Notes

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Structural Elucidation of the Reaction Products of Benzoxazole Derivatives with Dimethyl Acetylenedicarboxylate. V[1]

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Benzoxazole and *o*-aminophenol each reacted with dimethyl acetylenedicarboxylate (DMAD) to give the same product, which was previously suggested[2] to be a [1,4]benzoxazine [2,3-*b*]pyran derivative (**2**). An X-ray crystallographic analysis has now shown the structure of this compound to be trimethyl 2,3-dihydro-2-oxo-4*H*-1,4-benzoxazine-$\Delta^{3,\gamma}$-aconitate. A similar treatment of *o*-aminophenols and *β*-aminoalcohols with an excess of DMAD afforded new 1,4-benzoxazines and 1,4-oxazines, respectively.

Keywords——benzoxazole derivative; dimethyl acetylenedicarboxylate; X-ray analysis; *o*-aminophenol; *β*-aminoalcohol; 1,4-benzoxazine; 1,4-oxazine

As a part of our studies on heterocyclic compounds,[3] we reported the reaction of benzoxazole derivatives with dimethyl acetylenedicarboxylate (DMAD) in alcoholic solvents.[2]

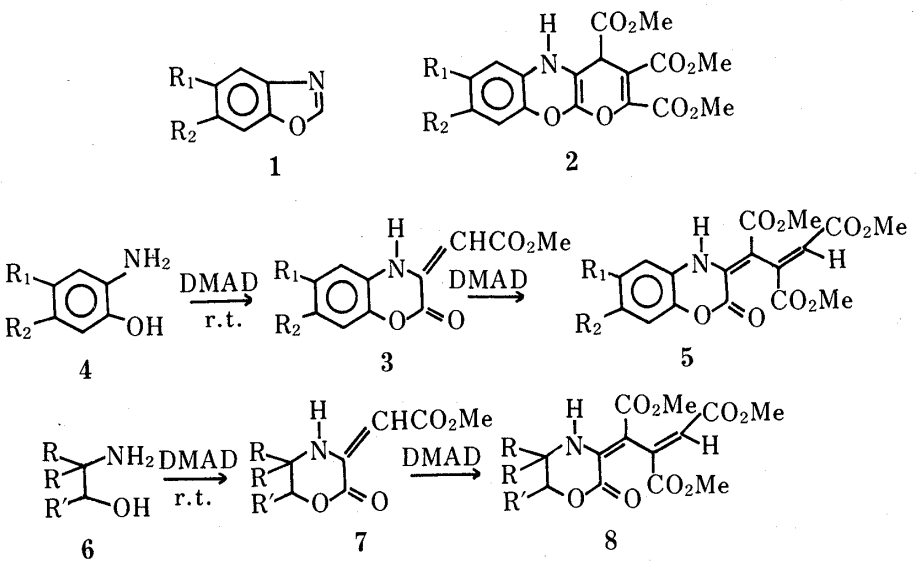
When 5- or 6-methylbenzoxazole (**1a**, **b**) was treated with DMAD in MeOH at room temperature, a crystalline solid was obtained in low yield. The products were suggested to be the tricyclic 4*H*-pyran derivatives (**2a**, **b**) formed by the Diels–Alder reaction of methyl 2,3-dihydro-5(or 6)-methyl-2-oxo-4*H*-1,4-benzoxazine-3-methylenecarboxylate (**3**) with DMAD.

However, it was recently found that no reaction of **3** occurred with dienophiles such as *p*-quinone, dimethylmaleate and cyclohexene, despite the reaction with DMAD. Thus, the proposed structure of **2** is suspect. In order to obtain the correct structure of **2**, we first attempted the synthesis of compound (**2**) in good yield. The same compound (**2a**, **b**) could be easily prepared by heating of *o*-aminophenol derivatives (**4a**, **b**) with an excess of DMAD in EtOH (benzene, *tert*-BuOH, dimethylformamide (DMF) and acetonitrile) and the best yield was obtained in dioxane. These compounds (**2a**, **b**) could also be prepared by heating of the initial Michael type addition product (**3a**, **b**) with DMAD in the above solvents.[4]

Next we carried out an X-ray crystallographic analysis. The chloro compound (**5c**) to be examined was prepared as follows.

4-Chloro-2-aminophenol (**4c**, 1.435 g) was treated with DMAD (5.0 ml) in refluxing dioxane (30 ml) overnight. After cooling of the reaction mixture, the precipitate (1.877 g) was collected, washed with EtOH and recrystallized from EtOH to give pure yellow rods (**5c**, mp = 159—160 °C). The filtrate and washing were combined and the solvent was evaporated off *in vacuo*. The residual oil was chromatographed on a thin layer (silica gel) plate with benzene–ethyl acetate (9 : 1) as the developer. A faster moving band gave the desired compound (**5c**, total 3.434 g).

