## **Electronic Supplementary Information**

# An insight into the mechanism of the aerobic oxidation of aldehydes catalyzed by *N*-heterocyclic carbenes

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## **Experimental procedures**

Liquid aldehydes were freshly distilled before their utilization. Reactions were monitored by TLC on silica gel 60 F254 with detection by charring with phosphomolybdic acid. Flash column chromatography was performed on silica gel 60 (230-400 mesh). <sup>1</sup>H (400 MHz) and <sup>13</sup>C (75 MHz) NMR spectra were recorded in CDCl<sub>3</sub> or DMSO- $d_6$  solutions at room temperature. Peaks assignments were aided by <sup>1</sup>H-<sup>1</sup>H COSY and gradient-HMQC/HMBC experiments. Aldehydes **3ak**, 1-methylimidazole, 1,6-dibromohexane, 1-butyl-3-methylimidazolium trifluoromethanesulfonate, and glutaric acid are commercially available (Sigma-Aldrich). Acids **7ak** and esters **11a-k** are known compounds.

#### 3,3'-dimethyl-1,1'-(hexane-1,6-diyl) diimidazolium glutarate(1)

A solution of 1-methylimidazole (11.1 mL, 0.14 mol), 1,6-dibromohexane (10.8 mL, 0.07 mol), and ethanol (20 mL) was stirred at room temperature for 4 days, and then concentrated. The resulting dibromide salt was then converted into the corresponding di-hydroxide salt by treatment with an equimolar amount of freshly prepared Ag<sub>2</sub>O in water. Insoluble AgBr was removed by filtration, and an equimolar amount of glutaric acid was added to the water solution of the di-hydroxide derivative. After further filtration of residual AgBr, water was removed under vacuum. Drying in a vacuum oven gave a high viscous liquid identified by NMR and ESI-MS as the 3,3'-dimethyl-1,1'- (hexane-1,6-diyl)diimidazolium glutarate **1** (25.5 g).

#### General procedure for the aerobic oxidation of aldehydes 3a-k catalyzed by 1.

A mixture of aldehyde **3** (0.40 mmol), 1,8-diazabicyclo[5.4.0]undec-7-ene (66  $\mu$ L, 0.44 mmol), diimidazolium glutarate **1** (151 mg, 0.40 mmol), activated 4-Å powdered molecular sieves (100 mg), anhydrous THF (2 mL), and anhydrous MeOH (1 mL) was warmed at 55 °C and stirred at that temperature for 16 h under air (air-filled balloon). The mixture was filtered through a pad of Celite, diluted with CH<sub>2</sub>Cl<sub>2</sub> (15 mL) and 1 M HCl (5 mL), cooled to room temperature, and then poured into a separatory funnel. The organic phase was separated and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 15 mL). The combined organic phases were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated to give the corresponding acid **7** and/or the ester **11** (Table 1). The reaction conversion and **7/11** ratio was determined by <sup>1</sup>H NMR analysis (DMSO-*d*<sub>6</sub>) using bromoform as the internal standard (5 mg/mL in methanol, analytical standard). The above crude mixture was eluted from a column of silica gel

with 15:1 cyclohexane-AcOEt to isolate the ester **11** and then with 10:1 AcOEt-AcOH to recover the acid **7** (Table 1).

#### Oxidation of aldehydes 3a,e catalyzed by bmim(OTf).

A mixture of aldehyde **3** (0.40 mmol), 1,8-diazabicyclo[5.4.0]undec-7-ene (66  $\mu$ L, 0.44 mmol), 1butyl-3-methylimidazolium trifluoromethanesulfonate (BMIM-OTf) (116 mg, 0.40 mmol), activated 4-Å powdered molecular sieves (100 mg), anhydrous THF (2 mL), and anhydrous MeOH (1 mL) was warmed at 55 °C and stirred at that temperature for 16 h under air (air-filled balloon). The mixture was filtered through a pad of Celite, diluted with CH<sub>2</sub>Cl<sub>2</sub> (15 mL) and 1 M HCl (5 mL), cooled to room temperature, and then poured into a separatory funnel. The organic phase was separated and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 15 mL). The combined organic phases were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated to give the corresponding acid **7** and/or the ester **11** (Table 1). The reaction conversion and **7/11** ratio was determined by <sup>1</sup>H NMR analysis (DMSO-*d*<sub>6</sub>) using bromoform as the internal standard (5 mg/mL in methanol, analytical standard).

#### Control experiments for evaluating the background oxidation of aldehydes 3a-l.

A mixture of aldehyde **3** (0.40 mmol), activated 4-Å powdered molecular sieves (100 mg), anhydrous THF (2 mL), and anhydrous MeOH (1 mL) was stirred at 55 °C for 16 h under air (air-filled balloon). The mixture was then cooled to room temperature, filtered through a pad of Celite, concentered, and analyzed by <sup>1</sup>H NMR (DMSO- $d_6$ ) to evaluate the **3**/7 ratio (Table S1).

