SUPPORTING INFORMATION

Unprecedented *in-situ* Oxidative Ring Cleavage of Isoxazolidines : Diastereoselective Transformation of Nitronic Acids and Derivatives into 3-Hydroxymethyl 4-Nitro Tetrahydrofurans and Pyrrolidines

Pierre-Yves Roger, Anne-Catherine Durand, Jean Rodriguez and Jean-Pierre Dulcère*.

General

NMR spectra were recorded on a *Brucker AC 300* (300 MHz) spectrometer, in CDCl₃. ¹³C spectra were made with a DEPT 135 sequence. IR spectra were performed on a *Perkin-Elmer 1600* Fourier transform spectrometer. Mass spectra were taken on an API III plus triple quadrupole (Sciex, Toronto, Canada) using ionspray source. Commercially available reagents were used without further purification. Dichloromethane (CH₂Cl₂) was dried by distillation from phosphorus pentoxide. Tetrahydrofurane (THF) was distilled from sodium benzophenone ketyl. Solvent evaporation was done under reduced pressure. Column chromatography was carried out with silica *Merck 230-400 mesh*.

Obtention of compounds 5, 6, 7 : to a stirred solution of potassium tertiobutylate (1.7 mmol, 1.7 eq.) and 3Å molecular sieves (0.6 g) in THF (5 mL) and tertiobutanol (1 mL) under argon at room temperature, allylic alcohol (1.5 mmol, 1.5 eq.) was added. The reaction mixture was cooled to 0°C and stirred for 20 min. **1** (1 mmol, 1 eq.) was added at 0°C and the reaction mixture was stirred from 0°C to room temperature for 4h. The reaction mixture was hydrolysed with 2M HCl (1.7 mmol, 1.7 eq.), filtered on a short pad of celite, rinced with Et_2O and diluted with water (10 mL). The reaction was then extracted with Et_2O (3x20 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered and evaporated to dryness. The crude product was purified by flash chromatography on silica gel using diethyl ether / petroleum ether as eluant.

2-allyloxy-1-nitro-cyclohexane (6a)

yield = 92% $C_9H_{15}NO_3$ (185 g.mol⁻¹), yellow oil IR (neat) : ν (cm⁻¹) 2860, 1550, 1380, 1090, 1060. **R**_f (PE/E : 3/7) : 0.60.



3-allyloxy-2-nitro-octane (**6b**)

yield = 65% $C_{11}H_{21}NO_3$ (215 g.mol⁻¹), yellow oil IR (neat) : v (cm⁻¹) 2959, 2864, 1643, 1555, 1393, 1095, 1030. **R**_f (PE/E : 3/7) : 0.75.





(1-allyloxy-2-nitro-propyl)-benzène (6c)

yield =100% $C_{12}H_{15}NO_3$ (221 g.mol⁻¹), yellow oil IR (neat) : v (cm⁻¹) 2985, 2867, 1552, 1451, 1388, 1291, 1072. **R**_f (PE/E : 3/7) : 0.90.



3-allyloxy-2-nitro-butane (6d)

yield = 85% $C_7H_{13}NO_3$ (159 g.mol⁻¹), yellow oil IR (neat) : v (cm⁻¹) 2961, 1549, 1451, 1388, 1261, 1067. **R**_f (PE/E : 3/7) : 0.75.





2-allyloxycyclohexanone (7a)

yield = 5% $C_9H_{14}NO_2$ (154 g.mol⁻¹), yellow oil The spectroscopic data are in accordance with those already described¹.

¹ Goshh, S.; Raychaudhuri, S.R.; Salomon, R.G. J. Org. Chem. **1987**, *52*, 83; Enholm, E.H.; Moran, K.M.; Whitley, P.E.; Battiste, M.A. J. Am. Chem. Soc. **1998**, *120*, 3807-08.



Preparation of compounds 5 : to a stirred solution of compound **8** or **9** (0.47 mmol, 1 eq.) in anhydrous CH_2Cl_2 (5 mL) under argon at room temperature, tetrabutyl ammonium fluoride 1M in THF (0.70 mmol, 1.5 eq.) was added slowly. The reaction mixture was stirred under argon at room temperature for 1h. The reaction was then diluted with water (10 mL), extracted with diethyl ether (3x20 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered and evaporated to dryness. The crude product was purified by flash chromatography on silica gel using diethyl ether / petroleum ether as eluant.

(3a-nitro-octahydro-benzofuran-3-yl)-methanol (5a)

yield = 47% $C_9H_{15}NO_4$ (201 g.mol⁻¹), yellow oil IR (neat) : v (cm⁻¹) 3439, 2942, 2869, 1536, 1435, 1054. **R**_f (PE/E : 3/7) : 0.35.











3-methyl-4-hydroxymethyl-3-nitro-2-pentyltetrahydrofurane (5b)

yield = 48% $C_{11}H_{21}NO_4$ (231 g.mol⁻¹), yellow oil IR (neat) : v (cm⁻¹) 3453, 2950, 2866, 1539, 1461, 1113, 1071. **R**_f (PE/E : 3/7) : 0.40.







