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Regioselective Oxidation of Azidodiols, Bromodiols and Triol Derivatives by Dimethyldioxirane

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Abstract: Azidodiols, bromodiols and triol derivatives were regioselectively monooxidised to the corresponding ketols using dimethyldioxirane. This regioselectivity is essentially determined by dipolar functionalities close to the potential reactive carbinol. These results make the reactivity of polyols with dimethyldioxirane highly predictable.

Keywords: dioxiranes, diols, triols.

In our previous papers[1, 2] we reported on the unique ability of dimethyldioxirane (DMD) to selectively monooxidise *sec*, *sec* 1,2 and 1,3 diols. This characteristic chemical behavior of DMD seems mainly due to its high sensitivity to polar and stereoelectronic effects.

The presence of either electron releasing (methyl, ERG substituted phenyl) or electron withdrawing group (carbonyl, carboxyl, EWG substituted phenyl, nitro[3]) close to the reactive site had a dramatic influence on the regioselectivity of the oxidation. With few exceptions, a carbinol directly linked to an ERG was better oxidised by DMD than that linked to an EWG.

These facts suggest a transition state that is polar in character, which is hardly consistent with a radical mechanism. They also prompted us to investigate the reactivity of polyfunctionalised diols, looking for a generalisation of the effects exerted by different

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dipolar moieties on the oxidation of carbinols by DMD. Every moiety in which an heteroatom is directly linked to a carbon atom shows a permanent dipole and its effect could be studied.

We report here on the regioselective oxidation of open chain and cyclic triol derivatives, azido diols and bromo diols by DMD, for their relevant synthetic potential. The results on open chain substrates are summarised in Table 1.[1] 1,2,3-Triol derivatives (**2a-c**) were regioselectively oxidised at the C-3 carbinol by DMD (0.08-0.09 M solution in acetone), affording the corresponding 3-oxodiols **3a-c** in good yields. This high regioselectivity is apparently due to the presence of the oxygenated moiety at C-1. The C-2 carbinols, close to those functionalities, are less reactive than C-3 ones toward DMD. This fact, together with the already known effect of the carbonyl group[1, 2] produces the regioselective monooxidation of such compounds.

The results for substrates **2a** and **2c** are particularly worthy of note, since they have three oxidisable moieties, although the lower reactivity of primary compared with secondary hydroxyl groups is well established. The azidodiol **2d** was oxidised to azidoketol **3d**, the azido group showing the same effect displayed by R-O moieties. Neither the azido group nor the α-carbinol were oxidised under these conditions, allowing a direct access to synthetically useful 1-azido-2-hydroxy-3-ketones.

An analogous effect was showed by bromine in 4-bromo-2,3-heptanetriol **2e**, which was quantitatively transformed by DMD into 4-bromo-3-hydroxyheptan-2-one **3e**. These results strongly support the hypothesis of a dipolar transition state, since both azido and R-O dipoles can inhibit the formation of a partial positive charge on the close potentially reactive carbon.

The results for compounds **2f-g** show that the effect of methoxyl and hydroxyl groups is displayed only on the α position, since oxidation of 1,3,4-triol derivatives furnished mixtures of products with low, if any, regioselectivity. Only in the case of oxyacetyl derivative **2h**, we obtained 4-oxo derivative **3h** almost quantitatively, with conversion around 60%.

This last unexpected result can hardly fit into an oxidation mechanism ruled by simple straightforward electron-withdrawing effects exercised by the oxyacetyl group. Instead oxidation by DMD appears to be strongly affected by the acetyl fragment of the oxyacetyl moiety.

Studies on the behavior of 2,3,4-*sec*, *sec*, *sec*-triol derivatives **2i-n** seemed challenging, since hitherto no general procedures for the regioselective monooxidation of such compounds were known.

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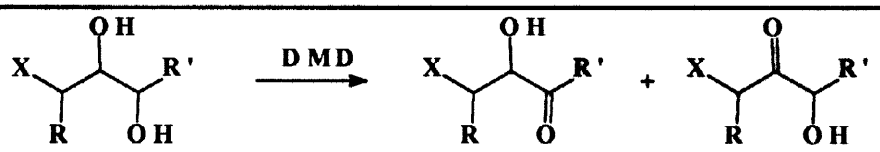
[1] Although it is well estabilished the solvent effects on dimethyldioxirane epoxidations, we noted no appreciable change in terms of conversion and regioselectivity in the oxidation of our products, changing the CH_2Cl_2/acetone ratio from 1:9 to 1:1. Examples of solvent effects are in Adam W, Smerz AK. J. Org. Chem. 1996; 61: 3506-3510 and Murray RW, Gu D. J. Chem. Soc. Perkin Trans. *2;* 1993:2203.

Table 1



2 3 4

entry	substrate	X	R	R^1	conv. (%)[a]	3[b]	4[b]
1	2a	OH	H	C_5H_{11}	90	66	-
2	2b	$OCOCH_3$	H	C_3H_7	90	92	-
3	2c	OCH_3	H	C_3H_7	90	84	16
4	2d	N_3	H	C_5H_{11}	>95	>95	-
5	2e	Br	C_3H_7[c]	CH_3	>95	>95	-
6	2f	CH_2OH	H	C_4H_7	75	50[d]	50[d]
7	2g	CH_2OCH_3	H	C_4H_7	60	50[e]	25[e]
8	2h	CH_2OCOCH_3	H	C_4H_7	60	>95[f]	-
9	2i	OH	CH_3[c]	CH_3	60	mixture	
10	2j	OCH_3	CH_3[c]	CH_3	60	mixture	
11	2k	$OCOCH_3$	CH_3[c]	CH_3	90	>95	-
12	2l	OH	CH_3[c]	C_5H_{11}	60	mixture	
13	2m	OCH_3	CH_3[c]	C_5H_{11}	60	>95	-
14	2n	$OCOCH_3$	CH_3[c]	C_5H_{11}	70	>95	-

a) Reactions were performed at r.t. on 0.5 mmol scale, adding aliquots of a 0.08M solution of dimethyldioxirane in acetone to the substrate dissolved in CH_2Cl_2 if necessary, and monitored by TLC and GC. Time reaction ranged around 24h. b) Yields are of isolated products. c) mixture of *syn,syn* and *anti,syn*. d) The products were characterised as diacetates. e) After 72h and DMD:substrate = 6:1.In this case 25% of diketone was also obtained. f) With conv. >90% a discrete amount of diketone was observed.

