# A Radical Clock for Reactions of Epoxy Derivatives Induced by Titanocene Chloride

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*Received 3 September 2008*

**Abstract:** A new radical clock based on pinene derivatives has been designed to measure the radical cyclization rate onto cyano and carbonyl groups and the radical elimination rate of OR and CN. In this system, the known rate constant of cyclobutylcarbinyl radical cleavage is used as the internal clock. At room temperature, the cyclization rate constants for 4-*exo* and 5-*exo* processes onto nitrile and aldehyde carbonyl groups are in the order of $10^7$ to $10^8$ $s^{-1}$. The radical elimination rate constants for CN, OH, OCHO, and OAc are in the order of $10^5$ to $10^8$ $s^{-1}$.

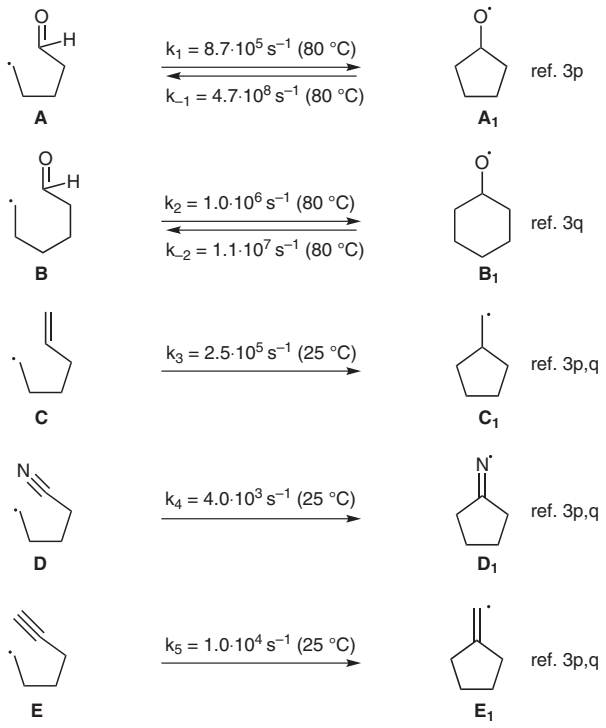
**Key words:** epoxides, titanium(III), radical clock, titanocene chloride, epoxynitriles, epoxyaldehydes, epoxyketones, epoxyesters

Radical reactions have become increasingly important in the last two decades,[1] and the knowledge of the rate constants of radical reactions is a crucial issue in mechanistic studies and synthetic applications.[2] Accordingly, standard methods for measuring the rates of radical reactions, such as electron spin resonance (ESR), laser flash photolysis and pulse radiolysis, have been extensively used.[2] Although direct methods are required for any kinetic scale, indirect competition methods have been developed to measure unknown rates. Radical clocks are used to describe a unimolecular radical reaction that is calibrated kinetically and, they can be applied in competition studies to time a particular reaction.[2] The kinetic method can now exceed the limits of picosecond laser-flash methods.[2]

Recently, the applications of radical methodology for the production of carbocycles in the synthesis of complex molecules have attracted much attention.[1] Carbonyl and cyano groups play an important role in organic chemistry. Radical cyclizations involving carbonyl and cyano groups have been studied from the synthetic and kinetic points of view.[3]

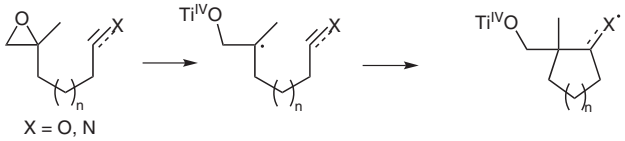
Scheme 1 shows the experimental rate constant for several related processes. The generation of the radicals for all these processes was done from alkyl halides with $Bu_3SnH$ and AIBN. As shown in Scheme 1, the ring closure of radical **A** or **B** is slower than the cleavage of $\mathbf{A_1}$ or $\mathbf{B_1}$. The last three processes are not reversible, and the latter two reactions are very slow.

