HETEROCYCLES, Vol. 81, No. 3, 2010, pp. 699 - 705. © The Japan Institute of Heterocyclic Chemistry
Received, 4th November, 2009, Accepted, 24th December, 2009, Published online, 28th December, 2009
DOI: 10.3987/COM-09-11869

SYNTHESIS OF 1,2-DIHYDRO-3-BENZOXEPINS BY THE REACTION OF 2-LITHIO-β-METHOXYSTYRENES WITH EPOXIDES FOLLOWED BY HYDRIODIC ACID CATALYZED CYCLIZATION

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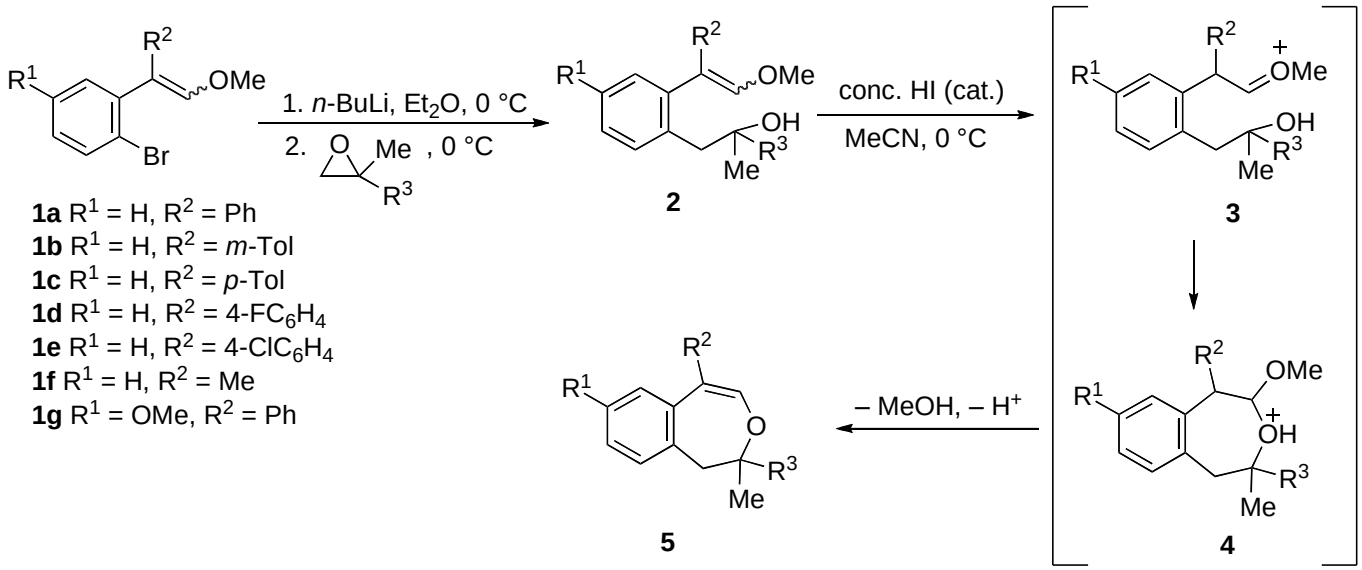
Abstract – 5-Substituted 1,2-dihydro-3-benzoxepins can be prepared in reasonable overall yields from α-substituted 2-bromo-β-methoxystyrenes. Thus, the reaction of α-substituted 2-lithio-β-methoxystyrenes, generated by the bromine-lithium exchange between α-substituted 2-bromo-β-methoxystyrenes and butyllithium, with epoxides gives the corresponding 2-(methoxyvinyl)phenethyl alcohols. These undergo cyclization with a loss of methanol on treatment with a catalytic amount of hydriodic acid to give the desired products.

