

REGIOSELECTIVITY IN FORMAL [3 + 2] CYCLOADDITION REACTION OF 5-ALKOXYOXAZOLES WITH DIETHYL OXOMALONATE AND 2,3-DICHLORO-5,6-DICYANO-1,4-BENZOQUINONE

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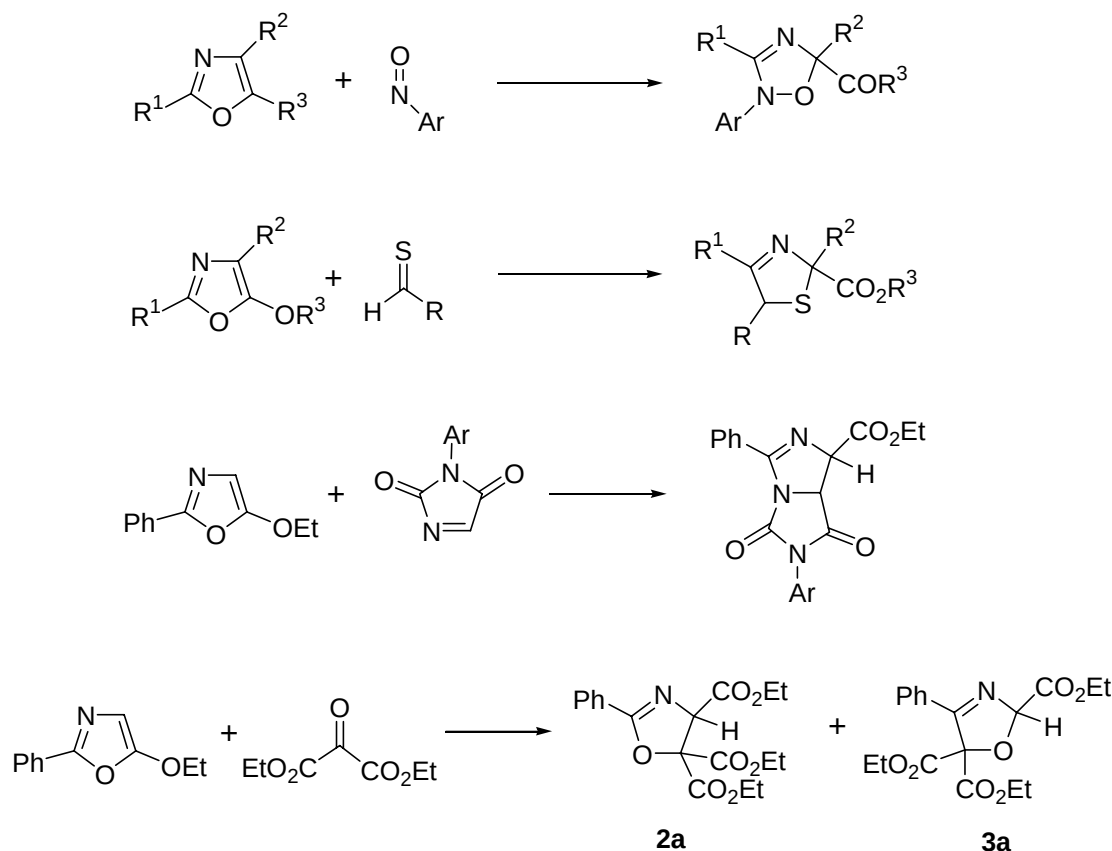
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Abstract- Tin(IV) chloride-catalyzed formal [3 + 2] cycloaddition of 5-alkoxy-2-(*p*-methoxyphenyl)- or 2-phenyloxazoles with diethyl oxomalonate gave 4,5,5-tris(alkoxycarbonyl)-2-oxazolines in high regioselectivity. Under similar conditions, 4-substituted 5-alkoxy-2-methyloxazoles showed a trend to shift the regioselectivity in favor for 3-oxazolines rather than 2-oxazolines. Reaction of 5-alkoxy-4-ethoxycarbonyloxazoles with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone proceeded only under high pressure to give 2-oxazolines exclusively.

Although it is well known that oxazoles undergo Diels-Alder reaction with olefins or acetylenes,¹ in this decade, we and others have found that the use of highly electron deficient dienophiles, such as tetracyanoethylene (TCNE),² 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (PTAD),³ diethyl azodicarboxylate (DEAD),^{3,4} nitrosobenzene,⁵ thioaldehydes,⁶ 1,5-dihydro-2*H*-imidazole-2,5-dione,⁴ diethyl oxomalonate (DEOM),^{4,7} and aldehydes⁸ gave no Diels-Alder adducts but formal [3 + 2] cycloadducts of the ring-opened oxazoles. In the reaction of unsymmetrical dienophiles such as nitrosobenzene, *para*-substituted nitrosobenzenes, thioaldehydes, and 1,5-dihydro-2*H*-imidazole-2,5-dione⁴ under thermal conditions, the formal [3 + 2] cycloadducts were obtained regioselectively probably depending on electronic character of dienophiles (Scheme 1). However, the reaction of oxazoles with DEOM under thermal conditions showed only poor regioselectivity. For example, 5-ethoxy-2-phenyloxazole (**1a**) underwent the cycloaddition under reflux in xylene to give mixture of 4,5,5-tris(ethoxycarbonyl)-2-oxazoline (**2a**) and 2,5,5-tris(ethoxycarbonyl)-3-oxazoline (**3a**) in a 1.2 : 1 ratio (Scheme 1, Table 1, Entry 2).⁴ On the other hand, we have already found Lewis acid-catalyzed reaction of 5-methoxy-2-(*p*-methoxyphenyl)oxazole with aldehydes gave only 2-oxazolines regioselectively.⁸ The primary factors to control the regioselectivity of the formal [3 + 2] cycloaddition with carbonyl compounds have not been understood. In this paper, we give full account of our

investigations of regio-control in the formal [3 + 2] cycloadditions of various 4-unsubstituted and 4-substituted 5-alkoxyoxazoles with DEOM.⁷ We also describe regioselectivity of the reactions with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).

