Supporting Informations

Differential oxidation conditions of substituted cyclobutanols derived from terpenes.

Juan A. Caturelli Kuran and Albertina G. Moglioni.*

*Departamento de Farmacología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956,
Buenos Aires, (C1113AAD), Argentina.*

<i>Table of Contents:</i>	Pages
1 General Methods	S-2
2 Experimental Procedure and Product Characterization	S-2
3 Spectra	S-5 to S-8
¹ H-NMR spectrum of 2a	S-5
¹³ C-NMR spectrum of 2a	S-5
¹ H-NMR spectrum of 2b	S-6
¹³ C-NMR spectrum of 2b	S-6
¹ H-NMR spectrum of 3a	S-7
¹³ C-NMR spectrum of 3a	S-7
¹ H-NMR spectrum of 3b	S-8
¹³ C-NMR spectrum of 3b	S-8

General Methods:

All the reactions were carried out in oven-dried flasks. Flash column chromatography was performed on Kieselgel 60 silica. Commercially available reagents were used as supplied (analytical or HPLC grade) without prior purification. Organic layers were dried over Na₂SO₄. Thin layer chromatography was performed on aluminium plates coated with 60 F₂₅₄ silica. Plates were visualised using UV light (254 nm), iodine, or 2.2 % v/v ethanolic *p*-anisaldehyde.

Optical rotations were recorded on a Perkin-Elmer 343 polarimeter with a 10 cm cell. Specific rotations are reported in 10⁻¹ deg cm² g⁻¹ and concentrations in g/100 mL. IR spectra were recorded on a Nicolet 380 FT-IR spectrometer as a thin film on NaCl plates. NMR spectra were recorded on a Bruker Avance 500 spectrometer in the deuterated solvent stated. Spectra were recorded at rt unless otherwise stated. The field was locked by external referencing to the relevant deuteron resonance. Chemical shifts (δ) are reported in ppm. [High resolution mass spectra were obtained on a Bruker micrOTOF-Q II™ spectrometer.](#) (1*S*,5*S*)-α-pinene and (1*S*,5*S*)-(-)-verbenone were purchased from Acros Organics and were used without purification.

Experimental Procedure and Product Characterization

Representative procedure A: Ru-based oxidation of cyclobutanols

A solution of RuO₄ in CCl₄ was prepared by mixing a solution of RuCl₃ hydrate (Ru content 45%, 178 mg, 0.86 mmol) in CCl₄ (100 mL) with a solution of NaIO₄ (900 mg, 4.2 mmol) in H₂O (100 mL). The two-phase system was stirred overnight, then the organic layer was separated and the aqueous layer was extracted with CCl₄ (2 x 30 mL). The combined organic extracts were used in the subsequent oxidation.

Supporting Information#

The RuO₄ solution (5.38 μmol/mL, 0.13 mol %) was added dropwise (5.2 mL) to a solution of the requisite cyclobutanol (1.0 equiv) in CHCl₃ (20 mL), then a solution of NaIO₄ (2.2 equiv) in H₂O (20 mL) was added. The two-phase system was stirred for 24 h at rt. The organic layer was run off and the aqueous layer was extracted with CH₂Cl₂. The combined organic extracts were washed with brine, then dried and concentrated under vacuum to provide a mixture of **2** and **3** as a yellow oil.

Representative procedure B: Cr-based oxidation of cyclobutanols

PDC (1.1 equiv) was added to a solution of the requisite cyclobutanol (1.0 equiv) in CH₂Cl₂ (81 mL). The resultant solution was bubbled with nitrogen and stirred for 4 h at rt. Celite[®] (3g) was added and stirring was continued for 5 min. The solution was vacuum filtered through Celite[®]. The clear organic solution was washed with brine, then dried and concentrated under vacuum to afford a mixture of **2** and **3** as a yellow oil.