(4-methyl-4-nitro-5-phenyltetrahydrofuran-3-yl)-methanol (5c)

yield = 37% $C_{12}H_{15}NO_4$ (237 g.mol⁻¹), yellow oil IR (neat) : v (cm⁻¹) 3441, 2939, 2883, 1540, 1268, 1069, 1026. **R**_f (PE/E : 3/7) : 0.45.





(4,5-dimethyl-4-nitrotetrahydrofuran-3-yl)-methanol (5d)

yield = 50% $C_7H_{13}NO_4$ (175 g.mol⁻¹), yellow oil IR (neat) : v (cm⁻¹) 3606, 3460, 2982, 1541, 1389, 1246, 1098. **R**_f (PE/E : 3/7) : 0.30.





1-(3a-nitro-octahydro-benzofuran-3-yl)-ethanol (5f)

yield = 66% $C_{10}H_{17}NO_4$ (215 g.mol⁻¹), yellow oil IR (neat) : v (cm⁻¹) 3414, 2939, 1537, 1453, 1346, 1103. **R**_f (PE/E : 3/7) : 0.35.







Preparation of compounds 9 : *Procedure A (with ClSiMe₃)* : to a stirred solution of compound **2** (0.5 mmol, 1 eq.) in anhydrous CH_2Cl_2 (5 mL) under argon at 0°C, DBU (0.6 mmol, 1.2 eq.) was added. The reaction mixture was stirred under argon at 0°C for 15min. ClSiMe₃ (1 mmol, 2 eq.) was then added at 0°C and the reaction mixture was stirred under argon at 0°C for 1min. CH_2Cl_2 was evaporated, petroleum ether (5 mL) was added to form a DBU-HCl precipitate. This precipitate was eliminated by filtration through a short pad of celite, and petroleum ether was evaporated to dryness.

Procedure B (with Me_2NSiMe_3) : to a stirred solution of compound 2 (0.5 mmol, 1 eq.) in anhydrous CH₂Cl₂ (5 mL)) under argon at 0°C, DBU (0.6 mmol, 1.2 eq.) was added. The reaction mixture was stirred under argon at 0°C for 15min. Me₂NSiMe₃ (1 mmol, 2 eq.) was then added at 0°C and the reaction mixture was stirred under argon from 0°C to room temperature for 4h. The reaction mixture was filtered on a small pad of silica gel and the solvent was removed under reduced pressure to dryness.

1-trimethylsilanyloxy-hexahydro-2,5-dioxa-1-aza-cyclopenta[c]indene (9a)

yield = 84% (procedure A) 100% (procedure B) $C_{12}H_{23}NO_3Si (257 \text{ g.mol}^{-1})$, yellow oil IR (neat) : $v (\text{cm}^{-1})$ 2940, 1549, 1378, 1253, 1088. $\mathbf{R}_f (\text{PE/E}: 3/7) : 0.85.$







6a-methyl-6-pentyl-1-trimethylsilanyloxy-tetrahydro-furo[3,4-*c*]isoxazole (**9b**)

yield = 62% (procedure A) 96% (procedure B) $C_{14}H_{29}NO_3Si (287 \text{ g.mol}^{-1})$, yellow oil IR (neat) : v (cm⁻¹) 2954, 1549, 1460, 1251, 1118, 1090, 1038. $\mathbf{R}_f (PE/E : 3/7) : 0.75.$







6a-methyl-6-phényl-1-trimethylsilanyloxy-tetrahydro-furo[3,4-*c*]isoxazole (**9c**)

yield = 82% (procedure A) 98% (procedure B) $C_{15}H_{23}NO_3Si (293 \text{ g.mol}^{-1})$, yellow oil IR (neat) : v (cm⁻¹) 2960, 1548, 1451, 1252, 1155, 1064. **R**_f (PE/E : 3/7) : 0.75.





6,6a-dimethyl-1-trimethylsilanyloxy-tetrahydro-furo[3,4-*c*]isoxazole (**9d**)

yield = 72% (procedure A) $C_{10}H_{21}NO_3Si (231 \text{ g.mol}^{-1})$, yellow oil IR (neat) : v (cm⁻¹) 2936, 1550, 1450, 1257, 1093, 1029. **R**_f (PE/E : 3/7) : 0.80.



3-methyl-1-trimethylsilanyloxy-hexahydro-2,5-dioxa-1-aza-cyclopenta[*c*]indene (**9e**)

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yield = 86% (procedure A)
97% (procedure B)
C_{13}H_{25}NO_3Si (271 \text{ g.mol}^{-1}), yellow oil
IR (neat) : v (cm<sup>-1</sup>) 2936, 2865, 1549, 1449, 1372, 1249, 1089.
\mathbf{R}_f (PE/E : 3/7) : 0.85.
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Preparation of compounds 10 : to a stirred solution of compound **2** (0.5 mmol, 1 éq.) in anhydrous CH_2Cl_2 (5 mL) under argon at 0°C, DBU (0.6 mmol, 1.2 éq.) was added. The reaction mixture was stirred under argon at 0°C for 15 min. ButMe₂SiCl (1 mmol, 2 éq.) was then added at 0°C and the reaction mixture was stirred under argon at 0°C for 15 min. The reaction mixture was filtered on a small pad of silica gel and the solvent was removed under reduced pressure to dryness. The crude product was purified by flash chromatography on silica gel using diethyl ether / petroleum ether as eluant.

