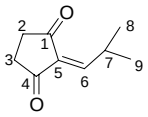
Supplementary data

Autoxidation of 2-alkylidene-1,3-cyclohexanediones as a green process to form bicyclic hemiketal endoperoxides.

Virginie Bernat,[a] Marion Costes[a] and Christiane André-Barrès.*

2-(2-methylpropylidene)cyclopentan-1,3-dione (5)



5

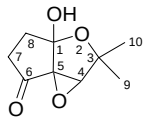
To isobutyraldehyde (309 mg, 4.285 mmol) solubilised in anhydrous dichloromethane (22 mL) is added piperidine (423 µL, 4.285 mmol) at room temperature, under argon. Cyclopentanedione (400 mg, 4.077 mmol) is solubilised in anhydrous dichloromethane (22 mL) and piperidine (403 µL, 4.077 mmol) is added. After 20 minutes, diketone solution is slowly poured on iminium solution. The mixture is shaken for thirty minutes then concentrated. Mannich base so obtained is dissolved in dichloromethane then treated by saturated NH_4Cl in HCl 1M solution. After 30 minutes, organic phase is washed with water then dried on magnesium sulfate, filtered and evaporated. Enone **5** (101 mg, 0.664 mmol) is obtained in 19% yield.

^{1}H NMR (300 MHz, $CDCl_3$, δ) : 1.09 (d, 6H, CH_3-8/9, $^3J_{HH}$ = 6.6 Hz) ; 2.41-2.77 (m, ABX system, 6H, CH2-2/3); 3.84 (m, 1H, CH-7) ; 7.08 (d, 1H, CH-6, $^3J_{HH}$ = 10.5 Hz)

Oxygen uptake on 5

Enone **5** (101 mg, 0.666 mmol), solubilised in dichloromethane, is left under air for ten days. After purification on column chromatography of sicagel (Petroleum ether/Ethyl acetate: 8/2) epoxide hemiketal **8** (23 mg, 0.125 mmol), epoxide **9** (5 mg, 0.030 mmol) and epoxide **10** (29 mg, 0.17 mmol) are obtained in respectively 25%, 8% and 26% yield.

Tetrahydro-6a-hydroxy-2,2-dimethyl-2H-4-oxiranyl-cyclopenta[b]furan-4(5H)-one (8)

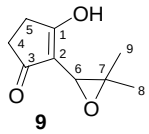


8

***R*$_f$ (PE/EtOAc: 7/3) =** 0.14

^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.36 (s, 3H, CH_3-9/10) ; 1.39 (s, 3H, CH_3-9/10) ; 2.13 (m, ABX system, 1H, CH_2-7) ; 2.56 (m, ABX system, 1H, CH_2-7) ; 2.65 (m, ABX system, 2H, CH_2-8) ; 3.84 (s, 1H, CH-4) ^{13}C NMR (75 MHz, $CDCl_3$, δ) : 24.0-25.4 (CH_3-9/10) ; 31.9 (CH_2-7) ; 37.7 (CH_2-8) ; 72.7 (C-5) ; 73.0 (CH-4) ; 81.4 (C-3) ; 105.1 (C-1) ; 205.4 (C-6) MS (ESI, MeOH, positive mode, *m/z*): 207 $[MNa]^+$ HRMS (DCI-CH_4, CH_2Cl_2, positive mode, *m/z*) : calculated for $C_9H_{13}O_4$ 185.0814, found 185.0824.

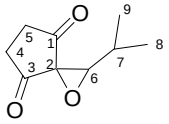
3-hydroxy-2-(3,3-dimethyloxiran-2-yl)cyclopent-2-enone (9)



9

R_f (PE/EtOAc: 7/3) = 0.36 ^{1}H NMR (500 MHz, $CDCl_3$, δ) : 1.31 (s, 3H, CH_3-8/9) ; 1.41 (s, 3H, CH_3-8/9) ; 2.15 (m, ABX system, 1H, CH_2-4) ; 2.54-2.73 (m, ABX system, 3H, CH_2-4/5) ; 3.46 (s, 1H, CH-6) ^{13}C NMR (75 MHz, $CDCl_3$, δ): 21.3-21.4 (CH_3-8/9) ; 28.6 (CH_2-4) ; 34.8 (CH_2-5) ; 63.3 (CH-6) ; 76.7 (C-7) ; 99.0 (C-2) ; 207.2 (C-1) ; 208.5 (C-3) MS (DCI/CH_4, CH_2Cl_2, positive mode, *m/z*) : 169 $[MH]^+$ HRMS (DCI/CH_4, CH_2Cl_2, positive mode, *m/z*) : calculated for $C_9H_{13}O_3$ 169.0865, found 169.0844.

