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SYNTHESIS OF 4-ALKYLIDENE-2-(DIMETHYLAMINO)METHYL-4*H*-3,1-BENZOXAZINES BY THE REACTION OF ALKYL 2-ISOCYANOPHENYL KETONES WITH ESCHENMOSER'S SALT

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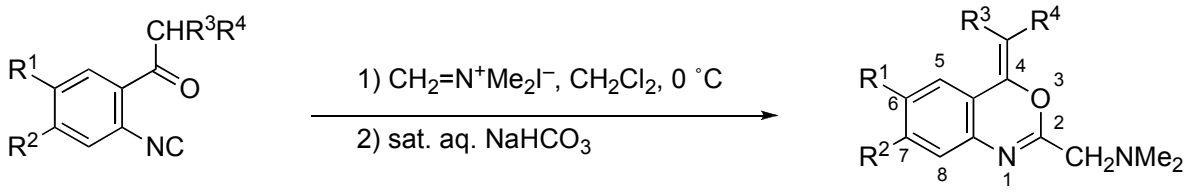
Abstract – 4-Alkylidene-2-(dimethylamino)methyl-4*H*-3,1-benzoxazines could be prepared in one-pot by simply treating alkyl 2-isocyanophenyl ketones with dimethyl(methylene)ammonium iodide (Eschenmoser's salt) in dichloromethane at 0 ˚C without any catalysts.

As part of an ongoing program aimed at developing new approaches to nitrogen heterocycles utilizing *o*-functionalized phenyl isocyanides,[1] we have recently described a synthesis of 2-(1-alkoxyalkyl)-4-alkylidene-4*H*-3,1-benzoxazines by the reaction of alkyl 2-isocyanophenyl ketones with vinyl ethers in the presence of a catalytic amount of (±)-camphor-10-sulfonic acid.[2] After this finding, we wished to extend this study and investigate the possibility of reacting alkyl 2-isocyanophenyl ketones with dimethyl(methylene)ammonium iodide (Eschenmoser's salt) for the preparation of 4*H*-3,1-benzoxazines carrying (dimethylamino)methyl group at the 2-position. We now report the results of our investigation, which offer a facile method for the synthesis of 4-alkylidene-2-(dimethylamino)methyl-4*H*-3,1-benzoxazines. Since compounds based on the 4*H*-3,1-benzoxazine have received much attention because of their significant biological utilities,[3] a number of efficient approaches for the construction of this system have recently been developed.[4] Although a few methods have been reported for the preparation of 4-alkylidene-4*H*-3,1-benzoxazine derivatives,[5] these methods are of limited generality.

The reactions used for the conversion of alkyl 2-isocyanophenyl ketones (**1**) (alkyl = methyl, ethyl, propyl, and 1-methylethyl) into 4-alkylidene-2-(dimethylamino)methyl-4*H*-3,1-benzoxazines (**2**) were carried out as shown in Scheme 1. The reactions of **1** with Eschenmoser's salt proceeded smoothly in dichloromethane at 0 ˚C without any catalysts and completed within 30 min. After workup using saturated aqueous sodium hydrogencarbonate followed by purification using column chromatography on silica gel, the desired 4*H*-3,1-benzoxazine derivatives (**2**) were obtained in the yields summarized in

Scheme 1. It indicates that the reactions generally provide satisfactory yields of the corresponding 4*H*-3,1-benzoxazine derivatives. Unfortunately, however, the yield of 7-chloro-2-(dimethylamino)methyl-4-(1-methylethylidene)-4*H*-3,1-benzoxazines (**2i**) was rather lower than those of the others, because of its instability under purification conditions. This may be ascribed to the steric repulsion between *E*-methyl substituent of the 1-methylethylidene moiety and 5-hydrogen. It should be noted that the reaction of **1b** with dimethyl(propylidene)ammonium iodide, generated in situ according to the procedure reported by Arend and Rish,[6] resulted in the formation of an intractable mixture of products.



