Crossed Acyloin Condensation of Aliphatic Aldehydes

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Crossed acyloins were efficiently prepared by the thiazolium-catalysed condensation of two different unhindered aldehydes, using one mol equivalent of one aldehyde with three mol equivalents of the other. Conversion into the corresponding nonsymmetrical 1,2-dioxime was achieved either by oxidation with bismuth(III) oxide or the Dess–Martin periodinane to give a 1,2-diketone that was then treated with hydroxylamine to give the oxime.

Introduction

For the synthesis of supramolecular cobaloximes,^[1,2] which we have designed for modelling coenzyme B_{12} -dependent enzymatic reactions,^[3] an efficient synthesis of nonsymmetrical 1,2-dioximes **1** was required. We report a route to these compounds via the corresponding crossed acyloins, which are accessed by an efficient condensation of two different aldehydes (see Scheme 1).



Scheme 1. Crossed acyloin condensation of two different aldehydes





Stetter and co-workers^[4–6] discovered a high yielding crossed acyloin condensation^[7] in which an aromatic aldehyde was treated with an excess of an aliphatic aldehyde in the presence of triethylamine and a catalytic quantity of the thiamine analogue 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride (2). This biomimetic process was rationalised as occurring by reaction of the more stable ylide, derived from the aromatic aldehyde, with the more reactive aliphatic aldehyde (Scheme 2).^[8] However, we have found that Stetter's method can be applied to the preparation of crossed acyloins 3a-f from two aliphatic aldehydes selected from 4a-e, propanal and decanal, even though the relative reactivities of the aldehyde functions are similar. An ex-

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ample of a symmetrically substituted acyloin **3g** was also prepared from a single aldehyde. Actually, Stetter and Dämbkes did report the condensation of two aliphatic aldehydes,^[4,5] but a common component of these reactions was a hindered aldehyde, for example norbornene-2-carboxaldehyde, with which self-condensation is presumably suppressed. We have found that the method of Stetter is effective even when two unhindered aldehydes are used. The method has been validated with a representative set of aldehydes.



R¹ = aromatic; R² = aliphatic

Scheme 2. Reaction of the ylide derived from an aromatic aldehyde with an aliphatic aldehyde



3a-g

3a: $R^1 = (CH_2)_3OPMB$, $R^2 = (CH_2)_6OTBDPS$ 3b: $R^1 = (CH_2)_3OPMB$, $R^2 = CH_2CH_3$ 3c: $R^1 = (CH_2)_3(1,3-dithian-2-yl)$, $R^2 = (CH_2)_6OTBDPS$ 3d: $R^1 = CH_2C(CH_3)_2CH_2OPMB$, $R^2 = (CH_2)_6OTBDPS$ 3e: $R^1 = (CH_2)_3OTIPS$, $R^2 = CH_2CH_3$ 3f: $R^1 = (CH_2)_3OTIPS$, $R^2 = (CH_2)_3OTIPS$ (PMB = 4-methoxybenzyl) (TBDPS = tert-butyldiphenylsilyl) (TIPS = triisopropylsilyl) 0 R + H 4a: $R = (CH_2)_3OPMB$ 4b: $R = (CH_2)_2(1,3-dithian-2-yl)$ 4c: $R = (CH_2)_6OTBDPS$ 4d: $R = CH_2C(CH_3)_2CH_2OPMB$

4e: $R = (CH_2)_3OTIPS$

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Results and Discussion

Using the method of Stetter and Dämbkes,^[4] we obtained a vield of 71% for the symmetrically substituted acyloin 3g starting from aldehyde 4e. To achieve the combination of two dissimilar aldehydes, Stetter and Dämbkes^[4] used a 3:1 ratio of reactants, without commenting on this choice. We have also used this ratio (see Exp. Section for a description of the general procedure) and obtained yields of crossed acyloin as high as 69% for 3a-c,e,f (based on the minor aldehyde; concerning acyloin 3d, see below). This at-firstsight surprising outcome can be easily rationalised by a statistical argument. Thus, an approximate 3:1 ratio of ylides is exposed to a 3:1 ratio of aldehydes. Although this necessarily leads primarily to a symmetrical acyloin from the major aldehyde, the minor aldehyde must give mainly a crossed acyloin (calculated yield based on the minor aldehyde = 86%; i.e. 6/7 of the acyloins derived from the minor aldehyde, if all ylide-aldehyde combinations occur at the same rate, as expected for unhindered aldehydes; note that two of the four possible combinations yield the crossed acyloin). This statistical argument was confirmed by a detailed study of the system using the combination of propanal and decanal. With a 3:1 ratio of propanal to decanal, 56% of crossed acyloin 3e was obtained. When the ratio was reversed (i.e. 3:1 decanal/propanal) the yield of crossed acyloin 3e was in the same range (58%). The fact that the yield of the crossed acyloins 3a-c,e,f was always less than the calculated yield can probably be explained by side reactions such as aldehyde oligomerisation. In one experiment the total amount of acyloins derived from the minor aldehyde was isolated and contained 76% crossed acyloin and 24% symmetrical acyloin. The lower yield (29%) of acyloin 3d is presumably due to steric hindrance in aldehyde 4d, which reduces the efficiency of the crossed condensation. Indeed, 35% of aldehyde 4d was recovered from the reaction and it did not yield any symmetrical acyloin.