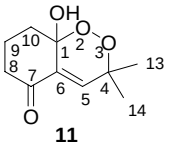
2-(3,3-dimethyloxiran-1-yl)cyclopentane-1,3-dione (10)



10

R_f (PE/EtOAc: 7/3) = 0.64 ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.85 (d, 3H, CH_3-8/9, $^3J_{HH}$ = 6.9 Hz); 1.14 (d, 3H, CH_3-8/9, $^3J_{HH}$ = 6.7 Hz); 1.95 (m, 1H, CH-7) ; 2.80-3.05 (m, ABX system, 4H, CH_2-4/5) ; 3.26 (d, 1H, CH-6, $^3J_{HH}$ = 8.9 Hz) ^{13}C NMR (75 MHz, $CDCl_3$, δ): 18.6-19.4 (CH_3-8/9) ; 26.4 (CH-7) ; 34.2-34.4 (CH_2-4/5) ; 63.1 (C-2) ; 78.1 (CH-6) ; 205.4-205.8 (C-1/3) MS (DCI/CH_4, CH_2Cl_2, positive mode, *m/z*): 169 $[MH]^+$ HRMS (DCI/CH_4, CH_2Cl_2, positive mode, *m/z*) : calculated for $C_9H_{13}O_3$ 169.0865, found 169.0869.

6,7,8,8a-tetrahydro-8a-hydroxy-3,3-dimethylbenzo[c][1,2]dioxin-5(3H)-one (11)

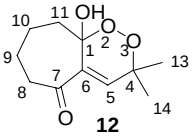


11

To isobutyraldehyde (171 µL, 1.873 mmol) solubilised in anhydrous dichloromethane (10 mL) is added piperidine (185 µL, 1.873 mmol) at room temperature, under argon. Cyclohexanedione (200 mg, 1.784 mmol) is solubilised in anhydrous dichloromethane (10 mL) and piperidine (176 µL, 1.784 mmol) is added. After 25 minutes, dione solution is slowly poured on iminium solution. The mixture is shaken for thirty minutes then concentrated. Mannich base obtained as a yellow solid besides 10% of bis-adduct. The mixture is then dissolved in dichloromethane, treated by saturated NH_4Cl in HCl 1M solution. After 30 minutes, organic phase is washed with water then dried on magnesium sulfate, filtered and evaporated. Enone is solubilised in dichloromethane and left under air for 36 hours. Then the raw mixture is concentrated and purified on silicagel column chromatography (Petroleum ether/Ethyl acetate: 8/2). Endoperoxide **11** (255 mg, 1.288 mmol) is obtained as a white solid in 72%yield.

R_f (PE/EtOAc: 8/2) = 0.06 ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.32 (s, 3H, CH_3-13/14) ; 1.45 (s, 3H, CH_3-13/14) ; 1.71 (m, 1H, ABX system, CH_2-10) ; 1.98 (m, 1H, ABX system, CH_2-9) ; 2.15 (m, 2H, ABX system, CH_2-9/10) ; 2.34 (m, 1H, ABX system, CH_2-8) ; 2.68 (m, 1H, ABX system, CH_2-8) ; 3.65 (s, 1H, OH) ; 6.57 (s, 1H, CH-5) ^{13}C NMR (75 MHz, $CDCl_3$, δ): 17.9 (CH_2-9) ; 23.8-24.2 (CH_3-13/14) ; 31.2 (CH_2-10) ; 39.6 (CH_2-8) ; 79.4 (C-4) ; 97.5 (C-1) ; 136.7 (C-6) ; 139.4 (CH-5) ; 198.7 (C-7) IR (diamond compression system, ν) : 3346 (OH) ; 3049 (=CH) ; 2974 à 2883 (CH_2 et CH_3) ; 1686 (α,β-unsaturated C=O) ; 1641 (C=C) ; 1129 (C-O alcohol ; 1101 (C-O peroxide) MS (ESI, MeOH, positive mode, *m/z*) : 221 $[MNa]^+$; 419 $[2MNa]^+$ HRMS (ESI, MeOH, positive mode, *m/z*) : calculated for $C_{10}H_{14}O_4Na$ 221.0790, found: 221.0784 T_f (Büchi) = 103°C