In previous papers, we reported that 2-lithio-β-methoxystyrene derivatives were versatile intermediates for the preparation of mainly heterocyclic compounds.[1] We first demonstrated that the reaction of these lithium compounds with various nitriles gives directly isoquinoline derivatives through a successive addition-substitution sequence.[1a] Subsequently, we found that isochromene,[1b] 2-methoxyindene,[1c] isoquinolin-1(2*H*)-one,[1d] and isothiochroman derivatives[1e] could be obtained by the reactions with other electrophiles, such as carbonyl compounds,[1b,c] isocyanates,[1d] and isothiocyanates,[1e] followed by hydriodic acid-catalyzed or -mediated cyclization of the resultant corresponding adducts, respectively. As a continuation of these studies, we envisaged that the reaction of 2-lithio-β-methoxystyrene derivatives with epoxides, followed by a similar cyclization with hydriodic acid should give 1,2-dihydro-3-benzoxepin derivatives. We wish to report here that the reaction of α-substituted 2-lithio-β-methoxystyrene derivatives with epoxides, such as isobutene oxide and propylene oxide, gave 1-[2-(2-methoxyvinyl)phenyl]propan-2-ol derivatives (**2**), which on treatment with a catalytic amount of

hydriodic acid to give 5-substituted 1,2-dihydro-3-benzoxepins (**5**) in reasonable yields. The previously synthesized compounds having this skeleton are ethyl 2-(7,8-dimethoxy-1,2-dihydro-3-benzoxepin-5-yl)acetate[2] and 6,9-diiodo-1,2-dihydro-3-benzoxepin.[3]

Our two-step synthesis of 1,2-dihydro-3-benzoxepin derivatives (**5**) from 2-bromo-β-methoxystyrene derivatives (**1**) was conducted as illustrated in Scheme 1. Thus, treatment of **1** with butyllithium in diethyl ether at 0 ˚C generated 2-lithio-β-methoxystyrene derivatives, which were then treated with epoxides, such as isobutene oxide and propylene oxide. The attack of these lithium compounds on these epoxides proceeded relative slowly (about 1 h) to produce the 1-[2-(2-methoxyvinyl)phenyl]propan-2-ol derivatives (**2**) after aqueous workup. Unfortunately, the reaction of 2-lithio-(β-methoxy-α-phenyl)styrene, derived from **1a**, with styrene oxide gave an intractable mixtures of products, though the reason for this is not clear yet.



Scheme 1

Table 1. Preparation of 1,2-Dihydro-3-benzoxepin Derivatives (**5**)

Entry	**1**	R^3 in epoxide	**2** (Yield/%;[a] *E*:*Z*[b])	**5** (Yield/%)[a]
1	**1a**	Me	**2a** (65; 5:5)	**5a** (60)
2	**1a**	H	**2b** (55; 3:7)	**5b** (42)
3	**1b**	Me	**2c** (57; 5:5)	**5c** (57)
4	**1b**	H	**2d** (58; 4:6)	**5d** (45)
5	**1c**	Me	**2e** (57; 5:5)	**5e** (54)
6	**1d**	Me	**2f** (63; 4:6)	**5f** (54)
7	**1e**	Me	**2g** (58; 4:6)	**5g** (60)
8	**1f**	Me	**2h** (58; 5:5)	**5h** (52)
9	**1f**	H	**2i** (59; 6:4)	**5i** (46)
10	**1g**	Me	**2j** (65; 4:6)	**5j** (61)

[a]Yields of isolated, purified products. [b]Approximate values.

These methoxyvinyl alcohols (**2**) thus obtained were treated with a catalytic amount of hydriodic acid in acetonitrile at 0 ˚C. The starting materials were consumed immediately as expected, and the desired products (**5**) were obtained, via intermediates (**3**) and (**4**), after the usual workup and subsequent purification by preparative TLC on silica gel. The results of the preparation of **5** from **1**, via **2**, are summarized in Table 1, which indicates that the yields of the both products (**2**) and (**5**) are generally moderate to fair. The cyclization products from the respective adducts of **1** with propylene oxide (**5b**, **5d**, and **5h**) were obtained in somewhat lower yields than those from **1** with isobutene oxide, though the reason for this is difficult to explain at the present time. The attempted cyclization of the adduct of **1a** with 1,2-epoxy-3-methoxypropane gave a poor result. When the adduct was subjected to similar cyclization conditions, a complex mixture of products was obtained. Not so high yields in the cyclization step forming **5** may be attributable to the liability of the methoxyvinyl moiety toward oligomerization under such acidic conditions. A similar explanation has been given previously in the preparation of 4-substituted isochromenes.[1b]

In conclusion, we have demonstrated the first general construction of 1,2-dihydro-3-benzoxepin derivatives. The present method may find some value in synthesis; the ready availability of the starting materials and simplicity of operations combine to make the present method useful. Further studies to utilize 2-lithio-β-methoxystyrene intermediates for the construction of rare or useful heterocyclic systems are in progress.

