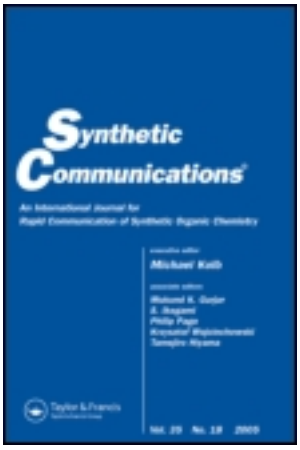

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Reductive Ring-Opening Reaction of 2,3-Epoxy-1,4-butanediones with $SbCl_3$-Bu_4NI in the Presence of $Na_2S_2O_3 \cdot 5H_2O$

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Reductive Ring-Opening Reaction of 2,3-Epoxy-1,4-butanediones with $SbCl_3$-Bu_4NI in the Presence of $Na_2S_2O_3 \cdot 5H_2O$

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Abstract: 1,4-Disubstituted 2,3-epoxy-1,4-butanediones were converted to 1,4-disubstituted 2-hydroxy-1,4-butanediones with $SbCl_3$-Bu_4NI in the presence of $Na_2S_2O_3 \cdot 5H_2O$. The ring opening of terminal epoxides can also be accomplished to afford the corresponding haloalcohol with $SbCl_3$ and tetrabutylammonium halides, Bu_4NX (X = Cl, Br, I) under the same reaction conditions.

Keywords: Antimony(III) chloride, 2,3-epoxy-1,4-butanedione, haloalcohol, tetrabutylammonium halide

Epoxides have been recognized as important intermediates in organic synthesis. In particular, the ring-opening of epoxides is a key reaction for the synthesis of marine natural products containing haloalcohol and polyalcohol moieties.[1] Therefore, regio- and stereoselective ring-opening reactions of epoxides were accomplished with various reagents and are still considered an intriguing study area.[1–4]

A variety of reductive reagents, such as $LiAlH_4$, $NaBH_4$, $LiBH_4$, BH_3, H_2/Raney Ni, and Li/NH_3, have been known to be useful for the reductive ring-opening of epoxides to alcohols.[2] Furthermore various metal halides, such as SmI_2, $InCl_3$, $InBr_3$, $CeCl_3$, $MgBr_2$, and $SmCl_3$, were used in the regio- and stereoselective ring-opening reaction of epoxides.[2,3]

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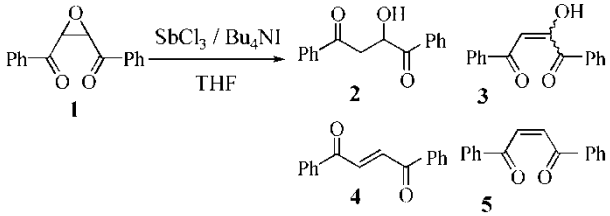
Selective azidolysis and conversion into haloalcohols of epoxides both were accomplished in the presence of quaternary ammonium halides Bu_4NX (X = F, Cl, Br, I).[4]

On the other hand, combinations of complex metal hydrides ($LiAlH_4$, $NaBH_4$) and antimony halides ($SbCl_3$, $SbBr_3$) were reported to be more effective for the conjugate reduction of 2-butene-1,4-diones and the reductive debromination of aromatic α-bromo ketones in comparison with those of complex metal hydrides and other metal halides ($AlCl_3$, $CuCl_2$, $FeCl_3$) in previous papers.[5] Antimony halides are more effective for organic synthesis and are easier to handle than other metal halides, such as $AlCl_3$ and $TiCl_4$. Moreover, the epoxidation of 2-butene-1,4-diones was also reported in a previous paper to be in the presence of a catalytic amount of BuN_4I.[6] Therefore, there has been much interest in the effect of the use of antimony(III) halide in the presence of quaternary ammonium halides for the reductive ring-opening reaction of 2,3-epoxy-1,4-butanediones.[7] In this article, we report the results of our studies concerning the ring-opening reaction of various epoxides with $SbCl_3$-Bu_4NX (X = Cl, Br, I).

