusively to product **5** (Table 1).

Table 1
The reaction conditions (in toluene) and the ratio of products **3** and **4** or **5** by ^{1}H NMR

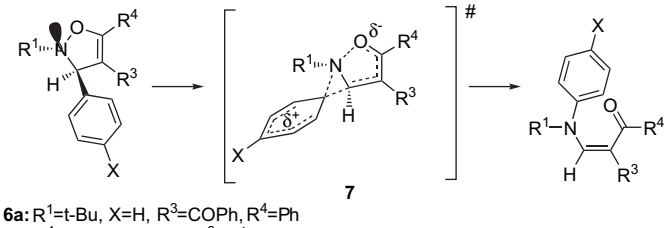
Compound	R^1	R^2	Reaction condition		Ratio (%)		
			Temp (°C)	Time (h)	**3**	**4**	**5**
1a	H	Me	105	150	100	—	0
1b	H	*t*-Bu	105	55	100	—	0
1c	H	4-NO_2–C_6H_4	131	11	100	—	0
1d	H	Ph	131	6	85	—	15
1e	H	4-MeO–C_6H_4	131	2.5	25	—	75
1f	H	4-NMe_2–C_6H_4	80	1	0	—	100
1g	Me	4-NO_2–C_6H_4	131	17	55	45	—
1h	Me	Ph	105	21	5	95	—
1i	Me	4-MeO–C_6H_4	105	2	0	100	—
1j	H	–CH=CH–Ph	105	12.5	0	—	100

The overall conversion equals to or more than 95%.

It should be noted that the relative amount of the rearrangement product **4** in case of *N*-methyl-substituted cycloadducts **1** (R^1=Me) is higher in comparison with corresponding *N*-unsubstituted derivatives (R^1=H).

2.1. Mechanism of the rearrangement

The migration of the aromatic substituent in **1** and **6** is most likely a concerted 1,2-shift. This reaction proceeds through transition state (TS) **7** (Scheme 2). Such TS can be achieved only in case of *syn*-position of the migrant R^2 and a lone electron pair on nitrogen N-4. In a number of cases, the *syn*-position of the substituent (especially hydrogen atom) relative to the lone electron pair leads to unstable 2,3-dihydroisoxazole derivatives, which thereby cannot be isolated.[1,10,11] At the same time, 2,3-dihydroisoxazole derivative **6a**, containing migrant and the lone electron pair in *anti*-position, is stable for several hours even at 80 °C.



6a: R^1=t-Bu, X=H, R^3=COPh, R^4=Ph
6b: R^1= t-Bu, X=NMe_2, R^3=R^4=CO_2Me
6c: R^1=Ph, X=NMe_2, R^3=R^4=CF_3
R^2=C_6H_4-X

Scheme 2.

Upon heating, 2,3-dihydroisoxazole derivative **6b** is shown to undergo the rearrangement with migration of the aryl substituent, but not the hydrogen atom. The same result was found by Kobayashi et al. for 2,3-dihydroisoxazole **6c**.[4] This is apparently due to much higher thermodynamic stability of the conformer in which the *para*-dimethylaminophenyl group and lone electron pair are situated on the same side of the isoxazoline ring plane. These examples unambiguously show the stereoselectivity of the reaction, which is typical for the 1,2-sigmatropic shifts.

3. Conclusion

Thus, upon heating, dimethyl 2,2,3,3-tetramethyl-7a-R-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate derivatives **1** undergo a rearrangement by two competing ways with the formation of either dimethyl 2-(2-R-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-3λ-5-imidazol-3-ylidene)-3-oxosuccinate derivatives **3** or dimethyl-2-oxo-3-(4,4,5,5-tetramethyl-1-R-imidazolidin-2-ylidene)-succinates **4**, the latter, in the case of *N*-unsubstituted derivatives, undergo further cyclization into methyl 2,2,3,3-tetramethyl-5,6-dioxo-1-R-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-7-carboxylate derivatives **5**; the ratio of the products being dependent on the nature of the substituents R^1 and R^2.