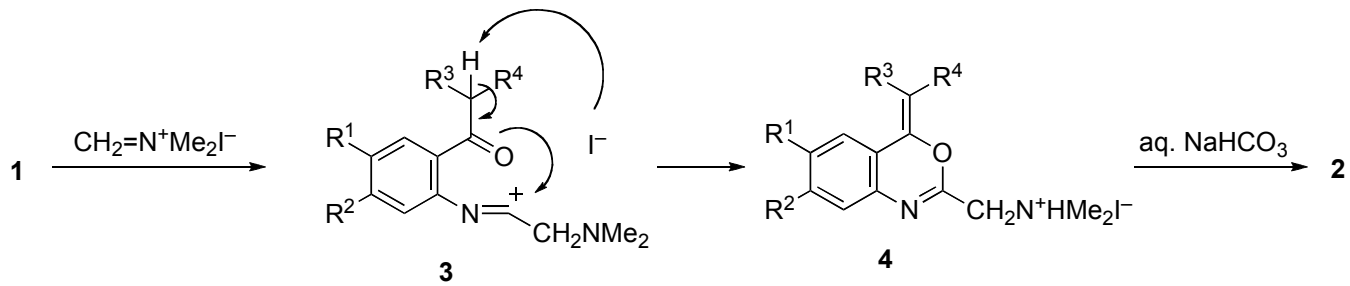
1

a $R^1 = R^2 = R^3 = R^4 = H$
b $R^1 = R^2 = H$, $R^3 = H$, $R^4 = Me$
c $R^1 = R^2 = H$, $R^3 = H$, $R^4 = Et$
d $R^1 = Cl$, $R^2 = R^3 = R^4 = H$
e $R^1 = Cl$, $R^2 = R^3 = H$, $R^4 = Me$
f $R^1 = Cl$, $R^2 = R^3 = H$, $R^4 = Et$
g $R^1 = H$, $R^2 = Cl$, $R^3 = H$, $R^4 = Me$
h $R^1 = H$, $R^2 = Cl$, $R^3 = H$, $R^4 = Et$
i $R^1 = H$, $R^2 = Cl$, $R^3 = R^4 = Me$
j $R^1 = R^2 = OMe$, $R^3 = H$, $R^4 = Me$

2a 52%
2b 75%
2c 55%
2d 61%
2e 66%
2f 72%
2g 60%
2h 59%
2i 37%
2j 56%

Scheme 1

In each of the reactions using the starting isocyano ketones (**1b**), (**1c**), (**1e-h**), and (**1j**), one of the two possible stereoisomers was exclusively obtained. The stereochemistry of the 4-alkylidene moiety of the corresponding products (**2b**), (**2c**), (**2e-h**), and (**2j**) was determined to be *Z* on the basis of NOE experiments. Thus, for example, an enhancement (12%) of the signal at δ 6.76 assignable to 5-hydrogen of compound (**2j**) was observed when the signal at δ 5.01 assignable to vinyl proton was irradiated.



Scheme 2

The formation of 4-alkylidene-4*H*-3,1-benzoxazine derivatives (**2**) from alkyl 2-isocyanophenyl ketones **1** and Eschenmoser's salt is thought to proceed as illustrated in Scheme 2. Thus, addition of isocyano carbon of **1** to iminium salts generates the imidoyl cation intermediate (**3**). Subsequent attack of the carbonyl oxygen on the cation center of this intermediate with a loss of a proton gives rise to the ammonium salt product (**4**), which is then treated with aqueous sodium hydrogencarbonate to give **2**.