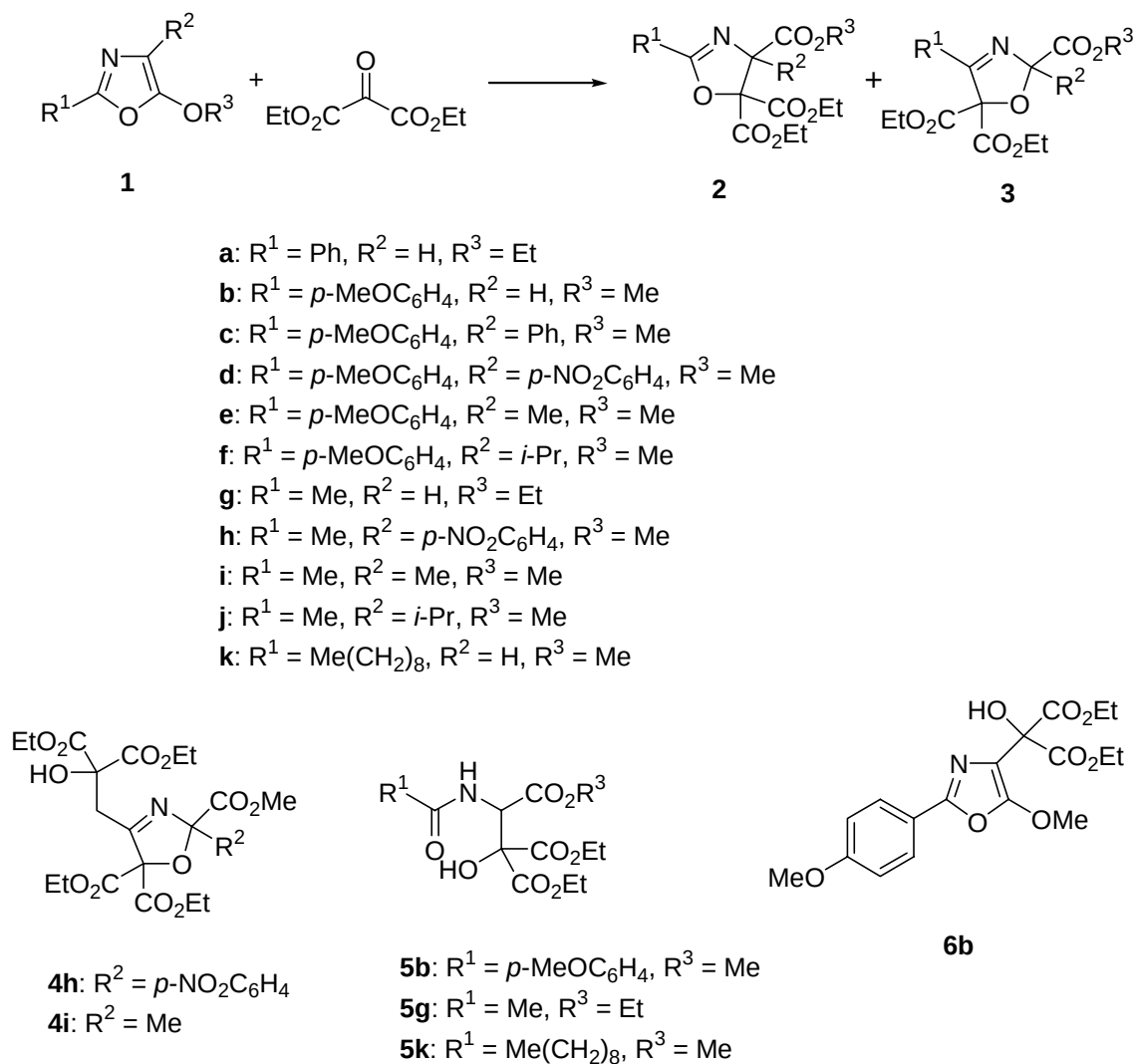


Scheme 1

RESULTS AND DISCUSSION

Reaction of 5-Alkoxy-2-aryloxazoles with DEOM. In contrast to the results of the thermal reaction described above, tin(IV) chloride-catalyzed reaction of oxazole (**1a**) with DEOM in MeCN gave only 2-oxazoline (**2a**) with complete regioselectivity (Table 1, Entry 1). Oxazole (**1b**) also underwent regioselective formal [3 + 2] cycloaddition under similar conditions to give 2-oxazoline (**2b**) exclusively (Entry 3). Regioselectivity of 4-phenyl-, 4-(*p*-nitrophenyl)-, and 4-methyl-substituted 5-methoxy-2-(*p*-methoxyphenyloxazoles (**1c** – **1e**) could be also controlled by using tin(IV) chloride to give only 2-oxazolines (**2c** – **2e**) (Entries 6, 8, and 9). It is interesting that the regioselectivity of the tin(IV) chloride-catalyzed reaction of **1c** was completely opposite from that under thermal conditions (Entries 6 vs 7). It is obvious that Lewis acid is extremely effective in controlling regioselectivity and accelerating rate of the reaction of 5-alkoxy-2-aryloxazoles as shown in Table 1. In the case of oxazole (**1f**), which substituted bulky isopropyl group at 4-position, a small amount of 3-oxazoline (**3f**) was produced (Entry 10). This is probably due to inhibition of the initial attack from the 4-position of oxazole to a carbonyl group by the steric interaction of 4-isopropyl group according to the proposed stepwise pathway.^{2,3,5,8} The regiochemistry of 2-oxazoline (**2f**) and 3-oxazoline (**3f**) was easily

determined by comparison with the chemical shift of ring sp^3 -carbons. Thus, **2f** showed these signals at 88.33 ppm (4-C) and 90.64 ppm (5-C), while **3f** showed those at 93.78 ppm (5-C) and 114.80 ppm (2-C). The observation of the lower field signal (114.80 ppm) obviously indicated the existence of the 3-oxazoline ring which include the carbon substituted by both oxygen and nitrogen. Consequently, the tin(IV) chloride-catalyzed reaction of 4-unsubstituted and 4-substituted 5-alkoxy-2-aryloxazoles (**1a** – **1f**) produced 2-oxazolines with high regioselectively regardless of the electronic factor of 4-substituents. High pressure was not so effective in the reaction of 5-alkoxy-2-aryloxazoles. For example, oxazole (**1b**) reacts under 0.85 GPa to give 2-oxazoline (**2b**) in a low yield along with hydrolysis product (**5b**) and oxazole (**6b**) (Entry 4). However, under similar conditions, the addition of $ZnCl_2$ accelerated the reaction to give 2-oxazoline (**2b**) in 67% yield with hydrolysis product (**5b**) (11% yield) (Entry 5).



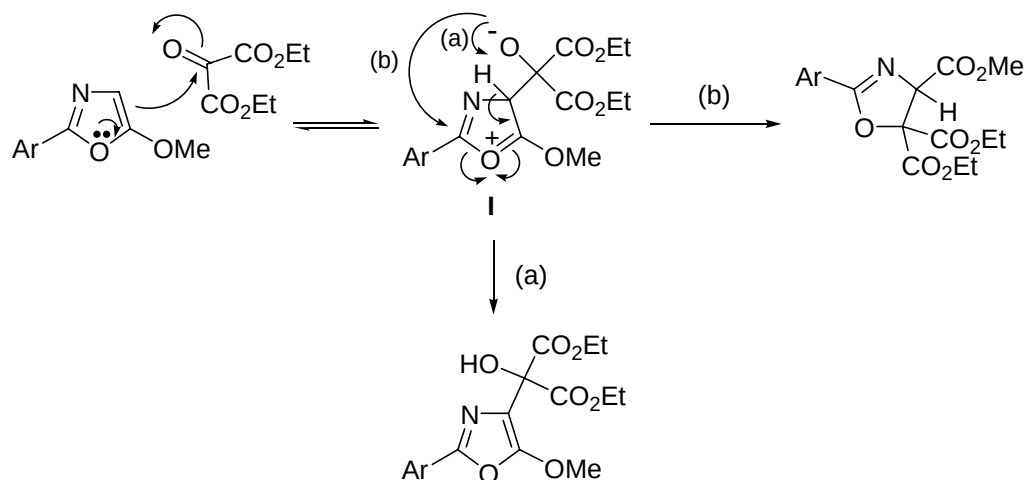
Scheme 2

Table 1. Reactions of 2-Aryloxazoles (**1a** – **1f**) with Diethyl Oxomalonate

Entry	Oxazole (1)	Conditions (Time/h) ^{a)}	Products	Yield/%	2 : 3 or 4	Recovered 1 /%
1	1a	SnCl ₄ (19)	2a	79	100:0	4
2 ^{b)}	1a	Reflux (44)	2a , 3a	96	55:45	–
3	1b	SnCl ₄ (19)	2b	79	100:0	5
4	1b	HP (44)	2b	12 ^{c,d)}	100:0	47
5	1b	HP, ZnCl ₄ (111)	2b	67 ^{c)}	100:0	7
6	1c	SnCl ₄ (20)	2c	95	100:0	–
7	1c	Reflux (69)	2c , 3c	23	1:99 ^{e)}	–
8	1d	SnCl ₄ (72)	2d	60	100:0	–
9	1e	SnCl ₄ (2)	2e	97	100:0	–
10	1f	SnCl ₄ (120)	2f , 3f	40	78:22	–

a) SnCl₄: In the presence of SnCl₄ (1 equiv) at rt in MeCN unless otherwise noted. HP: Under high pressure (0.85 GPa) at 60 °C in MeCN unless otherwise noted. HP, ZnCl₄: Under high pressure (0.85 GPa) in the presence of ZnCl₂ (1 equiv) at 40 °C in MeCN. Reflux: Under reflux in xylene. b) Results of Ref. 4. c) Hydrolysis product (**5**) was obtained (Entry 4: 13%, Entry 5: 11%). d) Product (**6b**) was also obtained in 5% yield. e) A trace amount of 2-oxazoline (**2c**) was detected by ¹H NMR.

The production of 4-substituted oxazole (**6b**) in the absence of ZnCl₂ and the acceleration of reactions by adding ZnCl₂ suggest the proposed stepwise mechanism^{2,3,5,8} involving nucleophilic attack of oxazole to carbonyl compounds (Scheme 3). Before cyclization of the initially formed zwitter ionic intermediate (**I**), protonation followed by aromatization could produce oxazole (**6b**) (path (a)). The Lewis acid not only activates carbonyl compounds but also accelerates the cyclization by coordination to the imino-nirtogen.



Scheme 3

Reaction of 5-Alkoxy-2-methyloxazoles with DEOM. 2-Methyl substituted oxazoles showed different trend in terms of regioselectivity (Table 2, Entries 1 – 10). The tin(IV) chloride-catalyzed reactions of 4-unsubstituted oxazole (**1g**) ($R^2 = H$) and 4-(*p*-nitrophenyl)oxazole (**1h**) ($R^2 = p\text{-NO}_2\text{C}_6\text{H}_4$) showed the same regioselectivity as that of 2-aryloxazoles (**1a** – **1f**) to give 2-oxazolines (**2g**) and (**2h**) along with a trace amount of 3-oxazolines (**3g**) and (**3f**), respectively. In the case of 4-methyloxazole (**1i**), however, the regioselectivity turns out opposite to give 3-oxazoline (**3i**) as a major product (Entry 8). The tin chloride(IV)-catalyzed reaction of 4-isopropyloxazole (**1j**) completely changed the regioselectivity to yield 3-oxazoline (**3j**) as a sole product (Entry 10). This may be attribute to the ease of the initial attack from 2-position of 2-methyloxazoles comparable with 2-aryloxazoles probably due to a steric factor of 2-substituents according to the proposed stepwise mechanism.^{2,3,5,8} Use of bulky organoaluminum catalyst, methylaluminum bis(2,4,6-tribromophenoxide), was also effective in favor for 3-oxazoline preferentially in the reaction of 4-(*p*-nitrophenyl)oxazole (**1h**) (Entry 5).