7,8,9,9a-tetrahydro-9a-hydroxy-3,3-dimethyl-3*H*-cyclohepta[c][1,2]dioxin-5(6H)-one (12)



12

To isobutyraldehyde (180 mg, 2.496 mmol) solubilised in anhydrous dichloromethane (13 mL) is added piperidine (247 µL, 2.496 mmol) at room temperature, under argon. Cycloheptanedione (300 mg, 2.378 mmol) is solubilised in anhydrous dichloromethane (13 mL) and piperidine (235 µL, 2.378 mmol) is added. After 25 minutes, diketone solution is slowly poured on iminium solution. The mixture is shaken for thirty minutes then concentrated. Mannich base obtained as a yellow solid is dissolved in dichloromethane then treated by saturated NH_4Cl in HCl 1M solution. After 30 minutes, organic phase is washed with water then dried on magnesium sulfate, filtered and evaporated. Enone is irradiated in dichloromethane at 350 nm (Rayonet) for 30 mn then left under air for five days. Raw mixture is then concentrated and purified on silicagel column chromatography (Petroleum ether/Ethyl acetate: 9/1). Endoperoxide **12** (201 mg, 0.95 mmol) is obtained as a white solid in 40% yield.

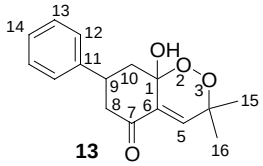
R_f (PE/EtOAc: 6/4) = 0.66 ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.31 (s, 3H, CH_3-13/14) ; 1.44 (s, 3H, CH_3-13/14) ; 1.35-1.63 (m, 2H, ABX system, CH_2-9/10) ; 1.80-1.93 (m, 1H, ABX system, CH_2-11) ; 1.95-2.14 (m, 3H, ABX system, CH_2-9/10/11) ; 2.60 (m, 1H, ABX system, CH_2-8) ; 2.94 (m, ABX system, 1H, CH_2-8) ; 3.48 (s, 1H, OH) ; 6.96 (s, 1H, CH-5) ^{13}C NMR (75 MHz, $CDCl_3$, δ): 23.2-23.9 (CH_3-13/14) ; 24.3 (CH_2-10) ; 25.6 (CH_2-9) ; 35.8 (CH_2-11) ; 43.3 (CH_2-8) ; 78.4 (C-4) ; 97.5 (C-1) ; 135.2 (C-6) ; 142.5 (CH-5) ; 199.1 (C-7) IR (KBr, ν) : 3387 (OH) ; 2989, 2860 (CH_2 et CH_3) ; 1676 (α,β-unsaturated C=O) ; 1619 (C=C) ; 1115 (C-O alcool) ; 1101 (C-O peroxyde) MS (ESI, MeOH, positive mode, *m/z*) : 235 $[MNa]^+$; 447 $[2MNa]^+$ HRMS (ESI, MeOH, positive mode, *m/z*) : calculated for $C_{11}H_{16}O_4Na$; 235.0946, found: 235.0949 T_f (Büchi) = 76°C