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. Low-resolution MS spectra 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-Bromo-β-methoxystyrenes (**1**) were prepared by a previously reported our procedure.[1] All other chemicals used in this study were commercially available.

Typical Procedure for the Preparation of 1-[2-(2-Methoxyvinyl)phenyl]propan-2-ol Derivatives (2). 1-[2-(2-Methoxy-1-phenylethenyl)phenyl]-2-methylpropan-2-ol (2a). To a stirred solution of **1a** (0.27 g, 0.92 mmol) in Et_2O (6 mL) at 0 ˚C was added dropwise *n*-BuLi (1.6M in hexane; 0.92 mmol). After 1 h, 2,2-dimethyloxiran (66 mg, 0.92 mmol) was added and stirring was continued for an additional 1 h.

The mixture was quenched with saturated aqueous NH_4Cl (15 mL) and extracted with Et_2O three times (10 mL each). The combined extracts were dried over anhydrous Na_2SO_4 and evaporated. The residue was purified by preparative TLC on silica gel to afford **2a** (0.16 g, 65%): a pale-yellow oil; a mixture of stereoisomers (*E*:*Z* = *ca*. 5:5); R_f 0.13 (1:5 AcOEt–hexane); IR (neat) 3427, 1633 cm^{-1}; ^1H NMR (500 MHz) δ 1.10 (3H, s), 1.15 (3H, s), 1.48 (0.5H, s), 1.83 (0.5H, s), 2.56 (1H, s), 2.57 (1H, s), 3.70 (1.5H, s), 3.77 (1.5H, s), 6.25 (0.5H, s), 6.67 (0.5H, s), 7.09–7.37 (9H, m). Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found: C, 80.73; H, 8.01.

1-[2-(2-Methoxy-1-phenylethenyl)phenyl]propan-2-ol (2b): a pale-yellow oil; a mixture of stereoisomers (*E*:*Z* = *ca*. 3:7); R_f 0.21 (1:4 AcOEt–hexane); IR (meat) 3404, 1636 cm^{-1}; ^1H NMR (500 MHz) δ 1.06 (0.9H, d, *J* = 6.0 Hz), 1.15 (2.1H, d, *J* = 6.0 Hz), 1.30 (0.3H, d, *J* = 4.1 Hz), 1.78 (0.7H, br s), 2.48 (0.3H, dd, *J* = 13.7, 8.2 Hz), 2.51 (0.7H, dd, *J* = 13.7, 8.9 Hz), 2.57 (0.3H, dd, *J* = 13.7, 4.6 Hz), 2.62 (0.7H, dd, *J* = 13.7, 3.7 Hz), 3.71 (2.1H, s), 3.78 (0.9H, s), 3.78–3.85 (0.3H, m), 3.91–3.96 (0.7H, m), 6.22 (0.3H, s), 6.70 (0.7H, s), 7.10–7.36 (9H, m). Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.49; H, 7.81.

2-Methyl-1-{2-[1-(3-Methylphenyl)-2-methoxyethenyl]phenyl}propan-2-ol (2c): a pale-yellow oil; a mixture of stereoisomers (*E*:*Z* = *ca*. 5:5); R_f 0.21 (1:7 AcOEt–hexane); IR (neat) 3418, 1634 cm^{-1}; ^1H NMR (500 MHz) δ 1.11 (3H, s), 1.16 (3H, s), 1.51 (0.5H, s), 1.87 (0.5H, s), 2.28 (3H, s), 2.57 (2H, s), 3.70 (1.5H, s), 3.77 (1.5H, s), 6.22 (0.5H, s), 6.66 (0.5H, s), 6.87 (1H, d, *J* = 7.8 Hz), 6.93–6.99 (1.5H, m), 7.10–7.17 (2H, m), 7.24–7.34 (3.5H, m). Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 81.87; H, 7.38.

