Synthesis and Reactions of Novel Substituted 3-Hydroxy-5-iminoalkanoic Esters

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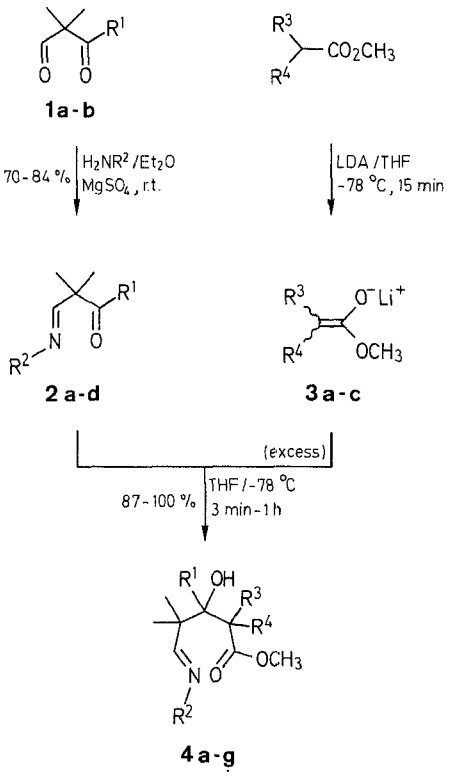
The title compounds **4** were prepared from β-iminoketones **2** by reaction with simple α-lithiated esters **3** through a thermally controlled process. Some reactions of the title compounds **4** are also reported, in spite of their facile thermolysis.

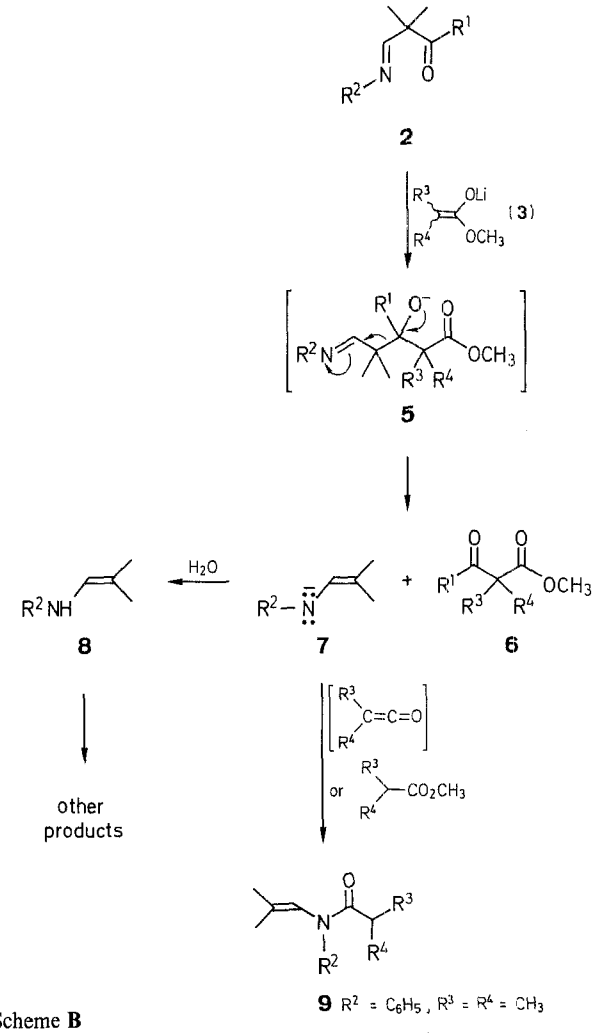
We recently undertook[1] a systematic study on the reaction of iminoketones and related bifunctional electrophiles with ester enolates in order to explore methods for the obtention of synthetically useful, simple polyfunctional compounds. Within the framework of this investigation, we have explored the reaction of simple α-lithiated esters **3** (lithium ester enolates) with β-iminoketones **2** which are unable to undergo tautomerization involving the central carbon atom. It may be expected that competitive aldol-like retrocondensation will constitute a serious shortcoming for these reactions of β-iminoketones, as occurs with β-dicarbonyl compounds upon treatment with bases.[2] We now report the synthesis of hitherto unknown 3-hydroxy-5-iminoalkanoic esters **4** through a thermally-controlled process in which competitive retrocondensation is practically absent in nearly every case. The potential interest of compounds **4** relies on the fact that they are both β-hydroxyesters and β-hydroxyimines, structures which have aroused interest both from the synthetic and the theoretical standpoint.[3]