4. Experimental section

4.1. General

^{1}H and ^{13}C NMR (200 and 50 MHz, respectively) spectra were recorded on Bruker AC-200, AV-300, AM-400 and WP-200 spectrometers; solvents were used as internal standards. IR spectra were recorded with a Bruker IFS 66 spectrometer for KBr pellets (concentration 0.25%, pellet thickness 1 mm). Melting points were measured in a sealed capillary. Thin layer chromatography

monitoring was carried out on aluminium oxide plates (Fluka) and silica gel 60 F_{254} plates with chloroform and chloroform/MeOH mixtures (from 50:1 to 120:1) as eluents. The solutions were evaporated in vacuo in all cases.

4.2. X-ray diffraction

Single crystal diffraction data for the compounds **3d**, **4h**, **5d** and **5e** were collected on a SMART APEX CCD (Bruker AXS) automatic diffractometer (Mo Kα, λ=0.71073 Å, T=240 K). The structures were solved by direct methods and refined by the full-matrix least-squares method in an anisotropic approximation for non-hydrogen atoms. The H atoms' positions were calculated and refined together with non-hydrogen atoms in an isotropic approximation. All structure solution and refinement calculations were carried out with SHELX-97 and Bruker SHELXTL Version 6.14 program packages. Atomic coordinates, thermal parameters, bond lengths and bond angles have been deposited at the Cambridge Crystallographic Data Centre; CCDC's contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk].

4.2.1. Crystallographic data for *3d*

$C_{19}H_{24}N_2O_5$, FW=360.40, orthorhombic, $Pna2_1$ a=13.027(3), b=14.603(3), c=10.617(2) Å, V=2019.7(7) Å^3, Z=4, D_c=1.185 g/cm^3, μ=0.086 mm^{-1}, $2.09<\theta<29.50^\circ$, reflections collected/unique=22,408/5209, R_{int}=0.1463, 277 parameters, Goof=0.999, R indices ($I>2\sigma(I)$): R_1=0.0879, wR_2=0.1477, R indices (all data): R_1=0.1659, wR_2=0.746.

4.2.2. Crystallographic data for *4h*

$C_{20}H_{26}N_2O_5$, FW=374.43, orthorhombic, $Pna2_1$, a=15.856(4), b=9.165(2), c=13.510(3) Å, V=1963.2(8) Å^3, Z=4, D_c=1.267 g/cm^3, μ=0.091 mm^{-1}, $2.57<\theta<23.33^\circ$, reflections collected/unique=7901/2786, R_{int}=0.0322, 349 parameters, Goof=0.942, R indices ($I>2\sigma(I)$): R_1=0.0326, wR_2=0.0911, R indices (all data): R_1=0.0335, wR_2=0.0919.

4.2.3. Crystallographic data for *5d*

$C_{36}H_{40}N_4O_8$, FW=218.91, monoclinic, $P2_1/c$, a=10.422(2), b=9.556(2), c=16.783(4) Å, β=106.557(4)°, V=1602.3(6) Å^3, Z=4, D_c=1.361 g/cm^3, μ=0.097 mm^{-1}, $2.04<\theta<23.33^\circ$, reflections collected/unique=6779/2319, R_{int}=0.0742, 298 parameters, Goof=0.938, R indices ($I>2\sigma(I)$): R_1=0.0412, wR_2=0.0863, R indices (all data): R_1=0.0571, wR_2=0.0925.

4.2.4. Crystallographic data for *5e*

$C_{40}H_{44}N_4O_{10}$, FW=238.92, monoclinic, $P2_1/c$, a=10.383(3), b=12.011(4), c=15.037(5) Å, β=105.912(6)°, V=1803.5(10) Å^3, Z=4, D_c=1.320 g/cm^3, μ=0.096 mm^{-1}, $2.20<\theta<23.39^\circ$, reflections collected/unique=7604/2590, R_{int}=0.0769, 324 parameters, Goof=0.973, R indices ($I>2\sigma(I)$): R_1=0.0425, wR_2=0.0958, R indices (all data): R_1=0.0541, wR_2=0.1012.