In the present work, we have demonstrated an efficient synthetic method that allows access to 4-alkylidene-4*H*-3,1-benzoxazines carrying (dimethylamino)methyl group at the 2-position. The synthesis can be achieved by simply mixing alkyl 2-isocyanophenyl ketones and Eschenmoser's salt without any catalysts. The operational simplicity, together with the ready availability of the starting materials, makes this new procedure attractive.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were determined with a Shimadzu FTIR-8300 spectrophotometer. The ^{1}H NMR spectra were determined in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz or a JEOL LA400 FT NMR spectrometer operating at 400 MHz. The ^{13}C NMR spectra were determined in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz or a JEOL LA400 FT NMR spectrometer operating at 100 MHz. Low-resolution MS spectra (EI, 70 eV or CI) and a high-resolution MS spectrum were measured by a JEOL JMS AX505 HA spectrometer. TLC was carried out on a Merck Kieselgel 60 PF_{254}. Column chromatography was performed using Merck Kieselgel 60 (0.063–0.200 mm). All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

Starting Materials. 2-Isocyanophenyl ketones (**1a, b**, **d**, **e**, **g**, and **j**) were prepared by the procedure reported previously by us.[2] 1-(2-Aminophenyl)-1-butanone was prepared according to the procedure reported by Sikkar and Martinson.[7] All other chemicals used in this study were commercially available.

2-Isocyanophenyl Ketones (1c, f, h, and i). These compounds were prepared from the respective 2-aminophenyl ketones, which were prepared from 2-aminobenzonitriles and appropriate Grignard reagents according to the procedure reported by Sikkar and Martinson,[7] by the procedure reported previously by us.[2] Thus, 2-aminophenyl ketones were treated with HCO_2H in refluxing toluene under azeotropic conditions to give the corresponding formamides, which in turn were dehydrated with $POCl_3$ in THF at 0 ˚C in the presence of Et_3N to give the desired isocyanides.

***N*-(2-Butanoylphenyl)formamide:** 86% yield; colorless crystals; mp 44–45 ˚C (hexane); IR (KBr) 3176, 1686, 1655 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.02 (t, *J* = 7.3 Hz, 3H), 1.77 (sext, *J* = 7.3 Hz, 2H), 3.01 (t, *J* = 7.3 Hz, 2H), 7.17 (dd, *J* = 7.8, 7.3 Hz, 1H), 7.56 (dd, *J* = 8.2, 7.3 Hz, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 8.49 (s, 1H), 8.74 (d, *J* = 8.2 Hz, 1H), 11.66 (br s, 1H). Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H,

6.85; N, 7.32. Found: C, 68.98; H, 6.96; N, 7.49.

1-(2-Isocyanophenyl)-1-butanone (1c): 75% yield; a yellow oil; R_f 0.30 (C_6H_6); IR (neat) 2124, 1699 cm^{-1}; ^1H NMR (500 MHz) δ 1.01 (t, J = 7.3 Hz, 3H), 1.78 (sext, J = 7.3 Hz, 2H), 2.99 (t, J = 7.3 Hz, 2H), 7.47 (dd, J = 7.8, 1.4 Hz, 1H), 7.50 (ddd, J = 7.8, 7.3, 1.4 Hz, 1H), 7.53 (ddd, J = 7.8, 7.3, 1.4 Hz, 1H), 7.69 (dd, J = 7.8, 1.4 Hz, 1H). HR-MS. Calcd for $C_{11}H_{11}NO$: M, 173.0841. Found: *m/z* 173.0820.

1-(2-Amino-5-chlorophenyl)-1-butanone: 82% yield; yellow crystals; mp 66–67 ˚C (hexane–Et_2O); IR (KBr) 3451, 3337, 1640, 1615 cm^{-1}; ^1H NMR (500 MHz) δ 1.01 (t, J = 7.3 Hz, 3H), 1.75 (sext, J = 7.3 Hz, 2H), 2.88 (t, J = 7.3 Hz, 2H), 6.27 (br s, 2H), 6.60 (d, J = 8.7 Hz, 1H), 7.20 (dd, J = 8.7, 2.3 Hz, 1H), 7.69 (d, J = 2.3 Hz, 1H). Anal. Calcd for $C_{10}H_{12}ClNO$: C, 60.76; H, 6.12; N, 7.09. Found: C, 60.58; H, 6.18; N, 7.02.