The ring-opening reaction of *cis*-1,4-diphenyl-2,3-epoxy-1,4-butanedione (**1**), chosen as a representative 2,3-epoxy-1,4-butanedione for this study, with $SbCl_3$-Bu_4NI in various stoichiometric ratios was carried out in the presence of $Na_2S_2O_3 \cdot 5H_2O$. The results are summarized in Table 1. Epoxybutanedione **1** was mostly recovered unchanged at the molar ratio of **1**, Bu_4NI, $Na_2S_2O_3 \cdot 5H_2O$, and $SbCl_3$ (1 : 1 : 1.8 : 0.2, run 1). A mixture of hydroxydiketone **2** and hydroxyenedione **3** was obtained even in the presence of 2.0 molar equivalents of Bu_4NI over **1** (run 2). Because the yields of hydroxydiketones **2** and **3** were not satisfactory in the presence of a catalytic amount of $SbCl_3$, the reaction of epoxydiketone **1** was carried out with 1.0–2.0 molar equivalents of $SbCl_3$ over **1**. At less than 2.0 molar equivalents of $SbCl_3$ and Bu_4NI over **1**, hydroxydiketone **2** was not obtained in high yields (runs 3–5). At the 2.0 molar equivalents of $SbCl_3$ and Bu_4NI over **1**, epoxydiketone **1** was converted to hydroxydiketone **2** in good yield (run 6), whereas at less than equimolar of Bu_4NI over $SbCl_3$, hydroxydiketone **2** was not afforded in good yields (runs 7 and 8). Therefore, the reaction of epoxydiketone **1** with 3.0 molar equivalents of $SbCl_3$ and Bu_4NI over **1** was expected to give hydroxydiketone **2** in satisfactory yield. At 3.0 molar equivalents of $SbCl_3$ and Bu_4NI over **1**, hydroxydiketone **2** was obtained in the expected 90% yield (run 9). Furthermore, the yield of **2** was also satisfactory at excess molar equivalents of Bu_4NI over $SbCl_3$ (run 10). Subsequent experiments were carried out to clarify the effect of $SbCl_3$, Bu_4NI, and $Na_2S_2O_3 \cdot 5H_2O$. Epoxydiketone **1** was recovered unchanged only with 4.0 molar equivalents of $SbCl_3$ over **1** in the presence of $Na_2S_2O_3 \cdot 5H_2O$ (run 11). Epoxydiketone **1** was also recovered unchanged only with 4.0 molar equivalents of Bu_4NI over **1** in the presence of $Na_2S_2O_3 \cdot 5H_2O$ (run 12). In the absence of $Na_2S_2O_3 \cdot 5H_2O$, the yield of **2** with $SbCl_3$ and Bu_4NI was not fully satisfactory, accompanied by *cis*-enedione **5** (**2**: 43%, **5**: 49%). The reaction of epoxydiketone **1** even

Table 1. Reductive ring-opening reaction of *cis*-1,4-diphenyl-2,3-epoxy-1,4-butanedione **1** with $SbCl_3$-Bu_4NI in THF at 0–23°C[a]



Run	Molar ratio/**1**		Yield (%)[b]				
	$SbCl_3$	Bu_4NI	**2**	**3**	**4**	**5**	**1**
1	0.2	1.0	8	8	—	—	83
2	0.2	2.0	28	54	—	—	—
3	1.0	2.0	46	—	2	8	33
4	1.5	0.5	52	3	5	3	18
5	1.5	1.0	59	5	10	—	22
6	2.0	2.0	83	12	3	—	—
7	3.0	1.0	37	6	2	—	45
8	3.0	2.0	63	7	5	4	7
9	3.0	3.0	90	—	3	3	—
10	3.0	4.0	90	—	—	—	—
11	4.0	—	—	—	—	—	99
12	—	4.0	—	—	—	—	98

[a] **1**: 0.4 mmol; THF: 15 mL; in the presence of $Na_2S_2O_3 \cdot 5H_2O$ (0.72 mmol); time: 65 h.