Based on our experiences with the acyloin reactions described, we recommend the following protocol: (i) The aldehyde which is more expensive (or time-consuming to synthesise) should be the minor aldehyde in the condensation reaction. (ii) If the two different aldehydes are both easily accessible, the aldehyde with the smaller molecular mass should be the major aldehyde. Thus the amount of crude product is reduced, facilitating the chromatographic fractionation of the acyloins. (iii) If one aldehyde is a small molecule like propanal, the use of more than three equivalents might be advantageous because the corresponding symmetrical acyloin can be removed under vacuum. (iv) If both aldehydes are valuable one might choose a 2:1 or even 1:1 ratio of aldehydes.

The aldehydes $4\mathbf{a} - \mathbf{e}$ required for the preparation of acyloins $3\mathbf{a} - \mathbf{d}$ were prepared by standard methods. Aldehyde $4\mathbf{a}$ was accessed starting from commercially available butane-1,4-diol which was reacted with 0.25 equivalents of sodium hydride and then with 0.25 equivalents of 4-methoxybenzyl chloride to give mainly the mono-O-4-methoxybenzyl ether in 79% yield. Swern oxidation of the remaining alcohol function yielded aldehyde 4a (78%). Selective hydrolysis of 2-[2-(1,3-dioxolan-2-yl)ethyl]-1,3-dithiane with 60% acetic acid (70 °C, 18 h) was used to access aldehyde **4b**.^[9,10] Aldehyde **4c** was synthesised by silvlation of 7-hydroxyheptanal^[11] with tert-butyldiphenylsilyl chloride in DMF with imidazole as base. All attempts to improve the yield of 53% (variation of base and solvent) failed. Aldehyde 4d was prepared starting from 2-(3-hydroxy-2,2-dimethylpropyl)-1,3-dithiane.^[12] First the hydroxyl group was converted into a 4-methoxybenzyl ether. In contrast to butane-1,4-diol (see above) the neopentyl-like alcohol function 2-(3-hydroxy-2,2-dimethylpropyl)-1,3-dithiane could of only be protected in a moderate yield of 47% using catalytic amounts of KI. Finally, removal of the dithiane function was achieved upon treatment of the thioacetal with HgO/ BF₃·Et₂O in wet THF to give aldehyde 4d in 50% yield. Monosilylation of butane-1,4-diol with triisopropylsilyl chloride, followed by Dess-Martin oxidation^[13] of the intermediate silyl-alcohol gave aldehyde 4e.



Conversion of the acyloins into the corresponding dioxime was exemplified with acyloins 3a, 3b, 3f and 3g. Numerous methods were explored for oxidation of these acyloins to the corresponding 1,2-diketone (5a-d), but the best methods utilised either an excess of bismuth(III) oxide (3.5 mol equiv.),^[4,14] which was added to a 1.3 M solution of the acyloin (3a or 3b) in 2-ethoxyethanol/acetic acid (10:3, v/v) at 105 °C, or the Dess-Martin periodinane^[13] (acyloins 3f and 3g). Under the conditions using bismuth oxide, oxidation to the 1,2-diketone was complete within 35 minutes and damage to the protecting groups was insignificant. The crude diketones 5a and 5b were immediately converted into dioximes 1a and 1b (overall yield 77% and 69%, respectively) with an excess of hydroxylamine in methanol (two days at room temp.), with the pH maintained at 5 by periodic addition of 4-dimethylaminopyridine. Diketones 5c and 5d were purified by medium pressure chromatography and converted into the corresponding dioximes (1c and 1d) with hydroxylamine in pyridine.