While in the case of symmetric or non symmetric triols **2i** ,**2l** and 2,3,4-pentanetriol-2-methyl ether **2j** we noted poor regioselectivities in the oxidation, 2-oxyacetyl-3,4-diols **2k** and **2n** were quantitatively transformed into ketols **3k** and **3n**, respectively.

These results demonstrate a low deactivation effect exerted by secondary R-O groups (with R=H, CH_3), with DMD unable to discriminate outer carbinols of 2,3,4-*sec*, *sec*, *sec*-triols. Only monoacetyl-triols **2k** and **2n** gave expected regioselectivity, pointing out the extraordinary synthetic usefulness of oxyacetyl group in such transformations.

Worthy of note, although unexpectedly and hardly rationalisable, was the regioselective monooxidation of 2-methoxy-3,4-nonanediol **2m**, which gave, in good yield, the corresponding ketol **3m**. All reactions were performed on diastereomeric mixtures, since

dedicated experiments showed that different relative stereochemistry of functional groups did not influence the course of the reactions.

Studies on the generality of such behavior for more complex structures are in progress in order to exploit this reaction for synthetic purposes.

The chemical behavior of cyclic compounds proves the high sensitivity of DMD to geometrical environment of the active site. Indeed, as shown in Table 2, 1,2,3-cyclohexanetriol **5a** was almost quantitatively converted by DMD into 2,3-dihydroxycyclohexan-1-one **6a**, the reaction showing much higher regioselectivity than in the case of the open chain derivative **2i**.

These results exclude the hypothesis of a process which is totally ruled by simple straightforward effects exerted by dipolar substituents.

A preferential geometrical approach of dioxirane was already proposed[4] in theoretical studies on oxyfunctionalisation of tertiary alkyl positions. **5a** gave a 1:1 mixture of diastereomeric products, meaning that the relative configuration *syn* or *anti* of the vicinal hydroxyl groups does not influence the reactivity of DMD. All other compounds were reacted as mixture of diastereoisomers with *syn* configuration of the diol moiety. In all cases we did not observe a different reaction rate between *anti,syn* and *syn,syn* compounds.

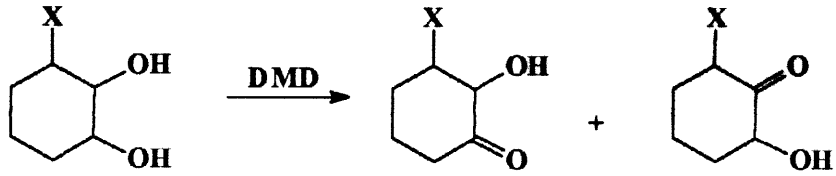
The higher regioselectivity obtained for cyclic compounds compared with that for open chain ones could be explained on the basis of conformational freedom degrees. As for example on 1,2,3 *sec,sec,sec* triols the approach of DMD on the central position of cyclic substrates is disfavoured by the polar vicinal groups.

On open chain compounds the free rotation around single bonds makes it possible a conformation in which the deactivating effects are minimised and the central carbinol can be approached by the reagent, too.

Although it is hard to propose a favoured or disfavoured relative orientation between DMD and dipolar moieties around the reactive carbinol, there seems to be no doubt about its existence.

High, expected regioselectivity was also noted in the oxidation of azidodiol **5c**, while in the case of 3-methoxy-1,2-cyclohexanediol **5b** a discrete amount of 3-methoxy-2-oxo-cyclohexanol **7b** was obtained, together with the expected 2-hydroxy-3-methoxycyclohexanone **6b**. In the case of **5f** the standard procedure gave a complex mixture of products. The use of the acetonic solution of isolated DMD allowed us to perform the reaction at –30 °C, obtaining a quantitative yield of **6f**.

Table 2



5 6 7

entry	substrate[a]	X	conv. (%)	6	7
1	5a	OH	>95	>95%	-
2	5b	OCH_3	90	82	18
3	5c	N_3	>95	>95	-
4	5d (*syn,syn*)	$OCOCH_3$	>95	>95	-
5	5e (*anti,syn*)	$OCOCH_3$	>95	>95	-
6	5f	Br	>95	>95	-

a) mixture of *syn,syn* and *anti,syn* if not specified

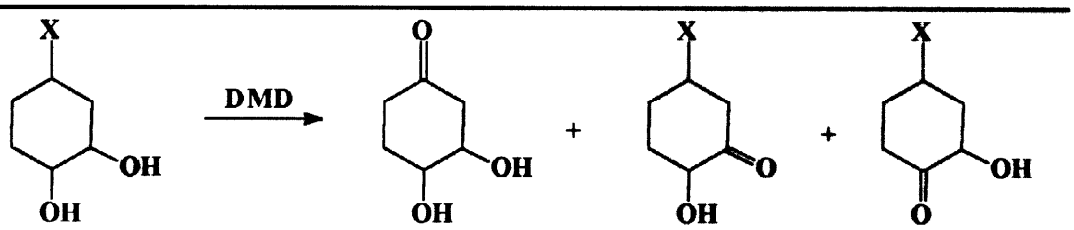
Although it is well known[5] that the oxidation of alcohols by DMD leaves the configuration of vicinal sites unchanged, we wanted to confirm this behavior for our compounds, using *syn, syn* 1,2,3-cyclohexanetriol-1-acetate **5d** and *anti, syn* 1,2,3-cyclohexanetriol-1-acetate as starting materials. Thus, acetate **5d** was oxidised by DMD affording exclusively *syn* 2-hydroxy-3-oxyacetylcyclohexanone **6d**, while the acetate **5e** gave *anti* 2-hydroxy-3-oxyacetylcyclohexanone **6e**. In both cases, the relative configuration of the vicinal centres remained unchanged.