Over the last ten years the attention of organic chemists has been drawn to the reactions of radicals generated from




**Scheme 1** Rate constants

epoxides with titanocene chloride.[4] However, no kinetic studies of this process have been carried out. In this paper we present a new radical clock to measure the rate of some radical reactions induced by titanocene, such as the cyclizations shown in Scheme 2.[5]

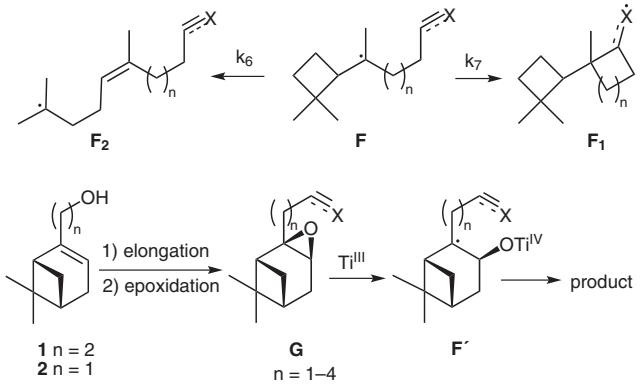



**Scheme 2** Radical cyclizations onto polar multiple bonds

Our radical clock consists of the irreversible cleavage of the cyclobutylcarbinyl radical.[6]

To check the kinetics of the radical cyclizations of aldehydes, ketones, and nitriles,[5] we decided to use intramolecular competition systems, such as the radical **F**, shown in Scheme 3, as our tools.

*SYNLETT* 2008, No. 20, pp 3208–3212
Advanced online publication: 26.11.2008
DOI: 10.1055/s-0028-1087410; Art ID: G29508ST



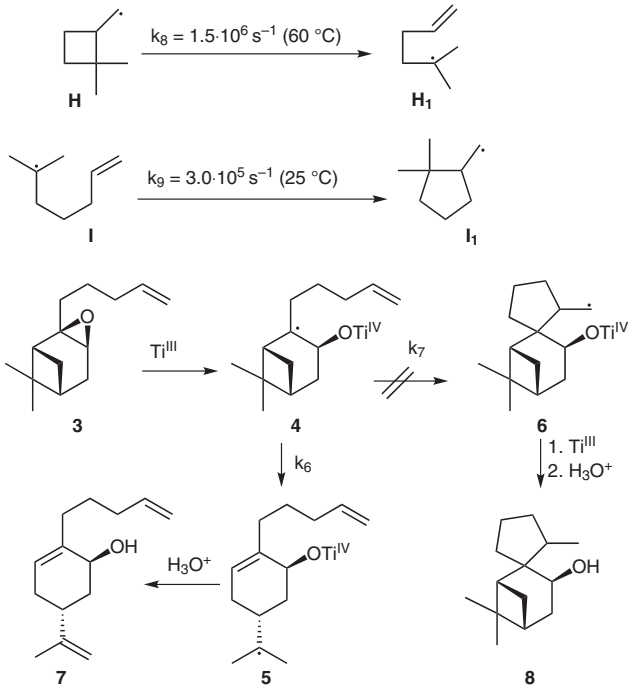

**Scheme 3** Intramolecular competition system

In **F**, the radical could be added to the polar multiple bond (aldehyde, ketone, nitrile) to give $\mathbf{F_1}$ or the cyclobutane could be cleaved to give $\mathbf{F_2}$. The ratio of the C≡X addition product $\mathbf{F_1}$, relative to the cleavage product $\mathbf{F_2}$, should reflect the ratio of the rate constants of the two processes: $k_6/k_7 = [\mathbf{F_2}]/[\mathbf{F_1}]$.

Our substrates **G**, the precursors of the radical **F′**, were prepared according to standard procedures from (1*R*)-(–)-nopol (**1**, n = 2) and (1*R*)-(–)-myrtenol (**2**, n = 1), two readily available terpenoids. These starting materials were selected because their hydroxyl function permits easy elongation of the chain and the incorporation of any functional group, and also owing to the strategic situation of the C=C double bond, which affords an epoxide at the correct site. In all cases, the epoxydation step was absolutely stereoselective and was *cis* with respect to the methylene bridge.[7] The homolytic cleavage of the oxirane ring in the above substrates with titanocene chloride would be totally regioselective in the direction towards the tertiary radical, as has been reported for trisubstituted epoxides.[4,5]

The rate constant for the cleavage of the radical cyclobutylcarbinyl model **H** has been reported[6] (Scheme 4). It should be possible to use this known cleavage system as an intramolecular radical clock to extrapolate the radical cyclization rate constants of aldehydes, ketones, and nitriles.

