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Nitrogen heterocycles by palladium-catalysed oxidative cyclization-alkoxycarbonylation of acetylenic ureas[1]

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Abstract

Acetylenic ureas readily undergo oxidative cyclization-alkoxycarbonylation reactions in the presence of PdI_2 (or Pd/C)-KI as catalyst in methanol under mild conditions (65°C and 24 bar of a 3:1 mixture of CO and air). Cyclization occurs by *trans*-attack of oxygen or *cis*-attack of nitrogen functions on the triple bond, followed by stereospecific carbonylation, resulting in *E* or *Z*-stereochemistry, respectively. In the case of diacetylenic ureas condensed ring formation occurs. The triple bond can also react stereospecifically with carbon monoxide and methanol to form a maleic group by *cis*-attack leading to *Z*-stereochemistry.

Keywords: Nitrogen heterocycles; Palladium catalyst; Oxidative carbonylation reaction; Cyclization reactions; Acetylenic urea

1. Introduction

We have previously shown that palladium-catalysed carbonylation of acetylenic amines and amides leads to β- and γ-lactams and to oxazolines, respectively [1] (Scheme 1).

On the basis of the versatility of this reaction and in view of the general interest in simple catalytic synthesis of other heterocycles we have addressed our attention to acetylenic ureas as substrates.

2. Results and discussion

We observed that acetylenic ureas **1** are very useful substrates to generate both oxazolines and cyclic ureas, containing an *E* or *Z*-(methoxycarbonyl)methylene chain, respectively.

Working in methanol with carbon monoxide and oxygen (from air) at 65°C in the presence of PdI_2 or 10% Pd/C + 10 KI we obtained two types of products, depending on whether the cyclization was initiated by N- or O-attack on the triple bond according to Scheme 2.

Although other alcohols can replace methanol and other alkyls can replace the geminal methyl groups no systematic study was carried out on this aspect.

The structures of **2**, **2′** and **3** were determined by IR, ^{1}H-, ^{13}C-NMR and mass spectroscopies and correspond to the expected properties of oxazolamines and cyclic ureas [2–4]. Compound **2′** corresponds to methoxycarbonylation at the exocyclic nitrogen of **2**. The strong similarity of ^{13}C-NMR absorption of the quaternary carbon bearing the geminal groups of **2c** and **2c′** and their difference from **3c** points to the presence of **2** rather than its tautomer with exocyclic RN=C double bond.

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[1] Dedicated to Professor Bruce King in recognition of his outstanding contribution to organometallic chemistry.

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The configuration of products **2**, **2′** turns out to be *E* as previously ascertained for oxazolines [1], while for **3** it is *Z* as determined by X-ray analysis of **3e** [5]. The *E* configuration must be attributed to *trans*-attack of the oxygen function on the palladium-coordinated triple bond, followed by vinylpalladium formation and stereospecific alkoxycarbonylation (Scheme 3), while the *Z* one seems to imply an initial *cis*-attack of a palladium bonded nitrogen function [6].

Oxygen-attack on the triple bond to form oxazolines [2] or nitrogen-attack to form cyclic ureas [3,4] in acid or base-catalysed reactions were previously reported. The presence of the geminal methyl groups α to the triple bond is a requisite for the success of the reaction [7]. In the absence of their orienting effect on the substrate only products deriving from double carbonylation of the triple bond are formed [8].

An interesting developement was observed when the reaction was carried out with a diacetylenic urea: both nitrogen atoms became reactive and underwent ring closure (Scheme 4).

The structure of the main product **7** was determined by X-ray diffraction. It contains two *E* and *Z* (methoxycarbonyl)methylene chains bonded to condensed oxazoline and pyrimidinone ring, respectively.

Fig. 1 reports a perspective view of **7**, along with the labelling scheme. Table 1 lists geometric parameters obtained by crystallographic analysis. The stereochemistry of the double bonds C2–C8 and C13–C14 is defined by the torsion angles C3–C2–C8–C9 = 0.5(3)° and C6–C13–C14–O5 = 2.5(3)°. The two condensed rings are planar within 0.09 Å, with the exception of C2, lying 0.47 Å out of the mean plane. Methyls C11 and C12 are in equatorial and axial positions, respectively, with reference to the six-membered ring. As a consequence of the distortion at C2, the double bond vector C2–C8 points away from C12, forming an angle of 36° with the mean ring plane, while the vector C3–O2 is slightly tilted (8°) towards C12. The carboxylic group bound to C13 lies in the plane of the fused rings, with O5 oriented on the same side of C16 and C17, roughly equidistant from them. Any displacement from this local minimum conformation by rotation around C13–C14 would require one of the two short distances O5...C16 = 3.083(2) or O5...C17 = 3.170(2) Å, to decrease slightly, with a consequent increase in steric repulsion. Similarly, for the carboxylic group at C8, the bond C8–C9 is oriented on the same side of O2, and the plane containing the group is rotated away from the double bond plane by about 60° due to the intramolecular contact O2...O4 = 2.700(2) Å. The conformation of this group is also determined by the interactions O3...C10 (x, $-y-0.5$, $z-0.5$) = 3.141(3) Å and O4...C11 (x, $-y+0.5$, $+z+0.5$) = 3.290(2) Å, which are the only intermolecular contacts below 3.4 Å occurring between non-hydrogen atoms in the crystal packing.

The structures of products **4**, **5** and **6** were unequivocally established by NMR spectroscopy. In particular the presence of dihydropyrimidine rings was ascertained on the basis of ^{1}H-NMR absorptions of the CH=CH group of **5** (doublets at δ 4.73, $J = 7.8$ Hz and δ 5.93, $J = 7.8$ Hz) and of the typical low field ^{1}H-NMR absorption of =CH (7.13 δ) of **6**. *E*-stereochemistry for [(methoxycarbonyl)methylene]oxazolines [1] and *Z* stereochemistry for the bicarboxylated double bond [8] are a clear indication of the perfect stereoselectivty of the reaction and of the underlying mechanism.