The ability of DMD to select between two adjacent functional groups with similar reactivity allows an easy access to highly functionalised building blocks. Results on cyclic 1,2,4-cyclohexanetriol **8a** (Table 3) prove the possibility to selectively oxidise isolated secondary carbinols in the presence of *sec, sec* diol units, which remain unchanged.

On the other hand the oxidation of monomethoxy derivative **8b** gave a mixture of products, with low regioselectivity. Monoacetyl derivative **8c** was also transformed into a mixture of monooxidised products, the 4-oxyacetyl-2-hydroxycyclohexanone **9c** being the main one.

Cyclic azido-diols **12** and **13** (figure 1) confirmed the reactivity of their linear counterparts, affording quantitatively azidoketols **14** and **15** respectively.

Table 3



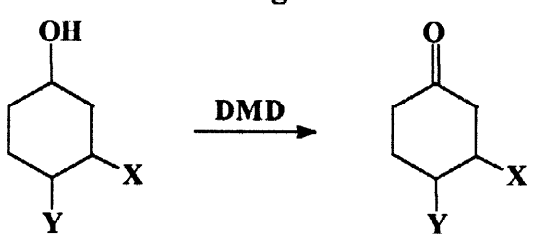
8 9 10 11

entry	substrate[a]	X	conv. (%)	9	10	11
1	8a	OH	50	>95	-	-
2	8b	OCH_3	50	mixture		
3	8c	$OCOCH_3$	>95	-	50	50

a) mixture of *syn,syn* and *anti,syn* diastereoisomers

In conclusion, all this experimental evidence on the oxidation of open chain and cyclic triol derivatives strongly supports the hypothesis of a mechanism not complitely ruled by straightforward electron-withdrawing effects exerted by the substituents. The observed regioselectivity of these reactions on structures with low conformational freedom makes a mechanism involving a dipolar transition state[1] highly probable. The general value of such hypothesis makes the reactivity of polyols and naked sugars with DMD highly predictable. Our major interest in this field is to study possible applications with optically pure diols,[6] in order to obtain useful chiral building blocks.

Figure 1



12; X=OH, Y=N_3 **14**; X=OH, Y=N_3
13; X=N_3, Y=OH **15**; X=N_3, Y=OH

EXPERIMENTAL

General: NMR: Varian XL 300; all spectra were recorded in $CDCl_3$ with tetramethylsilane as internal standard. Column chromatography: Merck silica gel 60, 0.040-0.063 nm (230-400 mesh). Analytical TLC: Kiesegel F254 (Merck), detection UV absorption (λ=254 nm) or H_2SO_4. GC-MS: HP 5890 and 5971 mass detector.

Starting materials: **2g** is commercial. **2a, 2b, 2c, 2h, 2i, 2j, 2k, 5a, 5b, 5d, 8a, 8b, 8c** were prepared according to literature procedures (acetylation[7], methylation[8], catalytic osmylation[9]) from the commercially available 1-octen-3-ol (for **2a**), *trans*-2-hexen-1-ol (for **2b** and **2c**), *trans*-3-octen-1-ol (for **2g** and **2h**), 3-penten-2-ol (for **2i**), *trans*-3-penten-1-ol (for **2j** and **2k**), 2-cyclohexen-1-ol (for **5a, 5b** and **5d**) or the easily prepared 3-cyclohexen-1-ol[10] (for **8a, 8b** and **8c**)

Typical procedure for the acetylation of unsaturated alcohols: to 1.00 g (7.8 mmol) of *trans*-3-octen-1-ol a mixture of 5 ml of pyridine and 5 ml of acetic anhydride was added. The reaction mixture was kept at room temperature over a period of 3 h, then ice/water was added and the organic layer was separated with ethyl acetate. After a double washing with diluite HCl aq. and $NaHCO_3$ s.s., the organic layer was neutralised with brine and dried over anhydrous Na_2SO_4. No further purification was necessary and after evaporation of the solvent, 1.260 g (95%) of *trans*-3-octen-1-ol acetate was obtained as a colorless oil. ^{1}H-nmr δ (ppm): 4.2 (m, 1H, C^2-H), 3.6 (dd, J= 11.2 Hz, 6.8Hz, 2H, C^1-H), 3.3 (s, 3H, CH_3O), 1.3-1.6 (m, 4H, C^4-H, C^5-H), 0.9 (t, J=6.8Hz, 3H, C^6-H). ^{13}C-nmr δ (ppm): 170.0 (C=O), 133.1-122.3 (C^3, C^4), 63.8 (C^1), 30.9, 30.8, 28.9, 22.2, 20.5, 14.2. Yields of about 95% were also obtained for the other products.

Typical procedure for the methylation of unsaturated alcohols: to a mixture of 1.6 g of KOH, 1.08 g (7.8 mmol) of *trans*-3-octen-1-ol and 14 ml of dimethylsulfoxide, 1.82 g (12.8 mmol) of iodomethane was added dropwise. The mixture was allowed to react over a period of 12 h, then 50 ml of water was added. The organic layer was extracted with diethyl ether, washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent in vacuo, 886 mg (80%) of *trans*-1-methoxy-3-octene was obtained as a colorless oil, without any further purification. ^{1}H-nmr δ (ppm): 5.4-5.7 (m, 2H, C^3-H, C^4-H), 3.4 (t, J=7.3Hz, 2H, C^1-H), 3.1 (s, 3H, CH_3O), 2.65 (q, J=6.9Hz, 2H, C^2-H), 2.0 (q, J=6.9Hz, 2H, C^5-H), 1.2-1.4 (m, 4H, C^6-H, C^7-H), 0.9 (t, J=6.7Hz, 3H, C^8-H).

