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I^--Catalyzed Reaction of 5-Methoxyoxazoles with Organic Iodides – An Efficient Synthesis of Azalactones

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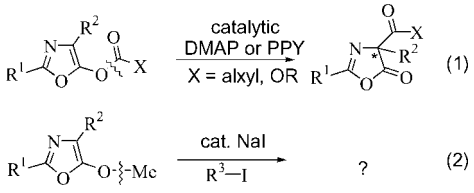
Keywords: Oxazoles / Organic iodides / Azalactones / Cleavage reactions / Heterocycles

An I^--catalyzed methoxy carbon–oxygen bond cleavage in 5-methoxyoxazoles leading to the synthesis of azalactones, precursors of quaternary amino acids, has been developed. A series of 4-substituted azalactones were obtained through the variation of the alkyl iodides and differently substituted 5-methoxyoxazoles. Further study indicated that azalactone **3aa** may be easily converted to benzoyl-protected quaternary amino acid **4aa**.

Introduction

Although the C–O bond cleavage of *O*-acylated oxazoles in the Steglich reaction has been widely investigated [Equation (1), Scheme 1],[1a,1c,2] the methyl–oxygen bond cleavage of 5-methoxyoxazole under the catalysis of mild and easily available NaI has never been reported [Equation (2), Scheme 1]. Recently, we have observed very mild cleavage of the methyl–oxygen bond of 2-methoxyfurans under the catalysis of I^-, which was followed by the formation of a new C–C bond with organic halides at the 5-position of the furans to afford butenolides.[3] It is well known that substitution at the α-carbon of α-amino acid derivatives introduces conformational constraints that can probe the molecular structure of receptor or enhance biological activity by helping to preorganize peptides for binding.[4,5] Therefore, chemists have been interested in the synthesis of α-alkylated α-amino acids and have developed many powerful methods for their preparation. Nitrogen-containing heterocycles such as azalactones and oxazoles are efficiently used as building blocks for the synthesis of α,α-disubstituted amino acids[6,7] and numerous efforts have been devoted to this area, such as α-allylation or α-arylation of azalactones,[8] cycloaddition of oxazolones,[9] and rearrangement of oxazoles.[1] Thus, it is desirable to develop new methods for the efficient synthesis of azalactones. Herein, we wish to report our recent results on the I^--catalyzed methyl–oxygen bond cleavage reaction in 5-methoxyoxazoles to afford 4-disubstituted azalactones.

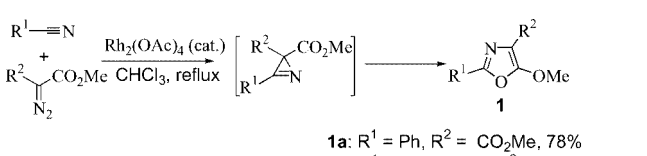


Scheme 1. Two routes for the synthesis of azalactones by C–O bond cleavage.

Results and Discussion

Synthesis of Starting Materials

5-Methoxyoxazoles **1a**–**e** used in this study were easily prepared by the $Rh_2(OAc)_4$-catalyzed one-pot cyclopropanation of the corresponding carbonitriles with α-diazo carboxylic acid esters followed by a rearrangement reaction (Scheme 2).[10]



1a: R^1 = Ph, R^2 = CO_2Me, 78%
1b: R^1 = 1-Naphthyl, R^2 = CO_2Me, 71%
1c: R^1 = Bn, R^2 = CO_2Me, 54%
1d: R^1 = Me, R^2 = CO_2Me, 63%
1e: R^1 = Ph, R^2 = SO_2Ph, 81%

Scheme 2. Synthesis of starting materials **1a**–**e**.

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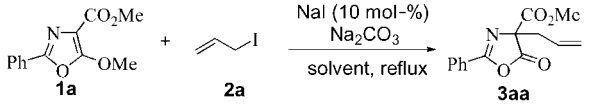
I⁻-catalyzed Methyl–Oxygen Bond Cleavage Reaction in 5-Methoxyoxazoles for the Synthesis of Azalactones

In our first attempt, the reaction of 2-phenyl-4-methoxycarbonyl-5-methoxyoxazole (**1a**) with 2 equiv. of allyl iodide (**2a**) under the catalysis of sodium iodide in THF[8] smoothly afforded product **3aa** in 59% yield (Entry 1, Table 1). It should be noted that C–C bond formation in this case occurred at the 4-position, which was different from the reaction of 2-methoxyfurans with alkyl iodides. On the basis of this interesting result, the solvent effects were further investigated and some typical results are listed in Table 1: it was concluded that acetone was the best solvent for this reaction and Na_2CO_3 was not necessary. The reaction did not occur in the absence of NaI (Entry 9, Table 1).