Scheme 5 accounts for the formation of products **4**–**7**, based on the assumption that the reaction starts from an oxazoline intermediate of type **2**.

Carbonylation and condensation steps are well established. Less common is the attack of the NH group on the external carbon of the triple bond, leading to products **5** and **6**. Examples of palladium-catalysed ring formation of this type are reported in the literature, however [9]. In the present case only the attack on the external triple bond leading to a six-membered ring is observed. This is probably due to the fact that the attacking nitrogen is part of the oxazolidinone ring and under these conditions the formation of a five-membered ring is less favorable than that of a six-membered one.

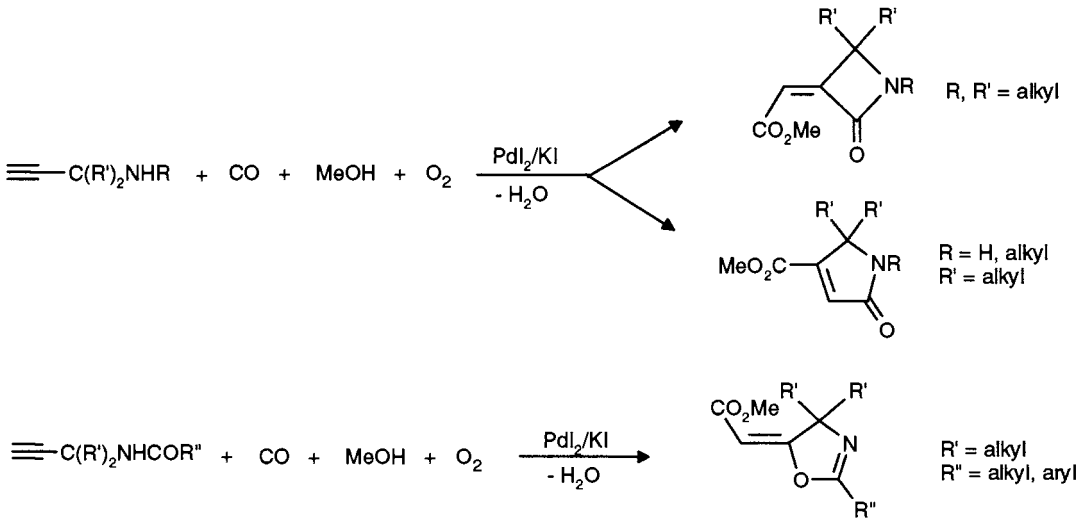
A transformation of **4** into **7** not requiring palladium does not occur significantly under the reaction conditions as ascertained by a blank experiment. Alternatively compound **7** could originate from another pathway, initiated by the methoxycarbonylation of a triple bond (Scheme 6).

However, the fact that monoacetylenic ureas reacted to form **3** by N-attack on the triple bond without previous CO insertion may be taken as an indirect evidence against the process depicted in Scheme 6. In both Schemes 5 and 6 the acylpalladium derivative corresponds to an inverted regiochemistry of carbonylation with respect to simple alkynes (initial attack of CO_2Me on the external rather than on the internal triple bond carbon). This is due to the steric effect of the geminal groups as already reported by us [10].

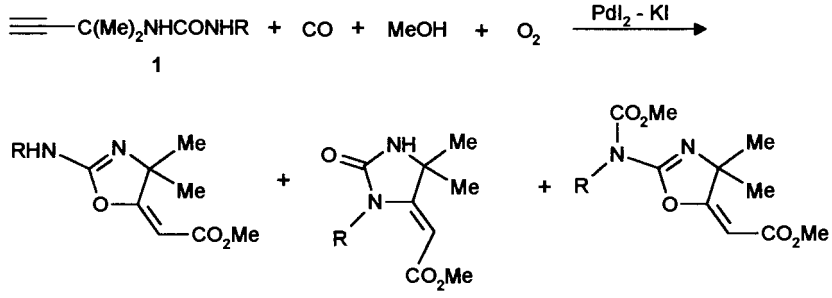
From a synthetic point of view the possibility to gain access to new heterocyclic rings of potentially biological interest [11] through a very simple, one-pot catalytic reaction offers a powerful tool to organic chemists.

3. Experimental details

Melting points were determined by an Electrothermal apparatus and are uncorrected. Elemental analyses were performed by a Carlo Erba Model EA 1108 Elemental Analyzer. GLC analyses were performed with a HR 3800 Dani Instrument equipped with a flame ionization detector using a methylsilicone (OV 101 sta-



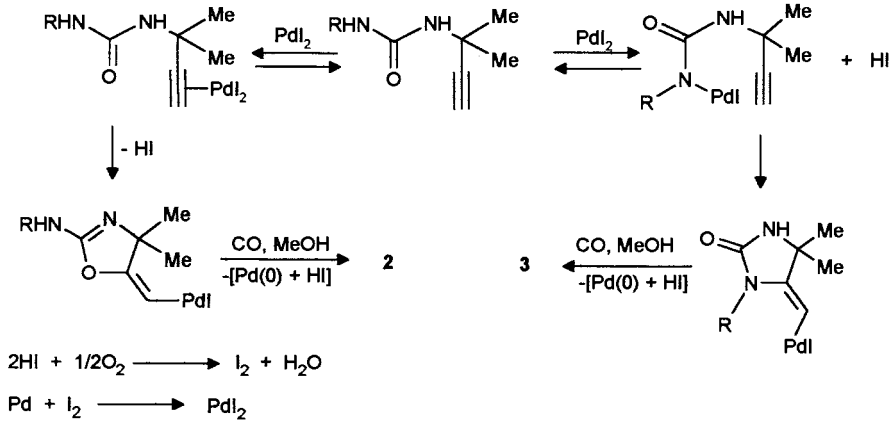
Scheme 1.