Endoperoxyde 13

To isobutyraldehyde (241 µL, 2.641 mmol) solubilised in anhydrous dichloromethane (13 mL) is added piperidine (261 µL, 2.641 mmol) at room temperature, under argon. 5-Phenylcyclohexanedione (497 mg, 2.641 mmol) is solubilised in anhydrous dichloromethane (13 mL) and piperidine (131 µL, 1.320 mmol) is added. After 25 minutes, diketone solution is slowly

poured on iminium solution. The mixture is shaken for ninety minutes then concentrated. Mannich base obtained as a yellow solid, is dissolved in dichloromethane then treated by saturated NH_4Cl in HCl 1M solution. After 30 minutes, organic phase is washed with water then dried on magnesium sulfate, filtered and evaporated. Enone is left under air for 24 hours. Raw mixture is then concentrated and purified on silicagel column chromatography (Petroleum ether/Ethyl acetate: 7/3). Endoperoxide **13** (386 mg, 1,407 mmol) is obtained as a white solid in 53% yield, besides Michael bis-adduct **13bis** (182 mg, 0.423 mmol) as a white solid in 16%.

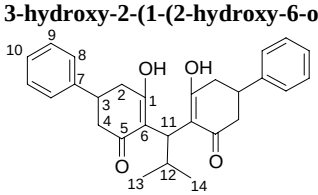
6,7,8,8a-tetrahydro-8a-hydroxy-3,3-dimethyl-7-phenylbenzo[c][1,2]dioxin-5(3H)-one (13)



13

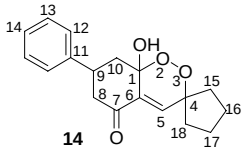
R_f (PE/EtOAc: 7/3) = 0.40 ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.41 (s, 3H, CH_3-15/16) ; 1.55 (s, 3H, CH_3-15/16) ; 2.04 (m, 1H, ABX system, CH_2-10) ; 2.46 (m, 1H, ABX system, CH_2-10) ; 2.55 (m, 1H, ABX system, CH_2-8) ; 2.94 (m, 1H, ABX system, CH_2-8) ; 3.61 (m, 1H, CH-9) ; 3.75 (1H, OH) ; 6.69 (s, 1H, CH-5) ; 7.29-7.39 (m, 5H, CH-12/13/14) ^{13}C NMR (75 MHz, $CDCl_3$, δ): 23.5 and 23.9 (CH_3-15/16) ; 35.6 (CH-9) ; 38.1 (CH_2-10) ; 47.6 (CH_2-8) ; 79.1 (C-4) ; 96.9 (C-1) ; 126.7-127.0-128.9 (CH-12/13/14) ; 135.9 (C-6) ; 139.3 (CH-5) ; 142.7 (C-11) ; 197.7 (C-7) IR (KBr, ν) : 3387 (OH) ; 3071, 3028, 3005 (=CH) ; 2980 to 2933 (CH, CH_2 and CH_3) ; 1687 (α,β-unsaturated C=O) ; 1635 (C=C) ; 1135 (C-O peroxide) ; 1103 (C-O, alcohol) ; 702 (O-O) MS (ESI, MeOH, positive mode, *m/z*) : 297 [MNa] $^+$; 571 [2MNa] $^+$ HRMS (ESI, MeOH, positive mode, *m/z*) : calculated for $C_{16}H_{18}O_4Na$ 297.1103, found: 297.1095 T_f (Büchi) = 149°C

3-hydroxy-2-(1-(2-hydroxy-6-oxo-4-phenylcyclohex-1-enyl)-2-methylpropyl)-5-phenylcyclohex-2-enone (13 bis)



R_f (PE/EtOAc: 7/3) = 0,74 ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.91 (d, 6H, CH_3-13/14, $^3J_{HH}$ = 6.4 Hz) ; 2.48-2.87 (m, 8H, ABX system, CH_2-4/6) ; 2.96 (m, 1H, CH-11) ; 3.25 (m, 2H, ABX system, CH-5) ; 3.48 (m, 1H, CH-12) ; 7.19-7.41 (m, 10H, CH-8/9/10) ; 12.96 (1H, OH) ^{13}C NMR (75 MHz, $CDCl_3$, δ): 21.9 (CH_3-13/14) ; 25.4 (CH-11) ; 38.2 (CH-3) ; 38.5 (CH-12) ; 40.2 and 40.7 (CH_2-2/4) ; 116.9 (C-6) ; 126.6-127.1-128.8 (CH-8/9/10) ; 142.1 (C-7) ; 189.8 (C-1) ; 191.0 (C-5) MS (ESI, CH_2Cl_2/MeOH, positive mode, *m/z*) : 453 [MNa] $^+$