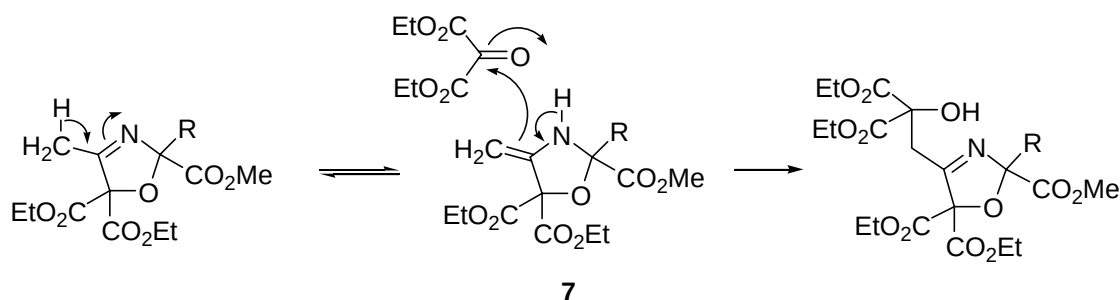
Table 2. Reactions of 2-methyl- or 2-nonyloxazoles (**1g** – **1k**) with Diethyl Oxomalonate

Entry	Oxazole (1)	Conditions (Time/h) ^{a)}	Products	Yield/%	2 : 3 or 4	Recovered 1 /%
1	1g	SnCl ₄ (72)	2g	16 ^{c)}	100:0	–
2	1g	HP, ZnCl ₂ (68.5)	2g, 3g	73 ^{c)}	96:4	–
3 ^{b)}	1g	Reflux (24)	3g	10	0:100 ^{d)}	–
4	1h	SnCl ₄ (33)	2h, 3h	56	94:6	21
5	1h	MATBr (62)	2h, 3h	40	30:70	19
6	1h	HP (120)	3h, 4h	47 ^{e)}	0:100	47
7	1h	HP (120) ^{f)}	4h	45	0:100	trace
8	1i	SnCl ₄ (46)	2i, 3i	89	34:66	–
9	1i	HP (74) ^{g)}	4i	68	0:100	–
10	1j	SnCl ₄ (96)	3j	78	0:100	–
11	1k	HP, ZnCl ₂ (90)	2k	55 ^{c)}	100:0	4

a) SnCl₄: In the presence of SnCl₄ (1 equiv) at rt in MeCN unless otherwise noted. HP: Under high pressure (0.85 GPa) at 40 °C in MeCN unless otherwise noted. HP, ZnCl₂: Under high pressure (0.85 GPa) in the presence of ZnCl₂ (1 equiv) at 40 °C in MeCN. Reflux: Under reflux in xylene. MATBr: In the presence of methylaluminum bis(2,4,6-tribromophenoxide) (AlMe₃ + 2,4,6-tribromophenol (2 equiv)) at rt in CH₂Cl₂. b) Results of Ref. 4. c) Hydrolysis product (**5**) was obtained (Entry 1: 31%, Entry 2: 9%, Entry 11: 23%). d) See Ref. 4.⁹ e) **3h** : **4h** = 21 : 26. f) Two equiv of diethyl oxomalonate was used. g) Three equiv of diethyl oxomalonate was used.

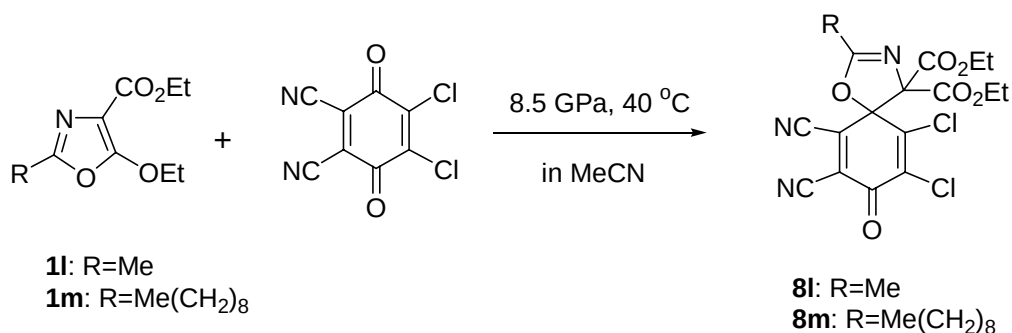
In the reaction of oxazole (**1g**) under high pressure, the addition of ZnCl₂ was also effective in producing 2-oxazoline (**2g**) in good yield, while the reaction did not proceed without ZnCl₂ (Entry 2). In the presence of ZnCl₂ under high pressure, 2-nonyloxazole (**1k**) also underwent cycloaddition with high regioselectivity to give 2-oxazoline (**2k**) along with its hydrolysis product (**5k**) (Entry 11). It is also interesting to note that 3-oxazolines were regioselectively formed under high pressure in the absence of

ZnCl₂ in the reaction of oxazoles (**1h**) and (**1i**) (Entries 6, 7, and 9). In these cases, initially produced 3-oxazolines (**3h**) and (**3i**) reacted further with diethyl oxomalonate to give 1:2 products (**4h**) and (**4i**) as major products. Production of the 1:2 products could be explained by nucleophilic attack of enamine (**7**), which is generated from 2-methyl-3-oxazolines by imine-enamine tautomerism, to dimethyl oxoxmalonate as shown in Scheme 4.



Scheme 4

Reaction of 5-Alkoxyoxazoles with DDQ. Reactions of 5-alkoxyoxazoles (**1a** – **1h**) with DDQ was also investigated. Unfortunately, under thermal, Lewis acid-catalyzed, and high pressure conditions, the reaction of **1a** – **1h** with DDQ did not give [3 + 2] cycloadducts but gave a complex mixture probably due to instability of cycloadducts under the reaction conditions. On the other hand, only at high pressure (8.6 GPa), the reaction of 2-alkyl-4-ethoxycarbonyl-5-methoxyoxazoles (**1l**) and (**1m**) gave desired [3 + 2] cycloadducts (**8l**) and (**8m**) in 59% and 20% yields, respectively (Scheme 5).



Scheme 5

The regiochemistry of the cycloadducts was determined by ¹³C NMR and 2D-INADEQUAT spectra. Thus, ¹³C NMR spectra of **8l** and **8m** showed 4-C at 93.91 and 93.96 ppm, and 5-C at 85.57 and 85.22 ppm, respectively. These values were consistent with those observed from the 2-oxazolines which were obtained by the reactions of 5-alkoxy-2-aryloxazoles with diethyl oxomalonate. Furthermore, 2D-INADEQUAT spectrum of **8l** showed correlation between C-4 (93.91 ppm) and C-5 (85.57 ppm) of a 2-oxazoline ring. These spectra obviously indicate that the products are not 3-oxazolines but 2-oxazoline derivatives. It should be also noted that these products were difficult to purify by silica gel chromatography, probably due to instability of the products. Only florisil could be used for flash

chromatographic purification and, even by this procedure, decomposition of the product seems to proceed slowly.

CONCLUSION

The above-described methodology involving the tin(IV) chloride-catalyzed formal [3 + 2] cycloaddition of 5-alkoxy-2-aryloxazoles with diethyl oxomalonate has the advantage of high yield and high regioselectivity over thermal reactions from the viewpoint of 2-oxazoline syntheses. It was also found that the bulkiness of 4-substituents greatly influences the regioselectivity in the reaction of 5-alkoxy-2-methyloxazoles which is catalyzed by tin(IV) chloride. The reaction of 4-ethoxycarbonyloxazoles (**8l**) and (**8m**) with DDQ proceeds only at high pressure to give 2-oxazolines exclusively.

EXPERIMENTAL

General. Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken with a Perkin-Elmer model 983 spectrophotometer. ¹H NMR spectra were recorded on a Varian EM-390 (90 MHz), a JEOL GX-500 (500 MHz), a JEOL GSX-400 (400 MHz) or JEOL EX-270 instrument (270 MHz), and ¹³C NMR on a JEOL GX-500, a JEOL GSX-400 or JEOL EX-270 spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. MS spectra were measured with a JEOL JMS-DX303 mass spectrometer. Elemental analyses were performed on a Yanaco CHN recorder MT-3. For preparative column chromatography, Wakogel C-300 and Silica gel 60 (Merck) were employed. Medium pressure liquid chromatography was carried out on Yamazen No. 540 pump using a column packed with Silica gel 60 (Merck, size 0.040 ~ 0.063 mm). Solvents were evaporated with Tokyo Rikakikai rotary evaporator at about 40 °C. All reactions except under high pressure were carried out under an argon atmosphere in dried glassware. Oxazoles (**1a** – **1k**) were prepared by the method reported previously.^{5,8}

General procedure for the tin(IV) chloride-catalyzed reaction of oxazole (**1a** – **1j**) with DEOM.

