Crossed Acyloin Condensation of Aliphatic Aldehydes

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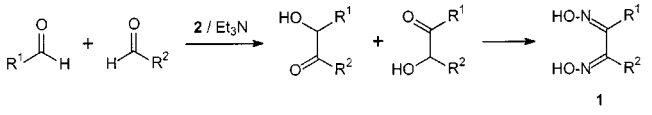
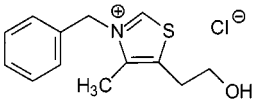
Crossed acyloins were efficiently prepared by the thiazolium-catalysed condensation of two different unhindered aldehydes, using one mol equivalent of one aldehyde with three mol equivalents of the other. Conversion into the corresponding nonsymmetrical 1,2-dioxime was achieved either by oxidation with 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



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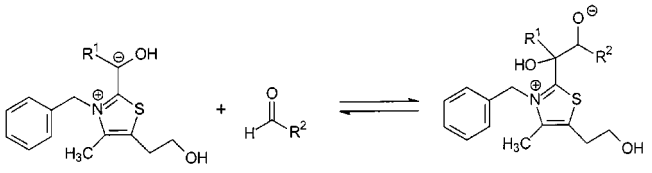
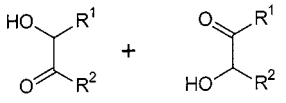
Stetter and co-workers[4–6] discovered a high yielding crossed acyloin condensation[7] in which an aromatic aldehyde was treated with an excess of an aliphatic aldehyde in the presence of triethylamine and a catalytic quantity of the thiamine analogue 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride (**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 example 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.



R^1 = aromatic; R^2 = 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: $R^1 = (CH_2)_2$(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: $R^1 = (CH_2)_8CH_3$, $R^2 = CH_2CH_3$
3f: $R^1 = (CH_2)_3OTIPS$, $R^2 = CH_2CH_3$
3g: $R^1 = (CH_2)_3OTIPS$, $R^2 = (CH_2)_3OTIPS$
(PMB = 4-methoxybenzyl)
(TBDPS = *tert*-butyldiphenylsilyl)
(TIPS = triisopropylsilyl)

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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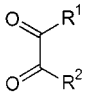
Results and Discussion

Using the method of Stetter and Dämbkes,[4] we obtained a yield 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-first-sight 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.

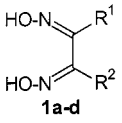
Based on our experiences with the acyloin reactions described, we recommend the following protocol: (i) The aldehyde which is more expensive (or time-consuming to synthesise) should be the minor aldehyde in the condensation reaction. (ii) If the two different aldehydes are both easily accessible, the 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 **4a−e** required for the preparation of acyloins **3a−d** were prepared by standard methods. Aldehyde **4a** 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 silylation 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 of 2-(3-hydroxy-2,2-dimethylpropyl)-1,3-dithiane could 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/BF_3·Et_2O 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**.



5a-d

5a: $R^1 = (CH_2)_3OPMB$, $R^2 = (CH_2)_6OTBDPS$
5b: $R^1 = (CH_2)_3OPMB$, $R^2 = CH_2CH_3$
5c: $R^1 = (CH_2)_3OTIPS$, $R^2 = CH_2CH_3$
5d: $R^1 = (CH_2)_3OTIPS$, $R^2 = (CH_2)_3OTIPS$



1a-d

1a: $R^1 = (CH_2)_3OPMB$, $R^2 = (CH_2)_6OTBDPS$
1b: $R^1 = (CH_2)_3OPMB$, $R^2 = CH_2CH_3$
1c: $R^1 = (CH_2)_3OTIPS$, $R^2 = CH_2CH_3$
1d: $R^1 = (CH_2)_3OTIPS$, $R^2 = (CH_2)_3OTIPS$

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 ^{13}C chemical shifts are reported downfield from Me_4Si in ppm and were determined using residual nondeuterated solvent or, when indicated, using Me_4Si 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 $60F_{254}$. 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 $R^1CHOHCOR^2$ and $R^1COCHOHR^2$.