All compounds **4** were obtained in dry tetrahydrofuran/hexane solution at − 78 °C by the reaction of iminoketones **2** with excess of enolates **3**, in nearly quantitative yield (Scheme **A**). Since chromatographic purification of these compounds on silica gel led to partial decomposition, they were used *in situ* to investigate



1–4	R^1	R^2	R^3	R^4
1a	C_6H_5			
1b	CH_3			
2a	C_6H_5	C_6H_5		
2b	C_6H_5	$C_6H_5CH_2$		
2c	CH_3	C_6H_5		
2d	CH_3	$C_6H_5CH_2$		
3a			H	H
3b			CH_3	H
3c			CH_3	CH_3
4a	C_6H_5	C_6H_5	H	H
4b	C_6H_5	$C_6H_5CH_2$	H	H
4c	CH_3	C_6H_5	H	H
4d	CH_3	$C_6H_5CH_2$	H	H
4e	C_6H_5	C_6H_5	CH_3	H
4f	CH_3	C_6H_5	CH_3	H
4g	CH_3	C_6H_5	CH_3	CH_3

Scheme **A**



Scheme **B**

their reactivity. The spectral properties of **4** are consistent with the hydroxy-imine ester structure. The starting β-iminoketones **2a–d** were obtained by condensation of the 3-oxoalkanals **1a, b** with appropriate primary amines according to a known procedure for **2a, b.**[4] The 3-oxoalkanals **1** were prepared by acylation[5] of 2-methyl-1-(4-morpholinyl)propene.[6] Lithium ester enolates **3a–c** were generated *in situ* from the related carboxylic esters and lithium diisopropylamide (LDA) in tetrahydrofuran.

When the reaction temperature was raised above −78 °C, formation of compounds **4** was accompanied, in every case, by the related retro-aldol fragmentation processes, the extension and rate of which increases, as expected, upon raising the temperature. The products isolated **(4, 6, 9)** and/or detected **(8)** in these processes are formulated in Scheme **B**. Enamide **9** was isolated along with the corresponding β-oxoester only in the reaction of **2a** with **3c** at −15 °C. Its formation can be accounted for by acylation of enamine anion **7** with dimethylketene generated *in situ* from anion **3c.**[7]

Of the various reactions essayed, only that of **2a** with **3c** failed to yield the corresponding addition products. From the beginning of reaction at −78 °C, the exclusive formation of fragmentations products was observed, and some unreacted **2a** was isolated. This fact may be accounted for by the high unstability of the intermediate alkoxide **5** as a consequence of the strong