1-{2-[1-(3-Methylphenyl)-2-methoxyethenyl]phenyl}propan-2-ol (2d): a pale-yellow oil; a mixture of stereoisomers (*E*:*Z* = *ca*. 4:6); R_f 0.21 (1:7 AcOEt–hexane); IR (neat) 3403, 1634 cm^{-1}; ^1H NMR (500 MHz) δ 1.07 (1.2H, d, *J* = 7.3 Hz), 1.15 (1.8H, d, *J* = 7.3 Hz), 1.30 (0.4H, br s), 1.78 (0.6H, br s), 2.28 (3H, s), 2.44–2.65 (2H, m), 3.69 (1.8H, s), 3.77 (1.2H, s), 3.82–3.88 (0.4H, m), 3.91–3.97 (0.6H, m), 6.19 (0.4H, s), 6.68 (0.6H, s), 6.88 (1.2H, d, *J* = 7.8 Hz), 6.93–6.99 (1.6H, m), 7.10–7.31 (5.2H, m). Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found: C, 80.61; H, 7.74.

2-Methyl-1-{2-[1-(4-Methylphenyl)-2-methoxyethenyl]phenyl}propan-2-ol (2e): a pale-yellow oil; a mixture of stereoisomers (*E*:*Z* = *ca*. 5:5); R_f 0.29 (1:5 THF–hexane); IR (neat) 3441, 1634 cm^{-1}; ^1H NMR (500 MHz) δ 1.11 (3H, s), 1.15 (3H, s), 1.51 (0.5H, s), 1.87 (0.5H, s), 2.298 and 2.303 (combined 3H, 2s), 2.57 (2H, s), 3.69 (1.5H, s), 3.76 (1.5H, s), 6.21 (0.5H, s), 6.64 (0.5H, s), 6.98 (1H, d, *J* = 8.2 Hz), 7.04 (1H, d, *J* = 8.2 Hz), 7.06 (1H, d, *J* = 8.2 Hz), 7.23 (1H, d, *J* = 8.2 Hz), 7.25–7.33 (4H, m). Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 81.00; H, 8.29.

1-{2-[1-(4-Fluorophenyl)-2-methoxyethenyl]phenyl}-2-methylpropan-2-ol (2f): a pale-yellow oil; a mixture of stereoisomers (*E*:*Z* = *ca*. 4:6); R_f 0.24 (1:6 AcOEt–hexane); IR (neat) 3389, 1637 cm^{-1}; ^1H NMR (500 MHz) δ 1.11 (2.4H, s), 1.16 (3.6H, s), 1.56 (0.4H, br s), 1.85 (0.6H, br s), 2.535 (1.2H, s),

2.542 (0.8H, s), 3.70 (1.8H, s), 3.78 (1.2H, s), 6.23 (0.4H, s), 6.61 (0.6H, s), 6.90–6.97 (2.8H, m), 7.05 (1.2H, dd, J = 8.7, 5.5 Hz), 7.20–7.37 (4H, m). Anal. Calcd for $C_{19}H_{21}FO_2$: C, 75.97; H, 7.05. Found: C, 75.75; H, 7.34.

1-{2-[1-(4-Chlorophenyl)-2-methoxyethenyl]phenyl}-2-methylpropan-2-ol (2g): a pale-yellow oil; a mixture of stereoisomers (*E*:*Z* = *ca*. 4:6); R_f 0.24 (1:5 AcOEt–hexane); IR (neat) 3410, 1635 cm^{-1}; ^1H NMR (500 MHz) δ 1.11 (2.4H, s), 1.15 (3.6H, s), 1.59 (0.4H, br s), 1.81 (0.6H, br s), 2.53 (2H, s), 3.71 (1.8H, s), 3.79 (1.2H, s), 6.25 (0.4H, s), 6.67 (0.6H, s), 7.02 (1.2H, d, J = 8.7 Hz), 7.18–7.35 (6.8H, m). Anal. Calcd for $C_{19}H_{21}ClO_2$: C, 72.03; H, 6.68. Found: C, 71.12; H, 6.63.

