in CH_2Cl_2 (20 mL). This solution was extracted with water (15 mL) and dried (Na_2SO_4) and the solvent removed in vacuo to give a brownish residue that was chromatographed (SiO_2, 1% CH_3OH/CH_2Cl_2 to 3% CH_3OH/CH_2Cl_2 gradient elution) to give unreacted **20** (0.15 g) and **21b** [0.45 g (57%, 72% based on recovered starting material)] as a white solid: ^1H NMR ($CDCl_3$) 7.64-7.71 (10 H, m, aromatic), 7.26-7.33 (10 H, m, aromatic), 3.50-3.56 (10 H, m, CH_2O), 3.26-3.37 (20 H, m, CH_2NTs), 2.64-2.76 (6 H, m, CH_2N), 2.40 (15 H, s, $ArCH_3$) ppm; ^{13}C NMR ($CDCl_3$) 143.7, 143.5, 143.3, 137.6, 135.7, 135.5, 129.9, 129.8, 129.7, 127.4, 127.3, 127.1, 70.0, 69.7, 59.3, 56.5, 53.7, 49.7, 49.3, 48.6, 48.0, 21.6, 21.5, 21.4 ppm; IR (KBr) 3449, 3032, 2926, 2872, 1599, 1495, 1456, 1340, 1155, 1089, 995 cm^{-1}. Anal. Calcd for $C_{53}H_{72}N_6O_{13}S_5 \cdot H_2O$: C, 53.97; H, 6.32; N, 7.12. Found: C, 54.00; H, 6.40; N, 7.00.

7-(2-Mercaptoethyl)-4,10,16,19,22-pentakis(*p*-tolylsulfonyl)-1,13-dioxa-4,7,10,16,19,22-hexaazacyclotetracosane (21c). A sealed vial containing a mixture of ethylene sulfide (26.6 mg, 0.44 mmol) and the macrocycle **20** (0.5 g, 0.44 mmol) was heated to 95 °C with stirring for 14 h when TLC indicated the reaction was completed. The product was obtained in the form of a yellow residue that was chromatographed (SiO_2, 100% CH_2Cl_2 to 1% CH_3OH/CH_2Cl_2 gradient elution) to give **21c** [0.35 g (68%)] as a white solid: ^1H NMR ($CDCl_3$) 7.63-7.71 (10 H, m, aromatic), 7.26-7.28 (10 H, m aromatic), 3.53 (8 H, m, CH_2O), 3.32, 3.25, 3.15 (22 H, m, CH_2S, CH_2NTs), 2.66 (6 H, m, CH_2N), 2.36 (15 H, s, $ArCH_3$) ppm; ^{13}C NMR ($CDCl_3$) 143.0, 142.8, 136.0, 135.0, 129.5, 129.3, 129.2, 129.1, 129.0, 128.9, 126.8, 126.7, 126.6, 126.5, 125.7, 69.47, 69.23, 52.89, 49.14, 49.00, 48.72, 48.11, 47.30, 20.93 ppm; IR (KBr) 3497, 3451, 3437, 2924, 2872, 1453, 1402, 1339, 1306, 1159, 1119, 1092, 1019, 990, 932 cm^{-1}. Anal. Calcd for $C_{53}H_{72}N_6O_{12}S_6$: C, 54.06; H, 6.16; N, 7.14. Found: C, 54.00; H, 6.18; N, 7.14.

7-(2-Aminoethyl)-1,13-dioxa-4,7,10,16,19,22-hexaazacyclotetracosane (5). Treatment of 300 mg of the compound **21a** (0.29 mmol) according to the method described in the preparation of **2** afforded 80 mg of the free base **5**: 71%; ^1H NMR (D_2O) 3.64 (8 H, m, CH_2O), 2.70-2.92 (28 H, m, CH_2N) ppm; ^{13}C NMR (D_2O) 71.49, 71.35, 57.05, 55.04, 54.95, 50.29, 50.24, 49.97, 49.66, 48.02 ppm; EIMS *m/e* (rel intens) 389 (21, M^+), 358 (16), 315 (11), 301 (100), 114 (79); HRMS (EI) *m/e* for $C_{18}H_{43}N_7O_2$ requires 389.348, found 389.346.