Table 1. β-Iminoketones **2** Prepared

Product	Yield[a] (%)	bp (°C)/Torr	Molecular Formula[b] or Lit. bp (°C)/Torr	IR (film)[c], ν(cm^{-1}) C=O	C=N	^{1}H-NMR ($CDCl_3$/TMS)[d] δ
2a	82	121–122/0.01	120/1.0[4]	1680	1640	1.60 (s, 6H, $2CH_3$); 6.83–7.47 (m, $8H_{arom}$); 7.77–7.87 (m, $3H_{arom}$ and CH=N)
2b	72	125–126/0.01	125/0.1[4]	1680	1650	1.47 (s, 6H, $2CH_3$); 4.50 (br s, 2H, $C\underline{H}_2C_6H_5$); 6.83–7.27 (m, $8H_{arom}$); 7.50–7.77 (m, $3H_{arom}$ and CH=N)
2c	84	95–96/0.05	$C_{12}H_{15}NO$ (189.3)	1710	1640	1.37 (s, 6H, $2CH_3$); 2.13 (s, 3H, CH_3CO); 6.70–7.13 (m, $5H_{arom}$); 7.57 (s, 1H, CH=N)
2d	70	71–72/0.01	$C_{13}H_{17}NO$ (203.3)	1705	1655	1.33 (s, 6H, $2CH_3$); 2.10 (s, 3H, CH_3CO); 4.60 (br s, 2H, $C\underline{H}_2C_6H_5$); 7.13–7.27 (m, $5H_{arom}$); 7.67 (br s, 1H, CH=N)

[a] Yield of isolated product **2** based on **1**.
[b] Microanalyses not obtained. All these compounds were unstable and were stored for days under nitrogen at −20 °C.
[c] Recorded on a Perkin Elmer 781 Infrared spectrophotometer.
[d] Obtained on a Varian T-60 A spectrometer.

Table 2. 3-Hydroxy-5-iminoalkanoic Esters **4** Prepared

Product	Mol Ratio **3:2**	Reaction Time (min)	Yield[a] (%)	mp (°C)[b]	Molecular Formula[c]	IR, ν(cm^{-1})[d] OH	C=O	C=N	^{1}H-NMR ($CDCl_3$/TMS)[e] δ, J(Hz)
4a	2.2	3	100 (95)	79–81 (EtOH)	$C_{20}H_{23}NO_3$ (325.4)	3480	1700	1645	1.13 (s, 3H, CH_3); 1.17 (s, 3H, CH_3); 2.87, 3.33 (dd, 2H, J = 16, CH_2); 3.37 (s, 3H, OCH_3); 4.60 (s, 1H, OH); 6.67–7.40 (m, $10H_{arom}$); 7.77 (s, 1H, CH=N)
4b	2.2	3	100	oil	$C_{21}H_{25}NO_3$ (339.4)	3460	1705	1650	1.07 (s, 3H, CH_3); 1.13 (s, 3H, CH_3); 2.87, 3.30 (dd, 2H, J = 16, CH_2CO); 3.47 (s, 3H, OCH_3); 4.63 (br s, 2H, $C\underline{H}_2C_6H_5$); 4.80 (s, 1H, OH); 7.13–7.40 (m, $10H_{arom}$); 7.87 (s, 1H, CH=N)
4c	2.2	3	100	oil	$C_{15}H_{21}NO_3$ (263.3)	3500	1725	1650	1.20 (s, 6H, $2CH_3$); 1.30 (s, 3H, CH_3); 2.47, 2.66 (dd, 2H, J = 15, CH_2); 3.67 (s, 3H, OCH_3); 4.43 (s, 1H, OH); 6.83–7.47 (m, $5H_{arom}$); 7.90 (s, 1H, CH=N)
4d	2.2	3	100	oil	$C_{16}H_{23}NO_3$ (277.4)	3490	1725	1650	1.13 (s, 3H, CH_3); 1.17 (s, 3H, CH_3); 1.30 (s, 3H, CH_3); 2.40, 2.64 (dd, 2H, J = 15, CH_2CO); 3.67 (s, 3H, OCH_3); 4.60 (br s, 3H, $C\underline{H}_2C_6H_5$ and OH); 7.23 (s, $5H_{arom}$); 7.77 (br s, 1H, CH=N)
4e	4.5	3	100[f]	77–79[g] (EtOH)	$C_{21}H_{25}NO_3$ (339.4)	3430	1730	1630[g]	0.97 (s, d, 6H, J = 7, CH_3 and $CHC\underline{H}_3$); 1.37 (s, 3H, CH_3); 3.50 (q, 1H, J = 7, $C\underline{H}CH_3$); 3.53 (s, 3H, OCH_3); 5.53 (s, 1H, OH); 6.93–7.60 (m, $10H_{arom}$); 7.90 (s, 1H, CH=N)[g]
4f	4.5	3	90[f]	oil	$C_{16}H_{23}NO_3$ (277.4)	3460	1720	1640[h]	7.87 (s, 1H, CH=N)[g]; 7.93 (s, 1H, CH=N)[i]
4g	4.5	60	87	oil	$C_{17}H_{25}NO_3$ (291.4)	3400	1710	1640	1.30, 1.35 (br s, s, 15H, $5CH_3$); 3.60 (s, 3H, OCH_3); 5.37 (br s, 1H, OH); 6.87–7.33 (m, $5H_{arom}$); 7.90 (s, 1H, CH=N)