As described above, 4-methyl-2-aminophenol (**4a**) and 4-chloro-2-aminophenol (**4c**) afforded **2a** and **5c**, respectively, under the same reaction conditions. The spectral data for **5c**



a : R_1=Me, R_2=H
b : R_1=H, R_2=Me
c : R_1=Cl, R_2=H
d : R_1=R_2=H
e : R_1=H, R_2=NO_2

R, R′=H or Me

Chart 1

TABLE I. Final Atomic Parameters ($\times 10^4$)

	X	Y	Z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	3502 (7)	4392 (8)	−598 (13)	559 (60)	413 (56)	462 (61)	−17 (47)	66 (51)	−138 (49)
C(2)	3883 (7)	3436 (8)	−421 (14)	659 (71)	386 (61)	457 (69)	62 (53)	109 (59)	−74 (54)
C(3)	4632 (6)	3278 (7)	906 (13)	525 (62)	292 (51)	523 (68)	85 (45)	258 (57)	−2 (48)
C(4)	5030 (5)	4013 (6)	2107 (11)	386 (45)	297 (45)	426 (55)	17 (37)	129 (42)	−15 (43)
C(5)	4648 (5)	4944 (7)	1896 (11)	359 (49)	299 (46)	375 (52)	−38 (37)	105 (43)	−15 (40)
C(6)	3901 (6)	5130 (7)	579 (12)	456 (56)	307 (53)	404 (57)	13 (42)	61 (48)	−50 (45)
C(7)	3858 (6)	6877 (7)	1365 (11)	353 (49)	344 (50)	358 (54)	−37 (39)	37 (44)	−90 (43)
C(8)	4673 (5)	6699 (6)	2762 (11)	282 (44)	307 (46)	334 (50)	−17 (36)	101 (41)	−8 (40)
C(9)	5066 (5)	7483 (7)	3774 (11)	199 (40)	361 (51)	357 (50)	−36 (37)	76 (38)	−36 (43)
C(10)	4736 (5)	8534 (7)	3467 (11)	279 (46)	350 (50)	362 (54)	−8 (39)	37 (42)	−106 (43)
C(11)	5115 (5)	9310 (7)	3012 (12)	289 (44)	390 (51)	412 (62)	53 (39)	32 (45)	−73 (47)
C(12)	5863 (5)	7286 (7)	5192 (11)	323 (44)	449 (54)	325 (53)	−43 (39)	91 (42)	−48 (44)
C(13)	6857 (6)	8042 (9)	7632 (12)	377 (52)	756 (82)	357 (57)	−58 (52)	−82 (46)	−111 (57)
C(14)	3916 (6)	8784 (8)	3818 (13)	360 (50)	502 (63)	512 (67)	−77 (45)	104 (49)	−226 (55)
C(15)	2932 (7)	8166 (11)	4981 (16)	362 (58)	1042 (100)	797 (94)	92 (61)	326 (64)	−91 (79)
C(16)	5910 (6)	9223 (7)	2664 (12)	430 (53)	358 (54)	413 (58)	−18 (44)	108 (47)	−81 (47)
C(17)	6788 (9)	10033 (10)	1366 (18)	992 (104)	689 (80)	1031 (114)	61 (73)	749 (94)	80 (77)
O(1)	3503 (4)	6068 (5)	358 (8)	399 (36)	324 (34)	510 (41)	113 (28)	−99 (32)	−124 (31)
O(2)	3464 (4)	7646 (5)	1073 (8)	429 (36)	309 (33)	505 (41)	91 (27)	−45 (32)	−72 (31)
O(3)	6245 (4)	6487 (5)	5502 (8)	363 (33)	390 (35)	442 (40)	45 (28)	33 (31)	−13 (31)
O(4)	6064 (4)	8095 (5)	6181 (8)	381 (34)	438 (37)	340 (37)	−9 (28)	8 (30)	−117 (30)
O(5)	3516 (4)	9554 (5)	3401 (11)	423 (38)	382 (39)	1102 (64)	76 (33)	267 (42)	−91 (42)
O(6)	3727 (5)	8030 (5)	4618 (8)	525 (55)	609 (44)	505 (39)	−28 (40)	169 (39)	−21 (34)
O(7)	6405 (4)	8514 (5)	3017 (9)	451 (38)	440 (39)	629 (47)	75 (32)	246 (36)	61 (36)
O(8)	5998 (5)	10023 (5)	1836 (9)	704 (47)	305 (37)	777 (52)	50 (32)	374 (42)	76 (36)
Cl(1)	5123 (2)	2080 (2)	1136 (4)	746 (18)	347 (13)	633 (18)	120 (12)	207 (15)	−49 (13)
N(1)	5003 (5)	5730 (5)	3017 (9)	375 (42)	281 (38)	407 (44)	−27 (32)	23 (36)	28 (35)