As a typical procedure, the reaction of 5-methoxy-2-(*p*-methoxyphenyl)oxazole (**1b**) is described below. To a solution of oxazole (**1b**) (0.205 g, 1.0 mmol) and DEOM (0.174 g, 1.0 mmol) in acetonitrile (10 mL) was added tin(IV) chloride (0.261 g, 0.12 mL, 1.0 mmol) at rt. After stirring for 19 h, the mixture was quenched with a saturated solution of NaHCO₃. The mixture was extracted with CH₂Cl₂ (30 mL x 3), the separated organic layer was dried over anhydrous MgSO₄, and the solvent was removed under a reduced pressure. The residue was chromatographed over silica gel using hexane-ethyl acetate (17/3 v/v) as an eluent to give 2-oxazoline (**2b**) (0.300 g, 79%).

General procedure for the reaction of oxazole with DEOM at high pressure. As a typical procedure, the reaction of 2,4-dimethyl-5-methoxyoxazoles (**1i**) is described below. A solution of oxazole (**1i**) (0.127 g, 1.0 mmol) and DEOM (0.348 g, 2.0 mmol) in acetonitrile (4.5 mL) was kept in a

Teflon capsule and pressurized hydraulically using Hikari Kouatsu high pressure reaction apparatus at 0.85 GPa and 40 °C for 74 h. The mixture was concentrated under a reduced pressure, and the residue was chromatographed over silica gel using hexane-ethyl acetate (17/3 v/v) as an eluent to give 3-oxazoline (**4i**) (0.322 g, 68%).

4,5,5-Tris(ethoxycarbonyl)-2-phenyl-2-oxazoline (2a): Colorless viscous oil; IR (Neat) 3646, 3473, 3063, 2982, 1749 (C=O), 1653 (C=N), 1603, 1579, 1493, 1450, 1369, 1217, 1098, 908, 861 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ = 1.29 (3H, t, J = 7.1 Hz, Me of OEt), 1.30 (3H, t, J = 7.1 Hz, Me of OEt), 1.32 (3H, t, J = 7.1 Hz Me of OEt), 4.18-4.40 (6H, m, CH₂ of OEt), 5.57 (1H, s, 4-H), 7.41-7.54 (3H, m, Ph-H), 8.04-8.05 (2H, m, Ph-H); ¹³C NMR (CDCl₃, 125.65 MHz) δ = 13.88, 13.93, 14.03 (each q, each Me of OEt), 62.02, 62.78, 63.28 (each t, each CH₂ of OEt), 75.50 (d, 4-C), 88.01 (d, ³ J_{C-H} = 2.3 Hz, 5-C), 126.10 (s, 1-C of Ph), 128.46, 129.00 (each d, *o*-, *m*-C of Ph), 132.36 (d, *p*-C of Ph), 164.70 (s, 2-C), 165.40 (dt, ³ J_{C-H} = 4.1 Hz, ³ J_{C-H} = 3.2 Hz, CO₂Et), 166.12 (dt, ³ J_{C-H} = 6.4 Hz, ³ J_{C-H} = 3.2 Hz, CO₂Et), 168.41 (dt, ² J_{C-H} = 6.9 Hz, ³ J_{C-H} = 3.2 Hz, CO₂Et); Found: M⁺, 363.1317. Calcd for C₁₈H₂₁ N O₇: M, 363.1318.

5,5-Bis(ethoxycarbonyl)-4-methoxycarbonyl-2-(*p*-methoxyphenyl)-2-oxazoline (2b): Pale yellow viscous oil; IR (Neat) 1750 (C=O), 1654 (C=N), 1608, 1512, 1306, 1260, 1220, 1174, 1098, 1071, 1028 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ = 1.29 (3H, t, J = 7.1 Hz, Me of OEt), 1.32 (3H, t, J = 7.1 Hz, Me of OEt), 3.77 (3H, s, OMe), 3.85 (3H, s, OMe), 4.21-4.40 (4H, m, CH₂ of OEt), 5.56 (1H, s, 4-H), 6.92 (2H, dt, J = 8.9 Hz, J = 2.8 Hz, Ar-H), and 7.99 (2H, dt, J = 8.9 Hz, J = 3.0 Hz, Ar-H); ¹³C NMR (CDCl₃, 125.65 MHz) δ = 13.90, 13.93 (each q, each Me of OEt), 52.72, 55.45 (each q, each OMe), 62.83, 63.27 (each t, each CH₂ of OEt), 75.36 (d, 4-C), 87.89 (d, ² J_{C-H} = 2.3 Hz, 5-C), 113.91, 130.86 (each d, *o*-, *m*-C of Ar), 118.37 (t, ² J_{C-H} = 8.3 Hz, 1-C of Ar), 163.05 (s, 4-C of Ar), 164.61 (dt, ³ J_{C-H} = 5.1 Hz, ³ J_{C-H} = 5.1 Hz, 2-C), 165.52 (dt, ³ J_{C-H} = 4.1 Hz, ³ J_{C-H} = 3.7 Hz, CO₂Et), 166.17 (dt, ³ J_{C-H} = 6.4 Hz, ³ J_{C-H} = 3.2 Hz, CO₂Et), 169.04 (dq, ² J_{C-H} = 6.9 Hz, ³ J_{C-H} = 4.1 Hz, CO₂Me); Anal. Calcd for C₁₈H₂₁NO₈: C, 56.99; H, 5.58; N, 3.69. Found: C, 56.56; H, 5.60; N, 3.74. Found: M⁺, 379.1265. Calcd for C₁₈H₂₁NO₈: M, 379.1267.

Diethyl methyl 1-hydroxy-2-(*p*-methoxybenzoyl)amino-1,1,2-ethanetricarboxylate (5b): Pale yellow viscous oil; IR (Neat) 3373 (OH, NH), 2981, 1750 (C=O), 1663 (C=O), 1607, 1528, 1499, 1465, 1443, 1258, 1178, 1147, 1029 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ = 1.21 (3H, t, J = 7.1 Hz, Me of OEt), 1.34 (3H, t, J = 7.1 Hz, Me of OEt), 3.73 (3H, s, OMe), 3.84 (3H, s, OMe), 4.17-4.37 (3H, m, CH₂ of OEt, OH), 4.35 (2H, q, J = 7.1 Hz, CH₂ of OEt), 5.93 (1H, d, J = 10.1 Hz, CHCO₂Me), 6.74 (1H, d, J = 10.1 Hz, NH), 6.92 (2H, dt, J = 8.9 Hz, J = 3.0 Hz, Ar-H), 7.75 (2H, dt, J = 8.9 Hz, J = 3.0 Hz, Ar-H); ¹³C NMR (CDCl₃, 125.65 MHz) δ = 13.92, 13.96 (each q, each Me of OEt), 52.89 (q, OMe), 55.46 (q, OMe), 56.11 (d, CHCO₂Me), 63.31, 63.40 (each t, each CH₂ of OEt), 80.53 (d, ² J_{C-H} = 4.1 Hz, COH), 113.94, 129.21 (each d, *o*-, *m*-C of Ar), 125.88 (t, ³ J_{C-H} = 7.4 Hz, 1-C of Ar), 162.76 (s, 4-C of Ar), 166.74 (s, CONH), 167.78 (dt, ³ J_{C-H} = 1.4 Hz, ³ J_{C-H} = 3.2 Hz, CO₂Et), 168.03 (dt, ³ J_{C-H} = 1.8 Hz, ³ J_{C-H} =

3.7 Hz, CO₂Et), 168.91 (dq, $^2J_{C-H} = 7.4$ Hz, $^3J_{C-H} = 3.2$ Hz, CO₂Me). Satisfactory analytical data was not obtained due to only a trace amount of **5b**.

4-[Bis(ethoxycarbonyl)]hydroxymethyl-5-methoxy-2-(*p*-methoxyphenyl)oxazole (6b): Pale yellow viscous oil; IR (Neat) 1750 (C=O), 1654 (C=N), 1611, 1500, 1304, 1255, 1174, 1103, 1028 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ = 1.33 (6H, t, $J = 7.1$ Hz, Me of OEt), 1.86 (1H, br s, OH), 3.84 (3H, s, OMe), 4.01 (3H, s, OMe), 4.35, 4.36 (each q, each $J = 7.1$ Hz, each CH₂ of OEt), 6.92 (2H, dt, $J = 8.9$ Hz, $J = 2.7$ Hz, Ar-H), 7.83 (2H, dt, $J = 8.9$ Hz, $J = 2.7$ Hz, Ar-H); ¹³C NMR (CDCl₃, 125.65 MHz) δ = 14.02 (q, Me of OEt), 55.38 (q, OMe), 60.95 (q, OMe), 63.00 (t, CH₂ of OEt), 76.20 (s, COH), 114.01 (s, 4-C), 114.13, 127.45 (each d, *o*-, *m*-C of Ar), 120.19 (t, $^3J_{C-H} = 7.8$ Hz, 1-C of Ar), 152.25 (t, $^3J_{C-H} = 4.6$ Hz, 2-C), 155.23 (q, $^3J_{C-H} = 4.1$ Hz, 5-C), 161.14 (s, 4-C of Ar), 168.61 (t, $^3J_{C-H} = 3.2$ Hz, CO₂Et). Satisfactory analytical data was not obtained due to hygroscopic property of **6a**.