However, the radical **H** is not exactly the same as **F′**, generated by cleavage of the epoxy myrtenol substrates. In the case of **F′**, the radical is tertiary and the cyclobutane is inserted in a cyclohexane. These characteristics could modify the rate of the cyclobutane cleavage. To determine this cyclobutane-cleavage rate more accurately, we prepared epoxy alkene **3**. The internal radical clock would be the 5-*exo* cyclization $\mathbf{I} \rightarrow \mathbf{I_1}$: after treatment of **3** with $Ti^{III}$, the radical **4** would be obtained (Scheme 4). The competitive pathways are the cyclobutane cleavage to the tertiary radical **5** ($k_6$), which further evolves through a loss of a hydrogen atom to **7**, and the irreversible 5-*exo* cyclization onto C=C to the primary radical **6** ($k_7$), which is further reduced to the tricyclic alcohol **8**.

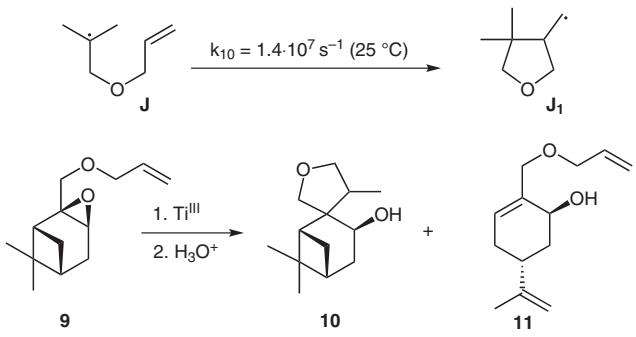



**Scheme 4** Radical reaction of epoxide **3** with $Ti^{III}$

Experimentally, the only product obtained in this reaction was the menthane derivative **7**.[8] This means that the rate constant $k_6$, of the cyclobutane cleavage of **4** is higher than that of the model $k_8$. Otherwise, the ratio of the expected compounds **7/8** would be 5:1 ($k_6/k_7$ = 5:1). To calculate the rate constant $k_6$, we used the faster radical clock $\mathbf{J} \rightarrow \mathbf{J_1}$ (Scheme 5).[2b]

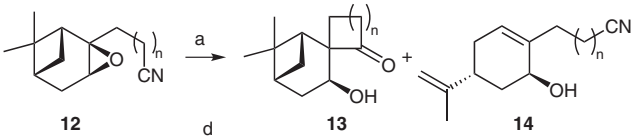
The reaction of **9** with $Ti^{III}$ gave a mixture of the cyclization product **10** and the cleavage product **11** at a ratio of 56:44, respectively.[8] Thus, the cyclobutane cleavage in substrate **9** was determined to be $k_6 = k_{10}\cdot[11]/[10] = 1.4\cdot10^7\ s^{-1}\cdot44/56 = 1.1\cdot10^7\ s^{-1}$. Henceforth, this rate constant was used as our internal radical clock to measure other radical reaction rates. The practical limits of this clock would be situated between $3\cdot10^5\ s^{-1}$ and $4\cdot10^8\ s^{-1}$; that is, 36 times below and above $1.1\cdot10^7\ s^{-1}$ ($k_6/k_{10}$).