Temperature factors are expressed as $T=\exp[-(U_{11}h^2+U_{22}k^2+U_{33}l^2+2U_{12}hk+2U_{13}hl+2U_{23}kl)]$. The e.s.d.'s given in the parentheses denote the least significant digits.

TABLE II. Bond Angles (°) (Estimated Standard Deviations in Parentheses)

C(2)–C(1)–C(6)=118.1 (8)	C(10)–C(9)–C(12)=118.6 (7)
C(1)–C(2)–C(3)=117.8 (9)	C(9)–C(10)–C(11)=125.9 (9)
C(4)–C(3)–Cl(1)=117.4 (6)	C(9)–C(10)–C(14)=117.5 (8)
C(4)–C(3)–C(2)=124.4 (9)	C(11)–C(10)–C(14)=116.4 (8)
Cl(1)–C(3)–C(2)=118.3 (8)	C(10)–C(11)–C(16)=124.2 (8)
C(3)–C(4)–C(5)=116.6 (7)	C(9)–C(12)–O(3)=125.5 (8)
C(4)–C(5)–C(6)=120.5 (8)	C(9)–C(12)–O(4)=110.1 (7)
C(4)–C(5)–N(1)=120.8 (7)	C(3)–C(12)–O(4)=124.1 (7)
C(6)–C(5)–N(1)=118.6 (8)	C(10)–C(14)–O(5)=123.7 (10)
C(5)–C(6)–O(1)=121.1 (8)	C(10)–C(14)–O(6)=110.2 (8)
C(5)–C(6)–C(1)=122.6 (9)	O(5)–C(14)–O(6)=126.0 (11)
O(1)–C(6)–C(1)=116.3 (7)	C(11)–C(16)–O(7)=126.1 (10)
C(8)–C(7)–O(1)=117.4 (7)	C(11)–C(16)–O(8)=110.0 (8)
C(8)–C(7)–O(2)=125.7 (8)	O(7)–C(16)–O(8)=123.8 (10)
O(1)–C(7)–O(2)=116.7 (7)	C(6)–O(1)–C(7)=122.1 (6)
C(7)–C(8)–C(9)=119.9 (7)	C(12)–O(4)–C(13)=117.5 (7)
C(7)–C(8)–N(1)=118.3 (7)	C(14)–O(6)–C(15)=115.4 (9)
C(9)–C(8)–N(1)=121.9 (7)	C(17)–O(8)–C(16)=116.0 (8)
C(7)–C(8)–N(1)=118.3 (7)	C(5)–N(1)–C(8)=122.0 (6)
C(8)–C(9)–C(12)=119.2 (8)	C(8)–C(9)–C(10)=122.1 (7)

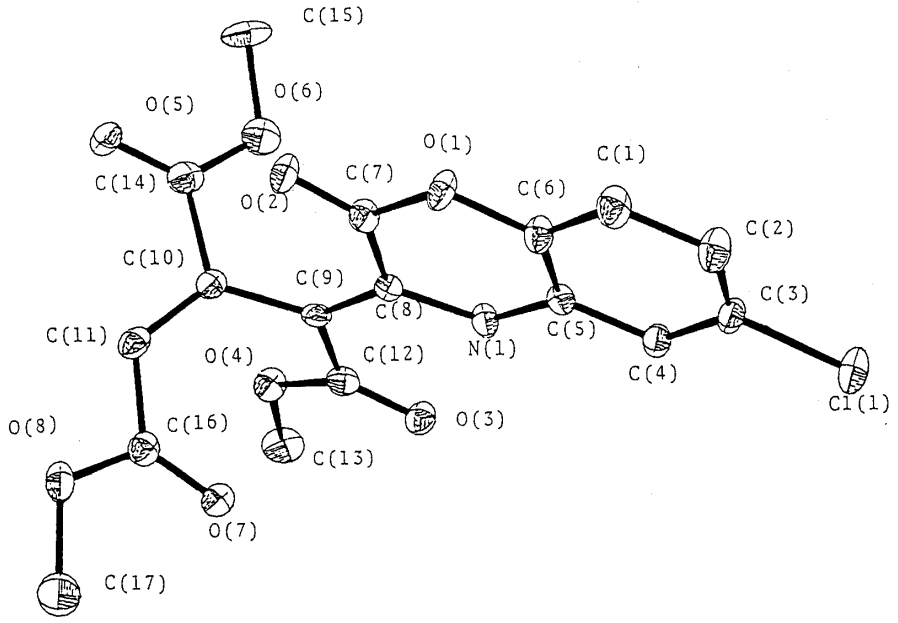


Fig. 1. A Perspective Drawing of the Molecule of **5c** with Hydrogen Atoms Omitted