5,5-Bis(ethoxycarbonyl)-4-methoxycarbonyl-2-(*p*-methoxyphenyl)-4-phenyl-2-oxazoline (2c): Colorless prism (benzene-hexane); mp 149.7-152.1 °C; IR (KBr) 3430, 1753 (C=O), 1647 (C=N), 1608, 1510, 1303, 1258, 1094, and 1018 cm⁻¹; ¹H NMR (CDCl₃, 270 MHz) δ = 0.78 (2H, t, $J = 7.3$ Hz, Me of OEt), 1.40 (3H, t, $J = 7.3$ Hz, Me of OEt), 3.47-3.68 (2H, m, CH₂ of OEt), 3.71 (3H, s, OMe), 3.87 (3H, s, OMe), 4.41 (2H, q, $J = 7.3$ Hz, CH₂ of OEt), 6.97 (2H, d, $J = 8.9$ Hz, Ar-H), 7.29-7.37 (3H, m, Ph), 7.69-7.72 (2H, m, Ph), 8.10 (2H, d, $J = 8.9$ Hz, Ar-H); ¹³C NMR (CDCl₃, 67.80 MHz) δ = 13.25 (t, $^2J_{C-H} = 3.1$ Hz, Me of OEt), 13.99 (t, $^2J_{C-H} = 3.1$ Hz, Me of OEt), 53.06 (q, OMe), 55.48 (q, OMe), 62.48 (q, $^2J_{C-H} = 4.3$ Hz, CH₂ of OEt), 62.69 (q, $^2J_{C-H} = 4.3$ Hz, CH₂ of Et), 86.88 (t, $^3J_{C-H} = 3.7$ Hz, 4-C), 93.19 (s, 5-C), 113.86, 131.03 (each d, *o*-, *m*-C of Ar), 118.85 (t, $^2J_{C-H} = 7.9$ Hz, 1-C of Ar), 127.60 (d, Ph), 128.42 (t, $^2J_{C-H} = 7.9$ Hz, Ph), 128.69 (d, Ph), 135.68 (s, Ph), 163.07 (s, 4-C of Ar), 165.07 (t, $^3J_{C-H} = 3.1$ Hz, CO₂Et), 165.42 (t, $^3J_{C-H} = 3.7$ Hz, 2-C), 166.00 (t, $^3J_{C-H} = 3.1$ Hz, CO₂Et), 170.22 (q, $^3J_{C-H} = 3.7$ Hz, CO₂Me); Anal. Calcd for C₂₄H₂₅NO₈: C, 63.29; H, 5.53; N, 3.08. Found: C, 63.23; H, 5.52; N, 3.08.

5,5-Bis(ethoxycarbonyl)-2-methoxycarbonyl-4-(*p*-methoxyphenyl)-2-phenyl-3-oxazoline (3c) was obtained as a mixture with **2c**. ¹H NMR (CDCl₃, 270 MHz) δ = 1.05 (3H, t, $J = 7.3$ Hz, Me of OEt), 1.28 (3H, t, $J = 7.3$ Hz, Me of OEt), 3.76 (3H, s, OMe), 3.84 (3H, s, OMe), 4.03 – 4.18 (2H, m, CH₂ of OEt), 4.27 – 4.37 (2H, m, CH₂ of OEt), 6.88 – 6.93 (2H, m, Ar-H), 7.31 – 7.41 (3H, m, Ar-H), 7.72 – 7.76 (2H, m, Ar-H), 8.02 – 8.09 (2H, m, Ar-H).

5,5-Bis(ethoxycarbonyl)-4-methoxycarbonyl-2-(*p*-methoxyphenyl)-4-(*p*-nitrophenyl)-2-oxazoline (2d): Colorless prisms (benzene-hexane); mp 141.2-143.2 °C; IR (KBr) 3443, 1752 (C=O), 1647 (C=N), 1607, 1513 (NO₂), 1351 (NO₂), 1306, 1259, 1219, 1173, 1092 cm⁻¹; ¹H NMR (CDCl₃, 270 MHz) δ = 0.81 (3H, t, $J = 7.3$ Hz, Me of OEt), 1.24 (3H, t, $J = 7.3$ Hz, Me of OEt), 3.58 – 3.72 (2H, m, CH₂ of OEt), 3.70 (3H, s, OMe), 3.88 (3H, s, OMe), 4.44 (2H, q, $J = 7.3$ Hz, CH₂ of OEt), 6.99 (2H, d, $J = 9.2$

Hz, Ar-H), 8.00 (2H, d, $J = 9.2$ Hz, Ar-H), 8.10 (2H, d, $J = 9.2$ Hz, Ar-H), 8.20 (2H, d, $J = 9.2$ Hz, Ar-H); Anal. Calcd for $C_{24}H_{24}N_2O_{10}$: C, 57.60; H, 4.83; N, 5.60. Found: C, 57.76; H, 4.86; N, 5.57.

5,5-Bis(ethoxycarbonyl)-4-methoxycarbonyl-2-(*p*-methoxyphenyl)-4-methyl-2-oxazoline (2e):

Colorless viscous oil; IR (Neat) 2981, 1750 (C=O), 1648 (C=N), 1608, 1577, 1509, 1450, 1422, 1368, 1258, 1172, 1139, 1090, 1027, 844, 792 cm^{-1} ; 1H NMR ($CDCl_3$, 270 MHz) $\delta = 1.29$ (3H, t, $J = 7.3$ Hz, Me of OEt), 1.31 (3H, t, $J = 7.3$ Hz, Me of OEt), 1.68 (3H, s, Me), 3.69 (3H, s, OMe), 3.85 (3H, s, OMe), 4.287 (2H, q, $J = 7.3$ Hz, CH_2 of OEt), 4.293 (2H, q, $J = 7.3$ Hz, CH_2 of OEt), 6.93 (2H, d, $J = 8.9$ Hz, Ar-H), 7.98 (2H, d, $J = 8.9$ Hz, Ar-H); ^{13}C NMR ($CDCl_3$, 67.80 MHz) $\delta = 13.88$ (t, $^2J_{C-H} = 3.1$ Hz, Me of OEt), 13.98 (t, $^2J_{C-H} = 3.1$ Hz, Me of OEt), 20.58 (q, Me), 52.69, 55.43 (each q, each OMe), 62.59, 62.84 (each q, each $^2J_{C-H} = 4.3$ Hz, each CH_2 of CO_2Et), 79.92 (q, $^2J_{C-H} = 4.9$ Hz, 4-C), 91.63 (q, $^3J_{C-H} = 4.3$ Hz, 5-C), 113.81, 130.79 (each d, *o*-, *m*-C of Ar), (d, $^2J_{C-H} = 4.9$ Hz, *p*- $MeOC_6H_4$), 118.72 (t, $^2J_{C-H} = 7.9$ Hz, 1-C of Ar), 162.94 (s, 4-C of Ar), 164.67 (t, $^3J_{C-H} = 4.3$ Hz, 2-C), 165.51, 165.59 (each t, each $^3J_{C-H} = 3.1$ Hz, each CO_2Et), 170.72 (s, CO_2Me); Found: M^+ , 393.1432. Calcd for $C_{19}H_{23}NO_8$: M , 393.1424.

5,5-Bis(ethoxycarbonyl)-4-methoxycarbonyl-2-(*p*-methoxyphenyl)-4-isopropyl-2-oxazoline (2f):

Colorless oil; IR (Neat) 2980, 2840, 1750 (C=O), 1663 (C=N), 1609, 1577, 1511, 1465, 1422, 1389, 1368, 1257, 1172, 1066, 1027, 843, 794, 738, 682 cm^{-1} ; 1H NMR ($CDCl_3$, 270 MHz) $\delta = 0.79$ (3H, d, $J = 6.6$ Hz, Me of *i*-Pr), 1.04 (3H, d, $J = 6.6$ Hz, Me of *i*-Pr), 1.23 (3H, t, $J = 7.3$ Hz, Me of OEt), 1.38 (3H, t, $J = 7.3$ Hz, Me of OEt), 2.68 (1H, sept, $J = 6.6$ Hz, CH of *i*-Pr), 3.78 (3H, s, OMe), 3.85 (3H, s, OMe), 4.19 (2H, qd, $J = 7.3$ Hz, $J = 2.0$ Hz, CH_2 of CO_2Et), 4.40 (2H, q, $J = 7.3$ Hz, CH_2 of OEt), 6.93 (2H, d, $J = 8.9$ Hz, Ar-H), 8.02 (2H, d, $J = 8.9$ Hz, Ar-H); ^{13}C NMR ($CDCl_3$, 67.80 MHz) $\delta = 13.78$ (t, $^2J_{C-H} = 2.4$ Hz, Me of OEt), 13.94 (t, $^2J_{C-H} = 2.4$ Hz, Me of OEt), 16.52 (q, Me of *i*-Pr), 18.73 (q, Me of *i*-Pr), 34.11 (d, CH of *i*-Pr), 52.33 (q, OMe), 55.43 (q, OMe), 62.48 (t, CH_2 of OEt), 62.87 (t, CH_2 of OEt), 88.33 (dq, $^2J_{C-H} = 8.5$ Hz, $^3J_{C-H} = 4.3$ Hz, 4-C), 90.64 (s, 5-C), 113.76, 130.76 (each d, *o*-, *m*-C of Ar), 118.66 (t, $^2J_{C-H} = 7.9$ Hz, 1-C of Ar), 161.95 (t, $^3J_{C-H} = 3.7$ Hz, 2-C), 162.80 (s, 4-C of Ar), 165.34 (t, $^3J_{C-H} = 3.7$ Hz, CO_2Et), 166.54 (t, $^3J_{C-H} = 3.7$ Hz, CO_2Et), 171.66 (s, CO_2Me); Found: M^+ , 421.1760. Calcd for $C_{21}H_{27}NO_8$: M 421.1737.