Typical procedure for the catalytic osmylation of methoxy and oxyacetyl alkenes[2]: to a stirred solution of 1.2 g (7.0 mmol) of *trans*-3-octen-1-yl acetate in 25 ml of acetone and 3 ml of water, 2.3 g (21.3 mmol) of 4-methylmorpholine-N-oxide and 0.1 ml of 25 wt.% sol. of OsO_4 in 2-methyl-2-propanol were added at room temperature. After 24 h, 10 ml of $Na_2S_2O_7$ s. s. was added to the reaction mixture. After 30 min., the mixture was washed three times with 100 ml of ethyl acetate and the organic layer was neutralised with NH_4Cl sat. sol. and dried over anhydrous Na_2SO_4. After evaporation of the solvent, 1.14 g (81%) of 1,3,4-octanetriol-1-acetate **2h** were obtained as a colorless oil, without further purification. ^{1}H-nmr δ (ppm): 4.05 (t, J=6.7Hz, 2H, C^1-H), 3.7 (s, 2H, OH), 3.45 (m, 2H, C^3-H, C^4-H), 1.55 (m, 2H,C^2-H), 1.0-1.3 (m, 6H, C^5-H, C^6-H, C^7-H), 1.9 (s, 3H, CH_3CO), 0.72 (t, J=6.7Hz, 3H, C^8-H). ^{13}C-nmr δ (ppm): 171.6 (COO), 74.3, 70.9 (C^3, C^4), 61.7 (C^1), 13.5 (C^8), 20.5 ($\underline{C}H_3CO$), 31.0, 29.5, 27.7, 22.2. Yields of about 80% were obtained with the other substrates, too.

2l, **2m** and **2n** were analogously prepared from *trans*-3-nonen-2-ol, which, in turn, was obtained from commercial *trans*-2-octenal by the following procedure: to a solution of 1.0 g (7.9 mmol) of *trans*-2-octenal in 15 ml of anhydrous diethyl ether, 11.9 ml (11.9 mmol) of 1.0 M sol. CH_3MgBr in butyl ether was added at 0°C dropwise. After 10 min, 8 ml of cold water was added. The organic layer was extracted with ethyl acetate and washed with $NaHCO_3$ s. s. and NaCl s. s. After drying over anhydrous Na_2SO_4 and evaporation of the solvent, 957 mg (85%) of *trans*-3-nonen-2-ol were obtained as a colorless oil. ^{1}H-nmr δ (ppm): 5.6 (m, 2H, CH=CH), 4.2 (m, 1H, $C\underline{H}$-OH), 2.1 (m, 2H, C^5-H), 1.2-1.4 (m, 4H, C^6-H, C^7-H), 1.2 (d, J=7.6Hz, 3H, C^1-H), 0.9 (t, J=7.0Hz, 3H, C^9-H).

2d, **5c**, **12** and **13** were prepared according to literature procedures (epoxidation[11] and epoxide ring-opening with NaN_3[12]) from the commercially available 1-octen-3-ol (for **2d**), 2-cyclohexen-1-ol (for **5c**) and the easily prepared 3-cyclohexen-1-ol[10] (for **12** and **13**).

2e was prepared from 2,3-epoxyhexanal[13] via regioselective epoxide ring-opening by $MgBr_2$ and, in situ, alkylation by CH_3MgBr[14].

5e was prepared via dihydroxylation with OsO_4[10] from commercially available 3-bromocyclohexene.

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[2] Although catalytic osmylation is easily performed with free alcohols, we preferred to prepare free triols via osmylation of the corresponding oxyacetyl alkenes and quantitative deacetylation with $NaOCH_3/CH_3OH$. This procedure allowed us to obtained higher overall yields of isolated triols.

Typical procedure for the epoxidation with dimethyldioxirane[15]: to a stirred solution of 750 mg (5.9 mmol) of 1-octen-3-ol in 1 ml of acetone at 0 °C a portion of 1.2 equivalents of dimethyldioxirane solution[16] (ca. 0.09 M in acetone) was added and the reaction mixture was kept stirring for 24 h. After evaporation of the solvent, the crude product was purified by chromatography, eluting with a mixture of petroleum ether and ethyl acetate, affording 730 mg (conv. 90%, yield 96%) of 1,2-epoxyoctan-3-ol as an oil.

Typical procedure for the epoxide ring-opening with NaN_3: to a solution of 600 mg (4.2 mmol) of 1,2-epoxyoctan-3-ol in 30 ml of anhydrous methanol, 907 mg (16.8 mmol) of Sodium azide and 819 mg (12.6 mmol) of NH_4Cl were added. The reaction mixture was kept stirring and refluxing for 48 h. The solvent was then evaporated in vacuo, 40 ml of diethyl ether were added, the organic layer was separated, washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent in vacuo, 707 mg (91%) of 1-azido-2,3-octanediol **2d** was obtained as oil. ^{1}H-nmr δ (ppm): 3.3-3.7 (m, 4H, C^1-H, C^2-H, C^3-H), 1.2-1.5 (m, 8H, C^4-H, C^5-H, C^6-H, C^7-H), 0.9 (t, J=6.1Hz, 3H, C^8-H). ^{13}C-nmr δ (ppm): 73.2, 72.9 (C^2, C^3), 54.1 (C^1), 33.4, 31.6, 25.5, 22.5 (C^4, C^5, C^6, C^7), 13.9 (C^8).

Typical procedure for the oxidation with dimethyldioxirane: to a stirred solution of substrate (0.5- 1.0 mmol) in 1 ml of acetone at room temperature (ca. 25 °C) a portion of 1.5 equivalents of dimethyldioxirane solution (ca. 0.09 M in acetone) was added. The reaction mixture was kept stirring for 12 h. Further amounts of reagent were added until the desired conversion was reached. Reactions were monitored by TLC and GC. The work up of all reactions consisted simply of evaporation of the solvent in vacuo. The crude products were purified by chromatography, when necessary, eluting with a mixture of Petroleum ether and ethyl acetate, or diethyl ether.