[b] Isolated products were purified by column chromatography on silica gel. Yields were also determined by ^1H NMR analysis of crude products.

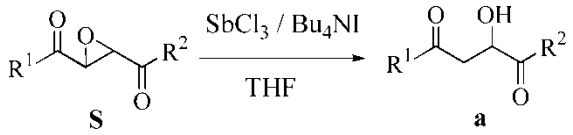
with $SbBr_3$-Bu_4NI instead of $SbCl_3$-Bu_4NI in the absence of $Na_2S_2O_3 \cdot 5H_2O$ did not afford hydroxydiketone **2** for 65 h at room temperature (recovered **1**: 60%, **5**: 30%). Hydroxydiketone **2** was predominantly obtained in the reductive ring opening of epoxydiketone **1** with $SbCl_3$-Bu_4NI in the presence of $Na_2S_2O_3 \cdot 5H_2O$ for 19 h at room temperature, but with a less satisfactory yield of **2** (64%) along with recovered **1** (31%). Accordingly, the optimum conditions for the reductive ring-opening of 2,3-epoxy-1,4-butanedione are as follows. The combination of $SbCl_3$ and Bu_4NI was found to be essential for reductive ring-opening of 2,3-epoxy-1,4-butanedione in the presence of $Na_2S_2O_3 \cdot 5H_2O$.[7] It needs about three molar equivalents of $SbCl_3$ and Bu_4NI over 2,3-epoxy-1,4-butanedione to give hydroxy-1,4-butanedione in high yield. Prolonged reaction time of more than 48–60 h is needed to obtain **2** in nearly quantitative yield at room temperature.

To clarify the effect of the combination of $SbCl_3$ and Bu_4NI in the presence of $Na_2S_2O_3 \cdot 5H_2O$ for the reductive ring opening of **1** to **2**, the reaction of epoxydiketone **1** was carried out with other metal halides and iodo compounds. Epoxydiketone **1** was recovered unchanged in greater than over 50% yields with other metal halides ($AlCl_3$, $CuCl_2$, $FeCl_3$)-Bu_4NI in the presence of $Na_2S_2O_3 \cdot 5H_2O$. Moreover, hydroxydiketone **2** was not afforded in good yields with the combination of $SbCl_3$ and I_2 or KI instead of Bu_4NI. Thus, the combination of $SbCl_3$ and Bu_4NI was found to be more effective for the reductive ring-opening reaction of epoxydiketone **1** to hydroxydiketone **2** than those of other metal halides—Bu_4NI or $SbCl_3$—other iodo reagents.

The reductive ring-opening reaction of various aromatic and aliphatic 2,3-epoxy-1,4-diones was carried out to elucidate the application of the combination $SbCl_3$ and Bu_4NI system. The results are shown in Table 2. The reaction of *trans*-1,4-diphenyl-2,3-epoxy-1,4-butanedione (**6**) and ethyl 3-benzoyl-2,3-epoxypropionate (**7**) also took place to give the corresponding 2-hydroxy-1,4-diones (**2**, **8**) in good yields under the same reaction conditions (runs 1 and 2). *trans*-2,3-Epoxy-1-phenyl-1,4-pentanedione (**9**) was similarly converted to a mixture of 3-hydroxy- and 2-hydroxy-1-phenyl-1,4-pentanediones (**10**, **11**, run 3). *trans*-3,4-Epoxy-2,5-decanedione (**12**) was also converted to a 1 : 1 mixture of 3-hydroxy- and 4-hydroxy-2,5-decanediones (**13**, **14**) in good yields (run 4). Thus, the combination of $SbCl_3$ and Bu_4NI was ascertained to be useful for the reductive ring opening of 2,3-epoxy-1,4-diones to hydroxy-1,4-diones.