Table 1. The optimization of the reaction conditions between **1a** and **2a**.[a]

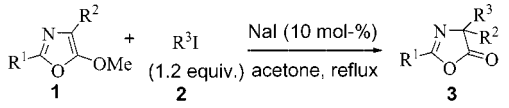


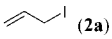
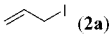
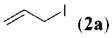
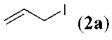
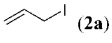
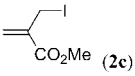
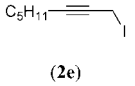
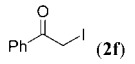
Entry	Na_2CO_3 [equiv.]	**2a** [equiv.]	Solvent	Time [h]	Yield of **3aa** [%]
1	0.5	2.0	THF	8	59
2	0.2	2.0	CH_2Cl_2	52	14
3	0.2	2.0	CH_3CN	7.3	63
4	0.2	2.0	toluene[b]	22.5	trace
5	0.2	2.0	dioxane[b]	7	49
6	0.2	2.0	DMF[b]	3	72
7	0.2	2.0	acetone	3.5	78
8	–	1.2	acetone	5	76
9[c]	–	1.2	acetone	44	NR

[a] The reaction was carried out with **1a** (0.25–0.5 mmol), Na_2CO_3 and **2a** in solvent (1–2 mL) heated at reflux. [b] The reaction was conducted at 80 °C. [c] The reaction was conducted in the absence of NaI.

With the optimized reaction conditions in hand, we further examined the scope of the reaction with a variety of differently substituted compounds **1** and organic iodides (Table 2). This reaction proceeded well with 2-aryl-, 2-benzyl- or 2-alkyl-5-methoxyoxazoles **1**, and provided desired azalactones **3** in satisfactory yields (Entries 1–4, Table 2). The reaction of phenylsulfonyl-substituted **1e** with **2a** appeared to be facile and afforded **3ea** in 91% yield (Entry 5, Table 2). Different organic iodides were also tested in this reaction (Entries 6–10, Table 2). Basically, sp^3 C-centered organic iodides could all participate in the reaction. However, methyl iodide showed a much lower reactivity (Entry 6, Table 2). It should be noted that 4-methylazolactone **3ab** was not formed in any of the other cases, though MeI would be formed in situ after the methyl–oxygen bond cleavage as proven in our previous research.[3] The reason may be that the in situ formed MeI evaporated from the reaction mixture due to its low b.p. (41–43 °C) under the current reaction conditions.

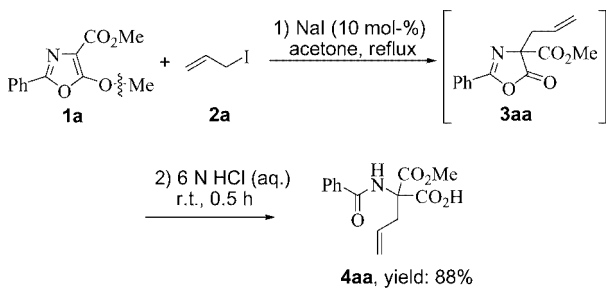
Table 2. The reaction of **1** and **2** for the synthesis of azalactones.[a]



Entry	Substrate **1**		Substrate **2**	Time	Yield of **3**
	R^1	R^2	R^3I	[h]	[%]
1	Ph	CO_2Me (**1a**)	 (**2a**)	5	76 (**3aa**)
2	1-Napthyl	CO_2Me (**1b**)	 (**2a**)	10	80 (**3ba**)
3	Bn	CO_2Me (**1c**)	 (**2a**)	9	62 (**3ca**)
4	Me	CO_2Me (**1d**)	 (**2a**)	10	50 (**3da**)
5	Ph	SO_2Ph (**1e**)	 (**2a**)	6	91 (**3ea**)
6[b]	Ph	CO_2Me (**1a**)	MeI (**2b**)	48	61 (**3ab**)
7[c]	Ph	CO_2Me (**1a**)	 (**2c**)	6	57 (**3ac**)
8	Ph	CO_2Me (**1a**)	ICH_2CO_2Et (**2d**)	16.5	59 (**3ad**)
9	Ph	CO_2Me (**1a**)	 (**2e**)	13.5	68 (**3ae**)
10	Ph	CO_2Me (**1a**)	 (**2f**)	6	65 (**3af**)

[a] The reactions were carried out with **1** (0.25–0.5 mmol) and **2** (1.2 equiv.) in 1–2 mL of acetone heated at reflux. [b] The reaction was carried out in a sealed tube heated at 80 °C. [c] 2 equiv. of **2c** were used in the reaction.