1,2-Dihydroxyoctan-3-one (**3a**): 60 mg (0.37 mmol) of **2a** in 12.3 ml of 0.09 M DMD sol. in acetone. React. time 24h. Conv. 90%. Chromatographic separation on silica gel gave 35 mg (66%) of **3a** as a colorless oil. ^{1}H-nmr δ (ppm): 4.18 (t, J=4.0Hz, 1H, C^2-H), 3.86-3.90 (2d, J=4.0 Hz, 2H, C^1-H), 2.45-2.55 (2t, J=7.0 Hz, 2H, C^4-H), 1.50-1.65 (m, 2H, C^5-H), 1.16-1.38 (m, 4H, C^6-H, C^7-H), 0.79-0.92 (m, 3H, C^8-H). ^{13}C-nmr δ (ppm): 210.5 (C^3), 77.5 (C^2), 63.4 (C^1), 37.9 (C^4), 31.1 (C^5), 22.2-22.8 (C^6, C^7), 13.6 (C^8). $C_8H_{16}O_3$ (160.2): calcd. C 59.98, H 10.07; found C 59.83, H 9.96.

2-Hydroxy-1-oxyacetylhexan-3-one (**3b**): 140 mg (0.79 mmol) of **2b** in 26.3 ml of 0.09 M DMD sol. in acetone. React. time 36h. Conv. 90%. Chromatographic separation on silica gel

gave 114 mg (92%) of **3b** as a colorless oil. ^{1}H-nmr δ (ppm): 4.5 (m, 3H, C^1-H, C^2-H), 2.5 (dt, J=4.6 Hz, 2.3 Hz, 2H, C^4-H) 2.0 (s, 3H, CH_3COO), 1.6 (sex, J=4.6Hz, 2H, C^5-H), 0.9 (t, J=4.6Hz, 3H, C^6-H). ^{13}C-nmr δ (ppm): 208.8 (C^3), 170.8 ($CH_3\underline{C}OO$), 75.1 (C^2), 65.0 (C^1), 40.1, 20.6, 16.8, 13.6. MS m^+/z (% rel. int): no mol. peak, 130 (4), 112 (27), 102 (28), 71 (100). - $C_8H_{14}O_4$ (174.2): calcd. C 55.16, H 8.10; found C 55.02, H 8.01.

2-Hydroxy-1-methoxyhexan-3-one (**3c**) and *3-hydroxy-1-methoxyhexan-2-one* (**4c**): 180 mg (1.22 mmol) of **2c** in 54 ml of 0.09 M DMD sol. in acetone. React. time 48h. Conv. 90%. Purification on silica gel gave 161 mg (90%) of an inseparable mixture of **3c** and **4c**. The ^{1}H NMR spectrum revealed that the crude was composed of a 84:16 ratio of **3c** and **4c**. **3c**; ^{1}H-nmr δ (ppm): 4.2 (m, 1H, C^2-H), 3.6 (dd, J=11.2Hz, 6.8Hz, 2H, C^1-H), 3.3 (s, 3H, CH_3O), 1.3-1.6 (m, 4H, C^4-H, C^5-H), 0.9 (t, J=6.8Hz, 3H, C^6-H). **4c** (characterised in mixture with **3c**); ^{1}H-nmr δ (ppm): 4.5 (s, 1H, C^1-H), 4.2 (m, 1H, C^2-H), 3.4 (s, 3H, CH_3O), 1.2-1.5 (m, 4H, C^4-H, C^5-H), 0.9 (t, J=6.8Hz, 3H, C^6-H).

1-Azido-2-hydroxyoctan-3-one (**3d**); 70 mg (0.37 mmol) of 2d in 16 ml of 0.09 M DMD sol. in acetone. React. time 48h. Conv. >95%. Chromatographic separation on silica gel gave 67 mg (>95%) of **3d** as a colorless oil. **3d**; ^{1}H-nmr δ (ppm): 4.3 (m, 1H, C^2-H), 3.7 (dd, J=10.5 Hz, 4.3Hz, 1H, C^1-H), 3.4 (dd, J=10.5Hz, 4.3Hz, 1H, C^1-H), 2.5 (dt, J=6.4Hz, 2.1Hz, 2H, C^5-H), 1.2-1.5 (m, 4H, C^6-H, C^7-H), 0.8 (t, J=6.4Hz, 3H, C^8-H).). ^{13}C-nmr δ (ppm): 208.9 (C^3), 76.3 (C^2), 53.1 (C^1), 37.9, 31.1, 22.9, 22.3, 13.7. MS m^+/z (% rel. int.): no mol. peak, 142 (14), 99 (100), 98 (78), 73 (13), 71 (62). $C_8H_{15}N_3O_2$ (185.2); calcd. C 51.88, H 8.16, N 22.69; found C 51.90, H 8.33, N 22.93.

4-Bromo-3-hydroxyheptan-2-one (**3e**); 120 mg (0.57 mmol) of **2e** in 25 ml of 0.09 M DMD sol. in acetone. React. time 48h. Conv. >95%. After evaporation of the solvent 116 mg (>95%) of **3e** were obtained as a colorless oil. **3e**; ^{1}H-nmr δ (ppm): 4.4 (d, J=2.3Hz, 1H, C^3-H), 2.3 (s, 3H, CH_3CO), 1.8-2.0 (m, 1H, C^4-H), 1.4-1.7 (m, 4H, C^6-H, C^5-H), 0.9 (t, J=5.7Hz, 3H, C^7-H). ^{13}C-nmr δ (ppm): 206.5 (C^2), 80.8 (C^3), 55.7 (C^4), 35.2, 27.3, 20.9, 13.2. $C_7H_{13}O_2Br$ (209.1); calcd. C 40.21, H 6.27; found C 40.08, H 6.15.