To examine the limitations and chemoselectivity for the reductive ring opening of epoxides with the combination of $SbCl_3$ and quaternary ammonium halides (Bu_4NX: X = I, Br, Cl) system, the reaction of various epoxides was carried out under the same reaction conditions. The results are shown in Table 3. At first, the reaction of epoxydiketone **6** was carried out with $SbCl_3$-Bu_4NX (X = Br, Cl). Epoxydiketone **6** was recovered unchanged, respectively. Bu_4NI also turned out to be the most useful for reductive ring opening of **6** in quaternary ammonium halides Bu_4NX (X = I, Br, Cl, runs 1 and 2). On the other hand, unexpectedly, carvone oxide (**15**) was converted to the respective haloalcohols **16–18** with $SbCl_3$-Bu_4NX (X = I, Br, Cl, runs 3–5). These results suggested that the reductive ring-opening reaction did not occur in terminal epoxides such as carvone oxide even with $SbCl_3$-Bu_4NI. To show the transformation of terminal epoxides to haloalcohols with this method, the reaction of 10, 11-epoxy-1-undecanol (**19**) was examined under the same reaction conditions. Terminal epoxide **19** was converted to the corresponding haloalcohols **20–22** as expected (runs 6–8). Consequently, the $SbCl_3$-Bu_4NX (X = I, Br, Cl) systems were found to be useful and regioselective methods for converting terminal epoxides into respective haloalcohols. The reaction of aliphatic cyclic epoxides (**23**, **25**) was also carried out to examine the limitations and chemoselectivity of this system. α-Ionone oxide **23** was not converted to iodoalcohol **24** in high

Table 2. Reductive ring-opening reaction of *trans*-2,3-epoxy-1,4-butanedione with $SbCl_3$-Bu_4NI in THF at 0–23°C[a]



S **a**

Run	Substrates R^1	Substrates R^2	(**S**)	Products R^1	Products R^2	(**a**)	Yield/%[b]
1	Ph	Ph	**6**	Ph	Ph	**2**	90
2	Ph	OEt	**7**	Ph	OEt	**8**	96
3	Ph	Me	**9**	Ph	Me	**10**	55
				Me	Ph	**11***	27
4	C_5H_{12}	Me	**12**	C_5H_{12}	Me	**13**	41
				Me	C_5H_{12}	**14***	39

[a]**S**: 0.4 mmol; molar ratio: 1 : 3 : 3 (**S**/$SbCl_3$/Bu_4NI); THF: 15 mL; in the presence of $Na_2S_2O_3 \cdot 5H_2O$ (0.72 mmol); time: 65 h.

[b]Isolated products were purified by column chromatography on silica gel. Yields were also determined by ^1H NMR analysis of crude products.

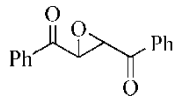
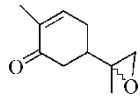
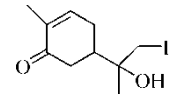
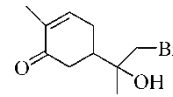
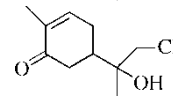
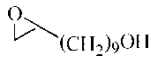
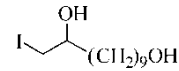
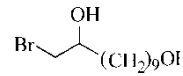
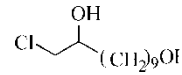
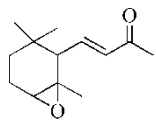
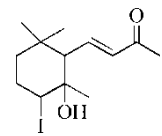
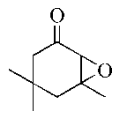
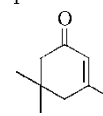
*2-Hydroxy-1-phenyl-1,4-pentanedione (**11**): $R_f = 0.41$ ($CH_3CO_2Et/CHCl_3$, 1 : 3). IR (neat, cm^{-1}) 3420, 1717, 1686, 1599, 1580, 1450, 1404, 1361, 1261, 1216, 1181, 1100, 1038, 1004, 988, 936, 758. ^1H NMR ($CDCl_3$) δ 2.25 (3H, s), 2.76 (1H, dd, $J = 17.5$, 7.4 Hz), 2.88 (1H, dd, $J = 17.5$, 3.5 Hz), 5.45 (1H, dd, $J = 7.4$, 3.5 Hz), 7.45–7.64 (3H, m), 7.91–7.97 (2H, m). ^{13}C NMR ($CDCl_3$) δ 30.99, 48.12, 69.99, 128.69, 128.87, 133.35, 133.94, 200.35, 205.80.