Representative procedure C: NaOCl-mediated oxidation of cyclobutanols

NaOCl (14 equiv) was added dropwise to a solution of the requisite cyclobutanol (1.0 equiv) in AcOH (6 mL) at 0 °C. The resultant solution was stirred at 0 °C for 2 h, and then extracted with CH₂Cl₂. The organic extract was washed with satd aq NaHCO₃, then dried and concentrated under vacuum.

Representative procedure D: DMP-mediated oxidation of cyclobutanols

DMP (1.3 equiv) was added to a solution of requisite cyclobutanol (1.0 equiv) in CH₂Cl₂ (10 mL) at 0 °C. The resultant solution was stirred at 0 °C for 1 h. The white precipitate was filtered then 10

Supporting Information#

% (w/v) aq Na₂S₂O₃ (6 mL) was added and the product mixture was stirred for 15 min. The organic layer was separated, washed with satd aq NaHCO₃ and brine, then dried and concentrated under vacuum.

Methyl 2-((1R)-2,2-dimethyl-3-oxocyclobutyl)acetate (2b): Following *general procedure D*, reaction of **1b** (270 mg, 1.57 mmol) and DMP (840 mg, 1.98 mmol) afforded **2b** as an oil (210 mg, 79%). [α]_D = - 1.4 (*c* 0.65, MeOH); ¹H NMR (500 MHz, CDCl₃): δ 1.03 (s, 3H), 1.19 (s, 3H), 2.48 (m, *J*= 7.4 Hz, 4.9 Hz, 2H), 2.56 (dd, *J*= 10.5 Hz, 8.5 Hz, 1H), 2.73 (dd, *J*= 17.9 Hz, 6.6 Hz, 1H), 3.18 (dd, *J*= 17.6 Hz, 8.2 Hz, 1H), 3.65 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 17.1, 23.2, 32.3, 35.2, 48.4, 51.7, 61.0, 172.7, 213.9; IR: 2956, 2924, 2852, 1778, 1736, 1464, 1186 cm⁻¹. All spectroscopical data are in accordance with that described for its enantiomer.^[1]

(3S)-Methyl tetrahydro-5,5-dimethyl-2-oxofuran-4-carboxylate (3a): Following *general procedure C*, reaction of **1a** (320 mg, 2.02 mmol) and NaOCl {17% (w/v) in H₂O, 12 mL, 27 mmol} afforded **3a** as a pale yellow oil (242 mg, 70 %). [α]_D = +4.0 (*c* 0.46, CHCl₃); ¹H NMR (500 MHz, CDCl₃): δ 1.29 (s, 3H), 1.58 (s, 3H), 2.69 (dd, *J*= 17.9 Hz, 8.7 Hz, 1H), 3.07 (dd, *J*= 17.9 Hz, 9 Hz, 1H), 3.18 (t, *J*= 9 Hz, 1H), 3.74 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 23.3, 28.4, 31.7, 50.4, 52.4, 84.3, 170.3, 173.9; IR: 2956, 1780, 1735, 1437, 1361, 1172, 1120 cm⁻¹. All spectroscopical data are in accordance with that described for its enantiomer.^[2]

References

1. Pirrung, M. C.; Chang, V. K.; DeAmicis, C. V. Mechanism and synthetic applications of the photochemical generation and X-H insertion reactions of oxacarbenes. *J. Am. Chem. Soc.* **1989**, *111*, 5824–5831.
2. Jacobine, A. M.; Lin, W.; Walls, B.; Zercher, C. K. Formation of γ -lactones through CAN-mediated oxidative cleavage of hemiketals. *J. Org. Chem.* **2008**, *73*, 7409–7412.

Supporting Information#

Supporting Information#

¹H NMR spectrum of **3a** (500 MHz, CDCl₃)

¹³C NMR spectrum of **3a** (125 MHz, CDCl₃)

Supporting Information#

3b

^1H NMR spectrum of **3b** (500 MHz, CDCl_3)

^{13}C NMR spectrum of **3b** (125 MHz, CDCl_3)