1,3-Dihydroxyoctan-4-one (**3f**) and *1,4-dihydroxyoctan-3-one* (**4f**); 100 mg (0.62 mmol) of **2f** in 21 ml of 0.09 M DMD sol. in acetone. React. time 24h. Conv. 75%. Purification on silica gel gave an inseparable mixture of **3f** and **4f** (ca. 1:1: ratio), which were characterised as dioxyacetyl derivatives via ^{1}H NMR. *1,3-dioxyacetyloctan-4-one*; ^{1}H-nmr δ (ppm): 5.1 (t, J=5.0 Hz, 1H, C^3-H), 4.3 (t, J=5.0Hz, 2H, C^1-H), 2.75 (q, J=5.0Hz, 2H, C^5-H), 1.6 (quin,

J=7.5Hz, 2H, C^6-H), 2.0 (s, 6H, $2CH_3COO$), 1.3-1.5 (m, 4H, C^2-H, C^7-H), 0.9 (t, J=7.5Hz, 3H, C^8-H). *1,4-dioxyacetyloctan-3-one*; ^{1}H-nmr δ (ppm): 4.9 (m, 1H, C^4-H), 4.1 (m, 2H, C^1-H), 2.4 (q, J=7.5 Hz, 2H, C^2-H), 2.0 (s, 6H, $2CH_3COO$), 1.4-1.5 (m, 6H, C^5-H, C^6-H, C^7-H), 0.9 (t, J=7.5 Hz, 3H, C^8-H).

1-Methoxy-3-hydroxyoctan-4-one (**3g**) and *1-methoxy-4-hydroxyoctan-3-one* (**4g**); 235 mg (1.34 mmol) of **2g** in 41 ml of 0.08 M DMD sol. in acetone. React. time 24h. Conv. 60%. Chromatographic separation on silica gel gave 70 mg (50%) of **3g** and 35 mg (25%) of **4g** as oils. **3g**; ^{1}H-nmr δ (ppm): 4.2 (m, 1H, C^3-H), 3.7 (d, J=2.8Hz, 1H, OH), 3.5 (m, 2H, C^1-H), 3.3 (s, 3H, CH_3O), 2.6 (m, 1H, C^5-H), 2.1 (m, 1H, C^2-H), 1.8 (m, 1H, C^2-H), 1.6 (m, 2H, C^6-H), 1.3 (sex, J=7.1Hz, 2H, C^7-H), 0.9 (t, J=7.0Hz, C^8-H). ^{13}C-nmr δ (ppm): 212.9 (C^4), 74.2 (C^3), 68.2 (C^1), 58.7 (CH_3O), 37.5, 33.8, 25.7, 22.3, 13.8. $C_9H_{18}O_3$ (174.2); calcd. C 62.04, H 10.41; found C 61.94, H 10.36. **4g**; ^{1}H-nmr δ (ppm): 4.2 (m, 1H, C^4-H), 3.7 (t, J=5.7Hz, 2H, C^1-H), 3.5 (d, J=5.7Hz, 1H, OH), 3.3 (s, 3H, CH_3O), 2.7 (dt, J=5.7Hz, 2.8Hz, 2H, C^2-H), 1.3-1.6 (m, 6H, C^5-H, C^7-H), 0.9 (t, J=5.7Hz, 3H, C^8-H). ^{13}C-nmr δ (ppm): 210.9 (C^3), 67.4 (C^4), 60.3 (C^1), 58.9 (CH_3O), 38.2, 33.0, 26.9, 22.5, 13.8. $C_9H_{18}O_3$ (174.2); calcd. C 62.04, H 10.41; found C 61.99, H 10.37.

1-Oxyacetyl-3-hydroxyoctan-4-one (**3h**); 100 mg (0.49 mmol) of **2h** in 8.2 ml of 0.09 M DMD sol. in acetone. React. time 24h. Conv. 60%. After evaporation of the solvent 59 mg (>97%) of **3h** was obtained as an oil. **3h**; ^{1}H-nmr δ (ppm): 4.15-4.30 (m, 3H, C^1-H, C^3-H), 2.5 (dd, J=10.5Hz, 6.3Hz, C^5-H), 1.8-2.2 (m, 2H, C^2-H), 1.6 (quin, J=6.4Hz, 2H, C^6-H), 1.3 (sex, J=6.4Hz, C^7-H), 0.9 (t, J=6.4Hz, 3H, C^8-H). ^{13}C-nmr δ (ppm): 211.9 (C^4), 171.0 ($CH_3\underline{C}OO$), 73.2 (C^3), 60.0 (C^1), 37.3, 32.3, 25.5, 22.1, 20.6, 13.5. $C_{10}H_{18}O_4$ (202.2); calcd. C 59.39, H 8.97; found C 59.19, H 8.85.

3-Hydroxy-4-oxyacetylpentan-2-one (**3k**); 130 mg (0.80 mmol) of **2k** in 14.5 ml of 0.09 M DMD sol. in acetone. React. time 24h. Conv. >95%. After evaporation of the solvent 124 mg (>95%) of **3k** was obtained as an oil. ^{1}H-nmr δ (ppm): 5.2 (dq, J=11.1Hz, 5.6Hz, 1H, C^4-H), 4.4 (d, J=5.6Hz, 1H, C^3-H), 2.2 (s, 3H, C^1-H), 2.0 (s, 3H, CH_3COO), 1.1 (d, J=5.6Hz, 3H, C^5-H). ^{13}C-nmr δ (ppm): 206.9 (C^2), 171.0 ($CH_3\underline{C}OO$), 78.7 (C^3), 70.5 (C^4), 26.2, 20.9, 13.4. $C_7H_{12}O_4$ (160.2); calcd. C 52.49, H 7.55; found C 52.35, H 7.43.

3-Hydroxy-2-methoxynonan-4-one (**3m**); 120 mg (0.63 mmol) of **2m** in 14 ml of 0.09 M DMD sol. in acetone. React. time 36h. Conv. 60%. Chromatographic separation on silica gel gave 69 mg (>95%) of **3m** as an oil. 3m; ^{1}H-nmr δ (ppm): 4.3 (m,1H, C^3-H), 3.55 (quin,

J=6.4Hz, 1H, C^2-H), 3.4 (s, 3H, CH_3O), 2.55 (m, 2H, C^5-H), 1.1 (d, J=6.4Hz, 3H, C^1-H), 1.3-1.7 (m, 6H, C^6-H, C^7-H), 0.9 (t, J=6.4Hz, 3H, C^9-H). $C_{10}H_{20}O_3$ (188.3); calcd. C 63.80, H 10.71; found C 63.67, H 10.55.