4-Hydroxy-2,5-decanedione (**14**): $R_f = 0.48$ ($CH_3CO_2Et/CHCl_3$, 1 : 3). IR (neat, cm^{-1}) 3414, 2960, 2934, 2874, 1717, 1460, 1406, 1365, 1247, 1172, 1112, 1073, 1038, 959. ^1H NMR ($CDCl_3$) δ 0.88 (3H, t, $J = 7.2$ Hz), 2.22 (3H, s), 2.85 (1H, dd, $J = 13.5$, 5.9 Hz), 2.95 (1H, dd, $J = 13.5$, 4.1 Hz), 4.35 (1H, dd, $J = 5.9$, 4.1 Hz).

yield (run 9), whereas the reaction of isophorone oxide **25** with $SbCl_3$-Bu_4NI took place to give isophorone **26** unexpectedly (run 10). These results sufficiently accounted for the regioselective ring opening of terminal epoxides to haloalcohols with $SbCl_3$-Bu_4NX (X = I, Br, Cl).

In conclusion, the $SbCl_3$-Bu_4NI system in the presence of $Na_2S_2O_3 \cdot 5H_2O$ provided an alternative procedure for reductive ring opening of 2,3-epoxy-1,4-butanediones to hydroxy-1,4-butanediones chemoselectively. The $SbCl_3$-Bu_4NX (X = I, Br, Cl) systems were also useful and [regioselective for the ring opening of terminal epoxides to the respective haloalcohols under the same reaction conditions].

Table 3. Ring-opening reaction of epoxides with $SbCl_3$-Bu_4NX in THF at 0–23°C[a]

Run	Substrates	(**S**)	Bu_4NX[b]	Products	Yields/%[c]
1		**6**	B	Recovered	**6**/85
2		**6**	C	Recovered	**6**/88
3		**15**	A		**16**/66
4		**15**	B		**17**/78
5		**15**	C		**18**/90
6		**19**	A		**20**/65
7		**19**	B		**21**/82
8		**19**	C		**22**/84
9		**23**	A		**24***/40[d]
10		**25**	A		**26**/77[e]

[a]**S**: 0.4 mmol; molar ratio: 1 : 3 : 3 (**S**/$SbCl_3$/Bu_4NX); THF: 15 mL; in the presence of $Na_2S_2O_3 \cdot 5H_2O$ (0.72 mmol); time: 65 h.

[b]A = Bu_4NI, B = Bu_4NBr, C = Bu_4NCl.

[c]Isolated products were purified by column chromatography on silica gel. Yields were also determined by ^1H NMR analysis of crude products.

[d]Recovered **23**: 39%.

[e]Recovered **25**: 20%.

*Iodoalcohol (**24**): $R_f = 0.33$ ($CHCl_3$/EtOAc, 5 : 1). IR (neat, cm^{-1}) 3474, 2950, 2334, 1659, 1458, 1365, 1309, 1265, 1220, 1176, 1106, 1058, 990, 938, 853. ^1H NMR ($CDCl_3$) δ 0.89 (3H, s), 1.07 (3H, s), 1.38 (3H, s), 2.29 (3H, s), 1.41–1.43 (1H, m), 1.75–1.90 (2H, m), 2.24–2.38 (1H, m), 2.40 (1H, d, $J = 10.5$ Hz), 4.43 (1H, t, $J = 2.0$ Hz), 6.12 (1H, d, $J = 16.0$), 6.94 (1H, dd, $J = 16.0$, 10.5 Hz). ^{13}C NMR ($CDCl_3$) δ 23.14, 27.15, 28.77, 32.11, 33.64, 34.35, 36.94, 44.27, 52.95, 73.40, 134.75, 145.96, 198.36.