о н х За-і	→ THF-MeOH (2:1), 4 Å MS air, 55 °C, 16 h	O X 7a-i	
Entry	substrate	Х	7 (%) <sup>a</sup>
1	3a	2-Br	10
2	3b	2-Cl	11
3	3c	2-NO <sub>2</sub>	<5
4	3d	2-OMe	<5
5	3e	4-Br	6
6	3f	4-Cl	7
7	3g	4-NO <sub>2</sub>	<5
8	3h	4-OMe	<5
9	3i	3-Br	8
10	3j	2,6-Cl <sub>2</sub>	5
11	3k	2,4,6-Me <sub>3</sub>	<5
12	31	Н	85

Table S1. Background oxidation of aldehydes 3a-l.

<sup>*a*</sup>Yield determined by <sup>1</sup>H NMR analysis (DMSO-*d*<sub>6</sub>).

**NOTE**: The high level of background oxidation of benzaldehyde **31** under our optimized conditions precluded its utilization in the present study.

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### NMR spectra



#### Mass spectrometric experiments

(+)-ESI and MS/MS mass spectra were acquired using a LCQ Duo (ThermoQuest, San Jose, CA, USA), equipped with an electrospray ionization source. Instrumental parameters: capillary voltage - 10 V, spray voltage 4.50 kV, capillary temperature of 150 °C, mass scan range from m/z 50 to 1000; N<sub>2</sub> was used as sheath gas. The samples were injected into the spectrometer by a syringe pump at a constant flow rate of 8 µL/min, using acetonitrile-MeOH (5:1) as eluting solvent. The appropriate aldehyde **3** and **1** were mixed in equimolar amounts of 10<sup>-3</sup> M. MS/MS experiments were carried out by using tickling voltages in the range 10-40 mV. HRMS were acquired in positive-ion mode on an ESI-Q-TOF LC-MS (Agilent Accurate Mass 6520). Gas Temperature: 300°C, Vcap 3500 V, Fragmentor 175V, Skimmer 65 V, OCT1 RF Vpp 750 V. Eluent, acetonitrile-MeOH (5:1). There are significant differences in the ESI spectra obtained with the two instruments. The Breslow intermediate containing an additional oxygen atom [**4**+O]<sup>+</sup> is well detectable in both cases. On the contrary the peroxo derivative [**4**+20]<sup>+</sup> is hardly measurable on an ESI-Q-TOF instrument.

substrate: 2-bromobenzaldehyde 3a



**Fig. S1**. (+)-ESI-MS full scan of the reaction of **3a** with **2**. The ions identified with circles are related to the 3,3'-dimethyl-1,1'-(hexane-1,6-diyl)diimidazolium derivative in association with its glutarate anion.



**Fig. S2**. HRMS (+)-ESI of the interval m/z 458-470 of the reaction. Calculated m/z 447.139561 and 449.13752; found 447.13901 and 449.13743 for <sup>79</sup>Br and <sup>81</sup>Br, respectively.



Calculated isotopic cluster ion distribution for  $[4a+O]^+ = 8a$ 



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**Fig. S3**. MS/MS of  $[4a+O]^+ = 8a$ , *m/z* 447 for <sup>79</sup>Br.



**Fig. S4**. MS/MS of  $[4a+2O]^+ = 5a$ , *m/z* 463 for <sup>79</sup>Br.



**Fig. S5**. MS/MS of  $[4a+2O]^+ = 5a$ , *m/z* 465 for <sup>81</sup>Br.



substrate: 2-chlorobenzaldehyde 3b



**Fig. S6**. MS/MS of  $[4b+O]^+ = 8b^{35}Cl$ , *m/z* 403.



**Fig. S7**. MS/MS of  $[4b+2O]^+ = 5b$ , *m/z* 419 for <sup>35</sup>Cl.



**Fig. S8**. MS/MS of  $[4b+2O]^+ = 5b$ , m/z 421 for <sup>37</sup>Cl.



substrate: 2-nitrobenzaldehyde 3c



**Fig. S9**. MS/MS of  $[4c+O]^+ = 8c$ , *m/z* 414.



**Fig. S10**. MS/MS of  $[4c+2O]^+ = 5c$ , *m/z* 430.







**Fig. S11**. MS/MS of  $[4d+O]^+ = 8d$ , *m/z* 399.



**Fig. S12**. MS/MS of  $[4d+2O]^+ = 5d$ , *m/z* 415.



substrate: 4-bromobenzaldehyde 3e



**Fig. S13**. (+)-ESI-MS full scan. The ions identified with circles are related to the 3,3'-dimethyl-1,1'- (hexane-1,6-diyl)diimidazolium derivative in association with its glutarate anion. Note the difference of the relative intensity of the cluster at m/z 447/449 compared to that shown in Fig. S1 for the 2-bromo benzaldehyde **3a**.



**Fig. S14**. MS/MS of  $[4e+2O]^+ = 5e$ , *m/z* 463 for <sup>79</sup>Br.



**Fig. S15**. MS/MS of  $[4e+2O]^+ = 5e$ , m/z 465 for <sup>81</sup>Br.



Fig. S16. MS/MS (12% relative CID energy ) of the doubly charged acyl intermediate 10e, m/z 215 for <sup>79</sup>Br.