Because azalactones can be regarded as the precursor to amino acids, we developed a tandem allylation/ring-opening reaction of **1a** with **2a** to form benzoyl-protected quaternary amino acid **4aa** (Scheme 3). The structure of **4aa** was further confirmed by its X-ray diffraction analysis (Figure 1).[11]



Scheme 3. Tandem allylation/ring-opening reaction of **1a** with **2a** to form **4aa**.

A plausible catalytic cycle for this reaction is depicted in Scheme 4.[8] The attack of I^- at the methyl group led to the cleavage of the methyl–oxygen bond in compound **1** with the formation of MeI and intermediate **5**, which reacts with organic iodide **2** to afford **3** and regenerate I^-.

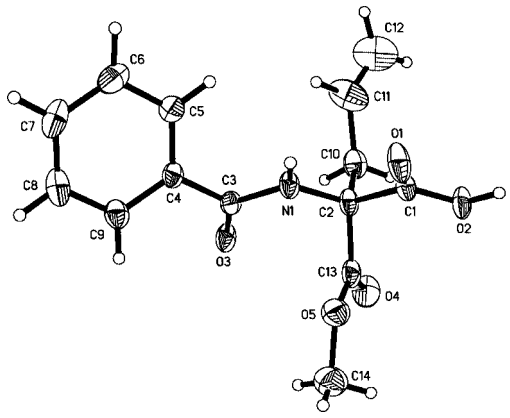
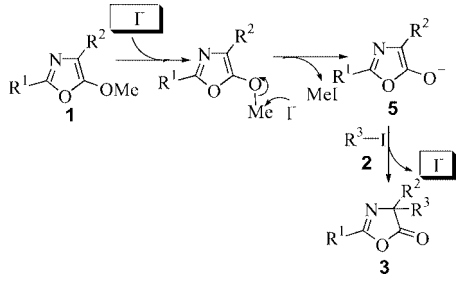


Figure 1. ORTEP representation of compound **4aa**.



Scheme 4. A plausible mechanism for the reaction of **1** and **2**.

Conclusions

In summary, we have developed a catalytic reaction of readily available organic iodides and differently substituted 5-methoxyoxazoles for the synthesis of azalactones. In this reaction, I^--catalyzed methoxy carbon–oxygen bond cleavage in 5-methoxyoxazoles and the new C–C bond formation at the 4-position were observed, which is different from our previous reported reaction of alkyl iodides with 2-methoxyfurans forming butenolides. Furthermore, a tandem reaction of **1a** with **2a** to afford amino acid derivative **4aa** in one-pot was realized. Further investigations are being pursued in our laboratory.

Experimental Section

5-Methoxy-4-(methoxycarbonyl)-2-phenyloxazole (1a).[10,12] **Typical Procedure:** A solution of dimethyl 2-diazomalonate (4.9 g, 31 mmol) in $CHCl_3$ (8 mL) was added with a syringe to a solution of benzonitrile (2.2 g, 21 mmol) and $Rh_2(OAc)_4$ (40 mg, 0.09 mmol) in $CHCl_3$ (2 mL) heated under reflux. After the addition was over, the mixture was stirred for 2 h while heated at reflux. After evaporation, the residue was purified by column chromatography on silica gel (petroleum ether/diethyl ether, 4:1) to afford 3.63 g (78%) of **1a**. Solid, m.p. 91–93 °C (petroleum ether/ethyl acetate) (98–99 °C[10]). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05–7.93 (m, 2 H), 7.50–7.40 (m, 3 H), 4.26 (s, 3 H), 3.91 (s, 3 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 161.9, 161.7, 150.8, 130.4, 128.7, 126.2, 125.8, 107.3, 59.7, 51.8 ppm. MS: *m*/*z* (%) = 233 (13.55) $[M]^+$, 105 (100). IR (KBr): $\tilde{\nu}$ = 1717, 1622, 1587, 1396, 1208, 1106 cm^{-1}.