are very similar to those of **2a** except that for the substituent signals (Me and Cl). The crystals of **5c** are monoclinic ($a=16.689(5)$ Å, $b=13.207(3)$ Å, $c=8.807(2)$ Å, $V_0=1808.20$ Å^3, $Z=4$, $D_{calc.}=1.411$, $D_{obs.}=1.42$ g/cm^3, $\beta=111.33(2)°$, space group $P2_{1/2}$).

The reflection data were collected on a Rigaku four-circle diffractometer using graphite monochromated Cu$K\alpha$ radiation. Those reflections having an intensity exceeding 3 times of the corresponding standard deviations were collected, and 1850 reflections out of 2418 reflections were used as data. The structure was solved by the heavy-atom (chlorine) method and refined by the block-diagonal least-squares method to a final R value of 0.092. The final atomic parameters are presented in Table I along with their standard deviations. The bond

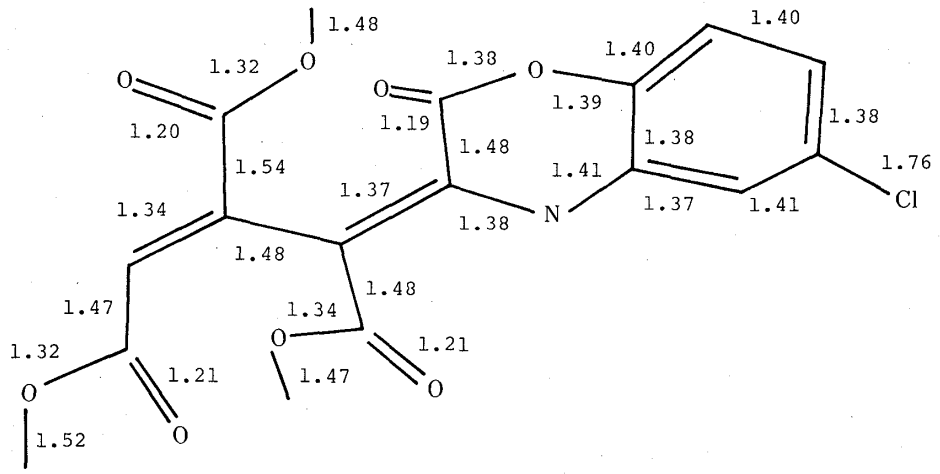
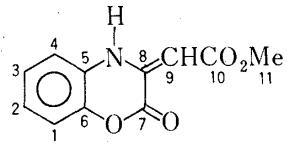
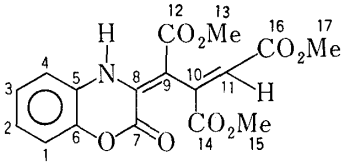


Fig. 2. Bond Lengths (Å)

TABLE III. Spectral Data for **3d** and **5d**

3d mp 164—164.5 °C	**5d** mp 144—145 °C
$C_{11}H_9NO_4$	$C_{17}H_{15}NO_8$
MS *m/e*: 219 (M^+)	MS *m/e*: 361 (M^+)
IR (cm^{-1}) ν_{max}^{KBr}: 3300, 1760, 1660, 1620	IR (cm^{-1}) ν_{max}^{KBr}: 2970, 1759, 1720, 1660, 1595
^{1}H-NMR ($CDCl_3$) δ: 3.78 (3H, s, O-Me); 5.96 (1H, s, =CH–); 7.03—7.20 (4H, m, ArH); 10.60 (1H, br, NH)	^{1}H-NMR ($CDCl_3$) δ: 3.70, 3.72 and 3.80 (9H, each s, O-Me × 3); 6.94 (1H, s, =CH–); 6.94—7.07 (4H, m, ArH); 11.72 (1H, br, NH)
^{13}C-NMR ($CDCl_3$) δ: 51.46 (C-11); 90.69 (C-9); 114.81 and 117.00 (C-2 and C-3); 122.75 and 125.63 (C-1 and C-4); 124.17 (C-8); 138.15 and 140.00 (C-5 and C-6); 156.80 (C-7); 170.21 (C-10)	^{13}C-NMR ($CDCl_3$) δ: 51.75, 52.14 and 52.78 (C-13, C-15 and C-17); 99.94 (C-9); 115.15 and 116.56 (C-2 and C-3); 122.85 and 125.67 (C-1 and C-4); 124.26 (C-8); 127.14 (C-11); 135.08 (C-10); 140.34 and 141.41 (C-5 and C-6); 155.49 (C-7); 165.78, 166.02 and 169.09 (C-14, C-16 and C-12)
	