**Radical cyclizations rates**: The reactions of the epoxy derivatives were performed by slow addition of a THF solution of titanocene chloride to a solution of the epoxy substrates at room temperature. The results for the




**Scheme 5** Radical reaction of epoxide **9** with $Ti^{III}$

**Table 1** Radical Cyclization Rates onto Nitrile[a]




12 d 13 14

| Entry | 12 | Yield of 13 (%) | Yield of 14 (%) | $k_{CN}/k_{cleav}$ | Extrapolated $k_{CN}$ |
|---|---|---|---|---|---|
| 1 | **12a** n = 1 | 12 | 67 | 0.18 | $0.2 \cdot 10^7$ |
| 2 | **12b** n = 2 | 42 | 11 | 3.82 | $4.2 \cdot 10^7$ |
| 3 | **12c** n = 3 | 0 | 76 | 0 | $<3 \cdot 10^5$ |

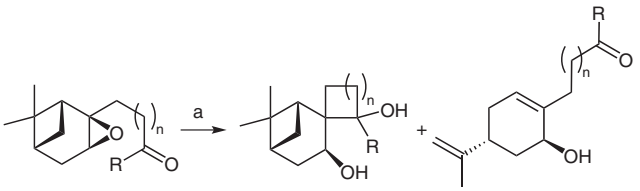
[a] Conditions: (a) 1. $Ti^{III}$, THF; 2. $H_3O^+$.

epoxynitriles are summarized in Table 1. The structures of **12**, **13**, and **14** were formulated on the basis of NMR data.[8]

The data from Table 1 indicate that 4-*exo* and 5-*exo* cyclizations onto nitrile are fast reactions and lie in the order of $10^7$ $s^{-1}$, while 6-*exo* cyclization is a slower process: $<10^5$ $s^{-1}$. The rate constant values found for 5-*exo* cyclization onto nitrile in our reaction conditions are very different from the reported $k = 4 \cdot 10^3$ $s^{-1}$ (25 °C)[9] for the same cyclization induced by $Bu_3SnH$. The acceleration of the titanocene-induced cyclization must be due to a coordination of $Ti^{III}$ with the cyano group, which enhances the radical-acceptor character of the cyano group by lowering its LUMO.[5e]

The results for epoxycarbonyl compounds are summarized in Table 2.

**Table 2** Radical Cyclization Rates onto Carbonyl Group[a]




15 16 17

| Entry | 15 | Yield of 16 (%) | Yield of 17 (%) | Extrapolated $k_{CO}$ |
|---|---|---|---|---|
| 1 | **15a** n = 1, R = H | 78 | 0 | $>4 \cdot 10^8$ |
| 2 | **15b** n = 2, R = H | 73 | 0 | $>4 \cdot 10^8$ |
| 3 | **15c** n = 3, R = H | 0 | 76 | $<3 \cdot 10^5$ |
| 4 | **15d** n = 1, R = Me | 0 | 75 | $<3 \cdot 10^5$ |
| 5 | **15e** n = 2, R = Me | 0 | 75 | $<3 \cdot 10^5$ |

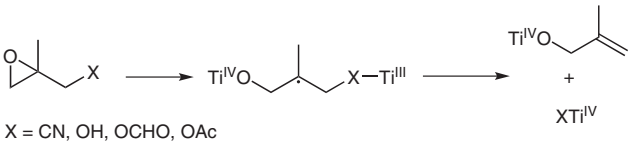
[a] Conditions: (a) 1. $Ti^{III}$, THF; 2. $H_3O^+$.

The data from Table 2 show that 4-*exo* and 5-*exo* cyclizations onto aldehyde carbonyl are very fast processes: lie above $4 \cdot 10^8$ $s^{-1}$ (25 °C). On the other hand, the 4-*exo* and 5-*exo* cyclizations onto ketone carbonyls are slow processes, like 6-*exo* cyclization onto the aldehyde carbonyl.

The rate constants extrapolated for 5-*exo* cyclization (Table 2, entry 2) are distant from those reported for the same reaction induced by $Bu_3SnH$ (see $k_1$, Scheme 1). The β-scission of the alkoxy radicals generated in the cyclization onto carbonyl, which occurred for the reactions induced by $Bu_3SnH$, does not take place with titanocene. As seen with cyano compounds, the coordination between the carbonyl group and $Ti^{III}$ should occur. The trapping rate of the alkoxy radical by $Ti^{III}$ should be faster than the β-scission (see $k_{-1}$, Scheme 1).