EXPERIMENTAL

IR spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-EX270 spectrometer, and the chemical shifts are given relative to the internal $SiMe_4$ standard. MS spectra were run on a Bruker Daltonics–APEX III and a JEOL-HX110.

General Procedure for the Synthesis of 2,3-Epoxy-1,4-butanedione[6]

To a solution of 2-butene-1,4-dione (1 mmol) and Bu_4NI (0.1 mmol) in THF (10 mL) at 0°C was added dropwise 30% aq. H_2O_2 (5–10 mmol) dissolved in THF (3 mL). After stirring for 20–36 h at 0–23°C, the reaction mixture was poured into 0.5 M of aq. KI. The resulting mixture was treated with 0.5 M of aq. $Na_2S_2O_3$ and extracted with ethyl acetate. The organic layer was washed with 0.5 M of aq. $Na_2S_2O_3$ and successively saturated aq. NaCl and dried by $MgSO_4$. After removal of solvent in vacuo, the residue was purified by recrystallization or column chromatography on silica gel (Wakogel C-200) with CCl_4 and $CHCl_3$ (1 : 1, v/v). Epoxydiketones were obtained in 56–91% yields.

Typical Procedure for the Ring Opening of Epoxide

To a solution of $SbCl_3$ (273 mg, 1.2 mmol), Bu_4NI (442 mg, 1.2 mmol) and $Na_2S_2O_3 \cdot 5H_2O$ (178 mg, 0.72 mmol) in THF (12 mL) at 0°C, 1,4-diphenyl-2,3-epoxy-1,4-butanedione **1** (100 mg, 0.4 mmol) in THF (3 mL) was added. The reaction mixture was treated with 1.0 M of aq. $NaHCO_3$ after stirring for 64 h at temperatures between 0°C and rt and extracted with ethyl acetate. The organic layer was washed with 0.5 M of aq. $Na_2S_2O_3$ and successively saturated aq. NaCl and dried over $MgSO_4$. After removal of the solvent in vacuo, the residue was purified by column chromatography on silica gel (Wakogel C-200) with CCl_4 and $CHCl_3$ (1 : 1, v/v). Hydroxydiketone **2** (91 mg, 0.36 mmol) was obtained in 90% yield.

2-Hydroxy-1,4-diphenyl-1,4-butanedione (**2**). Mp 92–93°C. $R_f = 0.25$ ($CHCl_3$). IR (KBr, cm^{-1}) 3406, 1682, 1599, 1448, 1325, 1305, 1203, 1108, 1048, 1009, 754. ^{1}H NMR ($CDCl_3$) δ 3.36 (1H, dd, $J = 16.2$, 5.4 Hz), 3.44 (1H, dd, $J = 16.2$, 6.0 Hz), 5.67 (1H, dd, $J = 6.0$, 5.4 Hz), 7.26–7.63 (6H, m), 7.91–8.01 (4H, m). ^{13}C NMR ($CDCl_3$) δ 43.50, 70.06, 128.26, 128.62, 128.67, 128.87, 133.51, 133.60, 133.87, 136.62, 197.14, 200.68. Anal. calcd. for $C_{16}H_{14}O_3$ C, 75.57; H, 5.55. Found: C, 75.48; H, 5.60.