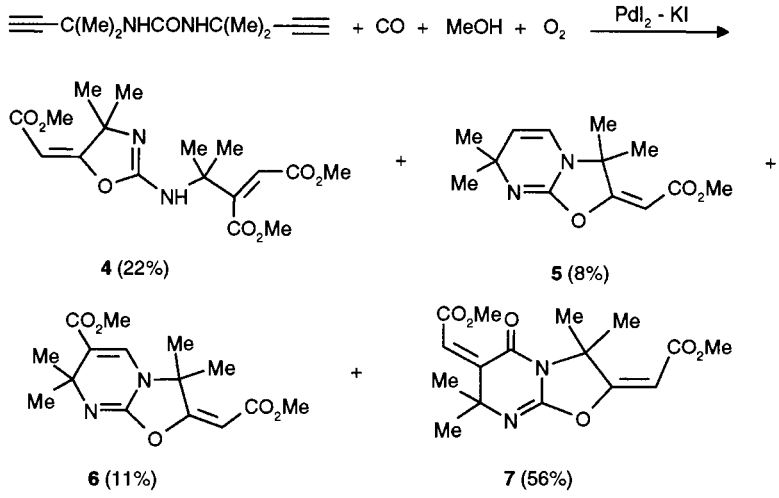
1		2 (%)[a]	3 (%)[a]	2' (%)[a]
a	R = n-Pr	a 70	23	3
b	R = CH_2Ph	b 33	53	-
c	R = Ph	c 34	7	33
d	R = p-MeC_6H_4	d 47	35	-
e	R = H	e	46	28

[a]) GLC yields based on starting ureas

Scheme 2.



Scheme 3.



Scheme 4.

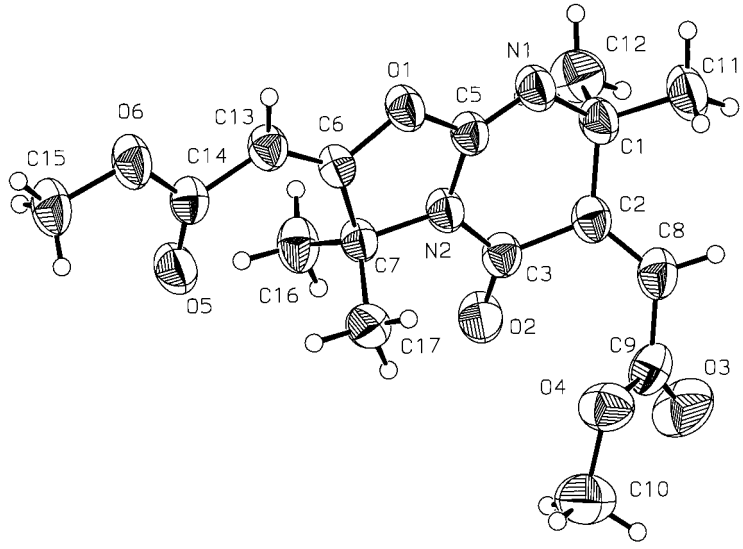


Fig. 1. ORTEP view of **7**, with anisotropic thermal displacement ellipsoids drawn at the 50% probability level.

tionary phase) capillary column. Quantitative determination of products and starting substrates were carried out by GLC with the internal standard method. ^{1}H-and ^{13}C-NMR spectra were obtained on a Brucker AC 300 spectrometer at 300 and 75.5 MHz, respectively, and were referenced to the residual proton and ^{13}C resonances of $CDCl_3$ (δ 7.25 and 77.5). Assignment of the absorptions in the ^{13}C-NMR spectra were made with the help of DEPT pulse experiments. Mass Spectra were obtained at an ionization energy of 70 eV on a Hewlett–Packard Mass Selective Detector 5971 Series interfaced with a Hewlett–Packard 5890 Series II GC. Relative intensities are in parentheses. IR spectra were recorded on a Nicolet 5PC FT-IR spectrometer.

3.1. Materials

Merck silica gel 60 (230–400 mesh) was used for preparative column chromatography. 10% Pd on carbon was purchased by Fluka. Propynylamines (Aldrich) were distilled and stored on K_2CO_3. The various *N*-alkyl-, *N*-aryl-*N*′-propynylureas, *N*,*N*′-bis(propynyl) urea and *N*-alkyl-, *N*-aryl-1,1-dimethylpropynylureas and *N*,*N*′-bis(1,1-dimethylpropynyl)urea were prepared according to literature methods [2–4,12].

3.2. Carbonylation reaction: general procedure

A 125 ml stainless-steel autoclave (Parr) equipped with a magnetic stirrer and thermostatted ($\pm$1°C) in a silicone oil bath (Fisher) was loaded with **1** (3.0 mmol) dissolved in MeOH (20 ml), PdI_2 (0.011 g, 0.03 mmol) or 10% Pd/C (0.031 g, 0.03 mmol) and KI (0.050 g, 0.3 mmol) under air, then it was pressurized with air (5 bar) and CO up to 23 bar total pressure and heated at 65°C for 36 h under stirring. The brown mixture was evaporated to dryness and the residue was extracted with CH_2Cl_2 and filtered. The organic products were

separated by column chromatography on silica gel using mixtures of *n*-hexane/ethyl acetate in suitable ratio as eluent. Compound **4** has been reported previously [1]. The spectral and analytical data for the other products are reported here.