2-Methyl-1-[2-(2-methoxy-1-methylethenyl)phenyl]propan-2-ol (2h): a pale-yellow oil; a mixture of stereoisomers (*E*:*Z* = *ca*. 5:5); R_f 0.29 (1:5 THF–hexane); IR (neat) 3441, 1668 cm^{-1}; ^1H NMR (500 MHz) δ 1.19 (3H, s), 1.23 (3H, s), 1.54 (0.5H, s), 1.85 (1.5H, d, J = 1.4 Hz), 1.91 (1.5H, d, J = 1.4 Hz), 2.00 (0.5H, s), 2.80 (1H, s), 2.88 (1H, s), 3.53 (1.5H, s), 3.66 (1.5H, s), 5.94 (0.5H, q, J = 1.4 Hz), 5.99 (0.5H, q, J = 1.4 Hz), 7.11–7.32 (4H, m). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.28; H, 9.09.

1-[2-(2-Methoxy-1-methylethenyl)phenyl]propan-2-ol (2i): a colorless oil; a mixture of stereoisomers (*E*:*Z* = *ca*. 6:4); R_f 0.25 (1:5 AcOEt–hexane); IR (neat) 3418, 1668 cm^{-1}; ^1H NMR (400 MHz) δ 1.23 (1.2H, d, J = 7.3 Hz), 1.25 (1.8H, d, J = 7.3 Hz), 1.48 (0.6H, br s), 1.84 (1.2H, d, J = 1.5 Hz), 1.90 (1.8H, d, J = 1.5 Hz), 1.99 (0.4H, br s), 2.63–2.86 (2H, m), 3.52 (1.2H, s), 3.66 (1.8H, s), 4.00–4.07 (1H, m), 5.91 (0.6H, q, J = 1.5 Hz), 6.00 (0.4H, q, J = 1.5 Hz), 7.08–7.27 (4H, m). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.71; H, 8.72.

1-[4-Methoxy-2-(2-methoxy-1-phenylethenyl)phenyl]-2-methylpropan-2-ol (2j): a pale-yellow oil; a mixture of stereoisomers (*E*:*Z* = *ca*. 4:6); R_f 0.20 (1:5 AcOEt–hexane); IR (neat) 3453, 1634 cm^{-1}; ^1H NMR (500 MHz) δ 1.09 (3.6H, s), 1.14 (2.4H, s), 1.45 (0.4H, s), 1.84 (0.6H, s), 2.48 (1.2H, s), 2.49 (0.8H, s), 3.71 (1.8H, s), 3.78 (1.2H, s), 3.82 (1.8H, s), 3.83 (1.2H, s), 6.27 (0.4H, s), 6.67 (0.6H, s), 6.81 (0.4H, d, J = 2.7 Hz), 6.85–6.88 (1.6H, m), 7.11 (1H, d, J = 7.8 Hz), 7.15–7.17 (1H, m), 7.22–7.27 (3.2H, m), 7.36 (0.8H, d, J = 7.3 Hz). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 77.02; H, 7.72.

Typical Procedure for the Preparation of Dihydrobenzoxepine Derivatives (5). 2,2-Dimethyl-5-phenyl-1,2-dihydro-3-benzoxepin (5a). To a stirred solution of **2a** (0.16 g, 0.60 mmol) in MeCN (6 mL) at 0 ˚ C was added a drop of concentrated hydriodic acid. After 5 min, saturated aqueous $NaHCO_3$ (10 mL) was added, and MeCN was evaporated. The organic materials were extracted with Et_2O twice (15 mL each). The combined extracts were washed with brine, dried over anhydrous Na_2SO_4, and evaporated. The residue was purified by preparative TLC on silica gel to afford **5a** (89 mg, 60%): a pale-yellow oil; R_f 0.34 (1:30 AcOEt–hexane); IR (neat) 1607 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.31 (6H, s), 2.92 (2H, s), 6.72 (1H, s), 6.94 (1H, dd, J = 8.7, 1.8 Hz), 7.12–7.18 (3H, m), 7.27–7.34 (5H, m); ^{13}C NMR δ 27.83, 46.85, 87.51, 124.38, 126.10, 126.17, 126.77, 128.26, 128.91, 129.42, 129.55, 137.86,

137.99, 140.77, 142.94; MS (EI) *m/z* 250 (M^+, 59), 207 (71), 192 (100). Anal. Calcd for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.19; H, 7.21.