3d	**5d**

lengths are shown in Fig. 2, and their standard deviations are between 0.020 and 0.010 Å. The bond angles are shown in Table II.

The molecular structure of this chloro compound (**5c**) was thus determined to be trimethyl 2,3-dihydro-6-chloro-2-oxo-4*H*-1,4-benzoxazine-$\Delta^{3,\gamma}$-aconitate by X-ray crystallographic analysis (Fig. 1).

Consequently, **2a** (or **b**) was elucidated to be trimethyl 2,3-dihydro-6(or 7)-methyl-2-oxo-4*H*-1,4-benzoxazine-$\Delta^{3,\gamma}$-aconitate (**5a**, **b**).

As shown in Table III, the infrared (IR) absorption at 1759 cm^{-1} in **5d** may be attributed to a lactone ring. The ^{1}H-nuclear magnetic resonance (^{1}H-NMR) showed three methyl ester signals at δ 3.70, 3.72 and 3.80, four aromatic protons at δ 6.94—7.07, and an amino proton at δ 11.72. The presence of a trisubstituted double bond was deduced from the signal at δ 6.94 in the ^{1}H-NMR of **5d**. The ^{13}C-NMR data are also compatible with the structure (**5d**); the signal

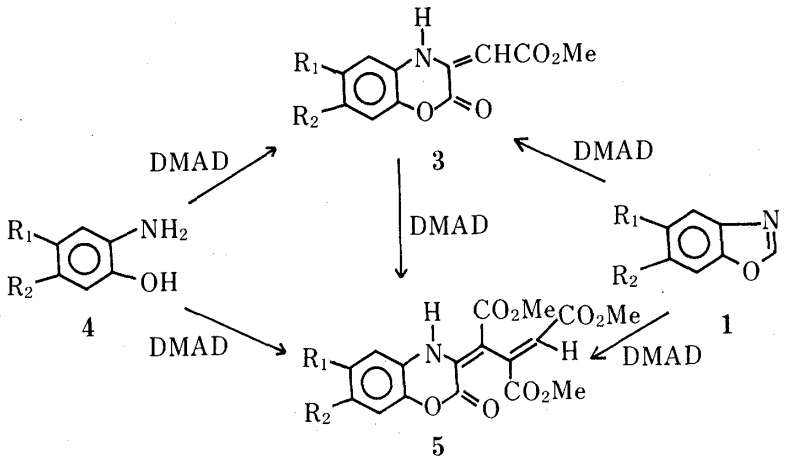
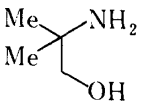
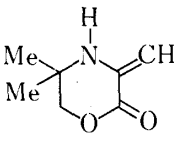
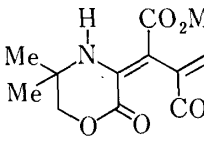
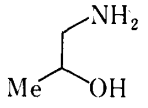
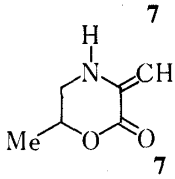


Chart 2

TABLE IV. Reaction Products and Yields (%)

4 and 6	3 and 7	5 and 8
4a	**3a** mp 148—149 °C (92.27)	**5a** mp 138—140 °C (36.87)[a]
4b	**3b** mp 168—169 °C (88.89)	**5b** mp 149—151 °C (41.80)
4c	**3c** mp 162—164 °C (quant.)	**5c** mp 159—160 °C (62.56)[b]
4d	**3d** mp 164—166 °C (89.11)	**5d** mp 145—147 °C (25.30)[c]
4e	**3e** mp 208—210 °C (84.02)	**5e** Oil
 **6**	 mp 97—98 °C (34.37) **7**	 mp 87.5—88.5 °C (41.70)[d] **8**
 **6**	 mp 88—90 °C (33.17) **7**	

Yield synthesized directly from **4** or **6** (*a*) 41.21, *b*) 44.67, *c*) 32.44, *d*) 72.00).

due to an olefin carbon (C-11) was observed at δ 127.14.