7-(2-Hydroxyethyl)-1,13-dioxa-4,7,10,16,19,22-hexaazacyclotetracosane (6). Treatment of 400 mg of the compound **21b** (0.34 mmol) according to the method described in the preparation of **2** afforded 85 mg of the free base **6**: 64%; ^1H NMR (D_2O) 3.56 (10 H, s, CH_2O), 2.48-2.72 (26 H, m, CH_2N) ppm; ^{13}C NMR (D_2O) 71.80, 71.75, 71.65 (CH_2O), 55.67, 54.59, 54.34, 50.17, 50.08, 49.85, 47.97 (CH_2N) ppm; EIMS *m/e* (rel intens) 391 (9, $M^+ + 1$), 373 (18), 316 (27), 302 (100), 247 (67), 243 (67) 229 (56); HRMS (CI/NH_3) *m/e* for $C_{18}H_{42}N_6O_3 + 1$ H requires 391.339, found 391.339.

7-(2-Mercaptoethyl)-1,13-dioxa-4,7,10,16,19,22-hexaazacyclotetracosane (7). Treatment of 300 mg of the compound **21c** (0.25 mmol) according to the method described in the preparation of **2** afforded 65 mg of the free base **7**: 65%; ^1H NMR (D_2O) 3.6-3.7 (8 H, m, CH_2O), 2.7-2.8 (28 H, m, CH_2N, CH_2S) ppm; ^{13}C NMR (D_2O) 71.87, 71.72, 55.29, 50.40, 50.29, 50.20, 49.79, 47.41, 46.59, 40.68 ppm; EIMS *m/e* (rel intens) 407 (100, $M^+ + 1$), 373 (55), 347 (28), 329 (28), 290 (28), 229 (50); HRMS (CI/NH_3) *m/e* for $C_{18}H_{42}N_6O_2S + 1$ H requires 407.317, found 407.313.

Acknowledgment. This work was supported by a grant from the National Institute of General Medical Sciences (GM 33922) at the University of Kansas and by the Centre National de la Recherche Scientifique (UA 422). We also acknowledge the technical assistance of Connie McConnell and the personnel of the Mass Spectral Laboratory of the University of Kansas.

Reaction of Dimethyl Acetylenedicarboxylate with 3,4-Disubstituted Isoxazolin-5-ones. A New Synthesis of 1,3-Oxazin-6-ones and 2,3-Dihydro-1,3-oxazin-6-ones

Egle M. Beccalli and Alessandro Marchesini*

Dipartimento di Chimica Organica e Industriale, Università degli Studi di Milano, 20133 Milano, Italy

Maria L. Gelmi

Istituto di Chimica Organica, Facoltà di Farmacia, 20133 Milano, Italy

Tullio Pilati

Centro CNR per lo Studio delle Relazioni tra Struttura e Reattività Chimica, 20133 Milano, Italy

Received July 22, 1986

Reaction of 3,4-disubstituted isoxazolin-5-ones with dimethyl acetylenedicarboxylate affords 2,2',3,3'-tetrahydro[2,2'-bi-1,3-oxazine]-6,6'-diones. A reaction path is proposed.

The reaction of acetylenecarboxylic esters with nitrogen-containing heterocycles[1] as well as the synthesis of heterocycles through nucleophilic addition to acetylenic esters[2] have been widely studied. However the reaction of isoxazolin-5-ones with acetylene carboxylic esters has not been reported.