2-Methyl-5-phenyl-1,2-dihydro-3-benzoxepin (5b): a pale-yellow oil; R_f 0.47 (1:29 AcOEt–hexane); IR (neat) 1607 cm^{-1}; ^1H NMR (500 MHz) δ 1.36 (3H, d, *J* = 6.4 Hz), 3.01–3.08 (*2*H, m), 4.46–4.49 (1H. m), 6.62 (1H, s), 6.88 (1H, d, *J* = 7.3 Hz), 7.05–7.11 (3H, m), 7.26–7.34 (5H, m); ^{13}C NMR δ 21.80, 43.79, 79.73, 119.83, 125.83, 126.02, 126.58, 128.23, 128.64, 129.51, 130.17, 137.35, 138.93, 141.92, 143.96; MS (EI) *m/z* 236 (M^+, 92), 207 (100). Anal. Calcd for $C_{17}H_{16}O$: C, 86.40; H, 6.82. Found: C, 86.32; H, 7.05.

2,2-Dimethyl-5-(3-methylphenyl)-1,2-dihydro-3-benzoxepin (5c): a pale-yellow oil; R_f 0.41 (hexane); IR (neat) 1606 cm^{-1}; ^1H NMR (400 MHz) δ 1.30 (6H, s), 2.33 (3H, s), 2.91 (2H, s), 6.71 (1H, s), 6.95 (1H, dd, *J* = 6.4, 2.3 Hz), 7.07–7.11 (3H, m), 7.12–7.18 (3H, m), 7.22 (1H, dd, *J* = 8.2, 7.3 Hz); ^{13}C NMR δ 21.39, 27.79, 46.83, 87.61, 124.67, 126.05, 126.15, 126.63, 127.55, 128.15, 128.96, 129.38, 130.24, 137.83, 137.95, 137.98, 140.61, 142.73; MS (EI) *m/z* 264 (M^+, 100). Anal. Calcd for $C_{19}H_{20}O_2$: C, 86.32; H, 7.63. Found: C, 86.09; H, 7.85.

2-Methyl-5-(3-methylphenyl)-1,2-dihydro-3-benzoxepin (5d): a pale-yellow oil; R_f 0.48 (1:19 AcOEt–hexane); IR (neat) 1606 cm^{-1}; ^1H NMR (400 MHz) δ 1.35 (3H, d, *J* = 6.6 Hz), 2.34 (3H, s), 3.02–3.06 (2H, m), 4.44–4.51 (1H, s), 6.61 (1H, m), 6.89 (1H, d, *J* = 6.9 Hz), 7.05–7.12 (6H, m), 7.22 (1H, dd, *J* = 7.7, 6.9 Hz); ^{13}C NMR δ 21.39, 21.78, 43.75, 79.73, 119.92, 125.78, 126.00, 127.25, 127.34, 128.10, 128.61, 129.56, 130.90, 137.41, 137.79, 138.89, 141.78, 143.79; MS (EI) *m/z* 250 (M^+, 100). Anal. Calcd for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.26; H, 7.09.

2,2-Dimethyl-5-(4-methylphenyl)-1,2-dihydro-3-benzoxepin (5e): a white solid; mp 79–80 ˚C (hexane–THF); IR (KBr) 1607 cm^{-1}; ^1H NMR (400 MHz) δ 1.30 (6H, s), 2.37 (3H, s), 2.90 (2H, s), 6.71 (1H, s), 6.95 (1H, dd, *J* = 6.9, 2.2 Hz), 7.12–7.18 (7H, m); ^{13}C NMR δ 21.10, 27.77, 46.82, 87.77, 124.70, 126.05, 126.15 (two overlapped C's), 128.92, 128.98, 129.39, 136.49, 137.71 (two overlapped C's), 138.02, 142.47; MS (EI) *m/z* 264 (M^+, 100). Anal. Calcd for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.03; H, 7.54.

5-(4-Fluorophenyl)-2,2-dimethyl-1,2-dihydro-3-benzoxepin (5f): a pale-yellow oil; R_f 0.24 (hexane); IR (neat) 1606 cm^{-1}; ^1H NMR (500 MHz) δ 1.30 (6H, s), 2.92 (2H, s), 6.67 (1H, s), 6.89 (1H, dd, *J* = 8.2, 2.3 Hz), 7.02 (2H, t, *J* = 8.7 Hz), 7.13–7.18 (3H, m), 7.23 (2H, dd, *J* = 8.7, 5.5 Hz); MS (EI) *m/z* 268 (M^+, 100). Anal. Calcd for $C_{18}H_{17}FO$: C, 80.57; H, 6.39. Found: C, 80.48; H, 6.42.