3.2.1. *E*-4,5-dihydro-4,4-dimethyl-5-methoxycarbonylmethylene-*N*-propyl-2-oxazolamine **2a**

Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.91 (t, $J = 7.0$ Hz, 3 H, Me); 1.50–1.60 (m, 2 H, CH_2); 1.58 (s, 6 H, 2 Me); 3.15 (t, $J = 7.0$ Hz, 2H, NCH_2); 3.64 (s, 3 H, OMe); 4.33 (s, 1 H, NH); 5.50 (s, 1 H, =CH). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ: 10.98 (Me); 22.66 (CH_2); 25.74 (2 Me); 44.31 (CH_2); 51.84 (OMe); 70.31 (qC); 92.56 (=CH); 154.36 (qC); 166.31 (qC); 178.13 (qC). MS (*m*/*e*): 226 (M^+, 9); 211 (100); 169 (10); 127 (14); 83 (15); 69 (12). IR (neat) cm^{-1}: 3359 (m); 2969 (w); 2935 (w); 1725 (s br); 1656 (s); 1533 (m); 1436 (m); 1351 (m); 1172 (s); 1103 (s); 1045 (m); 986 (m); 824 (m). Anal. Calcd. for $C_{11}H_{18}N_2O_3$: C, 58.41; H, 7.96; N, 12.39%. Found: C, 58.29; H, 8.00; N, 12.17%.

Table 1
Bond distances (Å) and angles (°) with s.u.'s in parentheses for 7

O1–C5	1.368(2)	N2–C5	1.382(2)
O1–C6	1.384(2)	N2–C7	1.485(2)
O2–C3	1.210(2)	C1–C2	1.521(2)
O3–C9	1.197(2)	C1–C11	1.524(3)
O4–C9	1.327(2)	C1–C12	1.536(3)
O4–C10	1.449(3)	C2–C3	1.503(2)
O5–C14	1.204(2)	C2–C8	1.327(2)
O6–C14	1.335(2)	C6–C7	1.524(2)
O6–C15	1.442(2)	C6–C13	1.331(2)
N1–C1	1.489(2)	C7–C16	1.527(2)
N1–C5	1.252(2)	C7–C17	1.528(2)
N2–C3	1.378(2)	C8–C9	1.483(3)
		C13–C14	1.467(2)
C5–O1–C6	110.6(1)	O1–C6–C13	117.2(1)
C9–O4–C10	116.5(2)	O1–C6–C7	109.6(1)
C14–O6–C15	115.6(1)	C7–C6–C13	133.2(1)
C1–N1–C5	116.1(1)	N2–C7–C6	99.0(1)
C5–N2–C7	112.4(1)	C6–C7–C17	111.1(1)
C3–N2–C7	126.6(1)	C6–C7–C16	112.5(1)
C3–N2–C5	120.5(1)	N2–C7–C17	109.2(1)
N1–C1–C12	107.7(1)	N2–C7–C16	110.2(1)
N1–C1–C11	106.3(1)	C16–C7–C17	113.8(1)
N1–C1–C2	111.3(1)	C2–C8–C9	125.3(2)
C11–C1–C12	110.4(2)	O4–C9–C8	112.2(2)
C2–C1–C12	108.5(1)	O3–C9–C8	123.6(2)
C2–C1–C11	112.5(2)	O3–C9–O4	124.1(2)
C1–C2–C8	125.2(2)	C6–C13–C14	125.7(2)
C1–C2–C3	116.1(1)	O6–C14–C13	110.3(1)
C3–C2–C8	118.8(1)	O5–C14–C13	127.4(2)
N2–C3–C2	112.4(1)	O5–C14–O6	122.2(2)
O2–C3–C2	124.9(1)		
O2–C3–N2	122.6(1)		
N1–C5–N2	130.1(1)		
O1–C5–N2	108.2(1)		
O1–C5–N1	121.7(1)		

3.2.2. *E*-4,5-dihydro-4,4-dimethyl-5-methoxycarbonylmethylene-*N*-methoxycarbonyl-*N*-propyl-2-oxazolamine **2′a**

Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.87 (t, $J = 7.4$ Hz, 3 H, Me); 1.48–1.56 (m, 2 H, CH_2); 1.68 (s, 6 H, 2 Me); 3.30 (t, $J = 7.1$ Hz, 2 H, NCH_2); 3.68 (s, 3 H, OMe); 3.69 (s, 3 H, OMe); 5.59 (s, 1 H, =CH). MS (*m*/*e*): 284 (M^+, 12); 269 (95); 253 (11); 195 (25); 184 (81); 141 (100); 83 (84); 69 (76); 59 (41). IR (neat) cm^{-1}: 2968 (w); 2937 (w); 1749 (s); 1715 (s); 1685 (m); 1627 (s); 1426 (m); 1342 (m); 1167 (s); 1099 (s); 917 (m); 820 (m). Anal. Calcd. for $C_{13}H_{20}N_2O_5$: C, 54.93; H, 7.04; N, 9.86%. Found: C, 54.81; H, 7.02; N, 9.57%.

3.2.3. *E*-4,4-Dimethyl-5-methoxycarbonylmethylene-1-(1-propyl)imidazolidin-2-one **3a**