***N*-(2-Butanoyl-4-chlorophenyl)formamide:** 87% yield; yellow needles; mp 100–103 ˚C (hexane–Et_2O); IR (KBr) 3231, 1694, 1667, cm^{-1}; ^1H NMR (500 MHz) δ 1.02 (t, J = 7.3 Hz, 3H), 1.77 (sext, J = 7.3 Hz, 2H), 2.99 (t, J = 7.3 Hz, 2H), 7.51 (dd, J = 8.7, 2.3 Hz, 1H), 7.89 (d, J = 2.3 Hz, 1H), 8.48 (s, 1H), 8.74 (d, J = 8.7 Hz, 1H), 11.54 (br s, 1H). Anal. Calcd for $C_{11}H_{12}ClNO_2$: C, 58.54; H, 5.36; N, 6.21. Found: C, 58.29; H, 5.37; N, 6.18.

1-(5-Chloro-2-isocyanophenyl)-1-butanone (1f): 83% yield; a pale-brown liquid; R_f 0.64 (1:1 Et_2O–hexane); IR (neat) 2124, 1703 cm^{-1}; ^1H NMR (500 MHz) δ 1.01 (t, J = 7.3 Hz, 3H), 1.77 (sext, J = 7.3 Hz, 2H), 2.98 (t, J = 7.3 Hz, 2H), 7.42 (d, J = 8.7 Hz, 1H), 7.50 (dd, J = 8.7, 2.3 Hz, 1H), 7.66 (d, J = 2.3 Hz, 1H). HR-MS. Calcd for $C_{11}H_{10}ClNO$: M, 207.0451. Found: *m/z* 207.0433.

1-(2-Amino-4-chlorophenyl)-1-butanone: 77% yield; pale-yellow crystals; mp 43–45 ˚C (hexane–Et_2O); IR (KBr) 3462, 3340, 1648, 1614 cm^{-1}; ^1H NMR (500 MHz) δ 1.00 (t, J = 7.3 Hz, 3H), 1.74 (sext, J = 7.3 Hz, 2H), 2.87 (t, J = 7.3 Hz, 2H), 6.36 (br s, 2H), 6.60 (dd, J = 8.7, 1.8 Hz, 1H), 6.65 (d, J = 1.8 Hz, 1H), 7.66 (d, J = 8.7 Hz, 1H). Anal. Calcd for $C_{10}H_{12}ClNO$: C, 60.76; H, 6.12; N, 7.09. Found: C, 60.63; H, 6.20; N, 6.95.

***N*-(2-Butanoyl-5-chlorophenyl)formamide:** 91 % yield; white needles; mp 35–38 ˚C (hexane–Et_2O); IR (KBr) 3192, 1697, 1655 cm^{-1}; ^1H NMR (500 MHz) δ 1.02 (t, J = 7.3 Hz, 3H), 1.75 (sext, J = 7.3 Hz, 2H), 2.97 (t, J = 7.3 Hz, 2H), 7.14 (dd, J = 8.7, 1.8 Hz, 1H), 7.87 (d, J = 8.7 Hz, 1H), 8.49 (s, 1H), 8.85 (d, J = 1.8 Hz, 1H), 11.75 (br s, 1H). Anal. Calcd for $C_{11}H_{12}ClNO_2$: C, 58.54; H, 5.36; N, 6.21. Found: C, 58.37; H, 5.37; N, 6.06.

1-(4-Chloro-2-isocyanophenyl)-1-butanone (1h): 77% yield; a yellow oil; R_f 0.43 (C_6H_6); IR (neat) 2129, 1695 cm^{-1}; ^1H NMR (500 MHz) δ 1.01 (t, J = 7.3 Hz, 3H), 1.76 (sext, J = 7.3 Hz, 2H), 2.97 (t, J = 7.3 Hz, 2H), 7.47 (dd, J = 7.8, 2.3 Hz, 1H), 7.48 (d, J = 2.3 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H). HR-MS. Calcd for $C_{11}H_{10}ClNO$: M, 207.0451. Found: *m/z* 207.0443.