We have previously reported on the synthesis of 2,5-diaryl-1,3-oxazin-6-ones from 4-arylisoxazolin-5-ones[3] and of 2-(dialkylamino)-1,3-oxazin-6-ones by Vilsmeier-Haack reaction of 3,4-disubstituted isoxazolin-5-ones.[4]

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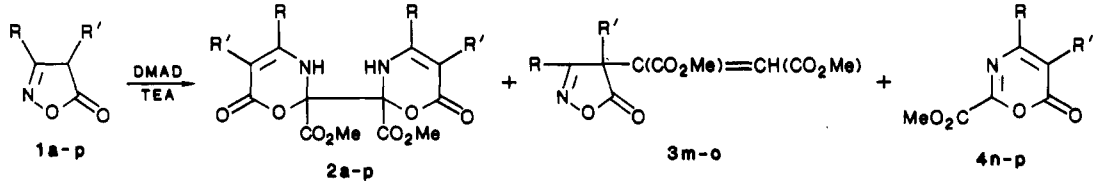
0022-3263/87/1952-1666$01.50/0

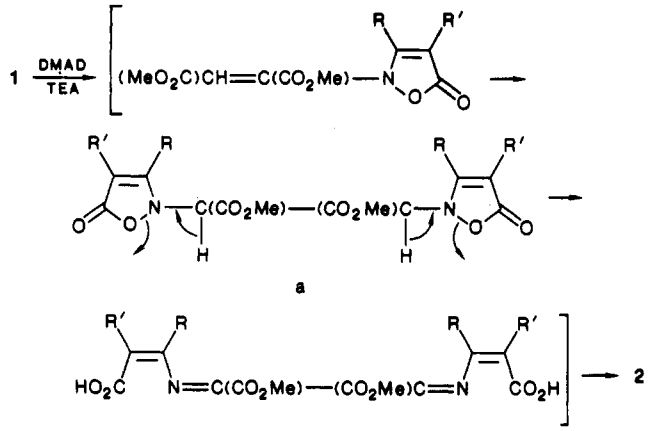
Table I. Products from Isoxazolin-5-ones 1 and DMAD



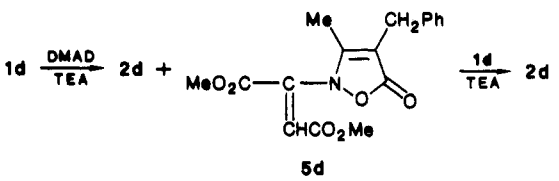
startg materl	R	R′	products (yield, %)	reactn solv	eluant	mp, °C
1a[6]	Me	Et	2a[b] (65)	Et_2O	CH_2Cl_2	186–187
1b[7]	Me	$C_{12}H_{25}$	2b[b] (81)	Et_2O	a	127–128
1c[8]	n-C_3H_7	CH_2Ph	2c[b] (83)	Et_2O–hexane (1:1)	a	186–187
1d[9]	Me	CH_2Ph	2d[c] (90)	CH_2Cl_2	a	227–228
1e[8]	Me	$C_{16}H_{33}$	2e[c] (88)	Et_2O–hexane (1:1)	a	112–114
1f[8]	Me	$(CH_2)_2CO_2Et$	2f[c] (70)	Et_2O	a	169–171
1g[8]	Me	$(CH_2)_2Ph$	2g[c] (60)	CH_2Cl_2	a	185–189
1h[8]	Me	CH_2CO_2Me	2h[c] (90)	CH_2Cl_2	a	198–205
1i[10]	Me	Ph	2i[b] (72)	CH_2Cl_2	a	208–209
1l[11]		$(CH_2)_4$	2l[c] (74)	CH_2Cl_2	CH_2Cl_2–Et_2O (1:1)	204–207[d]
1m[8]	t-C_4H_9	CH_2Ph	2m[b] (16)	Et_2O	a	165–166[d]
			3m (32)		CH_2Cl_2–hexane (1:1)	102–103[e]
1n[12]	Ph	Me	2n[c] (10)	CH_2Cl_2	hexane–Et_2O (4:1)	160–163[e]
			3n (27)			95–97[d]
			4n (25)			97–98[f]
1o[13]	Ph	Et	2o[b] (12)	CH_2Cl_2	hexane–Et_2O (4:1)	174–176[f]
			3o (40)			54–56[f]
			4o (30)			70–71[f]
1p[14]	Ph	CH_2Ph	2p[b] (24)	CH_2Cl_2	hexane–Et_2O (4:1)	194–196[f]
			4p (29)			120[f]

[a] Crystallized from the reaction mixture. [b] Pure isomer. [c] Mixture of isomers. [d] CH_2Cl_2–Et_2O. [e] Et_2O. [f] Et_2O–hexane.