**Radical fragmentation rates**: It has been reported that radicals generated by homolytic cleavage of epoxides with titanocene afford alkenes through the elimination of certain atoms or functional groups, such as H, CN, OH, OCHO, and OAc, following the mechanism shown in Scheme 6.[10]

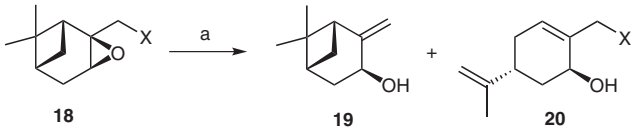
The kinetics of these fragmentation reactions corresponds to a radical reaction, as will be seen with our radical clock based on pinene derivatives.[5e]




**Scheme 6** Radical fragmentation

The substrates for the kinetic study were obtained from (1*S*)-(–)-α-pinene or from (1*R*)-(–)-myrtenol (**2**) by standard methods. The reactions of the epoxy derivatives were performed by slow addition of a THF solution of titanocene chloride to a solution of the epoxides. The results are summarized in Table 3.

**Table 3** Radical Elimination Rates[a]




18 19 20

| Entry | 18 | Yield of 19 (%) | Yield of 20 (%) | $k_{elim}/k_{cleav}$ | Extrapolated $k_{elim}$ |
|---|---|---|---|---|---|
| 1 | **18a** X = CN | 20 | 47 | 0.42 | $4.6 \cdot 10^6$ |
| 2 | **18b** X = OH | 90 | 0 | – | $>4 \cdot 10^8$ |
| 3 | **18c** X = OCHO | 25 | 45 | 0.55 | $5.7 \cdot 10^6$ |
| 4 | **18d** X = OAc | 13 | 62 | 0.24 | $2.2 \cdot 10^6$ |
| 5 | **18e** X = OBz | 0 | 73 | 0 | $<3 \cdot 10^5$ |

[a] Conditions: (a) 1. $Ti^{III}$, THF; 2. $H_3O^+$.

The data from Table 3 show that the fastest elimination corresponds to the hydroxyl group followed by the formate and cyano groups. It is interesting to note that, owing

to its kinetics, benzoate elimination is a slow reaction: $<10^5$ $s^{-1}$. An explanation for the rate of ester eliminations could be the stronger coordination of the oxygen carbonyl to $Ti^{III}$ passing from benzoate to formate. Using intramolecular competition experiments, we have determined the approximate rates of radical cyclizations to carbonyl and cyano groups and the radical elimination rates of CN, OH, OCHO, and OAc.

## Acknowledgment

Financial support for this work from the MCyT of Spain (PPQ2002-00290) (CTQ2005-05026/BQU) and the JCyL (SA079A06) is gratefully acknowledged. We also thank the MCyT of Spain and the Universidad de Salamanca for fellowships to R.R.C. and P.H.T.