4.3. General experimental procedure

The solution of 0.1–0.2 mmol of **1** in 1–2 ml of toluene, unless otherwise stated was heated (the conditions are shown in Table 1). In the cases when the temperature was 131 °C, the reaction was carried out in a sealed tube. After evaporation of a reaction mixture the products of rearrangement **3** and/or **4** (**5**) were separated by chromatographing on silica gel or alumina with $CHCl_3$/MeOH mixture as eluent.

4.3.1. Dimethyl 2-oxo-3-(2,4,4,5,5-pentamethyl-4,5-dihydro-1H-1λ-5-imidazol-1-ylidene)succinate *3a*

Starting from **1a**, following the general procedure and using $CHCl_3$/MeOH (50:1) as eluent for the chromatography on alumina, the product was obtained as a white powder (0.014 g, 25%). Mp 222.5–227 °C (with decomposition). IR (KBr) 3179, 2988, 2926, 2766, 2720, 1736, 1687, 1589, 1521, 1432, 1364, 1336, 1276, 1242, 1189, 1174, 1158, 1132, 1065 cm^{-1}. δ_H ($CDCl_3$): 1.13 (s, 3H, 4-CH_3 or 5-CH_3), 1.18 (s, 3H, 4-CH_3 or 5-CH_3), 1.25 (s, 3H, 4-CH_3 or 5-CH_3), 1.26 (s, 3H, 4-CH_3 or 5-CH_3), 1.97 (s, 3H, 2-CH_3), 3.59 (s, 3H, CO_2CH_3), 3.81 (s, 3H, CO_2CH_3), 10.40 (br s, 1H, NH); δ_C ($CDCl_3$): 12.2, 20.1, 20.6, 22.1, 23.3, 50.3, 51.7, 64.7, 72.9, 91.6, 166.3, 167.4, 169.6, 174.1. Anal. Calcd for $C_{14}H_{22}N_2O_5$: C, 56.36; H, 7.43; N, 9.39. Found: C, 56.61; H, 7.40; N, 9.22%.

4.3.2. Dimethyl 2-oxo-3-(2-tert-butyl-4,4,5,5-pentamethyl-4,5-dihydro-1H-1λ-5-imidazol-1-ylidene)succinate *3b*

Starting from **1b**, following the general procedure and using $CHCl_3$/MeOH (50:1) as eluent for the chromatography on alumina, the product was obtained as a white powder (0.043 g, 80%). Mp 275–277 °C (with decomposition). IR (KBr) 3148, 3000, 2944, 2881, 1734, 1675, 1536, 1518, 1437, 1397, 1373, 1335, 1271, 1223, 1191, 1177, 1157, 1064 cm^{-1}. δ_H (CD_3OH): 1.20 (s, 3H, 4-CH_3 or 5-CH_3), 1.23 (s, 3H, 4-CH_3 or 5-CH_3), 1.32 (s, 3H, 4-CH_3 or 5-CH_3), 1.37 (s, 3H, 4-CH_3 or 5-CH_3), 1.29 (s, 9H, $C(CH_3)_3$), 3.59 (s, 3H, CO_2CH_3), 3.78 (s, 3H, CO_2CH_3); δ_C (CD_3OH): 21.5, 22.0, 23.3, 23.9, 28.6, 36.7, 51.5, 53.0, 66.1, 76.1, 170.4, 171.9, 176.9, 177.0. Anal. Calcd for $C_{17}H_{28}N_2O_5$: C, 59.98; H, 8.29; N 8.23. Found: C, 60.02; H, 8.47; N, 8.22%.