As mentioned above, the treatment of benzoxazoles and *o*-aminophenols with DMAD afforded the same products (**5**) (Chart 2). It may be assumed that hydrolysis of the oxazole ring occurs first to give the *o*-aminophenol which would then condense with DMAD to form the intermediate (**3**). A further addition of DMAD to **3** would furnish **5**.

Furthermore, we could synthesize new benzoxazine analogs (**5**), as shown in Table IV, under the above reaction conditions. When aliphatic β-aminoalcohols (**6**) were used, trimethyl 2,3,5,6-tetrahydro-2-oxo-4*H*-1,4-oxazine-$\Delta^{3,\gamma}$-aconitates (**8**) were formed.

Experimental

Melting points were determined on a micro hot-stage apparatus (Mitamura, Tokyo) and are uncorrected. IR spectra (IR, ν_{max}) in KBr disks were recorded on a Hitachi 215 infrared spectrophotometer and are expressed as cm^{-1}. NMR spectra (^1H and ^{13}C) were measured on a JNM-FX100 spectrometer (JEOL, Tokyo) at 100 MHz and chemical shifts are expressed relative to 1% tetramethylsilane (TMS) as an internal standard; s = singlet, d = doublet, t = triplet,

br = broad, and m = multiplet. Mass spectra (MS) were obtained on a GCMS-9000 spectromerer (Shimadzu, Tokyo) by the direct insertion method. Elemental analyses were done by the staff of the Analytical Center of the School of Pharmaceutical Sciences, Kitasato University (Tokyo), to whom our thanks are due.

TLC was performed with Merck precoated Silica gel 60 F_{254} plates. Preparative thin-layer chromatography (TLC) was done with the same commercial product, 20 × 20 cm, with a thickness of 0.25 or 0.5 mm. All the chemcials used were of reagent grade, and were used without further purification.

Methyl 2,3-Dihydro-6-methyl-2-oxo-4*H*-1,4-benzoxazine-3-methylenecarboxylate (3a)——DMAD (3.7 ml) was added to an MeOH (20 ml) solution of 4-methyl-2-aminophenol (**4a**, 1.23 g) at room temperature. The mixture was stirred at room temperature overnight. A precipitate that developed in the reaction flask was collected and washed with MeOH to give 2.15 g (92.27%) of **3a**. The crude product was recrystallized from MeOH to give yellow needles; mp 148—149 °C, *Anal.* Calcd for $C_{12}H_{11}NO_4$ (233.22): C, 61.80; H, 4.75; N, 6.01. Found: C, 61.91; H, 4.82, N, 5.96. MS *m/e*: 233 (M^+). IR: 1755 (C=O), 1655 (C=O), 1620. ^{1}H-NMR ($CDCl_3$) δ: 2.33 (3H, s, C–Me), 3.80 (3H, s, O–Me), 5.92 (1H, s, =CH–), 6.71—7.25 (3H, m, ArH), 10.60 (1H, br, NH).

Methyl 2,3-Dihydro-7-methyl-2-oxo-4*H*-1,4-benzoxazine-3-methylenecarboxylate (**3b**): 88.89% yield, mp = 168—169 °C (needles from CH_2Cl_2–MeOH), *Anal.* Calcd for $C_{12}H_{11}NO_4$ (233.22): C, 61.80; H, 4.75; N, 6.01. Found: C, 61.88; H, 4.86; N, 5.85. MS *m/e*: 233 (M^+). IR: 1745 (C=O), 1650, 1630. ^{1}H-NMR ($CDCl_3$) δ 2.32 (3H, s, C–Me), 3.77 (3H, s, O–Me), 5.89 (1H, s, =CH–), 6.89 (3H, br, ArH), 10.58 (1H, br, NH).

Methyl 2,3-Dihydro-2-oxo-4*H*-1,4-benzoxazine-3-methylenecarboxylate (**3d**): 89.11% yield, mp = 164—166 °C (needles from CH_2Cl_2–MeOH), MS *m/e*: 219 (M^+). ^{1}H-NMR δ: 3.79 (3H, s, O–Me), 5.95 (1H, s, =CH–), 6.90—7.30 (4H, m, ArH), 10.65 (1H, br, NH).

Methyl 2,3-Dihydro-6-chloro-2-oxo-4*H*-1,4-benzoxazine-3-methylenecarboxylate (**3c**): Quantitative yield, mp = 162—164 °C (needles from EtOH), MS *m/e*: 253, 255 (M^+). IR: 1775 (C=O), 1650, 1620, 1605. ^{1}H-NMR ($CDCl_3$) δ: 3.65 (3H, s, O–Me), 5.82 (1H, s, =CH–), 6.80—7.10 (4H, m, ArH), 10.52 (1H, br, NH).