1-(*tert*-butyl-dimethyl-silanyloxy)-hexahydro-2,5-dioxa-1-aza-cyclopenta[c]indene (**10a**)

yield = 84% $C_{15}H_{29}NO_3Si$, (299 g.mol⁻¹), colorless oil IR (neat) : v (cm⁻¹) 2933, 1472, 1434, 1388, 1249,1174, 1087. **R**_f (PE/E : 3/7) : 0.70.





1-(*tert*-butyl-dimethyl-silanyloxy)-6a-methyl-6-pentyl-tetrahydro-furo[3,4-*c*]isoxazole (**10b**)

yield = 93% $C_{17}H_{35}NO_3Si (329 \text{ g.mol}^{-1})$, colorless oil IR (neat) : v (cm⁻¹) 2946, 2874, 1454, 1339, 1246, 1204, 1045 . **R**_f (PE/E : 3/7) : 0.75.



1-(*tert*-butyl-dimethyl-silanyloxy)-6a-methyl-6-phenyl-tetrahydro-furo[3,4-*c*]isoxazole (**10c**)

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yield = 69%

C_{18}H_{29}NO_3Si (335 \text{ g.mol}^{-1}), yellow oil

IR (neat) : v (cm<sup>-1</sup>) 2957, 2857, 1704, 1454, 1385, 1257, 1204, 1037.

R<sub>f</sub> (PE/E : 3/7) : 0.75.
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1-(*tert*-butyl-dimethyl-silanyloxy)-3-methyl-hexahydro-2,5-dioxa-1-aza-cyclopenta[c]indene (**10e**)

yield = 94% $C_{16}H_{31}NO_3Si (313 \text{ g.mol}^{-1})$, colorless oil IR (neat) : v (cm⁻¹) 2930, 2858, 1471, 1462, 1434, 1372, 1247, 1087. **R**_f (PE/E : 3/7) : 0.70.





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Compound 11a : compound **11a** was isolated as a dimer by filtration of crude compound **5**.

(3a-nitroso-octahydro-benzofuran-3-yl)-methanol (11a)

yield = 24% C₉H₁₃NO₃ (185 g.mol⁻¹), white solid (m.p.: decomposed around 170°C) IR (neat) : v (cm⁻¹) 3414, 2918, 1446, 1268, 1178, 1148, 1093. **R**_f (E) : 0.30.





Preparation of compound 13: to a stirred solution of compound **12** (1 mmol, 1 eq.) in anhydrous CH_2Cl_2 (10 mL) under argon at 0°C, DBU (1.2 mmol, 1.2 eq.) was added. The reaction mixture was stirred under argon at 0°C for 15min. ClSiMe₃ (2 mmol, 2 eq.) was then added at 0°C and the reaction mixture was stirred under argon at 0°C for 1 min. CH_2Cl_2 was evaporated, petroleum ether (10 mL) was added to form a DBU-HCl precipitate. This precipitate was eliminated by filtration on a short pad of celite, and petroleum ether was evaporated to dryness.

5-(toluene-4-sulfonyl)-1-trimethyl-silanyloxy-octahydro-2-oxa-1,5-diaza-cyclopenta[*c*]indene (**13a**)

 $\label{eq:constraint} \begin{array}{l} Yield = 31\% \\ C_{19}H_{30}N_2O_4SSi \ (410 \ g.mol^{-1}), \ yellow \ oil \end{array}$



Preparation of compound 14 : to a stirred solution of compound **13** (0.4 mmol, 1 eq.) in anhydrous CH_2Cl_2 (4 mL) under argon at room temperature, tetrabutyl ammonium fluoride 1M in THF (0.6 mmol, 1.5 eq.) was added slowly. The reaction mixture was stirred under argon at room temperature for 1h. The reaction was then diluted with water, extracted with diethyl ether. The organic phase was dried over anhydrous magnesium sulfate, filtered and evaporated to dryness. The crude product was purified by flash chromatography on silica gel using diethyl ether / petroleum ether as eluant.

[3a-nitro-1-(toluene-4-sulfonyl)-octahydro-indol-3-yl]-methanol (14a)

Yield = 52% $C_{16}H_{22}N_2O_5S$ (354 g.mol⁻¹), colorless oil IR (neat) : v (cm⁻¹) 3418, 2946, 2872, 1538, 1455, 1337, 1159, 1092, 1046. **R**_f (PE/E : 3/7) : 0.30.