5,5-Bis(ethoxycarbonyl)-2-methoxycarbonyl-4-(*p*-methoxyphenyl)-2-isopropyl-3-oxazoline (3f):

Colorless oil; IR (Neat) 2977, 2875, 2841, 1749 (C=O), 1605 (C=N), 1568, 1513, 1465, 1422, 1386, 1368, 1262, 1178, 1150, 1107, 1032, 943, 843 cm^{-1} ; 1H NMR ($CDCl_3$, 270 MHz) $\delta = 1.01$ (3H, d, $J = 6.9$ Hz, Me of *i*-Pr), 1.03 (3H, d, $J = 6.9$ Hz, Me of *i*-Pr), 1.23 (3H, t, $J = 7.3$ Hz, Me of OEt), 1.27 (3H, t, $J = 7.3$ Hz, Me of OEt), 2.68 (1H, sept, $J = 6.9$ Hz, CH of *i*-Pr), 3.76 (3H, s, OMe), 3.84 (3H, s, OMe), 4.21-4.33 (4H, m, CH_2 of OEt), 6.90 (2H, d, $J = 8.9$ Hz, Ar-H), 7.99 (2H, d, $J = 8.9$ Hz, Ar-H); ^{13}C NMR ($CDCl_3$, 67.80 MHz) $\delta = 13.79$, 13.85 (each q, each Me of OEt), 16.28, 16.36 (each q, each Me of *i*-Pr), 34.61 (d, CH of *i*-Pr), 52.45, 55.34 (each q, OMe), 62.53 (t, CH_2 of CO_2Et), 62.61 (t, CH_2 of CO_2Et), 93.78 (s, 5-C), 113.48, 131.85 (each d, *o*-, *m*-C of Ar), 114.80 (s, 2-C), 122.28 (t, $^2J_{C-H} = 7.9$ Hz,

1-C of Ar), 162.38 (s, 4-C of Ar), 163.82 (s, 4-C), 165.93 (t, $^3J_{C-H} = 3.7$ Hz, CO₂Et), 166.29 (t, $^3J_{C-H} = 3.7$ Hz, CO₂Et), 169.28 (s, CO₂Me); Found: M⁺, 421.1708. Calcd for C₂₁H₂₇NO₈: M, 421.1737.

5,5,4-Tris(ethoxycarbonyl)-2-methyl-2-oxazoline (2g): Colorless oil; IR (Neat) 3374, 1749 (C=O), 1670 (C=N), 1521, 1371, 1228, 1024 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ = 1.28 (3H, t, $J = 7.1$ Hz, Me of OEt), 1.29 (3H, t, $J = 7.1$ Hz, Me of OEt), 1.32 (3H, t, $J = 7.3$ Hz, Me of OEt), 2.15 (3H, d, $J = 1.6$ Hz, 2-Me), 4.15-4.40 (6H, m, CH₂ of OEt), 5.32 (1H, q, $J = 1.6$ Hz, 4-H); ¹³C NMR (CDCl₃, 125.65 MHz) δ = 13.82, 13.86, 13.91, 14.01 (each q, each Me), 61.98, 62.78, 63.27 (each t, each CH₂ of OEt), 75.11 (d, 4-C), 87.93 (d, $^2J_{C-H} = 2.3$ Hz, 5-C), 165.39 (dt, $^3J_{C-H} = 4.6$ Hz, $^3J_{C-H} = 3.2$ Hz, CO₂Et), 165.90 (dq, $^3J_{C-H} = 6.0$ Hz, $^2J_{C-H} = 7.4$ Hz, 2-C), 166.05 (dt, $^3J_{C-H} = 6.0$ Hz, $^3J_{C-H} = 3.7$ Hz, CO₂Et), 168.45 (s, CO₂Et). Satisfactory analytical data was not obtained due to instability of **2g**.

Triethyl 2-acetylamino-1-hydroxy-1,1,2-ethanetricarboxylate (5g): Colorless viscous oil; IR (Neat) 3367 (OH), 2983 (NH), 2939, 1750 (C=O), 1670 (C=O), 1526, 1465, 1447, 1136, 1216, 1159, 1097, 1024, 860 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ = 1.24 (3H, $J = 7.3$ Hz, Me of OEt), 1.27 (3H, t, $J = 7.1$ Hz, Me of OEt, OH), 1.34 (3H, t, $J = 7.1$ Hz, Me of OEt), 2.03 (3H, s, COMe), 4.15 – 4.38 (7H, m, CH₂ of OEt), 5.70 (1H, d, $J = 10.1$ Hz, CHNH), 6.26 (1H, d, $J = 10.1$ Hz, NH); ¹³C NMR (CDCl₃, 125.65 MHz) δ = 13.90, 13.96 (each q, each Me of OEt), 23.02 (q, COMe), 55.75 (d, CHNH), 62.22, 63.17, 63.27 (each t, each CH₂ of OEt), 80.39 (dd, $^2J_{C-H} = 2.8$ Hz, $^2J_{C-H} = 3.7$ Hz, COH), 167.86 (s, CO₂Et), 167.88 (s, CO₂Et), 168.16 (dt, $^2J_{C-H} = 6.9$ Hz, $^3J_{C-H} = 2.8$ Hz, CO₂Et), 169.97 (s, COMe). Satisfactory analytical data was not obtained due to hygroscopic property of **5g**.

5,5-Bis(ethoxycarbonyl)-4-methoxycarbonyl-2-methyl-4-(p-nitrophenyl)-2-oxazoline (2h): Colorless prism; A sharp melting point was not obtained probably due to lability of **2h**; IR (KBr) 1752 (C=O), 1742 (C=O), 1675 (C=N), 1520 (NO₂), 1353 (NO₂), 1289, 1235, 1220, 1104, 1014, 855 cm⁻¹; ¹H NMR (CDCl₃, 270 MHz) δ = 0.86 (3H, t, $J = 6.9$ Hz, Me of CO₂Et), 1.40 (3H, t, $J = 6.9$ Hz, Me of CO₂Et), 2.30 (3H, s, 2-Me), 3.67 (2H, q, $J = 6.9$ Hz, CH₂ of CO₂Et), 3.71 (3H, s, OMe), 4.42 (2H, q, $J = 6.9$ Hz, CH₂ of CO₂Et), 7.91 (2H, d, $J = 8.9$ Hz, Ar-H), 8.19 (2H, d, $J = 8.9$ Hz, Ar-H); ¹³C NMR (CDCl₃, 67.80 MHz) δ = 13.33, 13.96, 14.30 (each q, each Me), 53.44 (q, OMe), 62.93, 63.23 (each t, each CH₂ of CO₂Et), 86.16 (t, $^3J_{C-H} = 3.1$ Hz, 4-C), 93.13 (s, 5-C), 122.64, 129.97 (each d, *o*-, *m*-C of Ar), 142.46 (t, $^2J_{C-H} = 7.9$ Hz, 4-C of Ar), 147.90 (s, 1-C of Ar), 164.49 (t, $^3J_{C-H} = 3.1$ Hz, CO₂Et), 165.55 (t, $^3J_{C-H} = 3.1$ Hz, CO₂Et), 168.34 (q, $^2J_{C-H} = 7.3$ Hz, 2-C), 169.31 (q, $^3J_{C-H} = 3.7$ Hz, CO₂Me). Hydrolysis product was obtained by recrystallization. Pale yellow prisms (benzen-hexane), mp 118.0 – 120.0 °C, Anal. Calcd for C₁₈H₂₂N₂O₁₀: C, 50.71; H, 5.20; N, 6.57. Found: C, 50.99; H, 5.25; N, 6.49.