Scheme I



Scheme II



The isoxazolin-5-ones 1 were prepared by reaction between the corresponding β-keto esters and hydroxylamine hydrochloride in ethanol–water solution and in the presence of sodium acetate. The α-butanoylbenzenepropanoic acid ethyl ester and the α-pivaloylbenzenepropanoic acid ethyl ester have been obtained by alkylation with benzyl chloride of the sodium salts of the ethyl butanoylacetate and ethyl pivaloylacetate, repectively.

We have now found that the title compounds 1 react with 0.5 mol of dimethyl acetylenedicarboxylate (DMAD), in the presence of a base to give the (2,3-dihydro-1,3-oxazin-6-ones) 2, often in very good yields (Table I).

We suggest that the reaction proceeds via two successive Michael addition reactions to the DMAD to give the corresponding di-2-isoxazolinylsuccinates a. Double Michael addition reactions of nitrogen heterocycles to DMAD, to give di-2-isoxazolinylsuccinates, have been previously reported.[1] Base-catalyzed ring opening followed by cyclization affords the final products 2 (Scheme I).

The 2,2′-carbomethoxy structures have been assigned to **2a–p** on the basis of analytical and spectroscopic data, as well as chemical behavior. The IR spectra of these compounds exhibit absorption bands in the range 3300–3480 cm^{-1}, characteristic of NH groups, as well as two carbonylic absorption bands in the range 1697–1760 cm^{-1}.

Mass spectra (FAB) and elemental analyses show that compounds **2a–p** arise from 2 mol of isoxazolin-5-one 1 and 1 mol of DMAD. ^1H NMR spectra are consistent with the proposed structures and indicate the presence, in many cases, of two isomers (see Table IV, supplementary material). Structure **2a** has been confirmed by X-ray crystallography.

In the case of **1d**, utilizing a very large excess of DMAD, we were able to isolate, in very low yields, the *N*-alkenyl derivative **5d**, from which by reaction with a second mole of **1d**, compound **2d** was obtained in quantitative yields (Scheme II). The stereochemistry of double bond in **5d** has not been investigated.

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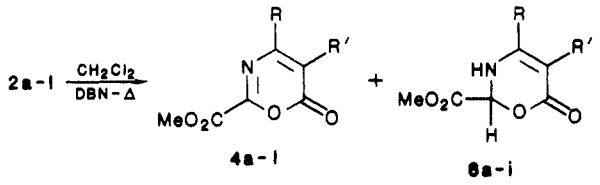
Table II. Cleavage Products from 2



startg materl	products (yield, %)	eluant	mp, °C
2a	**4a** (78)	hexane–Et_2O (2:1)	53–54[a]
	6a (58)		70–71[a]
2b	**4b** (78)	hexane–Et_2O (1:1)	67–69[a]
	6b (66)		50–52[b]
2c	**4c** (60)	CH_2Cl_2–Et_2O (20:1)	44–45[a]
	6c (78)		80[b]
2d	**4d** (65)	CH_2Cl_2–Et_2O (20:1)	65–67[a]
	6d (61)		84–86[c]
2e	**4e** (65)	CH_2Cl_2–Et_2O (20:1)	78–80[d]
	6e (59)		61–62[d]
2f	**4f** (82)	CH_2Cl_2–Et_2O (10:1)	76–77[d]
	6f (97)		74–75[d]
2g	**4g** (73)	CH_2Cl_2–Et_2O (20:1)	86–88[a]
	6g (90)		77–79[a]
2h	**4h** (57)	CH_2Cl_2–Et_2O (10:1)	69–71[a]
	6h (74)		oil
2i	**4i** (59)	CH_2Cl_2–Et_2O (10:1)	94–96[a]
	6i (71)		134–137[e]
2l	**4l** (62)	CH_2Cl_2	120–122[d]

[a] Et_2O–hexane. [b] Hexane. [c] CH_2Cl–hexane. [d] Et_2O. [e] CH_2Cl_2–Et_2O.