5-(4-Chlorophenyl)-2,2-dimethyl-1,2-dihydro-3-benzoxepin (5g): a pale-yellow solid; mp 56–58 ˚C (hexane–Et_2O); IR (KBr) 1607 cm^{-1}; ^1H NMR (500 MHz) δ 1.29 (6H, s), 2.92 (2H, s), 6.68 (1H, s), 6.89 (1H, d, *J* = 8.2 Hz), 7.12–7.17 (3H, m), 7.20 (2H, d, *J* = 8.2 Hz), 7.29 (2H, d, *J* = 8.2 Hz); MS (EI) *m/z* 284 (M^+, 69), 241 (87), 226 (100). Anal. Calcd for $C_{18}H_{17}ClO$: C, 75.92; H, 6.02. Found: C, 75.63; H, 6.14.

2,2,5-Trimethyl-1,2-dihydro-3-benzoxepin (5h): a pale-yellow oil; R_f 0.49 (hexane); IR (neat) 1620 cm^{-1}; ^1H NMR (500 MHz) δ 1.23 (6H, s), 2.02 (2H, d, J = 1.4 Hz), 2.81 (3H, s), 6.47 (1H, s), 7.09 (1H, d, J = 7.3 Hz), 7.13 (1H, td, J = 7.3, 1.4 Hz), 7.26 (1H, ddd, J = 7.8, 7.3, 1.4 Hz), 7.30 (1H, dd, J = 7.8, 1.4 Hz); ^{13}C NMR δ 19.27, 27.71, 47.21, 84.40, 113.33, 125.57, 125.63, 126.33, 129.52, 137.16, 138.47, 140.52; MS (CI) *m/z* 189 [$(M+1)^+$, 100]. Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 83.04; H, 8.72.

2,5-Dimethyl-1,2-dihydro-3-benzoxepin (5i): a colorless oil; R_f 0.43 (hexane); IR (neat) 1622 cm^{-1}; ^1H NMR (500 MHz) δ 1.31 (3H, d, J = 6.4 Hz), 2.02 (3H, s), 2.92 (1H, dd, J = 15.1, 6.4 Hz), 2.96 (1H, d, J = 14.7 Hz), 4.31 (1H, quint, J = 6.4 Hz), 6.49 (1H, s), 7.05 (1H, d, J = 7.3 Hz), 7.10 (1H, t, J = 7.3 Hz), 7.23 (1H, dd, J = 7.8, 7.3 Hz), 7.31 (1H, d, J = 7.8 Hz)); ^{13}C NMR δ 20.43, 21.67, 44.20, 77.81, 109.12, 125.37, 126.22, 126.28, 128.68, 137.58, 138.43, 141.48; MS (CI) *m/z* 175 [$(M+1)^+$, 100]. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.93; H, 8.11.

7-Methoxy-2,2-dimethyl-5-phenyl-1,2-dihydro-3-benzoxepin (5j): a pale-yellow oil; R_f 0.68 (1:5 AcOEt–hexane); IR (neat) 1607 cm^{-1}; ^1H NMR (500 MHz) δ 1.29 (6H, s), 2.86 (2H, s), 3.65 (3H, s), 6.49 (1H, d, J = 2.7 Hz), 6.71 (1H, s), 6.72 (1H, dd, J = 8.2, 2.7 Hz), 7.08 (1H, d, J = 8.2 Hz), 7.27–7.34 (5H, m); ^{13}C NMR δ 27.70, 46.01, 55.18, 87.53, 111.79, 114.33, 124.41, 126.81, 128.27, 129.54, 130.30, 130.57, 138.96, 140.53, 143.20, 158.00; MS (EI) *m/z* 280 (M^+, 100). Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.18; H, 7.29.

ACKNOWLEDGEMENTS

We are grateful to Mrs. Miyuki Tanmatsu of this university for determining mass spectra and performing combustion analyses.

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