5,5-Bis(ethoxycarbonyl)-2-methoxycarbonyl-4-methyl-2-(p-nitrophenyl)-3-oxazoline (3h): Colorless plate crystals (hexane); mp 77-78.5 °C; IR (KBr) 1765 (C=O), 1743 (C=O), 1650 (C=N), 1526 (NO₂), 1437, 1352 (NO₂), 1297, 1222, 1127, 1114, 1064, 1013, 990, 976, 855 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ = 1.21 (3H, t, $J = 7.1$ Hz, Me of OEt), 1.36 (3H, t, $J = 7.1$ Hz, Me of OEt), 2.37 (3H, s, 4-Me),

3.75 (3H, s, OMe), 4.18 – 4.27 (2H, m, CH₂ of OEt), 4.36 (2H, q, $J = 7.1$ Hz, CH₂ of OEt), 7.93 (2H, dt, $J = 8.9$ Hz, $J = 2.5$ Hz, Ar-H), 8.23 (2H, dt, $J = 8.9$ Hz, $J = 2.5$ Hz, Ar-H); ¹³C NMR (CDCl₃, 125.65 MHz) $\delta = 13.88$ (q, Me of OEt), 14.00 (q, Me of OEt), 16.48 (q, 4-Me), 53.45 (q, OMe), 63.01, 63.02 (each t, each CH₂ of OEt), 95.77 (q, $^3J_{C-H} = 2.3$ Hz, 5-C), 111.15 (t, $^3J_{C-H} = 3.4$ Hz, 2-C), 123.28, 127.76 (each d, *o*-, *m*-C of Ar), 143.97 (s, 4-C of Ar), 148.34 (s, 1-C of Ar), 164.49 (t, $^3J_{C-H} = 3.4$ Hz, CO₂Et), 164.54 (t, $^3J_{C-H} = 3.4$ Hz, CO₂Et), 167.58 (q, $^2J_{C-H} = 7.2$ Hz, 4-C), 167.59 (s, CO₂Me); Anal. Calcd for C₁₈H₂₀N₂O₉: C, 52.94; H, 4.94; N, 6.86. Found: C, 52.83; H, 4.93; N, 6.96.

5,5-Bis(ethoxycarbonyl)-4-[2,2-di(ethoxycarbonyl)-2-hydroxyethyl]-2-methoxycarbonyl-2-(*p*-nitrophenyl)-3-oxazoline (4h): Colorless prisms (benzene-hexane); mp 96.5-97.5 °C; IR (KBr) 3500 (OH), 1772 (C=O), 1759 (C=O), 1741 (C=O), 1657 (C=N), 1519 (NO₂), 1444, 1352 (NO₂), 1297, 1232, 1193, 1174, 1124, 1112, 1043, 1025, 1005 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) $\delta = 1.18$ (3H, t, $J = 7.1$ Hz, Me of OEt), 1.19 (3H, t, $J = 6.9$ Hz, Me of OEt), 1.31 (3H, t, $J = 7.1$ Hz, Me of OEt), 1.36 (3H, t, $J = 7.1$ Hz, Me of OEt), 3.47, 3.57 (2H, each d, each $J_{gem} = 17.6$ Hz, CH₂), 3.71 (3H, s, OMe), 4.12-4.26 (5H, m, CH₂ of OEt and OH), 4.31 (2H, q, $J = 7.1$ Hz, CH₂ of OEt), 4.36 (2H, q, $J = 7.1$ Hz, CH₂ of OEt), 7.84 (2H, dt, $J = 8.9$ Hz, $J = 2.3$ Hz, Ar-H), 8.22 (2H, dt, $J = 8.9$ Hz, $J = 2.3$ Hz, Ar-H); ¹³C NMR (CDCl₃, 125.65 MHz) $\delta = 13.81$, 13.86, 13.91, 13.98 (each q, each Me of OEt), 34.63 (t, CH₂), 53.42 (q, OMe), 62.68, 62.98, 63.12, 63.16 (each t, each CH₂ of OEt), 77.71 (s, COH), 96.20 (s, 5-C), 111.43 (t, $^3J_{C-H} = 2.7$ Hz, 2-C), 123.26, 127.79 (each d, *o*-, *m*-C of Ar), 143.72 (s, 4-C of Ar), 148.36 (s, 1-C of Ar), 163.88 (t, $^3J_{C-H} = 3.1$ Hz, CO₂Et), 164.20 (t, $^3J_{C-H} = 3.1$ Hz, CO₂Et), 167.04 (t, $^2J_{C-H} = 6.7$ Hz, 4-C), 167.17 (q, $^3J_{C-H} = 3.8$ Hz, CO₂Me), 168.86 (s, CO₂Et), 169.25 (s, CO₂Et); Anal. Calcd for C₂₅H₃₀N₂O₁₄: C, 51.55; H, 5.19; N, 4.81. Found: C, 51.30; H, 5.13; N, 4.86.

5,5-Bis(ethoxycarbonyl)-2,4-dimethyl-4-methoxycarbonyl-2-oxazoline (2i): Colorless oil; ¹H NMR (CDCl₃, 270 MHz) $\delta = 1.30$ (3H, t, $J = 6.9$ Hz, Me of CO₂Et), 1.32 (3H, t, $J = 6.9$ Hz, Me of CO₂Et), 1.57 (3H, s, Me), 2.16 (3H, s, Me), 3.71 (3H, s, OMe), 4.28 (2H, q, $J = 6.9$ Hz, CH₂ of CO₂Et), 4.30 (2H, q, $J = 6.9$ Hz, CH₂ of CO₂Et); ¹³C NMR (CDCl₃, 67.80 Mz) $\delta = 13.85$, 13.98, 14.07, 20.42 (each Me), 52.73 (OMe), 62.68, 62.91 (each CH₂ of CO₂Et), 165.25, 165.42 (each CO₂Et), 166.18 (2-C), 170.68 (CO₂Me). Satisfactory analytical data was not obtained due to instability of **2i**.

5,5-Bis(ethoxycarbonyl)-2,4-dimethyl-2-methoxycarbonyl-3-oxazoline (3i): Colorless oil; ¹H NMR (CDCl₃, 270 MHz) $\delta = 1.32$ (3H, t, $J = 7.3$ Hz, Me of CO₂Et), 1.33 (3H, t, $J = 7.3$ Hz, Me of CO₂Et), 1.76 (3H, s, Me), 2.32 (3H, s, Me), 3.74 (3H, s, OMe), 4.31 (4H, q, $J = 7.3$ Hz, CH₂ of CO₂Et); ¹³C NMR (CDCl₃, 67.80 MHz) $\delta = 13.94$, 13.98, 16.42, 23.40 (each q, each Me), 52.81 (q, OMe), 62.52, 62.93 (each t, each CH₂ of CO₂Et), 95.20 (q, $^3J_{C-H} = 1.8$ Hz, 5-C), 110.10 (q, $^2J_{C-H} = 4.9$ Hz, 2-C), 165.14 (t, $^3J_{C-H} = 3.1$ Hz, CO₂Et), 165.44 (t, $^3J_{C-H} = 3.1$ Hz, CO₂Et), 166.32 (q, $^2J_{C-H} = 7.3$ Hz, 4-C), 168.95 (s, CO₂Me). Satisfactory analytical data was not obtained due to instability of **3i**.

5,5-Bis(ethoxycarbonyl)-4-[2,2-di(ethoxycarbonyl)-2-hydroxyethyl]-2-methoxycarbonyl-2-methyl-3-oxazoline (4i): Pale yellow viscous oil; IR (Neat) 3485 (OH), 2985, 1743 (C=O), 1662 (C=N), 1447, 1369, 1284, 1221, 1137, 1107, 1049 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ = 1.277 (3H, t, J = 7.1 Hz, Me of OEt), 1.278 (3H, t, J = 7.1 Hz, Me of OEt), 1.316 (3H, t, J = 7.1 Hz, Me of OEt), 1.317 (3H, t, J = 7.3 Hz, Me of OEt), 1.71 (3H, s, 2-Me), 3.39, 3.53 (2H, each d, each J_{gem} = 17.4 Hz, CH_2), 3.70 (3H, s, OMe), 4.22 – 4.36 (8H, m, CH_2 of OEt), 4.44 (1H, br s, OH); ^{13}C NMR (CDCl_3 , 125.65 MHz) δ = 13.88, 13.91, 13.96 (each q, Me of OEt), 23.09 (q, 2-Me), 34.61 (t, CH_2), 52.75 (q, CO_2Me), 62.58, 62.62, 62.77, 63.07 (each t, each CH_2 of OEt), 78.05 (t, $^2J_{\text{C-H}}$ = 4.6 Hz, COH), 95.61 (s, 5-C), 110.38 (q, $^2J_{\text{C-H}}$ = 5.5 Hz, 2-C), 164.81 (t, $^3J_{\text{C-H}}$ = 2.3 Hz, CO_2Et), 164.82 (t, $^3J_{\text{C-H}}$ = 3.2 Hz, CO_2Et), 165.99 (t, $^2J_{\text{C-H}}$ = 7.4 Hz, 4-C), 168.41, 168.92, 169.10 (each s, C=O); Anal. Calcd for $\text{C}_{20}\text{H}_{29}\text{NO}_{12}$: C, 50.52; H, 6.15; N, 2.95. Found: C, 50.36; H, 6.06; N, 2.99.