5-Methoxy-4-(methoxycarbonyl)-2-(1′-naphthyl)oxazole (1b): The reaction of dimethyl 2-diazomalonate (2.20 g, 15 mmol), 1-naphthonitrile (6.63 g, 50 mmol), and $Rh_2(OAc)_4$ (33 mg + 33 mg, 0.15 mmol) in $CHCl_3$ (20 mL) afforded 3.01 g (71%) of **1b**. Solid, m.p. 141–144 °C (petroleum ether/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.19 (d, *J* = 8.7 Hz, 1 H), 8.03 (d, *J* = 7.2 Hz, 1 H), 7.90 (d, *J* = 15.4 Hz, 1 H), 7.87 (d, *J* = 15.4 Hz, 1 H), 7.63 (t, *J* = 7.5 Hz, 1 H), 7.57–7.44 (m, 2 H), 4.26 (s, 3 H), 3.93 (s, 3 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 161.9, 161.6, 150.5, 133.7, 131.2, 129.7, 128.4, 127.7, 127.3, 126.3, 125.9, 124.6, 122.5, 107.2, 59.7, 51.7 ppm. MS: *m*/*z* (%) = 283 (40.83) $[M]^+$, 155 (100). IR (KBr): $\tilde{\nu}$ = 1713, 1614, 1597, 1475, 1400, 1269, 1097 cm^{-1}. $C_{16}H_{13}NO_4$ (283.28): calcd. C 67.84, H 4.63, N 4.94; found C 67.97, H 4.59, N 4.85.

2-Benzyl-5-methoxy-4-(methoxycarbonyl)oxazole (1c): The reaction of dimethyl 2-diazomalonate (2.37 g, 15 mmol), 2-phenylacetonitrile (3.52 g, 30 mmol), and $Rh_2(OAc)_4$ (44 mg, 0.1 mmol) in $CHCl_3$ (10 mL) afforded 1.98 g (54%) of **1c**. Solid, m.p. 71–73 °C (hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 5 H), 4.10 (s, 3 H), 4.02 (s, 2 H), 3.87 (s, 3 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 161.7, 161.5, 151.8, 134.4, 128.5, 128.4, 127.0, 105.6, 59.4, 51.4, 34.4 ppm. MS: *m*/*z* (%) = 247 (26.15) $[M]^+$, 91 (100). IR (KBr): $\tilde{\nu}$ = 1719, 1634, 1591, 1263, 1092 cm^{-1}. $C_{13}H_{13}NO_4$ (247.25): calcd. C 63.15, H 5.30, N 5.67; found C 63.11, H 5.28, N 5.56.

5-Methoxy-4-(methoxycarbonyl)-2-methyloxazole (1d):[9] The reaction of dimethyl 2-diazomalonate (1.58 g, 10 mmol), acetonitrile (0.83 g, 20 mmol), and $Rh_2(OAc)_4$ (22 mg + 22 mg, 0.1 mmol) in $CHCl_3$ (10 mL) afforded 1.09 g (63%) of **1d**. Solid, m.p. 119–122 °C (petroleum ether/ethyl acetate) (119–122 °C[10]). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.13 (s, 3 H), 3.85 (s, 3 H), 2.37 (s, 3 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 161.8, 161.6, 150.5, 105.7, 59.6, 51.6, 13.8 ppm. MS: *m*/*z* (%) = 171 (24.00) $[M]^+$, 43 (100). IR (KBr): $\tilde{\nu}$ = 1713, 1640, 1597, 1470, 1401, 1236, 1093 cm^{-1}.

5-Methoxy-2-phenyl-4-(phenylsulfonyl)oxazole (1e): The reaction of 2-(phenylsulfonyl)-2-diazoacetic acid methyl ester (2.40 g, 10 mmol), benzonitrile (2.58 g, 25 mmol), and $Rh_2(OAc)_4$ (22 mg, 0.05 mmol) in $CHCl_3$ (10 mL) afforded 2.54 g (81%) of **1e**. Solid, m.p. 129–131 °C (hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10–8.00 (m, 2 H), 7.93–7.83 (m, 2 H), 7.65–7.47 (m, 3 H), 7.47–7.35 (m, 3 H), 4.26 (s, 3 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 158.3, 151.1, 141.2, 133.2, 130.7, 129.0, 128.6, 127.3, 125.8, 125.7, 114.7, 60.3 ppm. MS: *m*/*z* (%) = 315 (1.36) $[M]^+$, 105 (100). IR (KBr): $\tilde{\nu}$ = 1622, 1586, 1321, 1158 cm^{-1}. $C_{16}H_{13}NO_4S$ (315.34): calcd. C 60.94, H 4.16, N 4.44; found C 60.76, H 4.11, N 4.43.