With the isoxazolones **1a–l**, derivatives of the type **3**, arising from nucleophilic addition of C_4 of the isoxazolone ring to DMAD, are not isolated. These derivatives have been obtained only when a phenyl or a *tert*-butyl group is present at position 3 of the isoxazolone ring. (Table I). The reported results suggest that the path of the reaction between isoxazolin-5-ones and DMAD depends on the steric hindrance of the substituent at position 3 of the isoxazolone ring.

In the IR spectra of compounds **3**, a carbonyl absorption band at 1790–1800 cm^{-1} is present, in good agreement with the reported IR data of 3,4,4-trisubstituted isoxazolin-5-ones.[5] The derivatives **3m–o** are pure isomers, but the stereochemistry of the double bond has not been investigated. Unlike **5d**, these compounds do not react with a second mole of an isoxazolin-5-one.

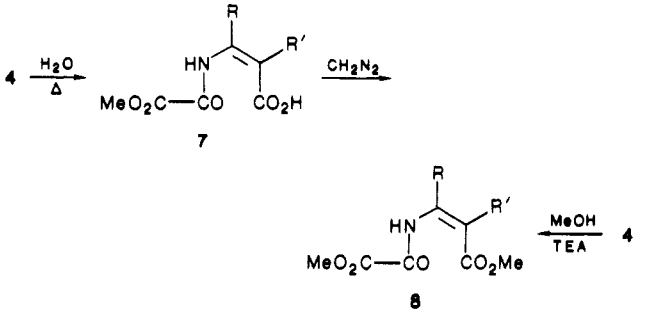
In the case of the 3-phenylisoxazolones **1n–p** the 2-carbomethoxy-1,3-oxazin-6-ones **4n-p** were also obtained (Table I).

Treatment of compounds **2** with a catalytic amount of base (DBN) in dichloromethane leads to an equimolecular amount of 2-carbomethoxy-1,3-oxazin-6-ones **4** and of 2-carbomethoxy-2,3-dihydro-1,3-oxazin-6-ones **6** (Table II).

In the ^1H NMR spectra of the derivatives **6** the N*H* is present as a doublet (J = 4 Hz) at 5.5–6.67 ppm and the C_3H also as a doublet (J = 4 Hz) at 5.43–5.59 ppm. After D_2O exchange the N*H* signals disappear and the C_3H signal shows up as a singlet. The dihydro derivatives **6** gave the oxazinones **4** by active MnO_2 oxidation.

The oxazinones **4** are readily hydrolyzed in H_2O to give the acids **7** (Table III). The corresponding methyl esters **8** were prepared from **7** by reaction with an ethereal solution of CH_2N_2. The same esters **8** were formed from **4** by reaction with methanol and basic catalysis (TEA) (Table III).

Table III. Ring-Opened Products of 1,3-Oxazin-6-ones 4



	7		8	
startg material	products (yield, %)	mp, °C	products	mp, °C
4a	**7a** (94)	143–145[a]	**8a**	64–65[a]
4b	**7b** (73)	95[a]	**8b**	60–61[a]
4c	**7c** (81)	146–147[a]	**8c**	71–72[a]
4d	**7d** (87)	134–135[b]	**8d**	87–88[a]
4e	**7e** (71)	100–101[a]	**8e**	72–73[e]
4f	**7f** (87)	150–151[c]	**8f**	89–90[c]
4g	**7g** (79)	143–144[b] dec	**8g**	79–80[a]
4h	**7h** (56)	173–174[b] dec	**8h**	114–115[a]
4i	**7i** (90)	172–173[c] dec	**8i**	114–115[a]
4l	**7l** (86)	168–170[d] dec	**8l**	97–98[a]
4n	**7n** (85)	146–148[a]	**8n**	90–91[a]
4o	**7o** (82)	137–139[a]	**8o**	88–89[a]
4p	**7p** (71)	155–157[a] dec	**8p**	132–133[b]

[a] Et_2O–hexane. [b] CH_2Cl_2–hexane. [c] Et_2O. [d] CH_2Cl_2–Et_2O. [e] Hexane.