5,5-Bis(ethoxycarbonyl)-2-methoxycarbonyl-4-methyl-2-iso-propyl-3-oxazoline (3j): Colorless oil; ^1H NMR (CDCl_3 , 270 MHz) δ = 0.94 (3H, d, J = 6.9 Hz, Me of *i*-Pr), 0.95 (3H, d, J = 6.9 Hz, Me of *i*-Pr), 1.31 (3H, t, J = 7.3 Hz, Me of CO_2Et), 1.33 (3H, t, J = 7.3 Hz, Me of CO_2Et), 2.33 (3H, s, Me), 2.57 (1H, sept, J = 6.9 Hz, CH of *i*-Pr), 3.77 (3H, s, OMe), 4.28 (2H, q, J = 7.3 Hz, CH_2 of CO_2Et), 4.32 (2H, q, J = 7.3 Hz, CH_2 of CO_2Et); ^{13}C NMR (CDCl_3 , 67.80 MHz) δ = 13.97, 13.99, 16.11, 16.41 (each q, each Me), 34.01 (d, CH of *i*-Pr), 52.55 (q, OMe), 62.64, 62.67 (each t, each CH_2 of OEt), 94.78 (s, 5-C), 115.08 (dq, $^2J_{\text{C-H}}$ = 9.2 Hz, $^3J_{\text{C-H}}$ = 4.3 Hz, 2-C), 164.99 (t, $^2J_{\text{C-H}}$ = 3.7 Hz, CO_2Et), 165.32 (t, $^2J_{\text{C-H}}$ = 3.7 Hz, CO_2Et), 166.48 (q, $^2J_{\text{C-H}}$ = 7.3 Hz, 4-C), 169.06 (s, CO_2Me). Satisfactory analytical data was not obtained due to instability of **3j**.

5,5-Bis(ethoxycarbonyl)-4-methoxycarbonyl-2-nonyl-2-oxazoline (2k): Colorless oil; IR (Neat) 2926, 2855, 1750 (C=O), 1677 (C=N), 1281, 1222, 1097, 939 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ = 0.88 (3H, t, J = 7.1 Hz, Me of *n*-nonyl), 1.20 – 1.45 (18H, m, Me of OEt, CH_2 of *n*-nonyl), 1.66 – 1.73 (2H, m, CH_2 of *n*-nonyl), 2.43 (2H, dt, J = 1.4 Hz, J = 7.8 Hz, CH_2 of *n*-nonyl), 3.74 (3H, s, OMe), 4.19 – 4.38 (4H, m, CH_2 , OEt), 5.35 (1H, t, J = 1.4 Hz, Me); ^{13}C NMR (CDCl_3) δ = 13.88, 13.92, 14.08 (each q, each Me), 22.67, 25.74, 27.83, 28.96, 29.19, 29.26, 29.42, 31.89 (each t, each CH_2 of *n*-nonyl), 52.66 (q, OMe), 62.81, 63.24 (each t, each CH_2 of OEt), 74.97 (d, 4-C), 87.69 (d, $^2J_{\text{C-H}}$ = 2.3 Hz, 5-C), 165.46 (dt, $^3J_{\text{C-H}}$ = 4.6 Hz, $^3J_{\text{C-H}}$ = 3.2 Hz, CO_2Et), 166.12 (dt, $^3J_{\text{C-H}}$ = 6.4 Hz, $^3J_{\text{C-H}}$ = 3.2 Hz, CO_2Et), 168.94 (s, CO_2Me), 169.31 (s, 2-C). Satisfactory analytical data was obtained as the hydrolyzed product of **2k**. Anal. Calcd for $\text{C}_{20}\text{H}_{35}\text{NO}_5$: C, 57.53; H, 8.45; N, 3.35. Found: C, 57.70; H, 8.29; N, 3.48.

Diethyl methyl 1-hydroxy-2-decanoylamino-1,1,2-ethanetricarboxylate (5k): Colorless viscous oil; IR (Neat) 3365 (OH, NH), 2927, 2852, 1750 (C=O), 1670 (C=O), 1525, 1222, 1171, 1156 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ = 0.88 (3H, t, J = 7.3 Hz, Me of *n*-nonyl), 1.19 – 1.41 (18H, m, Me of OEt, CH_2 of *n*-nonyl), 1.57 – 1.66 (2H, m, CH_2 of *n*-nonyl), 2.17 – 2.27 (2H, m, CH_2 of *n*-nonyl), 3.71 (3H, s, OMe), 4.19 – 4.36 (5H, m, CH_2 of OEt, OH), 5.74 (1H, d, J = 10.1 Hz, CHCO_2Me), 6.14 (1H, d, J = 10.1 Hz, NH); ^{13}C NMR (125.65 MHz, CDCl_3) δ = 13.92, 13.95, 14.07 (each q, each Me), 22.67, 25.63,

29.20, 29.27, 29.34, 29.46, 31.88, 36.56 (each t, each CH₂ of *n*-nonyl), 52.80 (q, OMe), 55.58 (d, CHCO₂Me), 63.26, 63.30 (each t, each CH₂ of OEt), 80.34 (dd, ²J_{C-H} = 3.2 Hz, ²J_{C-H} = 4.1 Hz, COH), 167.78, 167.86 (each s, each CO₂Et), 168.81 (dq, ²J_{C-H} = 6.9 Hz, ²J_{C-H} = 4.1 Hz, CO₂Me), 173.01 (s, NHCO). Anal. Calcd for C₂₀H₃₅NO₅: C, 57.53; H, 8.45; N, 3.35. Found: C, 57.70; H, 8.29; N, 3.48.

General procedure for the reaction of oxazole with DDQ at high pressure. As a typical procedure, the reaction of 4-ethoxycarbonyl-5-methoxy-2-methyloxazoles (**11**) is described below. A solution of oxazole (**11**) (0.199 g, 1.0 mmol) and DDQ (0.227 g, 1.0 mmol) in acetonitrile (4.5 mL) was kept in a Teflon capsule and pressurized hydraulically using Hikari Kouatsu High Pressure reaction apparatus at 0.85 GPa and 30 °C for 4 days. The mixture was concentrated under a reduced pressure, and the residue was purified by flash chromatography over florisil using hexane-ethyl acetate (7/3 v/v) as an eluent to give 2-oxazoline **8l** (0.252 g, 68%).

6,7-Dichloro-9,10-dicyano-2-methyl-1,3-oxazaspiro[4,5]deca-2,6,9-trien-8-one (8l): Colorless needles (benzene-hexane); mp 140-141 °C, IR (KBr) 1765 (C=O), 1737 (C=O), 1698 (C=O, C=N), 1236, 1202 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ = 1.26 (3H, t, *J* = 7.1 Hz, Me of OEt), 1.33 (3H, t, *J* = 7.2 Hz, Me of OEt), 2.34 (3H, s, Me), 4.20 – 4.40 (4H, m, CH₂ of OEt); ¹³C NMR (125.65 MHz, CDCl₃) δ = 13.74, 13.79, 13.85 (each q, each Me), 64.37, 64.93 (each t, each CH₂ of OEt), 85.57 (s, 5-C), 93.91 (s, 4-C), 109.90 (s, CN), 110.96 (s, CN), 122.17 (s, 9-C), 133.37 (s, 7-C), 138.21 (s, 10-C), 147.34 (s, 6-C), 163.51 (t, ³J_{C-H} = 3.2 Hz, CO₂Et), 164.19 (t, ³J_{C-H} = 3.7 Hz, CO₂Et), 165.90 (q, ²J_{C-H} = 7.4 Hz, 2-C), 169.06 (s, C=O). Anal. Calcd for C₁₇H₁₃N₃O₆Cl: C, 47.91; H, 3.07; N, 9.86. Found: C, 48.06; H, 3.16; N, 9.92.

6,7-Dichloro-9,10-dicyano-2-nonyl-1,3-oxazaspiro[4,5]deca-2,6,9-trien-8-one (8m): Pale yellow prisms (benzene-hexane); mp 80.5 – 81.5 °C, IR (KBr) 2937, 2929, 1770 (C=O), 1744 (C=O), 1697 (C=O), 1677 (C=N), 1261, 1236, 1205, 1176 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ = 0.88 (3H, t, *J* = 7.1 Hz, Me of *n*-nonyl), 1.21 – 1.83 (17H, m, CH₂ of *n*-nonyl and Me of OEt), 1.33 (3H, t, *J* = 7.1 Hz, Me of OEt), 2.56 – 2.66 (2H, m, CH₂ of *n*-nonyl), 4.19 – 4.38 (4H, m, CH₂ of OEt); ¹³C NMR (125.65 Hz, CDCl₃) δ = 13.68, 13.72, 14.00 (each q, each Me), 22.59, 25.52, 27.87, 28.94, 29.04, 29.16, 29.30, 31.78 (each t, each CH₂ of OEt), 64.24, 64.82 (each t, each CH₂ of OEt), 85.22 (s, 5-C), 93.96 (s, 4-C), 109.86 (s, CN), 110.92 (s, CN), 122.07 (s, 9-C), 133.24 (s, 7-C), 138.26 (s, 10-C), 147.47 (s, 6-C), 163.55 (t, ³J_{C-H} = 3.2 Hz, CO₂Et), 164.28 (t, ³J_{C-H} = 3.7 Hz, CO₂Et), 168.96 (s, 2-C), 169.02 (s, C=O). Anal. Calcd for C₂₅H₂₉N₃O₆Cl: C, 55.77; H, 5.43; N, 7.80. Found: C, 55.64; H, 5.25; N, 7.87.

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 9. The structure of the adduct assigned to 2-oxazoline by Hassner should be corrected to 3-oxazoline on the basis of its ¹³C NMR spectrum.⁷