4.3.3. Dimethyl 2-oxo-3-(2-(4-nitrophenyl)-4,4,5,5-pentamethyl-4,5-dihydro-1H-1λ-5-imidazol-1-ylidene)succinate *3c*

Starting from **1c**, following the general procedure and using $CHCl_3$/MeOH (50:1) as eluent for the chromatography on alumina, the product was obtained as a white powder, which was recrystallized from toluene/$CHCl_3$ (0.016 g, 50%). Mp 222.5–224.5 °C (with decomposition). IR (KBr) 2980, 2948, 2846, 2721, 1739, 1676, 1612, 1556, 1521, 1436, 1340, 1238, 1167, 1122, 1057 cm^{-1}. δ_H ($CDCl_3$): 1.08 (s, 3H, 4-CH_3 or 5-CH_3), 1.23 (s, 3H, 4-CH_3 or 5-CH_3), 1.25 (s, 3H, 4-CH_3 or 5-CH_3), 1.38 (s, 3H, 4-CH_3 or 5-CH_3), 3.51 (s, 3H, CO_2CH_3), 3.60 (s, 3H, CO_2CH_3), 7.72 (d, ^3J=8.7 Hz, 2H, Ar), 8.07 (d, ^3J=8.7 Hz, 2H, Ar), 11.18 (br s, 1H, NH); δ_C ($CDCl_3$): 20.0, 20.7, 21.8, 23.1, 50.5, 51.5, 65.7, 73.8, 93.4, 123.0, 129.6, 130.6, 149.9, 163.6, 168.6, 166.9, 173.6. Anal. Calcd for $C_{19}H_{23}N_3O_7$: C, 56.29; H, 5.72; N, 10.37. Found: C, 56.43; H, 5.92; N, 10.24%.

4.3.4. Dimethyl 2-oxo-3-(2-phenyl-4,4,5,5-pentamethyl-4,5-dihydro-1H-1λ-5-imidazol-1-ylidene)succinate *3d*

Starting from **1d**, following the general procedure, the product was obtained as a white powder, which was recrystallized from hexane/acetone (0.006 g, 20%). Mp 238–240 °C. IR (KBr) 3165, 2992, 2948, 2907, 2844, 2726, 1742, 1674, 1610, 1592, 1540, 1521, 1436, 1398, 1373, 1351, 1272, 1237, 1199, 1129, 1058 cm^{-1}. δ_H ($CDCl_3$): 1.07 (s, 3H, 4-CH_3 or 5-CH_3), 1.15 (s, 6H, 4-CH_3 or 5-CH_3), 1.21 (s, 3H, 4-CH_3 or 5-CH_3), 3.39 (s, 3H, CO_2CH_3), 3.51 (s, 3H, CO_2CH_3), 7.11–7.47 (m, 5H, Ph), 10.55 (br s, 1H, NH); δ_C ($CDCl_3$): 20.0, 20.8, 21.8, 23.0, 50.1, 51.3, 64.8, 73.3, 93.3, 124.7, 128.1, 128.1, 132.3, 165.0, 167.5, 169.1, 174.0. Anal. Calcd for $C_{19}H_{24}N_2O_5$: C, 63.32; H, 6.71; N, 7.77. Found: C, 63.13; H, 6.66; N, 7.62%.

4.3.5. Dimethyl 2-oxo-3-(2-(4-methoxyphenyl)-4,4,5,5-pentamethyl-4,5-dihydro-1H-1λ-5-imidazol-1-ylidene)succinate *3e*

Starting from **1e**, following the general procedure and using $CHCl_3$/MeOH (50:1) as eluent for the chromatography on silica gel, the product was obtained as a yellowish oil (0.039 g, 22%), which was crystallized in hexane at −95 °C and recrystallized from heptane/EtOAc to give colourless crystals. Mp 183–185 °C. IR (KBr)

3104, 2947, 2852, 1736, 1677, 1612, 1586, 1506, 1435, 1397, 1373, 1339, 138, 1263, 1171, 1121, 1055 cm^{-1}. δ_H ($CDCl_3$): 1.12 (s, 3H, 4-CH_3 or 5-CH_3), 1.18 (s, 3H, 4-CH_3 or 5-CH_3), 1.22 (s, 3H, 4-CH_3 or 5-CH_3), 1.24 (s, 3H, 4-CH_3 or 5-CH_3), 3.47 (s, 3H, CO_2CH_3), 3.64 (s, 3H, CO_2CH_3), 3.70 (s, 3H, OCH_3), 6.68 (d, ^3J=8.8 Hz, 2H, Ar), 7.50 (d, ^3J=8.8 Hz, 2H, Ar), 10.28 (br s, 1H, NH); δ_C ($CDCl_3$): 20.0, 21.1, 21.7, 23.1, 50.1, 51.3, 55.1, 64.4, 73.0, 93.6, 113.6, 116.7, 130.5, 162.8, 164.2, 167.6, 161.2, 174.2. Anal. Calcd for $C_{20}H_{26}N_2O_6$: C, 61.53; H, 6.71; N 7.18. Found: C, 61.29; H, 6.96; N, 7.01%.