Experimental Section

General: NMR spectra were recorded on Bruker AC 250 or DRX 500 instruments. ¹H and ¹³C chemical shifts are reported downfield from Me₄Si in ppm and were determined using residual nondeuterated solvent or, when indicated, using Me₄Si as an internal standard. IR spectra were recorded on Beckman Aculab 8 or Bruker IFS 88 (FT) spectrometers. Mass spectra and high resolution mass spectra were recorded on a Finnigan MAT 90 electron impact machine. Analytical thin layer chromatography was performed on commercial Merck plates coated with silica gel 60F₂₅₄. Column chromatography was carried out on Merck silica gel 60. The solvents used for chromatography were distilled before use. Ethanol was distilled from magnesium ethoxide and kept over 3 Å molecular sieves. Triethylamine was distilled from, and kept over, KOH. 3-Benzyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium chloride, hydroxylamine hydrochloride and DMAP were purchased from Fluka. Propanal and decanal were freshly distilled before use. Glassware was dried by flaming or assembling straight from the oven and flushing with argon.

General Procedure for Preparing Crossed Acyloins: One mol equiv. of one aldehyde was mixed with 3 mol equiv. of the other aldehyde in ethanol under argon (overall aldehyde concentration 1 M). The condensation was initiated by addition of catalyst 2 (0.1 mol equiv.) followed by triethylamine (0.6 mol equiv.). After heating the reaction mixture at reflux for 16 h, addition of water and extraction with ethyl acetate gave a crude product, which was fractionated into crossed acyloin and symmetrical acyloins by flash chromatography on silica (elution with cyclohexane/ethyl acetate). According to their spectroscopic data (see below) the acyloins were mixtures of isomers R¹CHOHCOR² and R¹COCHOHR².

5-Hydroxy-1-[(4-methoxyphenyl)methoxy]-11-(tert-butyldiphenylsilanyloxy)undecan-4-one (3a): This compound was prepared from 1 mol equiv. 4a and 3 mol equiv. 4c; yield based on 4a: 69%, colourless oil. $- {}^{1}$ H NMR (250 MHz, CDCl₃): $\delta = 1.01$ [s, 9 H, C(CH₃)₃], 1.19-1.99 (m, 12 H, $6 \times CH_2$), 2.27-2.61 (m, 2 H, $CH_2-C=O$), 3.42 (t, J = 5.4 Hz, 2 H, CH_2 OPMB), 3.37 and 3.63 (2 d, J =3.6 Hz, Σ 1 H, OH), 3.53 (t, J = 5.4 Hz, 2 H, CH₂OSi), 3.78 (s, 3 H, OCH₃), 4.12 [m, 1 H, CH(OH)CH₂], 4.38 and 4.40 (2 s, Σ 2 H, OCH_2Ph), 6.85 (d, J = 8.9 Hz, 2 H, arom. H of *m*-Bn), 7.20 (m, 2 H, arom. H of o-Bn), 7.37 (m, 6 H, arom. H of Si-Ph), 7.63 (m, 4 H, arom. H of Si-Ph). $-{}^{13}$ C NMR (63 MHz, CDCl₃): $\delta = 19.23$, 23.53, 23.82, 24.90, 25.30, 25.58, 25.68, 26.89, 28.96, 29.23, 30.71, 32.34, 32.49, 33.69, 34.55, 37.82, 55.23, 63.79, 63.87, 69.38, 72.58, 76.17, 76.48, 113.79, 127.60, 129.29, 129.53, 130.38, 134.07, 135.57, 159.20, 212.40. – IR (film): $\tilde{v} = 2931$, 2857, 1710, 1612, 1513, 1472, 1463, 1428, 1390, 1361, 1302, 1248, 1173, 1111, 1036, 1008, 998, 823, 741, 703, 687, 614 cm⁻¹. – MS (EI): m/z (%) = 519 (0.2) $[M - C_4H_9]^+ - MS (+FAB/3-nitrobenzyl alcohol): m/z (\%) = 599$ (0.9) [M + Na]⁺, 249 (5), 199 (12), 135 (13), 121 (100). - HRMS (+FAB): calcd. for C₃₅H₄₈NaO₅Si [M + Na]⁺ 599.3169; found 599.3182. - C₃₅H₄₈O₅Si (576.85): C 72.88, H 8.39; found C 72.71, H 8.20.