3-cyclopentyl- 6,7,8,8a-tetrahydro-8a-hydroxy-7-phenylbenzo[c][1,2]dioxin-5(3H)-one (14)

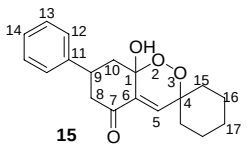


14

The same protocol as precedent is followed using cyclopentanecarboxaldehyde (284 µL, 2.656 mmol) and 5-phenylcyclohexanedione (500 mg, 2,656 mmol). After two days for oxygen uptake and purification on silicagel column chromatography (Petroleum ether/Ethyl acetate: 8/2), endoperoxide **14** (525 mg, 1.748 mmol) is obtained as a white solid in 66% yield.

R_f (PE/EtOAc: 8/2) = 0.25 ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.55-1.94 (m, 8H, CH_2-15/16/17/18) ; 1.98 (m, ABX system, 1H, CH_2-10); 2,31 (m, ABX system, 1H, CH_2-10) ; 2.52 (m, 1H, ABX system, CH_2-8) ; 2.88 (m, 1H, ABX system, CH_2-8) ; 3.56 (m, 1H, CH-9) ; 3.75 (s, 1H, OH) ; 6.67 (s, 1H, CH-5) ; 7.21-7.40 (m, 5H, CH-12/13/14) ^{13}C NMR (75 MHz, $CDCl_3$, δ): 24.4 and 24.8 (CH_2-16/17) ; 35.7 (CH-9) ; 35.7 and 35.8 (CH_2-15/18) ; 38.1 (CH_2-10); 47.5 (CH_2-8) ; 90.2 (C-4) ; 97.2 (C-1) ; 126.7 ; 127.1 and 128.9 (CH-12/13/14) ; 136.1 (C-6) ; 139.0 (CH-5) ; 142.7 (C-11) ; 197.6 (C-7) IR (KBr, ν) : 3353 (OH) ; 3054 (=CH) ; 2976 to 2871 (CH, CH_2 and CH_3) ; 1685 (α,β-insaturated C=O) ; 1637 (C=C) ; 1100 (C-O peroxide) ; 1043 (C-O alcohol) ; 764 (O-O) MS (ESI, CH_2Cl_2/MeOH, positive mode, *m/z*) : 323 [MNa] $^+$; 623 [2MNa] $^+$ HRMS (ESI, MeOH, positive mode, *m/z*) : calculated for $C_{18}H_{20}O_4Na$ 323.1259, found: 323.1271 T_f (Büchi) = 127°C

3-cyclohexyl- 6,7,8,8a-tetrahydro-8a-hydroxy-7-phenylbenzo[c][1,2]dioxin-5(3H)-one (15)

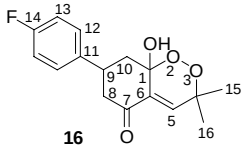


15

The same protocol as precedent is followed using cyclohexanecarboxaldehyde (250 mg, 2.229 mmol) and 5-phenylcyclohexanedione (400 mg, 2.123 mmol). After two days for oxygen uptake and purification on silicagel column chromatography (Petroleum ether/Ethyl acetate: 8/2), endoperoxide **15** (481 mg, 1.530 mmol) is obtained as a white solid in 72% yield.