4.3.6. Dimethyl 2-(2-(4-nitrophenyl)-3,4,4,5,5-pentamethyl-4,5-dihydro-1H-1λ-5-3λ-5-imidazol-1-ylidene)-3-oxosuccinate **3g**

Starting from **1g**, following the general procedure and using $CHCl_3$/MeOH (120:1) as eluent for the chromatography on silica gel, the product was obtained as a yellow powder, which was recrystallized from hexane/EtOAc (0.022 g, 29%). Mp 131.5–133.5 °C. IR (KBr) 3055, 2984, 2945, 1737, 1672, 1573, 1534, 1436, 1349, 1297, 1208, 1186, 1146, 1113, 1082, 1036 cm^{-1}. δ_H ($CDCl_3$): 1.35 (s, 3H, 4-CH_3 or 5-CH_3), 1.36 (s, 3H, 4-CH_3 or 5-CH_3), 1.43 (s, 3H, 4-CH_3 or 5-CH_3), 1.48 (s, 3H, 4-CH_3 or 5-CH_3), 2.89 (s, 3H, NCH_3), 3.47 (s, 3H, CO_2CH_3), 3.61 (s, 3H, CO_2CH_3), 7.65 (br s, 2H, Ar), 8.26 (d, ^3J=9.0 Hz, 2H, Ar); δ_C ($CDCl_3$): 19.7, 20.0, 20.5, 20.5, 23.3, 50.2, 51.4, 70.8, 72.5, 91.9, 123.6, 129.0, 130.3, 149.7, 165.0, 166.8, 168.7, 174.9. Anal. Calcd for $C_{20}H_{25}N_3O_7$: C, 57.27; H, 6.01; N, 10.02. Found: C, 57.25; H, 6.03; N, 10.24%.

4.3.7. Dimethyl 2-(1-(4-nitrophenyl)-3,4,4,5,5-pentamethylimidazolidin-2-ylidene)-3-oxosuccinate **4g**

Starting from **1g**, following the general procedure and using $CHCl_3$/MeOH (120:1) as eluent for the column chromatography on silica gel, the product was obtained as a yellow powder, which was recrystallized from hexane/EtOAc (0.005 g, 7%). Mp 168–169.5 °C. IR (KBr) 3088, 2990, 2951, 1732, 1681, 1592, 1544, 1523, 1499, 1449, 1341, 1298, 1231, 1200, 1154, 1134, 1080, 1021 cm^{-1}. δ_H ($CDCl_3$): 1.25 (s, 3H, 4-CH_3 or 5-CH_3), 1.35 (s, 3H, 4-CH_3 or 5-CH_3), 1.38 (s, 3H, 4-CH_3 or 5-CH_3), 1.39 (s, 3H, 4-CH_3 or 5-CH_3), 3.05 (s, 3H, NCH_3), 3.38 (s, 3H, CO_2CH_3), 3.72 (s, 3H, CO_2CH_3), 7.36 (d, ^3J=8.7 Hz, 2H, Ar), 8.21 (d, ^3J=8.7 Hz, 2H, Ar); δ_C ($CDCl_3$): 19.4, 20.6, 20.7, 22.0, 28.9, 50.2, 51.6, 69.0, 69.1, 81.5, 124.2, 127.5, 142.2, 146.7, 165.0, 165.4, 167.5, 179.4. Anal. Calcd for $C_{20}H_{25}N_3O_7$: C, 57.27; H, 6.01; N, 10.02. Found: C, 57.31; H, 6.12; N, 9.97%.