3-Hydroxy-2-oxyacetylnonan-4-one (**3n**); 140 mg (0.64 mmol) of **2n** in 21.3 ml of 0.09 M DMD sol. in acetone. React. time 48h. Conv. 70%. Chromatographic separation on silica gel gave 94 mg (>95%) of **3n** as an oil. ^{1}H-nmr δ (ppm): 5.2 (dq, J=5.8Hz, 1.9Hz, 1H, C^2-H), 4.4 (m, 1H C^3-H), 3.6 (d, J=3.8Hz, 1H, OH), 2.5 (dt, J=7.7Hz, 3.8Hz, 2H, C^5-H), 1.6 (q, J=7.7 Hz, 2H, C^6-H), 1.2-1.4 (m, 4H, C^7-H, C^8-H), 1.1 (d, J=5.8Hz, 3H, C^1-H), 0.9 (t, J=5.8Hz, 3H, C^9-H). ^{13}C-nmr δ (ppm): 209.1 (C^4), 170.7 ($CH_3\underline{C}OO$), 78.3 (C^3), 70.7 (C^2), 39.1, 31.2, 23.2, 22.3, 21.2, 13.8, 13.5. . MS m^+/z (% rel. int.): no mol. peak, 117 (27), 116 (26), 99 (18), 98 (17), 85 (24), 84 (24). $C_{11}H_{20}O_4$ (216.3); calcd. C 61.09, H 9.32; found C 60.91, H 9.20.

2,3-Dihydroxycyclohexanone (**6a**); 150 mg (1.14 mmol) of **5a** in 20.2 ml of 0.09 M DMD sol. in acetone. React. time 48h. Conv. >95%. After evaporation of the solvent 141 mg (quantitative yield) of **6a** was obtained as an oil. **6a**; *trans* isomer: ^{1}H-nmr δ (ppm): 4.00 (dd, J=10.0 Hz, 1.0 Hz, 1H, C^2-H), 3.5 (m, 1H, C^3-H), 2.3-2.5 (m, 2H, C^6-H), 2.1-1.4 (m, 4H, C^5-H, C^4-H). ^{13}C-nmr δ (ppm): 210.2 (C^1), 82.7, 77.4 (C^2, C^3), 40.3, (C^6),33.1, 21.9 (C^4, C^5). *Cis* isomer, characterised in mixture with the *trans* isomer: ^{1}H-nmr δ (ppm) in D_2O: 4.0-3.9 (m, 1H, C^2-H), 3.7-3.6 (m, 1H, C^3-H). ^{13}C-nmr δ (ppm): 210.8 (C^1), 80.4 (C^2), 72.7 (C^3), 38.1 (C^6), 30.4 (C^4), 18.9 (C^5). $C_6H_{10}O_3$ (130.1); calcd. C 55.37, H 7.74; found C 55.22, H 7.62.

2-Hydroxy-3-methoxycyclohexanone (**6b**) and *2-hydroxy-6-methoxycyclohexanone* (**7b**); 80 mg (0.55 mmol) of **5b** in 10.4 ml of 0.08 M DMD sol. in acetone. React. time 48h. Conv. 90%. Chromatographic purification of the crude product gave 72 mg of **6b** and **7b** as an oil. ^{1}H NMR analysis revealed a 82:18 ratio between **6b** and **7b**. **6b**; ^{1}H-nmr δ (ppm): 4.05 (d, J=6.0Hz, 1H, C^2-H), 3.4 (s, 3H, CH_3O), 3.1 (dt, J=6.0Hz, 3.0Hz, 1H, C^3-H), 2.5 (m, 2H, C^6-H). ^{13}C-nmr δ (ppm): 208.3 (C^1), 85.2, 80.7 (C^2, C^3), 57.9 (CH_3O), 38.5, 28.6, 20.5. **7b**; ^{1}H-nmr δ (ppm): 4.5 (dd, J=8.0Hz, 4.0Hz, 1H, C^2-H), 3.5 (s, 3H, CH_3O), 3.3-3.4 (m, 1H, C^3-H). ^{13}C-nmr δ (ppm): 206.9 (C^1), 84.3, 72.9 (C^2, C^6), 58.9 (CH_3O), 37.6, 36.2, 19.6.

3-Azido-2-hydroxycyclohexanone (**6c**); 100 mg (0.64 mmol) of **5c** in 21.3 ml of 0.09 M DMD sol. in acetone. React. time 48h. Conv. >95%. After evaporation of the solvent 99 mg of **6c** was obtained as an oil. ^{1}H-nmr δ (ppm): 4.1 (d, J=9.6Hz, 1H, C^2-H), 3.4 (dt, J=10.9Hz, 5.5 Hz, 1H, C^3-H), 2.5-2.7 (m, 2H, C^6-H), 2.0-2.2 (m, 2H, C^5-H), 1.6-1.8 (m, 2H, C^4).

^{13}C-nmr δ (ppm): 207.3 (C^1), 79.9 (C^2), 67.1 (C^3), 38.3, 29.2, 21.9. $C_6H_9N_3O_2$ (155.1); calcd. C 46.45, H 5.85, N 27.08; found C 46.20, H 6.03, N 27.38.

Cis-2-hydroxy-3-oxyacetylcyclohexanone (**6d**); 88 mg (0.62 mmol) of **5d** in 6.9 ml of 0.09 M DMD sol. in acetone. React. time 24h. Conv. >95%. After evaporation of the solvent, 86 mg (quantitative yield) of **6d** was obtained as an oil. **6d**; ^{1}H-nmr δ (ppm): 5.45-5.50 (m, 1H, C^3-H), 4.19 (d, J=4Hz, 1H, C^2-H), 1.8-2.4 (m, 4H, C^4-H, C^5-H), 1.95 (s, 3H, $\underline{CH_3}COO$).). ^{13}C-nmr δ (ppm): 208.5 (C^1), 170.1 ($\underline{C}OO$), 78.3 (C^2), 75.7 (C^3), 38.7 (C^6), 27.3 (C^4), 21.3 ($\underline{C}H_3COO$, C^5). $C_8H_{12}O_4$ (172.2); calcd. C 55.81, H 7.02; found C 55.74, H 6.93.