4-Hydroxy-7-[(4-methoxyphenyl)methoxy]heptan-3-one (3b): This compound was prepared from 1 mol equiv. **4a** and 3 mol equiv. propanal; yield based on **4a**: 56%, colourless oil. - ¹H NMR (250 MHz, CDCl₃, Me₄Si): $\delta = 0.92$ (t, J = 7.3 Hz) and 1.09 (t, J = 7.4 Hz, $\Sigma 3$ H, CH₃CH₂), 1.55–1.70 (2 m, $\Sigma 2$ H, CH₂CH₂OPMB), 1.90–1.95 [2 m, $\Sigma 2$ H, CH₂CH(OH)], 2.45–2.58 (2 m, $\Sigma 2$ H, CH₂-C=O), 3.46 (t, J = 5.9 Hz, 2 H, CH₂OPMB), 3.50 (d, J = 1.3 Hz, 1 H, OH), 3.80 (s, 3 H, OCH₃), 4.15 [m, 1 H, CH(OH)CH₂], 4.40 and 4.43 (2 s, $\Sigma 2$ H, OCH₂Ph), 6.86–6.89 (m, 2 H, arom. H

of *m*-Bn), 7.22–7.25 (m, 2 H, arom. H of *o*-Bn). – ¹³C NMR (63 MHz, CDCl₃): δ = 7.28, 8.67, 23.48, 25.0, 26.44, 30.52, 30.80, 34.30, 54.95, 68.47, 69.14, 72.28, 75.78, 77.05, 113.52, 129.03, 130.08, 130.15, 158.95, 211.95, 212.80. – IR (film): \tilde{v} = 3467, 2931, 2855, 1711, 1612, 1513, 1463, 1407, 1359, 1302, 1247, 1173, 1099, 1034, 984, 819 cm⁻¹. – MS (EI): *m/z* (%) = 266 (0.5) [M⁺], 208 (2), 137 (10), 135 (2), 122 (14), 121 (100), 78 (2), 77 (3), 59 (3), 57 (2), 43 (4). – HRMS (EI): calcd. for C₁₅H₂₂O₄ [M⁺] 266.1518, found 266.1524 – C₁₅H₂₂O₄ (266.33): C 67.65, H 8.33; found C 67.94, H 8.14.

1-(1,3-Dithian-2-yl)-4-hydroxy-10-(tert-butyldiphenylsilanyloxy)decan-3-one (3c): This compound was prepared from 1 mol equiv. 4b and 3 mol equiv. 4c; yield based on 4b: 63%, colourless oil. -¹H NMR (500 MHz, CDCl₃, Me₄Si): $\delta = 1.05$ [s, 9 H, C(CH₃)₃], 1.24-2.17 [m, 14 H, 4 × CH₂, CH₂CH(OH), S-CH₂-CH₂, $S-CH(S)-CH_2$, 2.40-2.50 and 2.64-2.75 (2 m, Σ 2 H, $CH_2-C=$ O), 2.80-2.87 (m, 4 H, S-CH₂), 3.65 (t, J = 6.4 Hz, 2 H, CH_2 -OSi), 4.03 (t, J = 6.9 Hz) and 4.06 (t, J = 7.0 Hz, $\Sigma 1$ H, S-CH-S), 4.17-4.18 [m, 1 H, CH(OH)CH₂], 7.36-7.43 (m, 6 H, arom. H of Si-Ph). 7.66–7.67 (m. 4 H, arom. H of Si-Ph). $-^{13}$ C NMR (126 MHz, CDCl₃, Me₄Si): $\delta = 19.21, 23.52, 24.80, 25.52,$ 25.64, 25.72, 25.86, 25.92, 26.87, 28.87, 28.91, 29.19, 29.85, 30.18, 30.26, 30.53, 30.69, 32.29, 32.45, 33.73, 34.49, 37.77, 46.21, 46.92, 63.75, 63.84, 75.64, 76.51, 127.58, 129.50, 134.05, 134.09, 135.55, 211.17, 211.82. – IR (film): $\tilde{v} = 3470$, 3134, 3070, 3047, 2998, 2931, 2857, 1711, 1589, 1472, 1462, 1428, 1390, 1361, 1276, 1243, 1187, 1112, 1008, 998, 938, 908, 824, 742, 704, 688, 622, 614 cm⁻¹. - MS (EI): m/z (%) = 544 (0.3) [M⁺], 487 (10) [M - C₄H₉]⁺, 311 (27), 276 (10), 275 (47), 200 (16), 199 (100), 183 (12), 147 (17), 139 (17), 135 (12), 132 (21), 131 (10), 119 (30), 69 (27). – HRMS (EI): calcd. for C₃₀H₄₄O₃S₂Si [M⁺] 544.2501, found 544.2534.