1-(2-Amino-4-chlorophenyl)-2-methyl-1-propanone: 87% yield; a pale-yellow liquid; R_f 0.40 (1:5 Et_2O–hexane); IR (neat) 3456, 3368, 1646, 1606 cm^{-1}; ^1H NMR (500 MHz) δ 1.19 (d, J = 6.9 Hz, 6H),

3.52 (sept, J = 6.9 Hz, 1H), 6.60 (br s, 2H), 6.61 (dd, J = 8.7, 1.8 Hz, 1H), 6.66 (d, J = 1.8 Hz, 1H), 7.69 (d, J = 8.7 Hz, 1H). Anal. Calcd for $C_{10}H_{12}ClNO$: C, 60.76; H, 6.12; N, 7.09. Found: C, 60.48; H, 6.23; N, 6.93.

***N*-[5-Chloro-2-(2-methylpropanoyl)phenyl]formamide:** 81% yield; colorless needles; mp 37–38 ˚C (hexane–Et_2O); IR (KBr) 3185, 1694, 1657 cm^{-1}; ^1H NMR (500 MHz) δ 1.22 (d, J = 6.9 Hz, 6H), 3.58 (sept, J = 6.9 Hz, 1H), 7.15 (dd, J = 8.7, 1.8 Hz, 1H), 7.87 (d, J = 8.7 Hz, 1H), 8.48 (s, 1H), 8.86 (d, J = 1.8 Hz, 1H), 11.73 (br s, 1H). Anal. Calcd for $C_{11}H_{12}ClNO_2$: C, 58.54; H, 5.36; N, 6.21. Found: C, 58.49; H, 5.35; N, 6.00.

1-(4-Chloro-2-isocyanophenyl)-2-methyl-1-propanone (1i): 82% yield; a pale-yellow liquid; R_f 0.55 (C_6H_6); IR (neat) 2124, 1699 cm^{-1}; ^1H NMR (500 MHz) δ 1.22 (d, J = 6.9 Hz, 6H), 3.42 (sept, J = 6.9 Hz, 1H), 7.45 (d, J = 2.3 Hz, 1H), 7.48 (dd, J = 8.2, 2.3 Hz, 1H), 7.56 (d, J = 8.2 Hz, 1H). HR-MS. Calcd for $C_{11}H_{10}ClNO$: M, 207.0451. Found: *m/z* 207.0463.

Typical Procedure for the Preparation of 4-Alkylidene-2-aminomethyl-4*H*-3,1-benzoxazines (2). 2-(Dimethylamino)methyl-4-methylene-4*H*-3,1-benzoxazine (2a). To a stirred solution of dimethyl(methylene)ammonium iodide (0.34 g, 1.8 mmol) in CH_2Cl_2 (4 mL) at 0 ˚C was added a solution of 1-(2-isocyanophenyl)ethanone (**1a**) (0.26 g, 1.8 mmol) in CH_2Cl_2 (4 mL) was added. After 5 min, saturated aqueous $NaHCO_3$ (15 mL) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 twice (10 mL each), and the combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography on silica gel to give **2a** (0.19 g, 52%); a pale yellow oil; R_f 0.30 (5:12 THF–hexane); IR (neat) 1660, 1651, 1605 cm^{-1}; ^1H NMR (500 MHz) δ 2.40 (s, 6H), 3.25 (s, 2H), 4.62 (d, J = 2.7 Hz, 1H), 4.79 (d, J = 2.7 Hz, 1H), 7.20 (ddd, J = 7.8, 7.3, 1.4 Hz, 1H), 7.26 (dd, J = 7.8, 1.4 Hz, 1H), 7.33 (ddd, J = 7.8, 7.3, 1.4 Hz, 1H), 7.45 (dd, J = 7.8, 1.4 Hz, 1H); MS (EI) *m/z* 202 (M^+, 27), 159 (100). Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85. Found: C, 71.13; H, 7.06; N, 13.75.