Reaction of 5-Methoxyoxazole with Organic Iodides

4-Allyl-4-(methoxycarbonyl)-2-phenyl-4*H*-oxazol-5-one (3aa). Typical Procedure: In a flame-dried argon-flushed flask, a solution of **1a** (117 mg, 0.5 mmol), allyl iodide **2a** (103 mg, 0.6 mmol), and NaI (8 mg, 0.05 mmol) in dry acetone (2 mL) (the solvent was refluxed over anhydrous $MgSO_4$ and distilled prior to use) was stirred for 5 h heated at reflux. After evaporation, the residue was purified by column chromatography (petroleum ether/Et_2O, 5:1) on silica gel to afford (98 mg, 76%) of **3aa**. Liquid. ^{1}H NMR (300 MHz, C_6D_6): δ = 8.00–7.93 (m, 2 H), 7.07–6.90 (m, 3 H), 5.72–5.53 (m, 1 H), 5.12 (d, *J* = 16.8 Hz, 1 H), 4.92 (d, *J* = 11.1 Hz, 1 H), 3.16 (dd, *J* = 13.8, 6.6 Hz, 1 H), 2.99 (dd, *J* = 13.8, 7.8 Hz, 1 H), 3.09 (s, 3 H) ppm. ^{13}C NMR (75.4 MHz, C_6D_6): δ = 174.0, 166.1, 163.6, 133.2, 129.8, 129.0, 128.4, 125.7, 121.5, 77.0, 53.0, 38.3 ppm. MS: *m*/*z* (%) = 259 (7.48) $[M]^+$, 105 (100). IR (neat): $\tilde{\nu}$ = 1827, 1756, 1653,

1245 cm^{-1}. $C_{14}H_{13}NO_4$ (259.26): calcd. C 64.86, H 5.05, N 5.40; found C 65.06, H 5.14, N 5.42.

Compound **3aa** is unstable and will decompose to give compound **4aa** when it is exposed to air for a long time. **4aa**: Solid, m.p. 115–118 °C (petroleum ether/ethyl acetate). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, J = 7.5 Hz, 2 H), 7.80–7.60 (br. s, 1 H), 7.57 (t, J = 7.5 Hz, 1 H), 7.50–7.40 (m, 3 H), 5.78–5.60 (m, 1 H), 5.23–5.15 (m, 2 H), 3.87 (s, 3 H), 3.24 (dd, J = 14.1, 7.5 Hz, 1 H), 3.13 (dd, J = 14.1, 7.5 Hz, 1 H) ppm. ^{13}C NMR (75.4 MHz, CD_3OD): δ = 170.1, 169.8, 168.7, 134.7, 133.3, 132.8, 129.9, 128.3, 120.2, 67.7, 53.8, 38.3 ppm. MS: m/z (%) = 277 (0.72) $[M]^+$, 105 (100). IR (KBr): $\tilde{\nu}$ = 3379, 1762, 1734, 1606, 1575, 1519, 1217 cm^{-1}. $C_{14}H_{15}NO_5$ (277.27): calcd. C 60.64, H 5.45, N 5.05; found C 60.79, H 5.48, N 5.02.