Experimental Section

Melting and boiling points are uncorrected. IR spectra were determined with a Perkin-Elmer 298 instrument, in Nujol mull for solids and liquid film for oils.

^1H NMR spectra were recorded on a Varian EM-390 or on a Bruker WP 80 SY spectrometer with tetramethylsilane as an internal standard. Mass spectra were determined with a VG-70 EQ instrument equipped with HF magnet and standard FAB source operating with xenon at 8 keV. Samples were dissolved in glycerol. Column chromatography was performed on Merck Kieselgel 60, 0.063–0.2 mm. Magnesium sulfate was used as the drying agent. Evaporation was carried out under vacuum in a rotatory evaporator.

Satisfactory combustion analytical data (±0.3%) for C, H, and N were obtained. Only representative spectral data are reported. Spectral data of other products are collected in Table IV (supplementary material).

α-Butanoylbenzenepropanoic Acid Ethyl Ester. This compound was prepared from ethyl butanoylacetate (sodium salt) and benzyl chloride in EtOH (reflux 6 h): 70%; bp 130–135 °C (1 mm); IR 1752, 1727 cm^{-1}; NMR ($CDCl_3$) δ 7.2 (m, 5), 4.17 (q, J = 7 Hz, 2), 3.8 (t, J = 7.5 Hz, 1), 3.2 (d, J = 7.5 Hz, 2), 2.42 (m, 2), 1.59 (m, 2), 1.2 (t, J = 7 Hz, 3), 0.83 (t, J = 7 Hz, 3).

α-Pivaloylbenzenepropanoic Acid Ethyl Ester. This compound was prepared from ethyl pivaloylacetate (sodium salt) and benzyl chloride in EtOH (reflux 8 h): 65%; bp 120–125 °C (0.5 mm); IR 1745, 1700 cm^{-1}; NMR ($CDCl_3$) δ 7.27 (m, 5), 4.18 (m, 3), 3.24 (d, J = 7.5 Hz, 2), 1.27 (t, J = 7 Hz, 3), 1.08 (s, 9).

Isoxazolin-5-ones 1c,e–h,m. These compounds were prepared by the previously reported method[15] from the corresponding β-keto esters in EtOH–H_2O, NH_2OH·HCl, and CH_3CO_2Na.

1c: from α-butanoylbenzenepropanoic acid ethyl ester; 60%; mp 43–44 °C (Et_2O–pentane).

1e: from α-acetylstearic acid methyl ester;[16] 80%, mp 60–61 °C (hexane).

1f: from α-acetylglutaric acid ethyl ester;[17] 75%; mp 45–46 °C (hexane).

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1g: from α-acetylbenzenebutanoic acid ethyl ester;[18] 85%; mp 90–92 °C (CH_2Cl_2–pentane).

1h: from α-acetylsuccinic acid ethyl ester;[19] 50%; mp 78 °C (Et_2O–pentane).

1m: from α-pivaloylbenzenepropanoic acid ethyl ester; reflux 48 h; 12%; 111 °C (Et_2O).

Reaction of Isoxazolin-5-ones 1 and DMAD. General Procedure. The isoxazolin-5-one **1** (10 mmol) was dissolved in the solvent (50 mL), and then DMAD (6 mmol) and triethylamine (0.05 mL) were added. After 24 h at room temperature the reaction mixture was filtered and the filtrate washed with the reaction solvent to give pure compound **2**. In some cases the reaction mixture was evaporated and the residue purified by column chromatography on silica gel (see Table I).

2f; IR 3340, 1750, 1710, 1698 cm^{-1}; NMR (Me_2SO) δ 8.6 (s, 1, exchange D_2O), 8.17 (s, 1, exchange D_2O), 4.07 (q, J = 7 Hz, 4), 3.76 (s, 6), 2.38 (m, 8), 2.12 (s, 6), 1.22 (t, J = 7 Hz, 6); mass spectrum, m/z 541 [$(M + H)^+$]. Anal. Calcd for $C_{24}H_{32}N_2O_{12}$: C, 53.33; H, 5.97; N, 5.18. Found: C, 53.21; H, 5.95; N, 5.14.