R_f (PE/EtOAc: 8/2) = 0.17 ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.30-2.09 (m, ABX system, 11H, CH_2-10/15/16/17) ; 2.34 (m, ABX system, 1H, CH_2-10) ; 2.53 (m, ABX system, 1H, CH_2-8) ; 2.90 (m, 1H, ABX system, CH_2-8) ; 3.58 (m, 1H, CH-9) ; 3.75 (s, 1H, OH) ; 6.69 (s, 1H, CH-5) ; 7.20-7.42 (m, 5H, CH-12/13/14) ^{13}C NMR (75 MHz, $CDCl_3$, δ): 21.0-21.2 (CH_2-16) ; 25.0 (CH_2-17) ; 31.8-32.9 (CH_2-15) ; 35.6 (CH-9) ; 38.1 (CH_2-10); 47.6 (CH_2-8) ; 80.3 (C-4) ; 97.2 (C-1) ; 126.7-127.1-128.9 (CH-12/13/14) ; 136.3 (C-6) ; 139.2 (CH-5) ; 142.7 (C-11) ; 197.8 (C-7) IR (diamond compression system, ν): 3380 (OH) ; 2934 to 2854 (CH, CH_2 and CH_3) ; 1684 (α,β-unsaturated C=O) ; 1642 (C=C) ; 1132 (C-O peroxide). MS (ESI, MeOH, positive mode, *m/z*) : 337 $[MNa]^+$; 651 $[2MNa]^+$ HRMS (ESI, MeOH, positive mode, *m/z*): calculated for $C_{19}H_{22}O_4Na$ 337.1416, found: 337.1474; calculated for $C_{38}H_{44}O_8Na$ 651.2934, found: 651.3004 T_f (Büchi) = 122°C

6,7,8,8a-tetrahydro-8a-hydroxy-3,3-dimethyl-7-(4-fluorophenyl)benzo[c][1,2]dioxin-5(3H)-one (16)

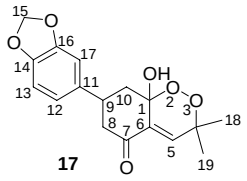


16

To isobutyraldehyde (175 mg, 2.439 mmol) solubilised in anhydrous dichloromethane (13 mL) is added piperidine (241 µL, 2.439 mmol) at room temperature, under argon. 5-Fluorophenylcyclohexanedione (503 mg, 2.439 mmol) is solubilised in anhydrous dichloromethane (13 mL) and piperidine (241 µL, 2.439 mmol) is added. After 25 minutes, diketone solution is slowly poured on iminium solution. The mixture is shaken for two hours then concentrated. Mannich base obtained as a yellow solid, is dissolved in dichloromethane then treated by saturated NH_4Cl in HCl 1M solution. After 30 minutes, organic phase is washed with water then dried on magnesium sulfate, filtered and evaporated. Enone is left under air for 6 days. Raw mixture is then concentrated and purified on silicagel column chromatography (Petroleum ether/Ethyl acetate: 8/2). Endoperoxide **16** (386 mg, 1,407 mmol) is obtained as a white solid in 64% yield.

R_f (PE/EtOAc: 7/3) = 0.28 ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.36 (s, 3H, CH_3-15/16) ; 1.49 (s, 3H, CH_3-15/16) ; 1.94 (m, 1H, system ABX, CH_2-10) ; 2,30 (m, 1H, ABX system, CH_2-10) ; 2,46 (m, 1H, ABX system, CH_2-8) ; 2.86 (m, 1H, ABX system, CH_2-8) ; 3.54 (m, 1H, CH-9) ; 3.77 (s, 1H, OH) ; 6.63 (s, 1H, CH-5) ; 7.01 (d, 1H, CH-12, $^3J_{HH}$ = 8.6 Hz) ; 7.04 (d, 1H, CH-12, $^3J_{HH}$ = 8.6 Hz) ; 7.18 (d, 1H, CH-13, $^3J_{HH}$ = 5.3 Hz) ; 7.21 (d, 1H, CH-13, $^3J_{HH}$ = 5.3 Hz) ^{13}C NMR (75 MHz, $CDCl_3$, δ): 23.5-23.9 (CH_3-15/16) ; 35.0 (CH-9) ; 38.2 (CH_2-10) ; 47.7 (CH_2-8) ; 79.2 (C-4) ; 96.8 (C-1) ; 115.6-115.8 (CH-13) ; 128.1-128.2 (CH-12) ; 135.7 (C-6) ; 138.4 (C-11) ; 139.5 (CH-5) ; 161.8 (d, C-14, $^1J_{CF}$ = 245 Hz) ; 197.4 (C-7) ^{19}F NMR (282 MHz, $CDCl_3$, δ, Reference : $CFCl_3$) : 115.5ppm. IR (KBr, ν) : 3343 (OH) ; 3049 (=CH) ; 2980 to 2867 (CH, CH_2 et CH_3) ; 1687 (α,β-unsaturated C=O) ; 1642 (C=C) ; 1106 (C-O peroxide) ; 1038 (C-O alcohol) MS (ESI, MeOH, positive mode, *m/z*) : 315 $[MNa]^+$; 607 $[2MNa]^+$ HRMS (ESI, MeOH, positive mode, *m/z*) : calculated for $C_{16}H_{17}O_4FNa$: 315.1009, found : 315.1030. Calculated for $C_{32}H_{34}O_8F_2Na$, 607.2119, found: 607.2141 T_f (Büchi) = 138°C