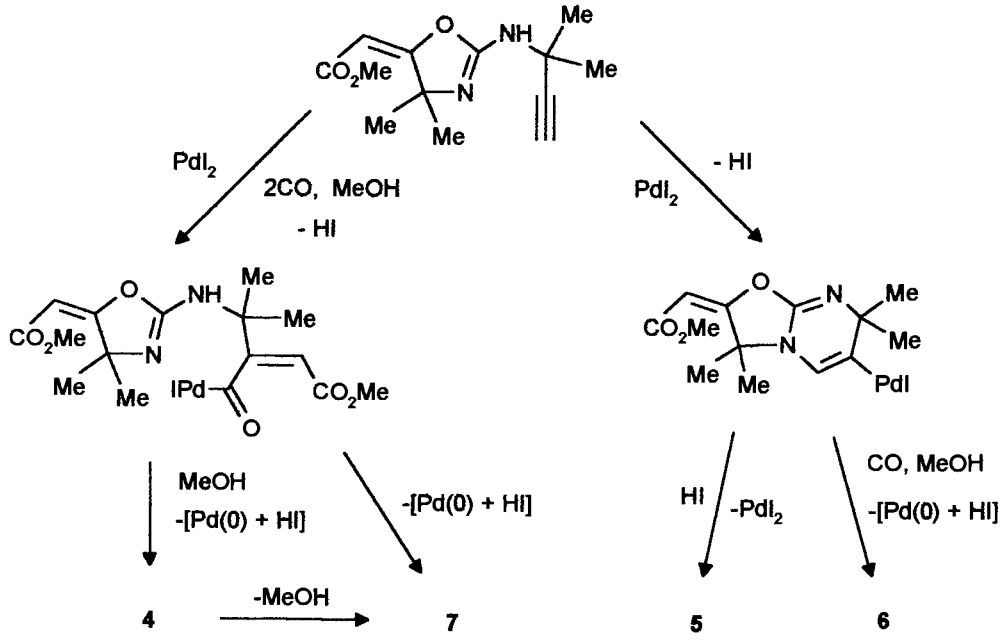
Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.90 (t, $J = 7.4$ Hz, 3 H, Me); 1.53–1.65 (m, 2 H, CH_2); 1.69 (s, 6 H, 2 Me); 3.42 (t, $J = 7.3$ Hz, 2 H, NCH_2); 3.64 (s, 3 H, OMe); 4.92 (s, 1 H, =CH), 6.08 (s, 1 H, NH). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ: 10.86 (Me); 19.31 (CH_2); 25.45 (2 Me); 41.56 (CH_2); 50.63 (OMe); 59.04 (qC); 86.77 (=CH); 156.21 (qC); 163.08 (qC); 166.35 (qC). MS (*m*/*e*): 226 (M^+, 32); 211 (28); 195 (33); 185 (82); 179 (27); 137 (77); 125 (31); 111(100). IR (neat) cm^{-1}: 3282 (m); 2989 (m); 1739 (s); 1714 (s); 1617 (s); 1424 (m); 1332 (m); 1161 (s); 1089 (s); 733 (m). Anal. Calcd. for $C_{11}H_{18}N_2O_3$: C, 58.34; H, 7.96; N, 12.39%. Found: C, 58.18; H, 8.02; N, 12.12%.

3.2.4. *E*-*N*-benzyl-4,5-dihydro-4,4-dimethyl-5-methoxycarbonylmethylene-2-oxazolamine **2b**

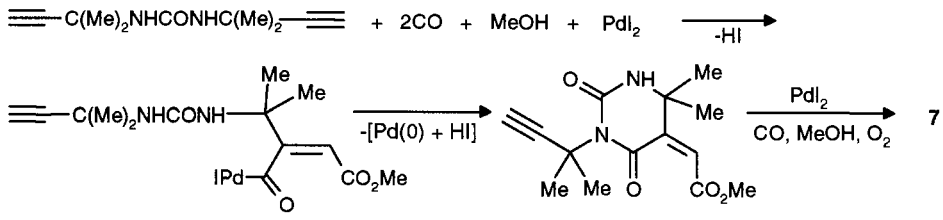
White solid, m.p. 99–102°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.64 (s, 6 H, 2 Me); 3.69 (s, 3 H, OMe); 4.36 (s, 1 H, NH); 4.42 (s, 2 H, CH_2); 5.56 (s, 1 H, =CH); 7.20–7.34 (m, 5 H, Ph). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ: 25.76 (2 Me); 46.73 (CH_2); 50.92 (OMe); 70.56 (qC); 92.95 (=CH); 127.47 (2 aromatic =CH); 127.63 (aromatic =CH); 128.62 (2 aromatic =CH); 137.60 (qC), 154.24 (qC); 166.28 (qC); 178.05 (qC). MS (*m*/*e*): 274 (M^+, 8); 259 (3); 243 (5); 215 (6); 91 (100); 65 (6). IR (neat) cm^{-1}: 3322 (m); 3198 (w); 2932 (w); 1801 (m); 1724 (s); 1657 (s); 1619 (m); 1524 (m); 1454 (m); 1252 (m); 1107 (s); 1048(m); 967 (m); 843 (w). Anal. Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.69; H, 6.57; N, 10.22%. Found: C, 65.52; H, 6.54; N, 10.08%.

3.2.5. *E*-1-benzyl-4,4-dimethyl-5-methoxycarbonylmethyleneimidazolidin-2-one **3b**

White solid, m.p. 128–130°C. ^{1}H-NMR (300 MHz,$CDCl_3$) δ: 1.72 (s, 6 H, 2 Me); 3.58 (s, 3 H, OMe); 4.67 (s, 2 H, CH_2); 4.88 (s, 1 H, =CH); 6.19 (s, 1 H, NH); 7.19–7.35 (m, 5 H, Ph). ^{13}C-NMR (75.5



Scheme 5.



Scheme 6.

MHz, $CDCl_3$) δ: 25.53 (2 Me); 43.76 (CH_2); 50.63 (OMe); 59.21 (qC); 88.56 (=CH); 126.56 (aromatic =CH); 127.47 (2 aromatic =CH); 128.67 (2 aromatic =CH); 135.07 (qC); 156.21 (qC); 162.15 (qC); 166.11 (qC). MS (*m/e*): 274 (M^+, 15); 259 (3); 243 (7); 215 (9); 199 (8); 91 (100); 65 (7). IR (neat) cm^{-1}: 3230 (m); 2950 (w); 1736 (s); 1711 (s); 1621 (s); 1440 (m); 1418 (m); 1340 (m); 1128 (s); 923 (w); 818 (w); 730 (w). Anal. Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.69; H, 6.57; N, 10.22%. Found: C, 65.49; H, 6.41; N, 10.01%.