3o; IR 1800, 1718 cm^{-1}; NMR ($CDCl_3$) δ 7.75 (m, 2), 7.52 (m, 3), 6.32 (s, 1), 3.84 (s, 3), 3.78 (s, 3), 2.2 (m, 2), 0.9 (m, 3); mass spectrum, m/z 331 (M^+). Anal. Calcd for $C_{17}H_{17}NO_6$: C, 61.63; H, 5.17; N, 4.23. Found: C, 61.41; H, 5.20; N, 4.19.

2-Alkenyl-4-benzyl-3-methylisoxazolin-5-one 5d. The 4-benzyl-3-methylisoxazolin-5-one (**1d**) (950 mg) was dissolved in dichloromethane (30 mL), and then DMAD (3 mL) and triethylamine (0.05 mL) were added. After 24 h at room temperature the solvent was evaporated. Column chromatography on silica gel of the residue [eluant, hexane, CH_2Cl_2, and CH_2Cl_2–Et_2O (10:1)] afforded **5d**: 125 mg; mp 127–128 °C (Et_2O); IR 1742, 1703, 1620, 1590 cm^{-1}; NMR ($CDCl_3$) δ 7.28 (m, 5), 5.98 (s, 1), 3.97 (s, 3), 3.81 (s, 3), 3.66 (s, 2), 1.2 (s, 3). Anal. Calcd for $C_{17}H_{17}NO_6$: C, 61.63; H, 5.17; N, 4.23. Found: C, 61.51; H, 5.18; N, 4.21. **2d** (790 mg) was also afforded.

2-Carbomethoxy-1,3-oxazin-6-ones 4 and 2-Carbomethoxy-2,3-dihydro-1,3-oxazin-6-ones 6 from Derivative 2. The 2,2′,3,3′-tetrahydro[2,2′-bi-1,3-oxazine]-6,6′-dione **2** (1 g) was suspended in dichloromethane (70 mL), and then DBN (0.05 mL) was added. After heating under reflux for 4 h (homogeneous solution), the solvent was evaporated. Silica gel column chromatography of the residue gave pure **4** and **6** (see Table II).

4f: IR 1735, 1715 cm^{-1}; NMR ($CDCl_3$) δ 4.15 (q, J = 7 Hz, 2), 4.07 (s, 3), 2.83 (m, 2), 2.62 (m, 2), 2.5 (s, 3), 1.3 (t, J = 7 Hz, 3); mass spectrum, m/z 269 (M^+). Anal. Calcd for $C_{12}H_{15}NO_6$: C, 53.53; H, 5.62; N, 5.20. Found: C, 53.60; H, 5.59; N, 5.19.

6f: IR 3230, 1745, 1720 cm^{-1}; NMR ($CDCl_3$) δ 5.97 (d, J = 4 Hz, 1, exchangeable in D_2O), 5.46 (d, J = 4 Hz, 1), 4.1 (q, J = 7 Hz, 2), 3.92 (s, 3), 2.58 (m, 2), 2.17 (m, 2), 1.29 (t, J = 7 Hz, 3); mass spectrum, m/z 271 (M^+). Anal. Calcd for $C_{12}H_{17}NO_6$: C, 53.13; H, 6.32; N, 5.16. Found: C, 53.05; H, 6.30; N, 5.12.

Water Ring Opening of Oxazinones 4. The oxazinone **4** (200 mg) was dissolved in dioxane (15 mL), and then water (10 mL) was added. The solution was heated to reflux for 4 h. The solvent was evaporated and water added (15 mL). The mixture was extracted with CH_2Cl_2 (2 × 20 mL) and dried and the solvent evaporated. Crystallization of the residue gave pure acid **7** (see Table III). Esterification of the acid **7** with an ethereal solution of CH_2N_2 gave pure ester **8** in quantitative yields (see Table III).