4-Allyl-4-(methoxycarbonyl)-2-(1′-naphthyl)-4*H*-oxazol-5-one (3ba): The reaction of **1b** (142 mg, 0.5 mmol), allyl iodide (**2a**; 101 mg, 0.6 mmol), and NaI (8 mg, 0.05 mmol) in dry acetone (2 mL) afforded 123 mg (80%) of **3ba**. Liquid. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.23 (d, J = 8.7 Hz, 1 H), 8.19 (d, J = 7.5 Hz, 1 H), 8.08 (d, J = 8.1 Hz, 1 H), 7.93 (d, J = 7.8 Hz, 1 H), 7.75–7.50 (m, 3 H), 5.80–5.64 (m, 1 H), 5.28 (d, J = 17.1 Hz, 1 H), 5.24 (d, J = 10.2 Hz, 1 H), 3.84 (s, 3 H), 3.20 (dd, J = 13.8, 6.9 Hz, 1 H), 3.03 (dd, J = 13.8, 7.8 Hz, 1 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 173.4, 165.9, 163.0, 134.1, 133.7, 130.8, 130.6, 129.2, 128.8, 128.4, 126.6, 125.9, 124.6, 121.8, 120.9, 77.1, 53.7, 38.3 ppm. MS: m/z (%) = 309 (14.36) $[M]^+$, 155 (100). IR (neat): $\tilde{\nu}$ = 1822, 1756, 1642, 1255 cm^{-1}. HRMS (MALDI/DHB): calcd. for $C_{18}H_{16}NO_4^+$ $[M + H]^+$ 310.1074; found 310.1066.

4-Allyl-2-benzyl-4-(methoxycarbonyl)-4*H*-oxazol-5-one (3ca): The reaction of **1c** (124 mg, 0.5 mmol), allyl iodide (**2a**; 103 mg, 0.6 mmol), and NaI (8 mg, 0.05 mmol) in dry acetone (2 mL) afforded 85 mg (62%) of **3ca**. Liquid. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 5 H), 5.58–5.40 (m, 1 H), 5.15 (d, J = 16.8 Hz, 1 H), 5.10 (d, J = 10.2 Hz, 1 H), 3.83 (s, 2 H), 3.75 (s, 3 H), 2.93 (dd, J = 13.8, 6.9 Hz, 1 H), 2.80 (dd, J = 13.8, 7.5 Hz, 1 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 173.4, 166.2, 165.5, 132.4, 128.9, 128.8, 128.7, 127.6, 121.7, 75.8, 53.5, 37.8, 35.6 ppm. MS: m/z (%) = 273 (9.02) $[M]^+$, 91 (100). IR (neat): $\tilde{\nu}$ = 1829, 1756, 1671, 1263, 1246 cm^{-1}. HRMS (MALDI/DHB): calcd. for $C_{15}H_{16}NO_4^+$ $[M + H]^+$ 274.1074; found 274.1076.

4-Allyl-4-(methoxycarbonyl)-2-methyl-4*H*-oxazol-5-one (3da): The reaction of **1d** (86 mg, 0.5 mmol), allyl iodide (**2a**; 101 mg, 0.6 mmol), and NaI (8 mg, 0.05 mmol) in dry acetone (2 mL) afforded 49 mg (50%) of **3da**. Oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.63–5.48 (m, 1 H), 5.23–5.14 (m, 2 H), 3.76 (s, 3 H), 2.90 (dd, J = 13.8, 6.6 Hz, 1 H), 2.76 (dd, J = 13.8, 7.5 Hz, 1 H), 2.24 (s, 3 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 173.6, 165.6, 164.8, 129.0, 121.7, 75.8, 53.5, 38.0, 15.1 ppm. MS: m/z (%) = 198 (1.10) $[M + 1]^+$, 127 (100). IR (neat): $\tilde{\nu}$ = 1831, 1753, 1679, 1259 cm^{-1}. HRMS (MALDI/DHB): calcd. for $C_9H_{12}NO_4^+$ $[M + H]^+$ 198.0761; found 198.0758.

4-Allyl-2-phenyl-4-(phenylsulfonyl)-4*H*-oxazol-5-one (3ea): The reaction of **1e** (158 mg, 0.5 mmol), allyl iodide (**2a**; 102 mg, 0.6 mmol), and NaI (8 mg, 0.05 mmol) in dry acetone (2 mL) afforded 141 mg (91%) of **3ea**. Solid, m.p. 108–110 °C(petroleum ether/ethyl acetate). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.00–7.87 (m, 4 H), 7.70–7.57 (m, 2 H), 7.57–7.40 (m, 4 H), 5.60–5.40 (m, 1 H), 5.23 (d, J = 16.5 Hz, 1 H), 5.18 (d, J = 9.9 Hz, 1 H), 3.21 (dd, J = 13.2, 8.1 Hz, 1 H), 3.10 (dd, J = 13.2, 6.0 Hz, 1 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 169.9, 165.1, 135.1, 134.0, 133.8, 130.5, 129.0, 128.9, 128.4, 127.7, 124.1, 122.7, 90.7, 34.8 ppm. MS: m/z (%) = 200 (28.15) $[M – SO_2Ph]^+$, 105 (100). IR (KBr): $\tilde{\nu}$ = 1825, 1630, 1328, 1149 cm^{-1}. $C_{18}H_{15}NO_4S$ (341.38): C 63.33, H 4.43, N 4.10; found C 63.42, H 4.42, N 4.05.