3.2.6. E-4,5-dihydro-4,4-dimethyl-5-methoxycarbonyl-methylene-N-phenyl-2-oxazolamine ***2c***

White solid, m.p. 111–113°C. ^{1}H-NMR (300 MHz,$CDCl_3$) δ: 1.70 (s, 6 H,2 Me); 3.71 (s, 3 H, OMe); 5.63 (s, 1 H, =CH); 6.45 (s, 1 H, NH); 7.00–7.40 (AA′ MM′ X system 5 H, Ph). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ: 25.76 (2 Me); 51.06 (OMe); 70.38 (qC); 93.38 (=CH); 118.77 (2 aromatic =CH); 122.98 (aromatic =CH); 128.99 (2 aromatic =CH); 138.56 (qC); 150.48 (qC); 166.20 (qC); 176.22 (qC). MS (*m/e*): 260 (M^+, 12); 245 (100); 144 (19); 128 (17); 119 (19); 93 (15); 77 (14); 69 (18); 59 (3). IR (neat) cm^{-1}: 3351 (s); 2985 (w); 2941 (w); 1708 (s); 1660 (s); 1608 (m); 1548 (s); 1448 (m); 1348 (m); 1231 (m); 1168 (m); 1110 (s); 1084 (m); 993 (m); 839 (w); 761 (m). Anal. Calcd. for $C_{14}H_{16}N_2O_3$: C, 64.62; H, 6.15; N, 10.77%. Found: C, 64.40; H, 6.12; N, 10.28%.

3.2.7. E-4,5-dihydro-4,4-dimethyl-5-methoxycarbonyl-methylene-N-methoxycarbonyl-N-phenyl-2-oxazolamine ***2′c***

White solid, m.p. 134–137°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.67 (s, 6 H, 2 Me); 3.67 (s, 3 H, OMe); 3.79 (s, 3 H, OMe); 5.61 (s, 1 H, =CH); 7.26–7.43 (m, 5 H, Ph). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ: 24.51 (2 Me); 51.05 (OMe); 53.95 (OMe); 71.83 (qC); 94.80 (=CH); 126.89 (2 aromatic =CH); 128.13 (aromatic =CH); 129.17 (2 aromatic =CH); 137.63 (qC); 151.20 (qC); 153.00 (qC); 166.02 (qC); 176.74 (qC). MS (*m/e*): 318 (M^+, 3); 303 (42); 287 (4); 259 (5); 231 (7); 184 (22); 159 (100); 141 (31); 118 (27); 97 (23); 77 (32); 69 (35); 59 (18). IR (neat) cm^{-1}: 3005 (w); 2954 (m); 1745 (s); 1721 (s); 1687 (m); 1658 (s); 1494 (m); 1441 (m); 1334 (s); 1302 (s); 1191 (m); 1166 (m); 1108 (m); 1071 (s); 917 (m); 851 (m); 765 (m); 696 (m). Anal. Calcd. for $C_{16}H_{18}N_2O_5$: C, 60.38; H, 5.66; N, 8.81%. Found: C, 60.22; H, 5.62; N, 8.43%.

3.2.8. *E*-4,4-dimethyl-5-methoxycarbonylmethylene-1-phenylimidazolidin-2-one **3c**

White solid, m.p. 136–138°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.81 (s,6 H, 2 Me); 3.59 (s, 3 H, OMe); 4.84 (s, 1 H, =CH); 5.97 (s, 1 H, NH); 7.21–7.26 (m, 2 H, 2 aromatic =CH); 7.39–7.53 (m, 3 H, 3 aromatic =CH). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ: 25.68 (2 Me); 50.69 (OMe); 59.41 (qC); 89.22 (=CH); 128.21 (2aromatic =CH); 128.58 (aromatic =CH); 129.72 (2 aromatic =CH); 133.62 (qC); 155.42 (qC); 164.00 (qC); 166.25 (qC). MS (*m*/*e*): 260 (M^+, 91); 245 (57); 229 (26); 213 (100); 201 (58); 186 (59); 176 (38); 158 (39); 144 (47); 77 (49); 59 (4). IR (neat) cm^{-1}: 3211 (m); 3112 (w); 2961 (w); 1739 (s); 1714 (s); 1625 (s); 1352 (m); 1315 (m); 1134 (s); 833 (w); 694 (m). Anal. Calcd. for $C_{14}H_{16}N_2O_3$: C, 64.62; H, 6.15; N, 10.77%. Found: C, 64.28; H, 6.09; N, 10.21%.

3.2.9. *E*-4,5-dihydro-4,4-dimethyl-5-methoxycarbonylmethylene-*N*-(4-methylphenyl)-2-oxazolamine **2d**

Pale yellow solid, m.p. 107–109°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.69 (s, 6 H, 2 Me); 2.29 (s, 3 H, Me); 3.70 (s, 3 H, OMe); 5.61 (s, 1 H, =CH); 6.63 (s, 1 H, NH); 7.09–7.11 and 7.25–7.27 (AA′XX′ system, 4 aromatit = CH). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ: 20.97 (Me); 26.22 (2 Me); 51.36 (OMe); 70.93 (qC); 93.52 (=CH); 119.36 (2 aromatic =CH); 128.87 (2 aromatic =CH); 132.88 (qC); 136.50 (qC); 151.04 (qC); 166.65 (qC); 176.95 (qC). MS (*m*/*e*): 274 (M^+, 24); 259 (100); 158 (17); 132 (21); 91 (34); 69 (48); 59 (12). IR (KBr) cm^{-1}: 3344 (m); 2941 (w); 1706 (s); 1657 (s); 1615 (m); 1539 (s); 1110 (s); 1048 (m); 998 (m); 813 (m). Anal. Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.69; H, 6.57; N, 10.22%. Found: C, 65.44; H, 6.54; N, 10.01%.