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. − ^1H NMR (250 MHz, $CDCl_3$): δ = 1.01 [s, 9 H, $C(CH_3)_3$], 1.19−1.99 (m, 12 H, 6 × CH_2), 2.27−2.61 (m, 2 H, CH_2−C=O), 3.42 (t, J = 5.4 Hz, 2 H, CH_2OPMB), 3.37 and 3.63 (2 d, J = 3.6 Hz, Σ 1 H, O*H*), 3.53 (t, J = 5.4 Hz, 2 H, CH_2OSi), 3.78 (s, 3 H, OCH_3), 4.12 [m, 1 H, $CH(OH)CH_2$], 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, $CDCl_3$): δ = 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): $\tilde{\nu}$ = 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 $C_{35}H_{48}NaO_5Si$ $[M + Na]^+$ 599.3169; found 599.3182. − $C_{35}H_{48}O_5Si$ (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, $CDCl_3$, Me_4Si): δ = 0.92 (t, J = 7.3 Hz) and 1.09 (t, J = 7.4 Hz, Σ 3 H, CH_3CH_2), 1.55−1.70 (2 m, Σ 2 H, CH_2CH_2OPMB), 1.90−1.95 [2 m, Σ 2 H, $CH_2CH(OH)$], 2.45−2.58 (2 m, Σ 2 H, CH_2−C=O), 3.46 (t, J = 5.9 Hz, 2 H, CH_2OPMB), 3.50 (d, J = 1.3 Hz, 1 H, OH), 3.80 (s, 3 H, OCH_3), 4.15 [m, 1 H, $CH(OH)CH_2$], 4.40 and 4.43 (2 s, Σ 2 H, OCH_2Ph), 6.86−6.89 (m, 2 H, arom. H of *m*-Bn), 7.22−7.25 (m, 2 H, arom. H of *o*-Bn). − ^{13}C NMR (63 MHz, $CDCl_3$): 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): $\tilde{\nu}$ = 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 $C_{15}H_{22}O_4$ $[M^+]$ 266.1518, found 266.1524 − $C_{15}H_{22}O_4$ (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, $CDCl_3$, Me_4Si): δ = 1.05 [s, 9 H, $C(CH_3)_3$], 1.24−2.17 [m, 14 H, 4 × CH_2, $CH_2CH(OH)$, S−CH_2−CH_2, 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−CH_2), 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, Σ 1 H, S−C*H*−S), 4.17−4.18 [m, 1 H, C*H*(OH)CH_2], 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, $CDCl_3$, Me_4Si): δ = 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): $\tilde{\nu}$ = 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) $[M - C_4H_9]^+$, 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 $C_{30}H_{44}O_3S_2Si$ $[M^+]$ 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, $CDCl_3$, Me_4Si): δ = 0.98 and 1.02 [2 s, Σ 6 H, $C(CH_3)_2$], 1.04 [s, 9 H, $C(CH_3)_3$], 1.15−1.81 [m, 10 H, 4 × CH_2, $CH_2CH(OH)$], 2.34−2.59 (m, 2 H, CH_2−C=O), 3.19−3.30 (m, 2 H, CH_2OPMB), 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, OCH_3), 4.07−4.17 [m, 1 H, C*H*(OH)CH_2], 4.21 (d, J = 4.0 Hz, 0.7 H, O*H*), 4.40 and 4.46 (2 s, Σ 2 H, OCH_2Ph), 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) $[M - C_4H_9]^+$, 409 (7), 311 (3), 249 (6), 231 (8), 199 (5), 122 (10), 121 (100), 109 (4). − HRMS (EI): calcd. for $C_{33}H_{43}O_5Si$ $[M - C_4H_9]^+$ 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. − ^1H NMR (500 MHz, $CDCl_3$): δ = 0.86 [t, J = 6.9 Hz, 6 H, 2 × $(CH_2)_8CH_3$], 0.92 [t, J = 7.4 Hz, 3 