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(8) **Reaction of Epoxides with $Cp_2TiCl$**
A mixture of $Cp_2TiCl_2$ (3.3 mmol) and Zn (6.60 mmol) in strictly deoxygenated THF (4 mL) was stirred at r.t. until the red solution turned green. In a separate flask, the epoxy compound (1 mmol) was dissolved in strictly deoxygenated THF (10 mL). The green $Ti^{III}$ solution was slowly added via cannula to the epoxide solution. After 30 min, an excess of sat. $NaH_2PO_4$ was added, and the mixture was stirred for 20 min. The product was extracted into $Et_2O$, washed with sat. $NaHCO_3$ and brine, dried ($Na_2SO_4$), and filtered. After removal of the solvent, the crude product was purified by flash chromatography.
Compound **10**: diastereomeric mixture (60:40). IR: 3408, 2923, 1462, 1053 $cm^{-1}$. MS (EI): *m/z* (%) = 192 (14) [$M^+$ – 18], 177 (7), 163 (3), 149 (12), 135 (17), 121 (16), 119 (25), 95 (31), 91 (82), 70 (65), 55 (100). HRMS (EI): *m/z* calcd for $C_{13}H_{22}O_2Na$ [$M^+$ + Na]: 233.1517; found: 233.1514. $^1H$ NMR (400 MHz, $CDCl_3$): δ (major isomer) = 0.94 (3 H, s), 1.10 (3 H, d, *J* = 7.2 Hz), 1.22 (3 H, s), 1.60–2.60 (7 H, m), 3.47 (1 H, dd, $J_1$ = 3.3 Hz, $J_2$ = 8.5 Hz), 3.51 (1 H, d, *J* = 9.1 Hz), 3.95 (1 H, dd, $J_1$ = 6.8 Hz, $J_2$ = 8.5 Hz), 4.22 (1 H, d, *J* = 9.1 Hz), 4.53 (1 H, dd, $J_1$ = 5.2 Hz, $J_2$ = 9.3 Hz) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 16.17 ($CH_3$), 23.83 ($CH_3$), 27.77 ($CH_3$), 30.66 ($CH_2$), 38.15 (C), 39.31 ($CH_2$), 40.14 (CH), 41.77 (CH), 51.50 (CH), 55.05 (C), 64.65 (CH), 72.86 ($CH_2$), 75.30 ($CH_2$) ppm. $^1H$ NMR (400 MHz, $CDCl_3$): δ (minor isomer) = 0.87 (3 H, d, *J* = 7.4 Hz), 0.88 (3 H, s), 1.21 (3 H, s), 1.60–2.90 (7 H, m), 3.31 (1 H, dd, $J_1$ = 3.7 Hz, $J_2$ = 8.4 Hz), 3.37 (1 H, d, *J* = 8.6 Hz), 3.77 (1 H, d, *J* = 8.6 Hz), 4.02 (1 H, dd, $J_1$ = 7.4 Hz, $J_2$ = 8.4 Hz), 4.28 (1 H, dd, $J_1$ = 5.3 Hz, $J_2$ = 9.3 Hz), ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 16.60 ($CH_3$), 23.91 ($CH_3$), 27.63 ($CH_3$), 30.51

($CH_2$), 36.37 (CH), 38.15 (C), 38.68 ($CH_2$), 39.46 (CH), 40.92 (CH), 55.32 (C), 72.69 (CH), 72.76 ($CH_2$), 79.34 ($CH_2$) ppm.

Compound **11**: IR: 3400, 1645 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 1.76 (3 H, s), 1.80–2.50 (5 H, m), 4.01 (1 H, m), 4.03 (2 H, s), 4.29 (1 H, s), 4.73 (1 H, s), 4.75 (1 H, s), 5.19 (1 H, d, *J* = 10.4 Hz), 5.27 (1 H, d, *J* = 15.6 Hz), 5.87 (1 H, br s), 5.89 (1 H, m) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 20.87 ($CH_3$), 30.86 ($CH_2$), 30.15 (CH), 35.57 ($CH_2$), 60.30 (CH), 71.38 ($CH_2$), 74.45 ($CH_2$), 109.03 ($CH_2$), 117.24 ($CH_2$), 129.49 (CH), 134.34 (CH), 134.94 (C), 149.01 (C) ppm. MS (EI): *m/z* (%) = 150 (22) [$M^+$ – 58], 135 (20), 131 (13), 108 (69), 93 (68), 91 (100), 68 (79), 55 (98). HRMS (EI): *m/z* calcd for $C_{13}H_{20}O_2Na$ [$M^+$ + Na]: 231.1355; found: 231.1353; $[\alpha]_D^{20}$ –49.2 (*c* 1.3, $CHCl_3$).

Compound **13a1**: IR: 3451, 2928, 2899, 1761, 1252, 1042 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.96 (3 H, s), 1.13 (1 H, d, *J* = 10.2 Hz), 1.21 (3 H, s), 1.64 (2 H, m), 1.94 (1 H, m), 2.24 (1 H, t, *J* = 5.7 Hz), 2.33 (1 H, m), 2.56 (2 H, m), 2.70 (1 H, m), 3.03 (1 H, m), 4.59 (1 H, dd, $J_1$ = 9.3 Hz, $J_2$ = 4.9 Hz) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 18.56 ($CH_2$), 23.35 ($CH_3$), 27.07 ($CH_3$), 29.82 ($CH_2$), 38.35 ($CH_2$), 38.53 (C), 40.44 (CH), 41.63 ($CH_2$), 50.24 (CH), 62.53 (CH), 75.80 (C), 212.49 (C) ppm. MS (EI): *m/z* (%) = 179 (2) [$M^+$ – 15], 161 (2), 134 (4), 133 (17), 119 (26), 105 (100), 91 (96), 77 (30), 67 (28), 55 (68). HRMS (EI): *m/z* calcd for $C_{12}H_{18}O_2Na$ [$M^+$ + Na]: 217.1199; found: 217.1206; $[\alpha]_D^{20}$ –10.1 (*c* 1.4, $CHCl_3$).