5-Hydroxy-1-[(4-methoxyphenyl)methoxy]-11-(tert-butyldiphenylsilanyloxy)-2,2-dimethylundecan-4-one (3d): This compound was prepared from 1 mol equiv. 4d and 3 mol equiv. 4c; yield based on 4d: 29%, colourless oil. - ¹H NMR (250 MHz, CDCl₃, Me₄Si): $\delta = 0.98$ and 1.02 [2 s, $\Sigma \in H$, C(CH₃)₂], 1.04 [s, 9 H, C(CH₃)₃], 1.15-1.81 [m, 10 H, $4 \times CH_2$, CH_2 CH(OH)], 2.34-2.59 (m, 2 H, CH₂-C=O), 3.19-3.30 (m, 2 H, CH₂OPMB), 3.54 (d, J = 5.0 Hz, 0.3 H, OH), 3.64 (t, J = 6.4 Hz, 2 H, CH_2 -OSi), 3.79 (s, 3 H, OCH₃), 4.07–4.17 [m, 1 H, CH(OH)CH₂], 4.21 (d, J = 4.0 Hz, 0.7 H, OH), 4.40 and 4.46 (2 s, Σ 2 H, OCH₂Ph), 6.85–6.90 (m, 2 H, arom. H of m-Bn), 7.20-7.24 (m, 2 H, arom. H of o-Bn), 7.33-7.45 (m, 6 H, arom. H of Si-Ph), 7.65-7.69 (m, 4 H, arom. H of Si-Ph). – MS (EI): m/z (%) = 547 (3) [M – C₄H₉]⁺, 409 (7), 311 (3), 249 (6), 231 (8), 199 (5), 122 (10), 121 (100), 109 (4). -HRMS (EI): calcd. for C₃₃H₄₃O₅Si [M - C₄H₉]⁺ 547.2880, found 547.2859.

4-Hydroxytridecan-3-one (3e): This compound was prepared from 1 mol equiv. decanal and 3 mol equiv. propanal or 1 mol equiv. propanal and 3 mol equiv. decanal; yield based on the minor aldehyde: 56% and 58%, respectively, colourless oil. $-^{1}$ H NMR (500 MHz, CDCl₃): $\delta = 0.86$ [t, J = 6.9 Hz, 6 H, $2 \times (CH_2)_8 CH_3$], 0.92 [t, J = 7.4 Hz, 3 H, CH(OH)CH₂CH₃], 1.10 (t, J = 7.3 Hz, 3 H, CO-CH₂CH₃), 1.24–1.45 (m, 26 H, 13 × CH₂), 1.48–1.55 and 1.76–1.83 [2 m, 2 H, CH(OH)CH₂CH₂), 1.55–1.62 and 1.86–1.91 [2 m, 4 H, CH(OH)CH₂CH₂), 3.48–3.50 (br m, 2 H, 2 × OH), 4.13–4.17 [m, 2 H, 2 × CH(OH)]. $-^{13}$ C NMR (126 MHz, CDCl₃): $\delta = 7.61$, 8.86, 14.07, 22.65, 23.61, 24.81, 26.74, 29.24, 29.27, 29.34, 29.38, 29.46, 29.50, 31.06, 31.84, 31.86, 33.88, 37.88, 76.24, 77.17, 212.44, 212.90. – IR (film): $\tilde{v} = 3481$, 2926, 2855, 1713, 1463, 1407, 1379, 1352, 1262, 1115, 1095, 1037, 983, 723

cm⁻¹. – MS (EI): m/z (%) = 214 (3) [M⁺], 158 (3), 157 (49), 155 (77), 97 (40), 88 (11), 85 (13), 83 (100), 71 (30), 69 (53), 59 (100), 58 (22), 57 (81), 55 (58), 43 (53), 41 (48). – HRMS (EI): calcd. for $C_{13}H_{26}O_2$ [M⁺] 214.1933, found 214.1944.