6,7,8,8a-tetrahydro-8a-hydroxy-3,3 dimethyl-7-(benzo[d][1,3]dioxol-5-yl)benzo[c][1,2]dioxin-5(3H)-one (17)

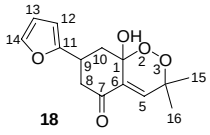


17

To isobutyraldehyde (163 mg, 2.260 mmol) solubilised in anhydrous dichloromethane (13 mL) is added piperidine (224 µL, 3.057 mmol) at room temperature, under argon. 5-(Benzo[d][1,3]dioxol-5-yl)cyclohexane-1,3-dione (500 mg, 2,153 mmol) is solubilised in anhydrous dichloromethane (13 mL) and piperidine (213 µL, 2.153 mmol) is added. After 25 minutes, diketone solution is slowly poured on iminium solution. The mixture is shaken for two hours then concentrated. Mannich base obtained as a yellow solid, is dissolved in dichloromethane then treated by saturated NH_4Cl in HCl 1M solution. After 30 minutes, organic phase is washed with water then dried on magnesium sulfate, filtered and evaporated. Enone is left under air for 2 days. Raw mixture is then concentrated and purified on silicagel column chromatography (Petroleum ether/Ethyl acetate: 8/2). Endoperoxide **17** (370 mg, 1.162 mmol) is obtained as a white solid in 54% yield.

R_f (PE/EtOAc: 7/3) = 0.20 ^{1}H NMR (300 MHz, $(CD_3)_2CO$, δ) : 1.28 (s, 3H, CH_3-18/19) ; 1.37 (s, 3H, CH_3-18/19) ; 1.96 (m, 2H, CH_2-10) ; 2.59 (m, 2H, CH_2-8) ; 3.31 (m, 1H, CH-9) ; 5.97 (s, 2H, CH_2-15) ; 6.55 (s, 1H, CH-5) ; 6.74-6.86 (m, 2H, CH-12/17) ; 6.97 (d, 1H, CH-13, $^3J_{HH}$ = 1.5 Hz) ; 7.04 (s, 1H, OH) ^{13}C NMR (75 MHz, $(CD_3)_2CO$, δ) : 22.7-23.9 (CH_2-18/19) ; 35.4 (CH-9) ; 38.6 (CH_2-10) ; 47.2 (CH_2-8) ; 78.0 (C-4) ; 96.0 (C-1) ; 100.7 (CH_2-15) ; 107.4 (CH-13) ; 108.1-120.0 (CH-12/17) ; 135.4 (C-6) ; 137.5 (C-11) ; 138.1 (CH-5) ; 145.7-147.4 (C-14/16) ; 197.8 (C-7) IR (KBr, ν) : 3322 (OH) ; 3051 (=CH) ; 2999 to 2790 (CH, CH_2 and CH_3) ; 1684 (α,β-insaturated C=O) ; 1644 (C=C ethylenic) ; 1102 (C-O peroxide) ; 1038 (C-O alcohol) MS (FAB, MNBA matrix, DMSO, positive mode, *m/z*) : 318 [M] T_f (Büchi) = 144°C

6,7,8,8a-tetrahydro-8a-hydroxy-3,3-dimethyl-7-(furan-2-yl)benzo[c][1,2]dioxin-5(3H)-one (18)

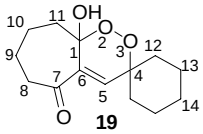


18

The same protocol as precedent is followed. After two days for oxygen uptake and purification on silicagel column chromatography (Petroleum ether/Ethyl acetate: 8/2), endoperoxide **18** (147 mg, 0.556 mmol) is obtained as a white solid in 22% yield.