Compound **13a2**: IR: ν = 3451, 2928, 2894, 1765, 1217 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ = 0.87 (3 H, s), 1.20 (1 H, d, *J* = 10.1 Hz), 1.28 (3 H, s), 1.50–2.40 (6 H, m), 2.54 (1 H, m), 3.01 (2 H, t, *J* = 8.9 Hz), 4.38 (1 H, dd, $J_1$ = 9.1 Hz, $J_2$ = 3.7 Hz) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 22.65 ($CH_3$), 26.59 ($CH_3$), 27.16 ($CH_2$), 27.88 ($CH_2$), 39.16 ($CH_2$), 39.65 (C), 39.80 (CH), 42.98 ($CH_2$), 48.56 (CH), 53.40 (C), 70.61 (CH), 213.39 (C) ppm. MS (EI): *m/z* (%) = 179 (3) [$M^+$ – 15], 151 (3), 134 (6), 133 (24), 119 (26), 105 (100), 91 (80), 77 (40), 67 (42), 55 (89). HRMS (EI): *m/z* calcd for $C_{12}H_{18}O_2Na$ [$M^+$ + Na]: 217.1199; found: 217.1195; $[\alpha]_D^{20}$ +40.7. (*c* 1.9, $CHCl_3$).

Compound **14a**: IR: ν = 3455, 2920, 2249, 1645, 1441, 1217, 1053 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 1.62 (1 H, dt, $J_1$ = 4.0 Hz, $J_2$ = 13.3 Hz), 1.73 (3 H, s), 1.90 (4 H, m), 2.10–2.60 (4 H, m), 4.09 (1 H, br s), 4.72 (1 H, s), 4.75 (1 H, s), 5.73 (1 H, m) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 16.71 ($CH_2$), 20.82 ($CH_3$), 30.47 ($CH_2$), 30.81 ($CH_2$), 35.04 (CH), 36.85 ($CH_2$), 66.90 (CH), 109.37 ($CH_2$), 119.73 (C), 128.03 (CH), 134.77 (C), 148.52 (C) ppm. MS (EI): *m/z* (%) = 173 (6) [$M^+$ – 18], 158 (6), 131 (9), 117 (22), 105 (21), 91 (100), 77 (23), 65 (22), 51 (23); HRMS (EI): *m/z* calcd for $C_{12}H_{17}NONa$ [$M^+$ + Na]:214.1208; found: 214.1205.

Compound **16a1**: IR: ν = 3439, 2929, 1455, 1260, 1052 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.90 (3 H, s), 1.21 (3 H, s), 1.66 (4 H, m), 1.90 (1 H, m), 1.98 (1 H, t, *J* = 5.8 Hz), 2.10–2.60 (4 H, m), 3.93 (1 H, t, *J* = 6.1 Hz), 4.68 (1 H, dd, $J_1$ = 9.2 Hz, $J_2$ = 5.4 Hz) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 22.62 ($CH_2$), 23.16 ($CH_3$), 27.49 ($CH_3$), 27.85 ($CH_2$), 29.90 ($CH_2$), 38.35 ($CH_2$, C), 40.76 (CH), 53.12 (CH, C), 62.02 (CH), 74.68 (CH) ppm. MS (EI): *m/z* (%) = 177 (3) [$M^+$ – 19], 163 (3), 149 (13), 134 (14), 121 (3), 108 (35), 92 (72), 91 (100), 67 (23), 55 (23). HRMS (EI): *m/z* calcd for $C_{12}H_{20}O_2Na$ [$M^+$ + Na]: 219.1356; found: 219.1338. Mp 146–150 °C; $[\alpha]_D^{20}$ –7.4 (*c* 0.6, $CHCl_3$).