3.2.10. *E*-4,4-dimethyl-5-methoxycarbonylmethylene-1(4-methylphenyl)-imidazolidin-2-one **3d**

Pale yellow solid, m.p. 149°C (dec). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.81 (s, 6 H, 2 Me); 2.38 (s, 3 H, Me); 3.59 (s, 3 H, OMe); 4.84 (s, 1 H, =CH); 5.15 (s, 1 H, NH); 7.10–7.12 and 7.27–7.29 (AA'XX' system, 4 aromatic =CH). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ: 21.11 (Me); 25.88 (2 Me); 50.72 (OMe); 59.30 (qC); 89.31 (=CH); 127.95 (2 =CH); 130.44 (2 =CH); 137.27 (qC); 139.07 (qC); 156.06 (qC); 163.88 (qC); 166.34 (qC). MS (*m*/*e*): 274 (M^+, 100); 259 (26); 243 (12); 227 (53); 216 (34); 200 (41); 172 (27); 158 (30); 91 (66); 65 (65)59 (16). IR (KBr) cm^{-1}: 3226 (m); 2926 (w); 1746 (s); 1623 (s); 1515 (m); 1428 (m); 1318 (m); 1132 (s); 826 (w); 717 (w). Anal, Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.69; H, 6.57; N, 10.22%. Found: C, 65.49; H, 6.54; N, 10.14%.

Table 2
Crystal data and structure refinement for 7

Empirical formula	$C_{17}H_{20}N_2O_6$
Formula weight	348.35
Temperature (K)	293(2)
Wavelength (Å)	1.54184
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	
a (Å)	19.274(5)
b (Å)	10.001(3)
c (Å)	8.968(2)
β (°)	101.08(5)
Volume (Å^3)	1696.4(8)
Z	4
Density (calcd., Mg m^{-3})	1.364
Absorption coefficient (mm^{-1})	0.875
F(000)	736
θ range for data collection (°)	5–70
Index ranges	$-23 \le h \le 23$, $0 \le k \le 12$, $0 \le k \le 10$
Measurement method	$\theta/2\theta$ scan
Reflections collected	3420
Independent reflections	3216
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3215/0/232
Goodness of fit on F^2	1.019
Final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0392$, $wR^2 = 0.1076$
R indices (all data)	$R_1 = 0.0514$, $wR^2 = 0.1293$
Largest ΔF peak and hole (e Å^{-3})	0.214 and −0.145

Table 3
Fractional atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters (Å$^2 \times 10^4$) (one third trace of the diagonalized matrix), with s.u.'s in parentheses for **7**

Atom	*x*/*a*	*y*/*b*	*z*/*c*	U_{eq}
O1	6436.3(5)	1502.6(10)	460.2(13)	484(3)
O2	8076.1(6)	−1749.0(11)	1375.0(16)	625(4)
O3	9901.5(7)	−1361.6(17)	2132.2(18)	879(6)
O4	9144.3(7)	−490.3(13)	3459.5(14)	664(5)
O5	5376.3(6)	−1194.5(13)	3092.2(16)	679(5)
O6	4518.2(6)	312.9(12)	2523.1(15)	593(4)
N1	7403.8(7)	1827.4(13)	−629.4(15)	498(4)
N2	7262.1(6)	−84.7(12)	878.7(14)	442(4)
C1	8082.6(8)	1268.1(16)	−913.4(18)	500(5)
C2	8416.3(8)	327.5(15)	357.0(18)	457(5)
C3	7921.8(8)	−629.4(15)	915.1(17)	457(5)
C5	7083.2(7)	1132.8(14)	182.1(16)	421(4)
C6	6173.3(7)	533.0(14)	1302.9(16)	413(4)
C7	6712.9(7)	−588.7(14)	1692.5(17)	419(4)
C8	9097.3(8)	299.4(18)	992.8(21)	552(6)
C9	9424.4(8)	−620.1(18)	2226.7(21)	579(6)
C10	9356(1)	−1470(3)	4650(3)	861(9)
C11	8553.2(9)	2462.2(19)	−1077.0(25)	685(7)
C12	7920(1)	472(2)	−2405(2)	701(7)
C13	5532.4(8)	736.1(15)	1606.2(19)	470(5)
C14	5160.6(8)	−164.3(15)	2478.1(18)	470(5)
C15	4097.5(9)	−490.3(19)	3347.1(23)	648(7)
C16	6429.5(9)	−1933.8(16)	1036.4(22)	576(6)
C17	7015.4(9)	−625.1(19)	3396.4(19)	577(6)

*3.2.11. E-4,5-dihydro-4,4-dimethyl-5-methoxycarbonylmethylene-N-methoxycarbonyl-2-oxazolamine **2′e***

White solid, m.p. 188–191 °C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.78 (s, 6 H, 2 Me); 3.72 (s, 3 H, OMe); 3.74 (s, 3 H, OMe); 5.79 (s, 1 H, =CH); 8.03 (s, 1 H, NH). MS (*m*/*e*): 242 (M^+, 12); 227 (4); 211 (11); 197 (13); 185 (10); 169 (19); 154 (100); 112 (17); 84 (27); 69 (15); 58 (41); 45 (24). IR (KBr) cm^{-1}: 3267 (m); 1755 (s), 1709 (s); 1662 (s); 1578 (s); 1324 (m); 1225 (s); 1190 (m); 1044 (m); 996 (w). Anal. Calc. for $C_{10}H_{14}N_2O_5$: C, 49.59; H, 5.79; N, 11.57%. Found: C, 49.31; H, 5.70; N, 11.44%.