Trans-2-hydroxy-3-oxyacetylcyclohexanone (**6e**); 100 mg (0.57 mmol) of **5e** in 9.6 ml of 0.09 M DMD sol. in acetone. React. time 24h. Conv. >95%. After evaporation of the solvent 99 mg (quantitative yield) of **6e** was obtained as an oil. **6e**; ^{1}H-nmr δ (ppm): 4.75 (m, 1H, C^3-H), 4.19 (dd, J=4Hz, 10Hz, 1H, C^2-H), 3.69 (d, J=4Hz, 1H, OH), 1.5-2.5 (m, 6H, C^4-H, C^5-H, C^6-H). ^{13}C-nmr δ (ppm): 207.6 (C^1), 170.6 ($CH_3\underline{C}OO$), 78.5, 77.1 (C^2, C^3), 38.3, 28.9, 21.0, 20.4. $C_8H_{12}O_4$ (172.2); calcd. C 55.81, H 7.02; found C 55.63, H 6.91.

3-Bromo-2-hydroxycyclohexanone (**6f**); to a stirred solution of 3-bromo-1,2-cyclohexandiol **5f** (120 mg, 0.62 mmol) in 1 ml of acetone at –30 °C, a portion of 1.5 eq. of DMD solution (0.09 M in acetone) was added and the reaction mixture was kept stirring for 24 hours. The excess of DMD was removed bubbling the reaction mixture with argon. After evaporation of the solvent in vacuo, 115 mg (quantitative yield) of **6f** was obtained as an oil without further purification. **6f**, *trans* isomer; ^{1}H-nmr δ (ppm): 4.82 (s, 1H, OH), 4.22 (dd, J=10Hz, 1Hz, 1H, C^2-H), 3.8 (ddd, J=10Hz, 9.5Hz, 4.5Hz, 1H, C^3-H), 2.7-2.0 and 1.7-1.5 (m, 6H). ^{13}C-nmr δ (ppm): 205.6 (C^1), 80.6 (C^2), 54.1 (C^3), 38.6, 34.8, 24.6.

3,4-Dihydroxycyclohexanone (**9a**); 80 mg (0.61 mmol) of **8a** in 10 ml of 0.09 M DMD sol. in acetone. React. time 24h. Conv. 50%. Chromatographic purification on silica gel gave 39 mg (>95%) of **9a** as an oil; ^{1}H-nmr δ (ppm) in D_2O: 4.3-4.2 (m, 2H, C^3-H, C^4-H), 2.7-2.3 (m, 4H, C^2-H, C^6-H), 1.8-2.0 (m, 2H, C^5-H). ^{13}C-nmr δ (ppm): 218.8 (C^1), 73.7, 71.1 (C^3, C^4), 47.8, 39.4, 29.6 (C^2, C^5, C^6). $C_6H_{10}O_3$ (130.1); calcd. C 55.37, H 7.74; found C 55.21, H 7.59.

2-Hydroxy-5-oxyacetylcyclohexanone (**10c**) and *2-hydroxy-4-oxyacetylcyclohexanone* (**11c**); 120 mg (0.69 mmol) of **8c** in 15.3 ml of 0.09 M DMD sol. in acetone. React. time 24h. Conv. >95%. Chromatographic purification on silica gel gave 60 mg of 1:1 mixture of **10c** and **11c** as an oil which were characterised as diacetates, by ^{1}H NMR analysis. **10c**,

diastereomeric mixture; ^{1}H-nmr δ (ppm): characteristic signals; δ = 7.1-7.3 (m, 1H, C^2-H), 5.4 (dd, J=13Hz, 6Hz, 0.5H, C^5-H, isomer A), 5.2 (m, 0.5H, C^5-H), 2.5 (m, 2H, C^6-H); **11c**, diastereomeric mixture; 7.1-7.3 (m, 1H, C^2-H), 5.6 (q, J=4Hz, 0.5H, C^4-H, isomer A), 5.3 (br, 0.5 H, C^4-H, isomer B), 2.7 (m, 2H, C^6-H).

4-Azido-3-hydroxycyclohexanone (**14**); 80 mg (0.51 mmol) of **12** in 8.5 ml of 0.09 M DMD sol. in acetone. React. time 24h. Conv. >95%. After evaporation of the solvent 79 mg (quantitative yield) of **14** was obtained as an oil. **14**; ^{1}H-nmr δ (ppm): 3.94 (m, 1H, C^3-H), 3.7 (dt, J=7.9Hz, 3.6Hz, 1H, C^4-H), 3.1-3.4 (s, 1H, OH), 2.7-2.8 (ddd, J=12.9Hz, 4.3Hz, 1.4Hz, 1H, C^2-H), 2.2-2.5 (m, 3H, C^2-H, C^6-H), 1.7-1.8 (m,2H, C^5-H). ^{13}C-nmr δ (ppm): 208.6 (C^1), 71.5 (C^3), 62.6 (C^4), 46.4, 37.5, 25.3. $C_6H_9N_3O_2$ (155.1); calcd. C 46.45, H 5.85, N 27.08; found C 46.28, H 5.64, N 26.87.

3-Azido-4-hydroxycyclohexanone (**15**); 80 mg (0.51 mmol) of **13** in 8.5 ml of 0.09 M DMD sol. in acetone. React. time 24h. Conv. >95%. After evaporation of the solvent 78 mg (quantitative yield) of **15** was obtained as an oil; ^{1}H-nmr δ (ppm): 207.3 (C^1), 70.2 (C^4), 64.2 (C^3), 42.9, 37.4, 28.8. $C_6H_9N_3O_2$ (155.1); calcd. C 46.45, H 5.85, N 27.08; found C 46.30, H 5.57, N 26.84.

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