(*Z*)-2-(Dimethylamino)methyl-4-ethylidene-4*H*-3,1-benzoxazine (2b): a pale-yellow oil; R_f 0.44 (4:5 C_6H_6–THF); IR (neat) 1672, 1643, 1603 cm^{-1}; ^1H NMR (400 MHz) δ 1.75 (d, J = 7.0 Hz, 3H), 2.43 (s, 6H), 3.27 (s, 2H), 5.22 (q, J = 7.0 Hz, 1H), 7.13 (ddd, J = 7.8, 6.9, 2.3 Hz, 1H), 7.20–7.23 (m, 2H), 7.32 (d, J = 7.8 Hz, 1H); MS (CI) *m/z* 217 [$(M+1)^+$, 100]. Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.27; H, 7.67; N, 12.86.

(*Z*)-2-(Dimethylamino)methyl-4-propylidene-4*H*-3,1-benzoxazine (2c): a pale-yellow oil; R_f 0.30 (Et_2O); IR (neat) 1668, 1643, 1603 cm^{-1}; ^1H NMR (500 MHz) δ 1.05 (t, J = 7.3 Hz, 3H), 2.23 (quint, J = 7.3 Hz, 2H), 2,42 (s, 6H), 3.26 (s, 2H), 5.18 (t, J = 7.3 Hz, 1H), 7.14 (ddd, J = 7,8, 7.3, 1.4 Hz, 1H), 7.20–7.25 (m, 2H), 7.34 (d, J = 7.8 Hz, 1H); MS (CI) *m/z* 231 [$(M+1)^+$, 100]. Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.16. Found: C, 72.97; H, 7.90; N, 12.03.

(*Z*)-6-Chloro-2-(dimethylamino)methyl-4-methylene-4*H*-3,1-benzoxazine (2d): a pale-yellow oil; R_f

0.28 (1:1 EtOAc–C_6H_6); IR (neat) 1651cm^{-1}; ^{1}H NMR (500 MHz) δ 2.39 (s, 6H), 3.23 (s, 2H), 4.67 (d, *J* = 2.7 Hz, 1H), 4.78 (d, *J* = 2.7 Hz, 1H), 7.19 (d, *J* = 8.2 Hz, 1H), 7.27 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.41 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR (125 MHz) δ 45.58, 61.37, 87.12, 122.21, 122.36, 127.69, 130.76, 132.91, 136.80, 150.36, 158.04; MS (CI) *m/z* 237 [(M+1)$^+$, 100]. Anal. Calcd for $C_{12}H_{13}ClN_2O$: C, 60.89; H, 5.54; N, 11.84. Found: C, 60.82; H, 5.73; N, 12.02.

(*Z*)-6-Chloro-2-(dimethylamino)methyl-4-ethylidene-4*H*-3,1-benzoxazine (2e): a pale-yellow oil; R_f 0.29 (Et_2O); IR (neat) 1672, 1650 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.75 (d, *J* = 6.9 Hz, 3H), 2.42 (s, 6H), 3.25 (s, 2H), 5.22 (q, *J* = 6.9 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 7.18 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.29 (d, *J* = 2.3 Hz, 1H); MS (EI) *m/z* 250 (M$^+$, 7.1), 207 (100). Anal. Calcd for $C_{13}H_{15}ClN_2O$: C, 62.28; H, 6.03; N, 11.17. Found: C, 62.36; H, 6.04; N, 11.15.

(*Z*)-6-Chloro-2-(dimethylamino)methyl-4-propylidene-4*H*-3,1-benzoxazine (2f): a pale-yellow oil; R_f 0.39 (Et_2O); IR (neat) 1668, 1643 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.05 (t, *J* = 7.3 Hz, 3H), 2.23 (quint, *J* = 7.3 Hz, 2H), 2.41 (s, 6H), 3.24 (s, 2H), 5.17 (t, *J* = 7.3 Hz, 1H), 7.14 (d, *J* = 8.7 Hz, 1H), 7.18 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.31 (d, *J* = 1.8 Hz, 1H); ^{13}C NMR (125 MHz) δ 13.90, 17.82, 45.55, 61.05, 105.76, 121.24, 123.33, 127.53, 129.51, 132.71, 136.47, 142.85, 158.14; MS (EI) *m/z* 264 (M$^+$, 8.8), 221 (100). Anal. Calcd for $C_{14}H_{17}ClN_2O$: C, 63.51; H, 6.47; N, 10.58. Found: C, 63.50; H, 6.51; N, 10.50.