4-Hydroxy-7-triisopropylsilanyloxyheptan-3-one (3f): This compound was prepared from 1 mol equiv. **4e** and 3 mol equiv. propanal; yield based on **4e**: 42%, colourless oil. - ¹H NMR (200 MHz, CDCl₃): $\delta = 0.82$ (m, 24 H, TIPS + CH₃), 1.70 (m, 6 H, 3 × CH₂), 2.31 (m, 2 H, CH₂-CH), 3.31 (d, J = 4.6 Hz, 1 H, CH-OH), 3.48 (m, 2 H, CH₂-OSi), 3.98 (m, 1 H, CH-OH). - ¹³C NMR: (126 MHz, CDCl₃) $\delta = 8.50, 8.97, 12.04, 18.08, 26.94, 27.84, 30.62, 31.75, 34.29, 62.17, 62.85, 212.54, 213.32. – IR (cap film): <math>\tilde{v} = 3481, 2942, 2891, 2866, 1713, 1463, 1367, 1248, 1106, 1038, 1013 cm⁻¹. – MS (+EI): <math>m/z$ (%) = 259 (71) [M⁺ – iPr], 241 (49), 217 (50), 111 (63), 103 (100), 75 (97), 61 (54). – C₁₆H₃₄O₃Si (302.53): C 63.52, H 11.33; found C 60.09, H 10.81; contains 1 molecule of water.

5-Hydroxy-1,8-bis(triisopropylsilanyloxy)octan-4-one (3g): This compound was prepared from **4e**; yield 71%, colourless oil. - ¹H NMR (200 MHz, CDCl₃): $\delta = 1.02$ (m, 42 H, 2 × TIPS), 1.90 (m, 6 H, 3 × CH₂), 2.60 (dt, *J* = 2.2 and 5.1 Hz, 1 H, C*H*CH₂), 3.69 (m, 5 H, OH and 2 × C*H*₂−OSi), 4.20 (m, 1 H, C*H*-OH). - ¹³C NMR (50.3 MHz, CDCl₃): $\delta = 11.99$, 18.04, 26.91, 28.35, 30.51, 34.29, 62.25, 62.89, 212.50. − IR (cap film): $\tilde{v} = 3483$, 2943, 2892, 2866, 2729, 1713, 1653, 1367, 1255, 1202, 1107, 1013 cm⁻¹. − MS (+EI): *m*/*z* (%) = 489 (0.5) [M + H]⁺, 445 (4), 427 (5), 271 (100), 253 (22), 157 (14), 145 (29), 123 (32), 71 (14), 59 (10). − C₂₆H₅₆O₄Si₂ (488.90): C 63.88, H 11.55; found C 60.42, H 10.62; contains 1 molecule of water.

General Procedures for the Conversion of Acyloins into 1,2-Dioximes. *Procedure A* (acyloins 3a and 3b): To a 1.3 M solution of the acyloin in 2-ethoxyethanol and acetic acid (10:3, v/v) at 105 °C was added bismuth(III) oxide (3.5 mol equiv.) in one portion. After 35 min. TLC showed complete consumption of starting material. The mixture was filtered hot and the filter cake washed with chloroform. The filtrate was washed neutral with aq. NaHCO₃ and water and dried (MgSO₄). The solvent was removed under reduced pressure to leave a yellow oil which was immediately taken up in methanol. After addition of H₂NOH·HCl (5 mol equiv.), the pH was adjusted to 5 by addition of DMAP. The mixture was stirred for two days at room temp. with periodic addition of DMAP to maintain the pH at 5. After addition of water and extraction with ethyl acetate the crude dioxime was purified by flash chromatography on silica using cyclohexane/ethyl acetate as eluent.

Procedure B (acyloins 3f and 3g): To a solution of the Dess Martin periodinane (1.2 mol equiv.) in dry dichloromethane was added dropwise the acyloin (1.0 mol equiv.) in dry dichloromethane over a 10 min. period. The resulting solution was stirred under N₂ for 1 h. The yellow-coloured mixture was concentrated and the residue chromatographed on silica gel eluting with ethyl acetate/petroleum ether (5:95) to give the diketone as a yellow oil. To the diketone (X, g) in dry ethanol (10X, mL) was added hydroxylamine hydrochloride (2X, g) and pyridine (2X, mL) and the resulting solution was stirred for 2 h. After this time the solution was concentrated, water was added and the solution extracted into ethyl acetate. The extracts were combined, dried (MgSO₄) and concentrated to give the product as a white solid.