Methyl 2,3-Dihydro-6-nitro-2-oxo-4*H*-1,4-benzoxazine-3-methylenecarboxylate (**3e**): 84.02% yield, mp = 208—210 °C (needles from MeOH), MS *m/e*: 264 (M^+). IR: 1765 (C=O), 1675, 1620. ^{1}H-NMR ($CDCl_3$) δ: 3.84 (3H, s, O–Me), 6.06 (1H, s, =CH–), 7.26 (1H, d, J = 9 Hz, ArH), 7.89 (1H, s, ArH), 7.92 (1H, d, J = 9 Hz, ArH).

Methyl 2,3,5,6-Tetrahydro-5,5-dimethyl-2-oxo-4*H*-1,4-oxazine-3-methylenecarboxylate (7, R = Me, R′ = H)——DMAD (12 ml) in EtOH (20 ml) was added to an EtOH (60 ml) solution of 2-amino-2-methyl-1-propanol (8.9 g) at room temperature. The mixture was stirred at room temperature overnight. The solvent was evaporated off *in vacuo* to leave a reddish solid (11.48 g), which was washed with EtOH and recrystallized from EtOH to give 5.13 g of **7**: white plates, mp = 97—98 °C, MS *m/e*: 199 (M^+). IR: 3300 (NH), 1735 (C=O), 1660 (C=O), 1640, 1615. ^{1}H-NMR ($CDCl_3$) δ: 1.32 (6H, each s, C–Me × 2), 3.66 (3H, s, O–Me), 4.22 (2H, s, –CH_2–), 5.54 (1H, s, =CH–), 8.22 (1H, m, NH).

Methyl 2,3,5,6-Tetrahydro-6-methyl-2-oxo-4*H*-1,4-oxazine-3-methylenecarboxylate (7, R = H, R′ = Me)——DMAD (6 ml) in EtOH (10 ml) was added to an EtOH (3 ml) solution of 1-amino-2-propanol (3.3 ml) at room temperature. The mixture was stirred at room temperature overnight. The solvent was evaporated off *in vacuo* to leave an oily residue (9.373 g). A part (1.036 g) of the residue was purified by preparative TLC with a mixture of ethyl acetate and benzene (1 : 4) as a developer. After repeated preparative TLC, pure product (0.3436 g) was crystallized from MeOH; mp = 88—90 °C (from MeOH), MS *m/e*: 185 (M^+). IR 3320 (NH), 1735 (sh), 1720 (C=O), 1655 (C=O), 1600. ^{1}H-NMR ($CDCl_3$) δ: 1.43 (3H, d, J = 6 Hz, C–Me, 3.36 (2H, m, –CH_2–), 3.78 (3H, s, O–Me), 4.76 (1H, m, –CH–), 5.71 (1H, s, =CH–), 8.34 (1H, br, NH).

Trimethyl 2,3-Dihydro-6-methyl-2-oxo-4*H*-1,4-benzoxazine-$\Delta^{3,\gamma}$-aconitate (5a)——Method A (**5a** from **3a**): DMAD (5.0 ml) was added to a dry dioxane (30 ml) solution of **3a** (2.33 g) and the mixture was refluxed overnight. The solvent was removed *in vacuo*, and the residue was washed with EtOH to give 1.289 g of **5a**. The crude product was recrystallized from EtOH; mp = 138—140 °C. The filtrate and washings were combined and the solvent was evaporated off *in vacuo*. The residual oil was chromatographed on a thin layer plate with benzene–ethyl acetate (9 : 1) as a developer to give 98.7 mg of **5a** (total 1.387 g, 36.97%).

Method B (**5a** from **4a**): DMAD (5.0 ml) was added to a dry dioxane (30 ml) solution of 4-methyl-2-aminophenol (**4a**, 1.23 g) and the mixture was refluxed overnight. After the same treatment as described above of the reaction mixture, 1.5466 g (41.21%) of **5a** was obtained; mp 138—140 °C, *Anal.* Calcd for $C_{18}H_{17}NO_8$ (375.32): C, 57.60; H, 4.57; N, 3.73. Found: C, 57.51; H, 4.57; N, 3.78. MS *m/e*: 375 (M^+). IR: 3400 (NH), 1750 (C=O), 1720 (C=O), 1660, 1595. ^{1}H-NMR ($CDCl_3$) δ: 2.32 (3H, s, C–Me), 3.71, 3.73 and 3.81 (9H, each s, O–Me × 3), 6.71—6.24 (3H, m, ArH), 6.93 (1H, s, =CH–), 11.71 (1H, br, NH). ^{13}C-NMR ($CDCl_3$) δ: 20.98, 51.80, 52.14, 52.78, 99.61, 109.16, 115.39, 116.22, 123.53, 126.99, 135.22, 135.71, 138.34, 141.51, 155.69, 165.78, 166.12, 169.09.