4.3.8. Dimethyl 2-(1-phenyl-3,4,4,5,5-pentamethylimidazolidin-2-ylidene)-3-oxosuccinate **4h**

Starting from **1h**, following the general procedure, the product was obtained as a white powder, which was recrystallized from heptane (0.035 g, 78%). Mp 171–172 °C. IR (KBr) 2988, 2951, 1735, 1673, 1579, 1539, 1506, 1431, 1396, 1376, 1350, 1297, 1209, 1152, 1133, 1071, 1022 cm^{-1}. δ_H ($CDCl_3$): 1.16 (s, 3H, 4-CH_3 or 5-CH_3), 1.34 (s, 3H, 4-CH_3 or 5-CH_3), 1.36 (s, 6H, 4-CH_3 or 5-CH_3), 3.02 (s, 3H, NCH_3), 3.34 (s, 3H, CO_2CH_3), 3.70 (s, 3H, CO_2CH_3), 7.15–7.17 (m, 2H), 7.30–7.35 (m, 3H); δ_C ($CDCl_3$): 19.4, 20.6, 22.0, 28.9, 49.8, 51.4, 68.4, 68.7, 127.7, 128.5, 128.8, 135.6, 165.4, 165.7, 168.0, 179.0. Anal. Calcd for $C_{20}H_{26}N_2O_5$: C, 64.15; H, 7.00; N, 7.48. Found: C, 64.47; H, 7.07; N, 7.47%.

4.3.9. Dimethyl 2-(1-(4-methoxyphenyl)-3,4,4,5,5-pentamethylimidazolidin-2-ylidene)-3-oxosuccinate **4i**

Starting from **1i**, following the general procedure, the product was obtained as a white powder, which was recrystallized from hexane/EtOAc (0.030 g, 46%). Mp 144–145.5 °C. IR (KBr) 2982, 2951, 2839, 1732, 1673, 1582, 1515, 1435, 1397, 1374, 1350, 1295, 1251, 1197, 1154, 1133, 1079, 1022 cm^{-1}. δ_H ($CDCl_3$): 1.12 (s, 3H, 4-CH_3 or 5-CH_3), 1.29 (s, 3H, 4-CH_3 or 5-CH_3), 1.31 (s, 3H, 4-CH_3 or 5-CH_3), 1.32 (s, 3H, 4-CH_3 or 5-CH_3), 2.98 (s, 3H, NCH_3), 3.35 (s, 3H, CO_2CH_3), 3.68 (s, 3H, CO_2CH_3), 3.74 (s, 3H, OCH_3), 6.80 (d, ^3J=8.8 Hz, 2H, Ar), 7.05 (d, ^3J=8.8 Hz, 2H, Ar); δ_C ($CDCl_3$): 19.4, 20.4, 20.6, 21.7, 28.7, 49.8, 51.4, 55.2, 68.2, 68.7, 81.0, 113.9, 127.8, 129.1, 159.4, 165.5, 165.7, 168.0, 178.7. Anal. Calcd for $C_{21}H_{28}N_2O_6$: C, 62.36; H, 6.98; N, 6.93. Found: C, 62.66; H, 7.06; N, 6.80%.

4.3.10. Methyl 2,2,3,3-tetramethyl-5,6-dioxo-1-phenyl-2,3,5,6-tetrahydro-1H-pyrrolo[1,2-a]imidazole-7-carboxylate **5d**

A solution of **1d** in 1 ml of DMSO was kept at 130 °C for 5 h. The resulting mixture was poured into 10 ml of $CHCl_3$ and extracted four times with 5 ml of water. The organic solution was dried with $MgSO_4$ and then evaporated. The crude product was purified chromatographically on silica gel, with $CHCl_3$/MeOH (100:1) and recrystallized from hexane/toluene (0.017 g, 25%). Mp 209–210.5 °C. IR (KBr) 3052, 2987, 2954, 1757, 1683, 1602, 1578, 1498, 1465, 1449, 1401, 1378, 1310, 1257, 1213, 1124 cm^{-1}. δ_H ($CDCl_3$): 1.30 (s, 6H, 2-CH_3 or 3-CH_3), 1.57 (s, 6H, 2-CH_3 or 3-CH_3), 3.26 (s, 3H, CO_2CH_3), 7.20–7.23 (m, 2H, Ph), 7.44–7.48 (m, 3H, Ph); δ_C ($CDCl_3$): 21.1, 22.2, 50.6, 63.8, 77.1, 86.6, 127.6, 129.1, 129.4, 135.2, 159.9, 161.0, 165.1, 177.5. Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.63; H, 6.12; N, 8.42%.