7-Triisopropylsilanyloxyheptane-3.4-dione (5a): This compound was prepared from **3f** as a yellow oil, yield $69\% - {}^{1}$ H NMR (500 MHz, CDCl₃): $\delta = 0.95$ (m, 24 H, TIPS + CH₃), 1.77 (quintet, 2 H, J = 6.4 Hz, CH₂), 2.70 (q, J = 7.0, 2 H, CH₂-CH₃) 2.79 (t, J = 7.0,

2 H, CH₂–C=O), 3.64 (t, J = 6.1 Hz, 2 H, CH₂–OSi). – ¹³C NMR (500 MHz, CDCl₃): $\delta = 6.95$, 12.01, 18.05, 26.47, 29.59, 32.86, 62.28, 199.86, 200.25. – IR (cap film): $\tilde{v} = 2943$, 2892, 1714, 1463, 1109, 1070, 1013, 892 cm⁻¹. – MS (+EI): m/z (%) = 257 (100) [M⁺ – *i*Pr], 243 (34), 213 (94), 173 (8), 103 (23), 57 (17). – C₁₆H₃₂O₃Si (300.51): C 63.95, H 10.73; found C 62.61, H 10.44; contains 1/2 molecule of water.

1,8-Bis(triisopropylsilanyloxy)octane-4,5-dione (5b): This compound was prepared from **3g** as a yellow oil, yield 94% – ¹H NMR (500 MHz, CDCl₃): $\delta = 0.97$ (m, 42 H, 2 × TIPS), 1.76 (q, J = 6.4, 4 H, 2 × CH₂), 2.79 (t, J = 7.1 Hz, 4 H, 2 × CH₂-C=O), 3.65 (t, J = 6.4 Hz, 4 H, 2 × CH₂-OTIPS). – ¹³C NMR (126 MHz, CDCl₃): $\delta = 11.98$, 18.01, 26.42, 32.71, 62.30, 200.53. – IR (cap film): $\tilde{v} = 2943$, 2891, 1714, 1463, 1107, 1069, 1038, 1013, 882 cm⁻¹. – MS (+EI): m/z (%) = 487 (33) [M + H]⁺, 443 (25), 313 (42), 269 (100), 243 (62), 217 (40), 139 (42). – C₂₆H₅₄O₄Si₂ (486.88): C 64.14, H 11.18; found C 62.54, H 11.07; contains 1 molecule of water.

11-(tert-Butyldiphenylsilanyloxy)-1-[(4-methoxyphenyl)methoxy]undecan-4,5-dione Dioxime 1a: White solid, 77%, m.p. 54 °C. - ¹H NMR (500 MHz, CDCl₃): $\delta = 1.09$ [s, 9 H, C(CH₃)₃], 1.38 [br m, 4 H, (CH₂)₂-(CH₂)₂-O], 1.52 [m, 2 H, CH₂-(CH₂)₄-O], 1.60 [m, 2 H, N=C-(CH₂)₄-CH₂], 1.89 (quintet, J = 7.5 Hz, 2 H, CH_2CH_2OPMB), 2.63 [t, J = 7.6 Hz, 2 H, $N=C-CH_2-(CH_2)_5$], 2.75 [t, J = 7.4 Hz, 2 H, N=C-CH₂-(CH₂)₂], 3.51 (t, J = 6.5 Hz, 2 H, CH_2OPMB), 3.68 (t, J = 6.6 Hz, 2 H, CH_2-OSi), 3.79 (s, 3 H, OCH₃), 4.47 (s, 2 H, CH₂Ph), 6.88 (d, J = 8.6 Hz, 2 H, arom. H of *m*-Bn), 7.29 (d, J = 8.6 Hz, 2 H, arom. H of *o*-Bn), 7.40 (m, 6 H, arom. H of Si-Ph), 7.71 (m, 4 H, arom. H of Si-Ph), 9.17 (s, 1 H, NOH), 9.18 (s, 1 H, NOH). - ¹³C NMR (126 MHz, CDCl₃): $\delta = 19.21, 20.63, 23.92, 25.53, 26.40, 26.90, 29.61, 32.48, 55.22,$ 64.08, 69.70, 72.38, 113.71, 127.60, 129.33, 129.52, 130.52, 134.09, 135.57, 157.58, 159.07. – IR (film): $\tilde{v} = 3296$, 3072, 2932, 2859, 1614, 1588, 1514, 1464, 1429, 1390, 1361, 1303, 1247, 1174, 1111, 1039, 989, 929, 905, 825, 741, 704, 687, 615 cm⁻¹. – MS (EI): *m*/ z (%) = 604 (0.1) [M⁺], 587 (1) [M - OH]⁺, 547 (2) [M - C₄H₉]⁺. - HRMS (EI): calcd. for C35H48N2O5Si [M+] 604.3353; found 604.3333 - C₃₅H₄₈N₂O₅Si (604.86): C 69.50, H 8.00, N 4.63; found C 69.21, H 7.98, N 4.43.