4-(Methoxycarbonyl)-4-methyl-2-phenyl-4*H*-oxazol-5-one (3ab): The reaction of **1a** (117 mg, 0.5 mmol), iodomethane (**2b**; 215 mg, 1.5 mmol), and NaI (8 mg, 0.05 mmol) in dry acetone (2 mL) in a sealed tube afforded 71 mg (61%) of **3ab**. Solid, m.p. 82–85 °C (hexane/diethyl ether). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.01 (d, J = 7.2 Hz, 2 H), 7.59 (t, J = 7.5 Hz, 1 H), 7.48 (t, J = 7.8 Hz, 2 H), 3.77 (s, 3 H), 1.76 (s, 3 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 174.9, 166.3, 163.1, 133.3, 128.8, 128.2, 125.1, 72.6, 53.6, 20.5 ppm. MS: m/z (%) = 233 (9.71) $[M]^+$, 105 (100). IR (KBr): $\tilde{\nu}$ = 1833, 1758, 1646, 1257 cm^{-1}. $C_{12}H_{11}NO_4$ (233.22): C 61.80, H 4.75, N 6.01; found C 61.83, H 4.85, N 5.90.

4-(Methoxycarbonyl)-4-(2′-methoxycarbonyl-2′-propenyl)-2-phenyl-4*H*-oxa-zol-5-one (3ac): The reaction of **1a** (117 mg, 0.5 mmol), 2-methoxycarbonyl allyl iodide (**2c**; 224 mg, 1.0 mmol), and NaI (8 mg, 0.05 mmol) in dry acetone (2 mL) afforded 87 mg (57%) of **3ac**. Oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.97 (d, J = 7.5 Hz, 2 H), 7.59 (t, J = 7.5 Hz, 1 H), 7.48 (t, J = 7.5 Hz, 2 H), 6.23 (s, 1 H), 5.76 (s, 1 H), 3.78 (s, 3 H), 3.64 (s, 3 H), 3.52 (d, J = 14.0 Hz, 1 H), 3.20 (d, J = 14.0 Hz, 1 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 173.5, 166.7, 165.6, 163.4, 133.6, 133.3, 130.0, 128.7, 128.1, 124.8, 76.0, 53.7, 51.9, 35.5 ppm. MS: m/z (%) = 317 (2.25) $[M]^+$, 105 (100). IR (KBr): $\tilde{\nu}$ = 1826, 1755, 1726, 1650, 1243 cm^{-1}. HRMS (MALDI/DHB): calcd. for $C_{16}H_{16}NO_6^+$ $[M + H]^+$ 318.0972; found 318.0973.

4-(Ethoxycarbonylmethyl)-4-(methoxycarbonyl)-2-phenyl-4*H*-oxazol-5-one (3ad): The reaction of **1a** (117 mg, 0.5 mmol), ethyl 2-iodoacetate (**2d**; 123 mg, 0.6 mmol), and NaI (8 mg, 0.05 mmol) in dry acetone (2 mL) afforded 90 mg (59%) of **3ad**. Liquid. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.87 (m, 2 H), 7.52–7.43 (m, 1 H), 7.37 (t, J = 7.5 Hz, 2 H), 4.02–3.87 (m, 2 H), 3.67 (s, 3 H), 3.29 (s, 2 H), 1.04 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 173.8, 168.4, 165.3, 165.1, 133.4, 128.8, 128.4, 125.1, 73.5, 61.4, 53.9, 38.1, 13.8 ppm. MS: m/z (%) = 305 (0.56) $[M]^+$, 105 (100). IR (KBr): $\tilde{\nu}$ = 1830, 1754, 1736, 1649, 1222 cm^{-1}. HRMS (MALDI/DHB): calcd. for $C_{15}H_{16}NO_6^+$ $[M + H]^+$ 306.0972; found 306.0969.