*3.2.12. E-4,4-dimethyl-5-methoxycarbonylmethyleneimidazolidin-2-one **3e***

White solid, m.p. 160–162°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.43 (s, 6 H, 2 Me); 3.71 (s, 3 H, OMe); 4.86 (s, 1 H, =CH); 6.13 (s, 1 H, NH); 9.10 (br, 1 H, NH). ^{13}C-NMR (75.5 Mhz, $CDCl_3$) δ: 28.88 (2 Me); 51.25 (OMe); 59.47 (qC); 84.23 (=CH); 156.57 (qC); 162.55 (qC); 165.83 (qC). MS (*m*/*e*): 184 (M^+, 17); 169 (78); 153 (7); 137 (100); 125 (10); 110 (8). IR (neat) cm^{-1}: 3404(m); 3351 (m); 1749 (s); 1718 (s); 1683 (s); 1647 (S); 1455 (m); 1272 (s); 1197 (s); 1182 (s); 1033 (m); 938 (w). Anal. Calc. for $C_8H_{12}N_2O_3$: C, 52.17; H, 6.52; N, 15.22%. Found: C, 52.12; H, 6.50; N, 15.14%.

*3.2.13. E-2-methoxycarbonylmethylene-2,3,4,7-tetrahydro-3,3,7,7-tetramethyloxazolo[3,2-a]pyrimidine **5***

White solid, m.p. 141–142°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.24 (s, 6 H, 2 Me); 3.67 (s, 3 H, OMe); 4.73 (d, $J = 7.8$ Hz, 1 H, =CH); 5.60 (s, 1 H, =CH); 5.93 (d, $J = 7.8$ Hz, =CH). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ: 23.37 (2 Me); 32.51 (2 Me); 51.16 (OMe); 55.13 (qC); 63.26 (qC); 94.67 (=CH); 111.42 (=CH); 117.32 (=CH); 149.58 (qC); 165.62 (qC); 170.66 (qC). MS (*m*/*e*): 250 (M^+, 2); 235 (41); 219 (3); 203 (9); 175 (7); 111 (100); 93 (21); 59 (4). IR (KBr) cm^{-1}: 2962 (w); 2928 (w); 1725 (s); 1658 (s); 1367 (s); 1265 (m); 1109 (s); 1086 (s); 952 (m); 853 (m). Anal. Calcd. for $C_{13}H_{18}N_2O_3$: C, 62.40; H, 7.20; N, 11.20%. Found: C, 62.29; H, 7.14; N, 11.14%.

*3.2.14. E-2-methoxycarbonylmethylene-6-methoxycarbonyl-2,3,4,7-tetrahydro-3,3,7,7-tetramethyloxazolo[3,2-a]pyrimidine **6***

White solid, m.p. 167–169°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.52 (s, 6 H, 2 Me); 1.74 (s, 6 H, 2 Me); 3.71 (s, 3 H, OMe); 3.72 (s, 3 H, OMe); 5.67 (s, 1H, =CH); 7.13 (s, 1H, =CH). MS (*m*/*e*): 308 (M^+, 1) 293 (57); 261 (9); 233 (8); 169 (100); 137 (37); 93 (52); 59 (16). IR (KBr) cm^{-1}: 2963 (w); 2926 (w); 1727 (s); 1659 (s); 1362 (s); 1264 (m); 1110 (s); 1025 (s); 937 (m); 828 (m). Anal. Calcd. for $C_{15}H_{20}N_2O_5$: C, 58.44; H, 6.49; N, 9.09%. Found: C, 58.12; H, 6.45; N, 8.92%.

*3.2.15. 2,3,4,5,6,7-Hexahydro-2E-6Z-dimethoxycarbonylmethylene-5-oxo-3,3,7,7-tetramethyloxazolo[3,2-a] pyrimidine **7***

White solid, m.p. 191°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.42 (s, 6 H, 2 Me); 1.97 (s, 6 H, 2 Me); 3.71 (s, 3 H, OMe); 3.80 (s, 3 H, OMe); 5.66 (s, 1 H, =CH); 6.25 (s, 1 H, =CH); MS (*m*/*e*): 336 (M^+, absent); 321 (100); 305 (12); 293 (16); 180 (31); 168 (24); 152 (25); 136 (21); 111 (24); 83 (41); 67 (44); 59 (61). IR (KBr) cm^{-1}: 2991 (w); 2902 (w); 1727 (s); 1694 (s); 1347 (s); 1262 (m); 1114 (s); 1013 (w); 826 (w). Anal. Calcd. for $C_{16}H_{20}N_2O_6$: C, 57.14; H, 5.95; N, 8.33%. Found: C, 56.98; H, 5.91; N, 8.19%.

3.3. X-ray crystallography

Suitable crystals for X-ray analysis were obtained by recrystallization from *n*-hexane/ethyl acetate. Automatic peak search and indexing procedures carried out on a Siemens AED diffractometer yielded a monoclinic primitive cell. Inspection of systematic absences and E statistics indicated unambiguously the space group as $P2_1/c$. Pertinent crystal data and basic information about data collection and structure refinement are given in Table 2. During data collection the intensity of one standard reflection was monitored to check crystal decomposition or loss of alignment. No intensity decay was detected. Polarization and Lorentz effects were included in data reduction.

The phase problem was solved by direct methods [13] and the structure was refined by full-matrix least-squares based on F^2 [14] with non-hydrogen atoms allowed for anisotropic vibration. Hydrogens attached to C8 and C13 were located by inspection of ΔF map and refined isotropically. All other hydrogen atoms were introduced in idealized positions and refined riding on their attached atoms. Neutral scattering factors were employed and anomalous dispersion terms were included for non-hydrogen atoms. Relevant atomic coordinates and equivalent isotropic thermal parameters are given in Table 3. Calculations were performed on ENCORE91 computer using programs SIR92 [13], SHELXL93 [14], PARST95 [15] and ZORTEP [16]. The complete list of atomic coordinates, geometric parameters and thermal displacement parameters have been deposited in CIF format as supplementary material.

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