7-[(4-Methoxyphenyl)methoxy]heptan-3,4-dione Dioxime (1b): White solid, 69%, m.p. 108 °C). $- {}^{1}$ H NMR (500 MHz, CD₃OD): $\delta = 0.92$ (t, J = 7.5 Hz, 3 H, CH₂CH₃), 1.68 (quintet, J = 7.2 Hz, 2 H, $CH_2CH_2CH_2$), 2.51 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 2.57 (t, J = 7.7 Hz, 2 H, N=C-CH₂CH₂), 3.36 (t, J = 6.7 Hz, 2 H, CH₂OPMB), 3.68 (s, 3 H, OCH₃), 4.31 (s, 2 H, CH₂Ph), 6.78–6.80 (m, 2 H, arom. H of *m*-Bn), 7.15–7.17 (m, 2 H, arom. H of *o*-Bn), 10.74 (s, 1 H, NOH), 10.81 (s, 1 H, NOH). - ¹³C NMR (126 MHz, CD₃OD): $\delta = 11.7, 17.9, 21.4, 27.8, 55.9, 71.4, 73.6, 115.0, 130.9,$ 131.9, 157.7, 159.5, 161.0. – IR (diffuse reflection): $\tilde{v} = 3227, 3086$, 2944, 2880, 1613, 1585, 1515, 1457, 1367, 1303, 1253, 1175, 1095, 1031, 969, 910, 901, 878, 851, 815 cm⁻¹. – MS (EI): m/z (%) = 277 (14) [M⁺], 142 (9), 141 (78), 126 (5), 122 (9), 121 (100). -HRMS (EI): calcd. for C15H21N2O3 [M+] 277.1552; found 277.1541 - C₁₅H₂₁N₂O₃ (277.34): C 61.21, H 7.53, N 9.52; found C 60.94, H 7.49, N 9.30.

7-Triisopropylsilanyloxyheptane-3,4-dione Dioxime (1c): This compound was prepared from **5a** as a white solid, yield 69%. – ¹H NMR (500 MHz, [D₆]DMSO): δ = 1.03 (m, 24 H, TIPS + CH₃), 1.65 (quintet, *J* = 7.3 Hz, 2 H, CH₂), 2.56 (m, 4 H, 2 × CH₂-C= N), 3.63 (t, *J* = 7.1 Hz, 2 H, CH₂-OSi), 11.31 (s, 1 H, N-OH), 11.35 (s, 1 H, N-OH). – ¹³C NMR (126 MHz, [D₆]DMSO): δ =

10.88, 11.41, 17.83, 19.75, 29.51, 29.56, 63.17, 155.25, 156.95. – IR (KBr disc): $\tilde{v} = 3283$, 2944, 2868, 1461, 1075, 1041, 1029, 909, 882 cm⁻¹. – MS (+EI): *m/z* (%) = 287 (11) [M⁺ – *i*Pr], 198 (100), 131 (30), 103 (54), 75 (75), 61 (54). – C₁₆H₃₄N₂O₃Si (330.54): C 58.14, H 10.37, N 8.47; found C 58.22, H 10.79, N 8.47.

1,8-Bis(triisopropylsilanyloxy)octane-4,5-dione Dioxime (1d): This compound was prepared from **5b** as a white solid, yield 57%. $-^{1}$ H NMR (500 MHz, CDCl₃): $\delta = 1.00$ (m, 42 H, 2 × TIPS), 1.62 (quintet, J = 7.4 Hz, 4 H, 2 × CH₂), 2.54 (t, J = 7.3 Hz, 4 H, 2 × CH₂-C=N), 3.60 (t, J = 7.0 Hz, 4 H, 2 × CH₂-OTIPS), 11.30 (s, 2 H, 2 × OH). $-^{13}$ C NMR (126 MHz, CDCl₃): $\delta = 11.36$, 17.83, 19.71, 29.58, 63.15, 155.24. - IR (KBr): $\tilde{v} = 3342$, 2962, 2946, 2867, 1606, 1461, 1118, 1072, 1027, 1019, 883 cm⁻¹. - MS (+EI): m/z (%) = 499 (2.7) [M⁺ - OH], 473 (46), 299 (44), 198 (75), 145 (77), 103 (81), 89 (52), 75 (100). - C₂₆H₅₆N₂O₄Si₂ (516.91): C 60.41, H 10.92, N 5.42; found C 60.88, H 10.92, N 5.24.

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