4-(Methoxycarbonyl)-4-(2′-octynyl)-2-phenyl-4*H*-oxazol-5-one (3ae): The reaction of **1a** (117 mg, 0.5 mmol), 1-iodooct-2-yne (**2e**; 142 mg, 0.6 mmol), and NaI (8 mg, 0.05 mmol) in dry acetone (2 mL) afforded 111 mg (68%) of **3ae**. Liquid. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, J = 7.5 Hz, 2 H), 7.63 (t, J = 7.5 Hz, 1 H), 7.52 (t, J = 7.5 Hz, 2 H), 3.80 (s, 3 H), 3.15 (t, J = 2.1 Hz, 2 H), 2.02–1.95 (m, 2 H), 1.30–1.17 (m, 2 H), 1–17–1.00 (m, 4 H), 0.72 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 173.4, 165.4, 164.0, 133.4, 128.8, 128.3, 125.0, 85.0, 76.1, 71.6, 53.8, 30.6, 28.1, 25.3, 22.0, 18.4, 13.8 ppm. MS: m/z (%) = 327 (0.56) $[M]^+$, 105 (100). IR (neat): $\tilde{\nu}$ = 1828, 1757, 1651, 1259 cm^{-1}. HRMS (MALDI/DHB): calcd. for $C_{19}H_{22}NO_4^+$ $[M + H]^+$ 328.1543; found 328.1543.

4-(Benzoylmethyl)-4-(methoxycarbonyl)-2-phenyl-4*H*-oxazol-5-one (3af): The reaction of **1a** (117 mg, 0.5 mmol), 2-iodo-1-phenylethanone (**2f**; 150 mg, 0.6 mmol), and NaI (8 mg, 0.05 mmol) in dry acetone (2 mL) afforded 110 mg (65%) of **3af** (eluent: petroleum ether/diethyl ether/methanol, 10:1:0.15). Solid, m.p. 178–181 °C (acetone). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.01 (d, J = 7.5 Hz, 2 H), 7.88 (d, J = 7.5 Hz, 2 H), 7.60–7.50 (m, 2 H), 7.50–7.33 (m, 4 H), 4.25 (d, J = 18.3 Hz, 1 H), 3.93 (d, J = 18.3 Hz, 1 H), 3.77 (s, 3 H) ppm. ^{13}C NMR (75.4 MHz, CD_3Cl_3): δ = 194.6, 174.3, 165.9, 165.3, 135.2, 134.0, 133.2, 128.74, 128.71, 128.4, 128.2, 125.4, 73.3, 54.0, 42.9 ppm. MS: m/z (%) = 337 (0.29) $[M]^+$, 309 (12.04) $[M – CO]^+$, 105 (100). IR (KBr): $\tilde{\nu}$ = 1824, 1755, 1683, 1647, 1240 cm^{-1}.

$C_{19}H_{15}NO_5$ (337.33): calcd. C 67.65, H 4.48, N 4.15; found C 67.52, H 4.56, N 3.98.

Procedure for the Synthesis of 2-(Benzamido)-2-(methoxycarbonyl)-pent-4-enoic Acid (4aa): In a flame-dried argon-flushed 50 mL flask, a solution of **1a** (1.68 g, 5 mmol), **2a** (1.01 g, 6 mmol), and NaI (76 mg, 0.5 mmol) in dry acetone (10 mL) was stirred for 8 h heated at reflux. After the starting material was completely consumed on the basis of the monitoring with TLC, aqueous solution of HCl (6 N, 10 mL) was added in the reaction. The resulting solution was stirred at room temp. for 0.5 h as monitored by TLC, extracted by CH_2Cl_2, and dried with anhydrous $MgSO_4$. After evaporation, the residue was purified by column chromatography (CH_2Cl_2/MeOH, 15:1) on silica gel to afford the product, which was further purified by recrystallization to afford 1.23 g (88%) of **4aa**.

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[11] X-ray data for compound **4aa**: $C_{14}H_{15}NO_5$, *Fw* = 277.27, Monoclinic, Space group *P*21/*n*, Mo-K_α, final *R* indices [$I > 2\sigma(I)$], *R*1 = 0.0621, *wR*2 = 0.1707, *a* = 10.4507(12) Å, *b* = 11.8193(13) Å, *c* = 11.3355(13) Å, $\alpha = 90°$, $\beta = 92.007(2)°$, $\gamma = 90°$ *V* = 1399.3(3) Å^3, *T* = 293(2) K, *Z* = 4, reflections collected/unique: 8315/3249 (R_{int} = 0.0665), parameters 220. CCDC-610577 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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