(*Z*)-7-Chloro-2-(dimethylamino)methyl-4-ethylidene-4*H*-3,1-benzoxazine (2g): a pale-yellow oil; R_f 0.50 (Et_2O); IR (neat) 1674, 1641, 1600 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.74 (d, *J* = 7.3 Hz, 3H), 2.42 (s, 6H), 3.26 (s, 2H), 5.21 (q, *J* = 7.3 Hz, 1H), 7.09 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.22 (d, *J* = 2.3 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (125 MHz) δ 9.72, 45.50, 61.02, 97.54, 120.53, 122.36, 126.04, 127.44, 134.86, 138.99, 144.32, 158.99; MS (EI) *m/z* 250 (M$^+$, 18), 207 (100). Anal. Calcd for $C_{13}H_{15}ClN_2O$: C, 62.28; H, 6.03; N, 11.17. Found: C, 62.23; H, 6.02; N, 10.96.

(*Z*)-7-Chloro-2-(dimethylamino)methyl-4-propylidene-4*H*-3,1-benzoxazine (2h): a colorless oil; R_f 0.44 (Et_2O); IR (neat) 1668, 1641 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.05 (t, *J* = 7.3 Hz, 3H), 2.22 (quint, *J* = 7.3 Hz, 2H), 2.41 (s, 6H), 3.25 (s, 2H), 5.15 (t, *J* = 7.3 Hz, 1H), 7.09 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.21 (d, *J* = 2.2 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz) δ 13.92, 17.77, 45.48, 61.01, 105.06, 120.46, 122.47, 126.04, 127.44, 134.92, 139.15, 143.23, 159.03; MS (CI) *m/z* 265 [(M+1)$^+$, 100]. Anal. Calcd for $C_{14}H_{17}ClN_2O$: C, 63.51; H, 6.47; N, 10.58. Found: C, 63.27; H, 6.56; N, 10.48.

7-Chloro-2-(dimethylamino)methyl-4-(1-methylethylidene)-4*H*-3,1-benzoxazine (2i): a colorless oil; R_f 0.26 (2:1:1 AcOEt–hexane–C_6H_6); IR (neat) 1662, 1634 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.87 (s, 3H), 1.95 (s, 3H), 2.40 (s, 6H), 3.25 (s, 2H), 7.14 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.22 (d, *J* = 2.3 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 1H); MS (EI) *m/z* 264 (M$^+$, 30), 221 (100). Anal. Calcd for $C_{14}H_{17}ClN_2O$: C, 63.51; H, 6.47; N, 10.58. Found: C, 63.50; H, 6.50; N, 10.29.

(*Z*)-2-(Dimethylamino)methyl-4-ethylidene-6,7-dimethoxy-4*H*-3,1-benzoxazine (2j): a pale-yellow solid; mp 74–76 °C (hexane–Et_2O); IR (KBr) 1674, 1649, 1611 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.74 (d, *J* =

7.3 Hz, 3H), 2.42 (s, 6H), 3.26 (s, 2H), 3.86 (s, 3H), 3.88 (s, 3H), 5.01 (q, J = 7.3 Hz, 1H), 6.76 (s, 1H), 6.79 (s, 1H); MS (EI) *m/z* 276 (M^+, 52), 233 (100). Anal. Calcd for $C_{15}H_{20}N_2O_3$: C, 65.20; H, 7.30; N, 10.14. Found: C, 65.20; H, 7.36; N, 9.87.

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