Ethyl 2-hydoxy-4-oxo-4-phenylbutanoate (**8**). $R_f = 0.17$ ($CHCl_3$). IR (neat, cm^{-1}) 3446, 3066, 2984, 2914, 1742, 1686, 1599, 1580, 1450, 1369, 1274, 1214, 1102, 1042, 1002, 936, 864, 758. ^{1}H NMR ($CDCl_3$) δ 1.29 (3H, t, $J = 7.2$ Hz), 3.45 (1H, dd, $J = 17.0$, 5.9 Hz), 3.54 (1H, dd, $J = 17.0$,

4.0 Hz), 4.26 (2H, q, $J = 7.2$ Hz), 4.66 (1H, dd, $J = 5.9$, 4.0 Hz), 7.43–7.62 (3H, m), 7.93–7.97 (2H, m). ^{13}C NMR ($CDCl_3$) δ 14.03, 42.12, 61.76, 67.15, 128.10, 128.62, 133.51, 136.38, 173.71, 197.44. HR-ESI-MS $[M + Na]^+$ m/z 245.0789 (calcd. for $C_{12}H_{14}O_4Na$: 245.0784).

3-Hydroxy-1-phenyl-1,4-pentanedione (**10**). $R_f = 0.41$ (CH_3CO_2Et/$CHCl_3$, 1 : 3). IR (neat, cm^{-1}) 3420, 1717, 1686, 1599, 1580, 1450, 1404, 1361, 1261, 1216, 1181, 1100, 1038, 1004, 988, 936, 758. ^{1}H NMR ($CDCl_3$) δ 2.33 (3H, s), 3.39 (1H, dd, $J = 17.5$, 5.9 Hz), 3.56 (1H, dd, $J = 17.5$, 3.5 Hz), 4.52 (1H, dd, $J = 5.9$, 3.5 Hz), 7.45–7.64 (3H, m), 7.91–7.97 (2H, m). ^{13}C NMR ($CDCl_3$) δ 25.55, 41.58, 73.85, 128.23, 128.60, 133.74, 136.28, 198.29, 209.57. Anal. calcd. for $C_{11}H_{12}O_3$; C, 68.73; H, 6.29. Found: C, 68.65; H, 6.40.

3-Hydroxy-2,5-decanedione (**13**). $R_f = 0.48$ ($CH_3CO_2Et/CHCl_3$, 1 : 3). IR (neat, cm^{-1}) 3414, 2960, 2934, 2874, 1717, 1460, 1406, 1365, 1247, 1172, 1112, 1073, 1038, 959. ^{1}H NMR ($CDCl_3$) δ 0.88 (3H, t, $J = 7.2$ Hz), 2.26 (3H,s), 2.45 (1H, dd, $J = 13.5$, 5.9 Hz), 2.55 (1H, dd, $J = 13.5$, 4.1 Hz), 4.00 (1H, dd, $J = 5.9$, 4.1 Hz). Anal. calcd. for $C_{10}H_{18}O_3$: 64.49; H, 9.74. Found: C, 64.33; H, 9.95.

Iodoalcohol (**16**). $R_f = 0.11$ ($CHCl_3$). IR (neat, cm^{-1}) 3438, 2976, 2924, 2898, 1663, 1452, 1435, 1417, 1373, 1305, 1259, 1189, 1104, 1058, 1009, 957, 907, 845, 803, 754, 714. ^{1}H NMR ($CDCl_3$) δ 1.34 (3H, s), 1.78 (3H, s), 2.24–2.75 (5H, m), 3.36 (1H, dd, $J = 10.8$, 2.7 Hz), 3.42 (1H, dd, $J = 10.8$, 3.5 Hz), 6.80 (1H, m). ^{13}C NMR ($CDCl_3$) δ15.52, 20.52, 23.70, 26.50, 39.57, 42.91, 71.21, 135.41, 144.07, 199.15. HR-ESI-MS m/z 317.0012 $[M + Na]^+$ (calcd. for $C_{10}H_{15}O_2I$ Na: 317.0009).