4.3.11. Methyl 1-(4-methoxyphenyl)-2,2,3,3-tetramethyl-5,6-dioxo-2,3,5,6-tetrahydro-1H-pyrrolo[1,2-a]imidazole-7-carboxylate **5e**

Starting from **1e**, following the general procedure and using $CHCl_3$/MeOH (80:1) as eluent for the chromatography on silica gel, the product was obtained as a yellow powder (0.105 g, 60%), which was recrystallized from EtOAc. Mp 204–205 °C. IR (KBr) 3076, 2982, 2946, 2846, 1754, 1729, 1696, 1578, 1513, 1466, 1377, 1306, 1254, 1175, 1128, 1030 cm^{-1}. δ_H ($CDCl_3$): 1.24 (s, 6H, 2-CH_3 or 3-CH_3), 1.50 (s, 6H, 2-CH_3 or 3-CH_3), 3.20 (s, 3H, CO_2CH_3), 3.79 (s, 3H, OCH_3), 6.90 (d, J=8.8 Hz, 2H, Ar), 7.10 (d, J=8.8 Hz, 2H, Ar); δ_C ($CDCl_3$): 20.9, 21.9, 50.4, 55.3, 63.5, 77.0, 86.3, 114.0, 127.4, 128.7, 159.8, 159.8, 160.9, 164.9, 177.3. Anal. Calcd for $C_{19}H_{22}N_2O_5$: C, 63.67; H, 6.19; N, 7.82. Found: C, 64.04; H, 6.25; N, 7.89%.

4.3.12. Methyl 1-(4-(dimethylamino)phenyl)-2,2,3,3-tetramethyl-5,6-dioxo-2,3,5,6-tetrahydro-1H-pyrrolo[1,2-a]imidazole-7-carboxylate **5f**

Starting from **1f**, following the general procedure (4 ml of benzene was a solvent, reaction time 2 h), the product was obtained as a yellow powder, which was recrystallized from hexane/EtOAc (0.122 g, 88%). Mp 189–191 °C. IR (KBr) 2982, 2923, 2810, 1755, 1688, 1586, 1523, 1458, 1359, 1254, 1215, 1193, 1122, 1020 cm^{-1}. δ_H ($CDCl_3$): 1.26 (s, 6H, 2-CH_3 or 3-CH_3), 1.53 (s, 6H, 2-CH_3 or 3-CH_3), 2.99 (s, 3H, $N(CH_3)_2$), 3.29 (s, 3H, CO_2CH_3), 6.66 (d, J=8.8 Hz, 2H, Ar), 7.01 (d, J=8.8 Hz, 2H, Ar); δ_C ($CDCl_3$): 20.9, 21.8, 40.0, 50.4, 63.4, 77.0, 86.4, 111.3, 122.8, 127.9, 150.2, 160.1, 160.9, 164.6, 177.3. Anal. Calcd for $C_{20}H_{25}N_3O_4$: C, 64.67; H, 6.78; N, 11.31. Found: C, 64.34; H, 6.80; N, 11.10%.

4.3.13. Methyl 2,2,3,3-tetramethyl-5,6-dioxo-1-[(E)-2-phenylvinyl]-2,3,5,6-tetrahydro-1H-pyrrolo[1,2-a]imidazole-7-carboxylate **5j**