Trimethyl 2,3-Dihydro-7-methyl-2-oxo-4*H*-1,4-benzoxazine-$\Delta^{3,\gamma}$-aconitate: 41.80% yield (Method A), mp 149—151 °C (from MeOH), MS *m/e*: 375 (M^+). IR: 1755 (C=O), 1720 (C=O), 1660, 1595. ^{1}H-NMR ($CDCl_3$) δ 2.33 (3H, s, C–Me), 3.71, 3.73 and 3.81 (9H, each s, O–Me × 3), 6.80—7.20 (4H, br, ArH and =CH–), 11.71 (1H, br, NH).

Trimethyl 2,3-Dihydro-6-chloro-2-oxo-4*H*-1,4-benzoxazine-$\Delta^{3,\gamma}$-aconitate (**5c**): 62.56% yield (Method A), 44.67% yield (Method B), mp = 159—160 °C (from EtOH), *Anal.* Calcd for $C_{17}H_{14}ClNO_8$ (395.77): C, 51.58; H, 3.56; N, 3.53. Found: C, 51.46; H, 3.44; N, 3.44. MS *m/e*: 395, 397 (M^+). IR: 1760 (C=O), 1720 (C=O), 1660. ^{1}H-NMR

($CDCl_3$) δ: 3.70, 3.71 and 3.81 (9H, each s, O–Me × 3), 6.95 (1H, s, =CH–), 6.98—7.27 (3H, m, ArH), 8.80 (1H, br, NH).

Trimethyl 2,3-Dihydro-2-oxo-4*H*-1,4-benzoxazine-$\Delta^{3,\gamma}$-aconitate (**5d**): 25.30% yield (Method A), 32.44% yield (Method B), mp = 145—147 °C (from EtOH), *Anal.* Calcd for $C_{17}H_{15}NO_8$ (361.30): C, 56.51; H, 4.18; N, 3.88. Found: C, 56.59; H, 4.26; N, 3.72. MS *m/e*: 361 (M^+). IR: 3400 (NH), 1755 (C=O), 1720 (C=O), 1660, 1595. ^{1}H-NMR ($CDCl_3$) δ: 3.70, 3.72 and 3.80 (9H, each s, O–Me × 3), 6.95—7.36 (5H, m, ArH and =CH–), 11.74 (1H, br, NH).

Trimethyl 2,3-Dihydro-6-nitro-2-oxo-4*H*-1,4-benzoxazine-$\Delta^{3,\gamma}$-aconitate (5e)——DMAD (5.0 ml) was added to a dry dioxane (30 ml) solution of **3c** (2.64 g) and the mixture was refluxed overnight. The solvent was evaporated off *in vacuo* to leave an oily residue (8.357 g). To purify the major product from the oily residue, we attempted crystallization, silica gel column chromatography or repeated preparative TLC, but these methods failed. We could obtain only an oily material contaminated by small amounts of impurities; MS *m/e*: 406 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 3.72, 3.75 and 3.82 (9H, each s, O–Me × 3), 6.96 (1H, s, =CH–), 7.22 (1H, d, J = 9 Hz, ArH), 7.95 (1H, s, ArH), 7.92 (1H, d, J = 9 Hz, ArH).

Trimethyl 2,3,5,6-Tetrahydro-5,5-dimethyl-2-oxo-4*H*-1,4-oxazine-$\Delta^{3,\gamma}$-aconitate (**8**, R = Me, R′ = H): 41.70% yield (Method A), 72.00% yield (Method B), mp = 87.5—88.5 °C (from CH_2Cl_2), MS *m/e*: 341 (M^+). IR: 3250 (NH), 1735 (C=O), 1715 (C=O), 1655, 1630, 1585. ^{1}H-NMR ($CDCl_3$) δ: 1.40 (6H, s, $>C<^{Me}_{Me}$), 3.64, 3.71 and 3.78 (9H, each s, O–Me × 3), 4.26 (2H, s, $-CH_2-$), 6.80 (1H, s, =CH–), 9.27 (1H, s, NH).

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