Bromoalcohol (**17**). $R_f = 0.50$ ($CH_3CO_2Et/CHCl_3$, 1 : 2). IR (neat, cm^{-1}) 3422, 2978, 2926, 1663, 1452, 1435, 1373, 1305, 1259, 1183, 1108, 1079, 1056, 1013, 961, 926, 907, 824, 801, 754. ^{1}H NMR ($CDCl_3$) δ 1.31 (3H, s), 1.78 (3H, s), 2.21–2.70 (5H, m), 3.45–3.57 (2H, m), 6.77 (1H, m). ^{13}C NMR ($CDCl_3$) δ15.51, 21.37, 27.24, 38.43, 41.99, 43.02, 71.96, 135.36, 145.03, 199.24. HR-ESI-MS m/z 269.0148 $[M + Na]^+$, 271.0129 $[(M + 2) + Na]^+$ (calcd. for $C_{10}H_{15}O_2Br$ Na: 269.0148).

Chloroalcohol (**18**). $R_f = 0.50$ ($CH_3CO_2Et/CHCl_3$, 1 : 2). IR (neat, cm^{-1}) 3442, 2978, 2928, 1663, 1452, 1435, 1373, 1307, 1259, 1183, 1154, 1108, 1058, 1013, 961, 930, 907, 828, 748, 714. ^{1}H NMR ($CDCl_3$) δ 1.27 (3H, s), 1.77 (3H,s), 2.18–2.67 (5H, m), 3.52–3.67 (2H, m), 6.77 (1H, m). ^{13}C NMR ($CDCl_3$) δ15.47, 21.87, 27.11, 39.19, 41.51, 52.29, 72.66, 135.14, 145.04, 199.63. HR-ESI-MS m/z 225.0654 $[M + Na]^+$, 227.0626 $[(M + 2) + Na]^+$ (calcd. for $C_{10}H_{15}O_2Cl$ Na: 225.0653).

Iodoalcohol (**20**). $R_f = 0.33$ ($CH_3CO_2Et/CHCl_3$, 1 : 3). IR (neat, cm^{-1}) 3332, 2928, 2858, 1460, 1417, 1185, 1056, 721.^{1}H NMR ($CDCl_3$) δ 1.13–1.55 (16H, m), 3.22 (1H, dd, $J = 10.8$, 6.4 Hz), 3.38 (1H, dd, $J = 10.8$, 5.4 Hz), 3.51 (1H, m), 3.62 (2H, t, $J = 6.7$ Hz). ^{13}C NMR ($CDCl_3$) δ16.49, 25.55, 25.62, 29.20, 29.27, 29.32, 32.65, 36.49, 62.89, 70.87. HR-ESI-MS m/z 337.0638 $[M + Na]^+$ (calcd. for $C_{11}H_{23}O_2I$ Na: 337.0636).

Bromoalcohol (**21**). $R_f = 0.32$ ($CH_3CO_2Et/CHCl_3$, 1 : 3). IR (neat, cm^{-1}) 3256, 2926, 2858, 1460, 1425, 1375, 1340, 1224, 1054, 721. ^1H NMR ($CDCl_3$) δ 1.30–1.57 (16H, m), 3.34–3.77 (5H, m). ^{13}C NMR ($CDCl_3$) δ 25.53, 25.68, 29.32, 29.40, 32.74, 35.07, 40.54, 62.98, 71.03. HR-ESI-MS m/z 289.0776 $[M + Na]^+$, 291.0756 $[(M + 2) + Na]^+$ (calcd. for $C_{11}H_{23}O_2Br$ Na: 289.0774).

Chloroalcohol (**22**). $R_f = 0.25$ ($CH_3CO_2Et/CHCl_3$, 1 : 3). IR (neat, cm^{-1}) 3302, 2930, 2858, 1464, 1056, 721. ^1H NMR ($CDCl_3$) δ 1.25–1.56 (16H, m), 3.44–3.79 (5H, m). ^{13}C NMR ($CDCl_3$) δ25.46, 25.68, 29.27, 29.34, 29.38, 29.43, 32.74, 34.19, 50.53, 63.02, 71.43. HR-ESI-MS m/z 245.1281 $[M + Na]^+$, 247.1251 $[(M + 2) + Na]^+$ (calcd. for $C_{11}H_{23}O_2Cl$ Na 245.1279).

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