R_f (PE/EtOAc: 1/1) = 0.66 RMN ^{1}H (300 MHz, $CDCl_3$, δ) : 1.35 (s, 3H, CH_3-15/16) ; 1.47 (s, 3H, CH_3-15/16) ; 1.93 (m, 1H, ABX system, CH_2-10) ; 2.43 (m, 1H, ABX system, CH_2-10) ; 2.55 (m, 1H, ABX system, CH_2-8) ; 2.96 (m, 1H, ABX system, CH_2-8) ; 3.65 (m, 1H, CH-9) ; 3.66 (1H, OH) ; 6.07 (d, 1H, CH-12, $^3J_{HH}$ = 3.2 Hz) ; 6.30 (d, 1H, CH-13, $^3J_{HH}$ = 3.2 Hz, $^3J_{HH}$ = 1.9 Hz) ; 6.64 (s, 1H, CH-5) ; 6.07 (d, 1H, CH-14, $^3J_{HH}$ = 1.9 Hz) ^{13}C NMR (75 MHz, $CDCl_3$, δ): 23.5 and 23,9(CH_2-15/16) ; 29.7 (CH-9) ; 36.0 (CH_2-10) ; 44.2 (CH_2-8) ; 79.2 (C-4) ; 96.6 (C-1) ; 104.7 (CH-12) ; 110.1 (CH-13) ; 135.7 (C-6) ; 139.6 (CH-5) ; 141.7 (CH-14) ; 155.7 (C-11) ; 196.8 (C-7) IR (KBr, ν) : 3357 (OH) ; 3157-3131-3055 (CH ethylenic) ; 2979, 2933 (CH, CH_2 and CH_3) ; 1689 (α,β-unsaturated C=O) ; 1640 (C=C) ; 1136 (C-O peroxide) ; 1102 (C-O alcohol) MS (ESI, CH_2Cl_2/MeOH, positive mode, *m/z*) : 287 $[MNa]^+$; 551 $[2MNa]^+$ HRMS (ESI, MeOH, positive mode, *m/z*) : calculated for $C_{14}H_{16}O_5Na$: 287.0895, found: 287.0912 T_f (Büchi) = 112°C

7,8,9,9a-tetrahydro-9a-hydroxy-3-cyclohexyl-3*H*-cyclohepta[c][1,2]dioxin-5(6H)-one (19)



19

Following the same protocol as previously, cyclohexanecarboxaldehyde (253 µL, 2.093 mmol) and 1,3-cycloheptanedione (240 mg, 1.903 mmol) gave enone in 62% yield from raw mixture ^{1}H NMR analysis. Enone is solubilised in dichloromethane and left under air. After 30 days, endoperoxyde **19** (110 mg, 0.0.436 mmol) is obtained as a pale yellow solid after purification silicagel column chromatography (EP/AcOEt : 9/1 then 8/2) in 23 % yield from cycloheptadione.

R_f (PE/EtOAc: 7/3) = 0.57 ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.58-2.48 (m, ABX system, 16H, CH_2-9/10/11/12/13/14) ; 2,85 (m, ABX system, 1H, CH_2-8) ; 3,22 (m, ABX system, 1H, CH_2-8) ; 4.18 (s, 1H, OH) ; 7.56 (s, 1H, CH-5) ^{13}C NMR (75 MHz, $CDCl_3$, δ): 21.0-21.1-24.4-25.1 (CH_2-9/10/13/14) ; 31.1-33.1 (CH_2-12) ; 35.8 (CH_2-11) ; 43.2 (CH_2-8) ; 79.3 (C-4) ; 97.7 (C-1) ; 137.4 (C-6) ; 142.4 (CH-5) ; 199.3 (C-7). MS (DCI/CH_4, CH_2Cl_2, positive mode, *m/z*) : 235 $[MH]^+$-H_2O.