Starting from **1j**, following the general procedure (4 ml of benzene was a solvent, reaction time 37 h), the product was obtained as a yellow powder, which was recrystallized from EtOAc (0.024 g, 53%). Mp 202.5–204 °C. IR (KBr) 3068, 2986, 2946, 1758, 1678, 1562, 1456, 1402, 1379, 1256, 1225, 1189, 1157, 1129 cm^{-1}. δ_H ($CDCl_3$): 1.47 (s, 6H, 2-CH_3 or 3-CH_3), 1.48 (s, 6H, 2-CH_3 or 3-CH_3), 3.68 (s, 3H, CO_2CH_3), 6.52 (d, J=14.7 Hz, 1H, CH), 7.26–7.43 (m, 5H, Ph), 7.50 (d, J=14.7 Hz, 1H, CH); δ_C ($CDCl_3$): 20.5, 21.9, 51.3, 63.8, 76.6, 87.3, 122.3, 126.4, 128.8, 126.6, 128.5, 134.0, 159.2, 162.2, 163.9, 177.2. Anal. Calcd for $C_{20}H_{22}N_2O_4$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.30; H, 6.10; N, 7.75%.

4.3.14. Dimethyl 2-tert-butyl-3-[4-(dimethylamino)phenyl]-2,3-dihydroisoxazole-4,5-dicarboxylate **6b**

The solution of 0.36 g (1.63 mmol) *N*-(4-{[*tert*-butyl(oxido)-imino]methyl}phenyl)-*N*,*N*-dimethylamine and 0.24 ml (1.96 mmol)

dimethyl but-2-ynedioate in 5 ml $CHCl_3$ was kept for 36 h at 20 °C. After evaporation of the reaction mixture the product was separated by chromatographing on alumina with hexane/EtOAc (4:1) as eluent. Compound **6b** was obtained as white powder, which was recrystallized from hexane (0.144 g, 24%). Mp 74–75 °C. IR (KBr) 2984, 2947, 2808, 1748, 1706, 1661, 1615, 1526, 1439, 1341, 1247, 1207, 1121, 1064, 1034 cm^{-1}. δ_H ($CDCl_3$): 1.15 (s, 9H, $C(CH_3)_3$), 2.92 (s, 6H, $N(CH_3)_2$), 3.56 (s, 3H, CO_2CH_3), 3.86 (s, 3H, CO_2CH_3), 5.22 (s, 1H, CH), 6.59 (d, J=8.8 Hz, 2H, Ar), 7.13 (d, J=8.8 Hz, 2H, Ar); δ_C ($CDCl_3$): 24.6, 40.3, 51.4, 52.3, 61.6, 67.1, 109.7, 112.2, 128.0, 129.3, 150.0, 151.6, 159.6, 162.5. Anal. Calcd for $C_{19}H_{26}N_2O_5$: C, 62.97; H, 7.23; N, 7.73. Found: C, 62.62; H, 7.33; N, 7.73%.

*4.3.15. Dimethyl 2-({tert-butyl[4-(dimethylamino)phenyl]amino}-methylene)-3-oxosuccinate **8b***

The solution of 0.10 g (0.28 mmol) **6b** in 1 ml toluene was heated for 14 h at 105 °C. After evaporation of the reaction mixture the product was separated by chromatographing on silica gel, using $CHCl_3$/MeOH as eluent (0.024 g, 24%). Mp 117–178 °C. IR (KBr) 3050, 2952, 2858, 2817, 1724, 1691, 1649, 1609, 1541, 1516, 1443, 1394, 1368, 1340, 1251, 1229, 1180, 1150, 1023 cm^{-1}. δ_H ($CDCl_3$): 1.35 (s, 9H, $C(CH_3)_3$), 2.92 (s, 6H, $N(CH_3)_2$), 3.14 (s, 3H, CO_2CH_3), 3.72 (s, 6H, CO_2CH_3), 6.58 (d, J=9.0 Hz, 2H, Ar), 6.86 (d, J=9.0 Hz, 2H, Ar), 8.34 (s, 1H, CH); δ_C ($CDCl_3$): 29.9, 40.2, 51.3, 52.0, 62.7, 67.1, 111.3, 129.2, 128.0, 149.8, 152.7, 165.0, 166.8. Anal. Calcd for $C_{19}H_{26}N_2O_5$: C, 62.97; H, 7.23; N, 7.73. Found: C, 62.99; H, 7.20; N, 7.49%.

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