Compound **16a2**: IR: n = 3445, 2929, 1453, 1260, 1051 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.81 (3 H, s), 1.29 (3 H, s), 1.44 (2 H, m), 1.60–1.90 (4 H, m), 2.09 (1 H, m), 2.34 (2 H, m), 2.46 (1 H, m), 3.94 (1 H, d, *J* = 8.2 Hz), 4.69 (1 H, dd, $J_1$ = 10.4 Hz, $J_2$ = 10.4 Hz) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 23.04 ($CH_3$), 26.44 ($CH_2$), 27.00 ($CH_3$, $CH_2$), 27.71 ($CH_2$), 38.81 ($CH_2$), 39.50 (CH), 39.54 (C), 43.99 (CH), 55.52 (C), 69.39 (CH), 71.48 (CH) ppm. MS (EI): *m/z* (%) = 163 (3) [$M^+$ – 33], 163 (2), 149 (1), 134 (10), 121 (4), 117 (27), 92 (51), 91 (100), 70 (23), 55 (43). HRMS (EI): *m/z* calcd for $C_{12}H_{20}O_2Na$ [$M^+$ + Na]: 219.1356; found: 219.1344. Mp 166–168 °C; $[\alpha]_D^{20}$ +33.5 (*c* 0.7, $CHCl_3$).

Compound **17c**: IR: 3383, 2923, 2858, 1729, 1469, 1391, 1372 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.89 (3 H, d, *J* = 6.6 Hz), 0.91 (3 H, d, *J* = 6.6 Hz), 1.20–2.20 (12 H, m), 2.44 (2 H, t, *J* = 8.9 Hz), 4.05 (1 H, br s), 5.56 (1 H, m), 9.77 (1 H, s) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 19.45 ($CH_3$), 19.89 ($CH_3$), 21.78 ($CH_2$), 27.55 ($CH_2$), 28.99 ($CH_2$), 31.94 (CH), 33.99 ($CH_2$), 34.06 (CH), 35.48 ($CH_2$), 43.71 ($CH_2$), 67.13 (CH), 125.69 (CH), 137.92 (C), 202.57 (CH) ppm. MS (EI): *m/z* (%) = 206 (9) [$M^+$ – 18], 188 (3), 163 (9), 153 (13), 145 (33), 121 (12), 117 (29), 93 (35), 91 (100), 67 (67), 55 (90). HRMS (EI): *m/z* calcd for $C_{14}H_{24}O_2Na$ [$M^+$ + Na]: 247.1674; found: 247.1681; $[\alpha]_D^{20}$ –51.9 (*c* 2.1, $CHCl_3$).

Compound **20d**: IR: 3407, 2927, 1729, 1457, 1247, 1040 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 1.73 (3 H, s), 1.50–2.40 (5 H, m), 2.07 (3 H, s), 4.20 (1 H, br s), 4.51 (1 H, d, *J* = 6.2 Hz), 4.72 (1 H, s), 4.73 (1 H, d, *J* = 6.2 Hz), 4.75 (1 H, s), 5.94 (1 H, br s) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 20.78 ($CH_3$), 20.94 ($CH_3$), 30.80 ($CH_2$), 34.99 (CH), 35.99 ($CH_2$), 64.78 (CH), 66.58 ($CH_2$), 109.27 ($CH_2$), 130.74 (CH), 133.76 (C), 148.61 (C), 171.11 (C) ppm. MS (EI): *m/z* (%) = 192 (2) [$M^+$ – 18], 167 (1), 150 (25), 132 (20), 117 (96), 91 (100), 68 (50), 53 (70). HRMS (EI): *m/z* calcd for $C_{12}H_{18}O_3Na$ [$M^+$ + Na]: 233.1148; found: 233.1161; $[\alpha]_D^{20}$ –108.5 (*c* 0.3, $CHCl_3$).

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