7f: IR 1712, 1640 cm^{-1}; NMR ($CDCl_3$) δ 12.8 (br s, 1, exchangeable in D_2O), 10.9 (br s, 1, exchangeable in D_2O), 4.2 (q, J = 7 Hz, 2), 4 (s, 3), 2.8 (m, 2), 2.62 (s, 3), 2.6 (m, 2), 1.32 (t, J = 7 Hz, 3); mass spectrum, m/z 287 (M^+). Anal. Calcd for $C_{12}H_{17}NO_7$: C, 50.17; H, 5.97; N, 4.88. Found: C, 50.08; H, 5.95; N, 4.85.

8f: IR 1718, 1710, 1663 cm^{-1}; NMR ($CDCl_3$) δ 13 (br s, 1, exchangeable in D_2O), 4.18 (q, J = 7 Hz, 2), 4 (s, 3), 3.88 (s, 3), 3.58 (s, 3), 2.73 (m, 2), 2.47 (m, 2), 1.3 (t, J = 7 Hz, 3); mass spectrum m/z 301 (M^+). Anal. Calcd for $C_{13}H_{19}NO_7$: C, 51.82; H, 6.36; N, 4.65. Found: C, 51.77; H, 6.34; N, 4.63.

2-Carbomethoxy-1,3-oxazin-6-ones 4 from 2-Carbomethoxy-2,3-dihydro-1,3-oxazin-6-ones 6. The oxazinone **4** (200 mg) was dissolved in CH_2Cl_2 (30 mL), and then active MnO_2 (1.5 g) was added. After being stirred at room temperature for 24 h, the mixture was filtered on Celite 535 and the solvent evaporated. Crystallization of the residue gave pure oxazinone **4**. The oxazinones **4** were obtained in 45–60% yields.

Crystallographic Determination of 2a. Crystals of the compound were obtained from THF. $C_{18}H_{24}N_2O_8$: M_r = 396.41; monoclinic, space group $C2/c$; a = 17.773 (1) Å; b = 11.764 (2) Å; c = 12400 (2) Å; β = 132.75 (1)°; v = 1903.8 (6) Å^3; Z = 4; D_{calcd} = 1.383 g/cm^3; $F(000)$ = 840; Mo Kα' = 0.71073 Å, μ = 1.02 cm^{-1}.

Data collection was performed at room temperature with a crystal of approximate dimensions 0.36 × 0.18 × 0.16mm on a Nonius CAD-4 automated diffractometer. Cell parameters and crystal orientation matrix were obtained from least-squares refinement of the setting angles of 25 reflections with 15° < θ < 19°. Intensity data were collected exploring the $+h,+k,l$ quadrant of the reciprocal space in the range 1.5° < θ < 30° by $\theta/2\theta$ scan technique. Three standard reflection monitored after every 2 h showed an intensity fluctuation of about 2%. 2763 unique reflections were collected, of which 1969 with $I > \sigma(I)$ were considered observed and used in the structure refinement. Data were corrected for Lorentz and polarization effects. The structure was solved by direct methods using the MULTAN program. The positions of all heavy atoms were obtained from the E-map derived from the set of phases with the highest figure of merit. Hydrogen atoms were obtained from a difference Fourier map. The refinement was performed by minimizing $\sum w(F_o-F_c)^2$ with weights $w = 4F_o/(\sigma(F_o^2) + 0.0004F_o^4)$. Heavy atoms were refined with anisotropic thermal parameters. Final discrepancy indices were R = 0.051 and R_w = 0.042. A final difference Fourier map was devoid of feature with electron densities greater than 0.2e/Å^3. The computation were carried out with the Nonius Structure Determination Package (SDP plus) and some inhouse program running on a Gould 32/97 computer.

The final coordinates, anisotropic thermal parameters, and a list of selected bond distances and angles are reported in Tables V, VI, and VII (supplementary material), respectively.

Supplementary Material Available: Tables IV–VII, spectral data for all compounds and crystallographic data for **2a** (5 pages). Ordering information is given on any current masthead page.

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