H, $CH(OH)CH_2CH_3$], 1.10 (t, J = 7.3 Hz, 3 H, CO-CH_2CH_3), 1.24−1.45 (m, 26 H, 13 × CH_2), 1.48−1.55 and 1.76−1.83 [2 m, 2 H, $CH(OH)CH_2(CH_2)_7$], 1.55−1.62 and 1.86−1.91 [2 m, 4 H, $CH(OH)CH_2CH_3$, CO-CH_2CH_2], 2.38−2.56 [m, 4 H, CO-CH_2CH_3, CO-$CH_2(CH_2)_7$], 3.48−3.50 (br m, 2 H, 2 × O*H*), 4.13−4.17 [m, 2 H, 2 × C*H*(OH)]. − ^{13}C NMR (126 MHz, $CDCl_3$): δ = 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): $\tilde{\nu}$ = 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. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.82 (m, 24 H, TIPS + CH_3), 1.70 (m, 6 H, 3 × C*H*$_2$), 2.31 (m, 2 H, C*H*$_2$-CH), 3.31 (d, *J* = 4.6 Hz, 1 H, CH-O*H*), 3.48 (m, 2 H, C*H*$_2$−OSi), 3.98 (m, 1 H, C*H*−OH). − ^{13}C NMR: (126 MHz, $CDCl_3$) δ = 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): $\tilde{\nu}$ = 3481, 2942, 2891, 2866, 1713, 1463, 1367, 1248, 1106, 1038, 1013 cm^{-1}. − MS (+EI): *m*/*z* (%) = 259 (71) [M$^+$ − *i*Pr], 241 (49), 217 (50), 111 (63), 103 (100), 75 (97), 61 (54). − $C_{16}H_{34}O_3Si$ (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. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.02 (m, 42 H, 2 × TIPS), 1.90 (m, 6 H, 3 × CH_2), 2.60 (dt, *J* = 2.2 and 5.1 Hz, 1 H, C*H*CH$_2$), 3.69 (m, 5 H, OH and 2 × C*H*$_2$−OSi), 4.20 (m, 1 H, C*H*-OH). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 11.99, 18.04, 26.91, 28.35, 30.51, 34.29, 62.25, 62.89, 212.50. − IR (cap film): $\tilde{\nu}$ = 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). − $C_{26}H_{56}O_4Si_2$ (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. $NaHCO_3$ and water and dried ($MgSO_4$). The solvent was removed under reduced pressure to leave a yellow oil which was immediately taken up in methanol. After addition of $H_2NOH{\cdot}HCl$ (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 N_2 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 ($MgSO_4$) 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, $CDCl_3$): δ = 0.95 (m, 24 H, TIPS + C*H*$_3$), 1.77 (quintet, 2 H, *J* = 6.4 Hz, C*H*$_2$), 2.70 (q, *J* = 7.0, 2 H, C*H*$_2$−CH$_3$) 2.79 (t, *J* = 7.0, 2 H, CH$_2$−C=O), 3.64 (t, *J* = 6.1 Hz, 2 H, C*H*$_2$−OSi). − ^{13}C NMR (500 MHz, $CDCl_3$): δ = 6.95, 12.01, 18.05, 26.47, 29.59, 32.86, 62.28, 199.86, 200.25. − IR (cap film): $\tilde{\nu}$ = 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). − $C_{16}H_{32}O_3Si$ (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% − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.97 (m, 42 H, 2 × TIPS), 1.76 (q, *J* = 6.4, 4 H, 2 × CH_2), 2.79 (t, *J* = 7.1 Hz, 4 H, 2 × CH$_2$−C=O), 3.65 (t, *J* = 6.4 Hz, 4 H, 2 × C*H*$_2$−OTIPS). − ^{13}C NMR (126 MHz, $CDCl_3$): δ = 11.98, 18.01, 26.42, 32.71, 62.30, 200.53. − IR (cap film): $\tilde{\nu}$ = 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). − $C_{26}H_{54}O_4Si_2$ (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. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.09 [s, 9 H, C(C*H*$_3$)$_3$], 1.38 [br m, 4 H, (C*H*$_2$)$_2$-(CH$_2$)$_2$−O], 1.52 [m, 2 H, C*H*$_2$-(CH$_2$)$_4$−O], 1.60 [m, 2 H, N=C-(CH$_2$)$_4$−C*H*$_2$], 1.89 (quintet, *J* = 7.5 Hz, 2 H, C*H*$_2$CH$_2$OPMB), 2.63 [t, *J* = 7.6 Hz, 2 H, N=C−C*H*$_2$-(CH$_2$)$_5$], 2.75 [t, *J* = 7.4 Hz, 2 H, N=C−C*H*$_2$-(CH$_2$)$_2$], 3.51 (t, *J* = 6.5 Hz, 2 H, C*H*$_2$OPMB), 3.68 (t, *J* = 6.6 Hz, 2 H, C*H*$_2$−OSi), 3.79 (s, 3 H, OC*H*$_3$), 4.47 (s, 2 H, C*H*$_2$Ph), 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). − ^{13}C NMR (126 MHz, $CDCl_3$): δ = 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): $\tilde{\nu}$ = 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 − C$_4$H$_9$]$^+$. − HRMS (EI): calcd. for $C_{35}H_{48}N_2O_5Si$ [M$^+$] 604.3353; found 604.3333 − $C_{35}H_{48}N_2O_5Si$ (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, CD_3OD): δ = 0.92 (t, *J* = 7.5 Hz, 3 H, CH$_2$C*H*$_3$), 1.68 (quintet, *J* = 7.2 Hz, 2 H, CH$_2$C*H*$_2$CH$_2$), 2.51 (q, *J* = 7.5 Hz, 2 H, C*H*$_2$CH$_3$), 2.57 (t, *J* = 7.7 Hz, 2 H, N=C−C*H*$_2$CH$_2$), 3.36 (t, *J* = 6.7 Hz, 2 H, C*H*$_2$OPMB), 3.68 (s, 3 H, OCH$_3$), 4.31 (s, 2 H, C*H*$_2$Ph), 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). − ^{13}C NMR (126 MHz, CD_3OD): δ = 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): $\tilde{\nu}$ = 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 $C_{15}H_{21}N_2O_3$ [M$^+$] 277.1552; found 277.1541 − $C_{15}H_{21}N_2O_3$ (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%. − ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 1.03 (m, 24 H, TIPS + CH_3), 1.65 (quintet, *J* = 7.3 Hz, 2 H, C*H*$_2$), 2.56 (m, 4 H, 2 × CH$_2$−C=N), 3.63 (t, *J* = 7.1 Hz, 2 H, C*H*$_2$−OSi), 11.31 (s, 1 H, N−OH), 11.35 (s, 1 H, N−OH). − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ =

10.88, 11.41, 17.83, 19.75, 29.51, 29.56, 63.17, 155.25, 156.95. − IR (KBr disc): $\tilde{\nu}$ = 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). − $C_{16}H_{34}N_2O_3Si$ (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%. − ^1H NMR (500 MHz, $CDCl_3$): δ = 1.00 (m, 42 H, 2 × TIPS), 1.62 (quintet, *J* = 7.4 Hz, 4 H, 2 × CH_2), 2.54 (t, *J* = 7.3 Hz, 4 H, 2 × CH_2−C=N), 3.60 (t, *J* = 7.0 Hz, 4 H, 2 × CH_2−OTIPS), 11.30 (s, 2 H, 2 × OH). − ^{13}C NMR (126 MHz, $CDCl_3$): δ = 11.36, 17.83, 19.71, 29.58, 63.15, 155.24. − IR (KBr): $\tilde{\nu}$ = 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). − $C_{26}H_{56}N_2O_4Si_2$ (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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