Fig. S17. MS/MS (13% relative CID energy) of the doubly charged acyl intermediate 10e, m/z 215 for <sup>79</sup>Br.



substrate: 4-chlorobenzaldehyde 3f



**Fig. S18**. MS/MS of  $[4f+2O]^+ = 5f$ , m/z 419 for <sup>35</sup>Cl.



**Fig. S19**. MS/MS of  $[4f+2O]^+ = 5f$ , m/z 421 for <sup>37</sup>Cl.











**Fig. S21**. MS/MS of  $[4g+2O]^+ = 5g$ , m/z 430.



Fig. S22. MS/MS of the doubly charged acyl intermediate 10g, m/z 198.5. The quality of the MS/MS is very poor due to overlapping with other signals. However, the two singly charged components at m/z 150 (ArCO<sup>+</sup>) and 247 (2) are discernible.





**Fig. S23**. MS/MS of  $[4h+2O]^+ = 5h$ , m/z 415.



Fig. S24. MS/MS (14% relative CID energy) of the doubly charged acyl intermediate 10h, *m/z* 191.



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substrate: 3-bromobenzaldehyde 3i



**Fig. S25**. MS/MS of  $[4i+2O]^+ = 5i$ , *m/z* 463 for <sup>79</sup>Br.



**Fig. S26**. MS/MS of  $[4i+2O]^+ = 5i$ , *m/z* 465 for <sup>81</sup>Br.





**Fig. S27**. MS/MS (15% relative CID energy) of the doubly charged acyl intermediate **10i**, m/z 215 for <sup>79</sup>Br.

substrate: 2,6-dichlorobenzaldehyde 3j



**Fig. S28**. MS/MS of  $[4j+O]^+ = 8j$ , *m/z* 437 for <sup>35</sup>Cl.



**Fig. S29**. MS/MS of  $[4j+20]^+ = 5j$ , m/z 453 for <sup>35</sup>Cl.







**Fig. S30**. MS/MS of  $[4k+O]^+ = 8k$ , *m/z* 411.



**Fig. S31**. MS/MS of  $[4k+2O]^+ = 8k$ , *m/z* 427.



(+) ESI-MS control experiments using acetonitrile-CD<sub>3</sub>OD (5:1), acetonitrile-CD<sub>3</sub>OH (5:1) or DMSO as eluting solvents

Since CH<sub>3</sub>OH and O<sub>2</sub> are isobaric (32 amu), the formation of the  $[4+2O]^+$  species was examined in the above mentioned solvents; diagnostic MS/MS fragmentations, in particular O<sub>2</sub> loss, were also evaluated. As shown in Fig. S32 for 2-bromobenzaldehyde **3a**, CD<sub>3</sub>OD is not suitable for this study since a progressive shift of the position of the ions is observed due to incorporation of deuterium on exchangeable hydrogens.

Fig. S32. Frames of the full scan mass spectrum of the reaction of 3a with 2 in acetonitrile-CD<sub>3</sub>OD (5:1).



Using acetonitrile-CD<sub>3</sub>OH or DMSO as eluting solvents, no mass shifts are observed and the  $[4+2O]^+$  ions are found at the correct m/z values for all aldehydes **3a-k**, thus confirming the incorporation of O<sub>2</sub> on the Breslow intermediate **4**. The case of 2-bromobenzaldehyde **3a** is reported. The relevant MS spectra (Figures 33 and 34) should be to be compared with Figure S5.



**Fig. S33.** MS/MS of  $[4a+2O]^+ = 5a$ , m/z 465 for <sup>81</sup>Br using acetonitrile-CD<sub>3</sub>OH (5:1) as eluent.

**Fig. S34.** MS/MS of  $[4a+2O]^+ = 5a$ , m/z 465 for <sup>81</sup>Br using DMSO as eluent. The peroxidic species **5a** is formed and detected; however, due to noise and interferences, DMSO is confirmed to be not suitable to promote the ESI process.



#### MS identification of genuine samples of model perbenzoic acids

(-)-ESI mass spectra were acquired using a LCQ Duo (ThermoQuest, San Jose, CA, USA), equipped with an electrospray ionization source. Instrumental parameters: capillary voltage -10 V, spray voltage -3.50 kV, capillary temperature of 150 °C, mass scan range from m/z 50 to 1000; N<sub>2</sub> was used as sheath gas. The samples was prepared by mixing a THF solution of benzoic acid with aqueous  $H_2O_2$  or by dissolving *m*-chloro perbenzoic acid (10<sup>-3</sup> M) in THF. Both solutions were injected into the spectrometer by a syringe pump at a constant flow rate of 8 µL/min.







Fig. S36. (-)-ESI mass spectrum of *m*-chloro perbenzoic acid.

## **DFT calculations**

Calculations have been performed using the Gaussian 03 package<sup>1</sup> with B3LYP functional employing the 6-311++G(d,p) basis set.

Fig. S37. Calculated equilibrium geometries for the possible intermediates arising from  $O_2$ -addition to the Breslow intermediate II.





A (+7.95 Kcal/mol)









#### References

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