[a] Yield without parentheses refer to crude product of ≧95% purity (^{1}H-NMR). Yield in parentheses refer to pure, isolated product.
[b] Uncorrected, measured with a Büchi apparatus.
[c] Microanalyses not obtained; compounds descompose during purification. All these compounds were unstable and were stored for days under nitrogen at −20 °C. Alternatively, they were used immediately after their preparation without purification.
[d] Recorded on a Perkin Elmer 781 Infrared spectrophotometer. KBr for compounds **4a, e** and liquid film for the other compounds.
[e] Obtained on a Varian T-60 A spectrometer.
[f] Mixture of diastereoisomers in the ratios of 55 : 45 for **4e** and 75 : 25 for **4f**.
[g] Data for the major diastereoisomer.
[h] Data for the mixture of diastereoisomers.
[i] Data for the minor diastereoisomer.

steric crowding when $R^1=C_6H_5$ and $R^3=R^4=CH_3$. The obtention of **4g** from the reaction of **2c** with **3c** could be the result of a certain relief of steric strain (with $R^1=CH_3$ instead of $R^1=C_6H_5$) as well as of diminished conjugation of the corresponding intermediate **5** which would make more difficult its formation by retrocondensation. Since products of addition to the imino group have been neither isolated nor detected the addition can be considered as totally site-selective in favor of the carbonyl group.

The reactivity of compounds **4** is strongly dependent on the ease of their thermolysis in various media and under under various

Table 3. Substituted 3-Hydroxy-5-alkanelactams **11** Prepared

Product	Time (h) Hydr.	Time (h) Cycl.	Yield[a] (%)	mp (°C)[b] (solvent)	Molecular Formula	IR (KBr)[d] ν(cm^{-1}) OH	IR (KBr)[d] ν(cm^{-1}) NC=O	^{1}H-NMR[e] δ, J(Hz)	^{13}C-NMR[f], δ C=O	^{13}C-NMR[f], δ C–OH
11a	8	4.5	75	218–219 (ethanol)	$C_{19}H_{21}NO_2$ (295.4)	3225	1640	0.80 (s, 3H, CH_3); 1.03 (s, 3H, CH_3); 2.50, 3.46 (dd, 2H, J = 18, CH_2CO); 3.04, 3.96 (dd, 2H, J = 12, CH_2N); 5.53 (s, 1H, OH); 7.13–7.70 (m, 10H$_{arom}$)	168.3	74.5
11b	14	4.5	55	160–162 (AcOEt/ hexane)	$C_{20}H_{23}NO_2$ (309.4)	3300	1620	0.77 (s, 3H, CH_3); 0.80 (s, 3H, CH_3); 2.48, 3.15 (dd, 2H, J = 18, CH_2CO); 2.64, 3.46 (dd, 2H, J = 12, CH_2N); 3.63 (s, 1H, OH); 4.21, 4.72 (dd, 2H, J = 14, $C\underline{H}_2C_6H_5$); 7.07–7.50 (m, 10H$_{arom}$)	169.3	75.8
11c	6	4.5	70	141–143 (AcOEt/ hexane)	$C_{14}H_{19}NO_2$ (233.3)	3370	1620	1.00 (s, 3H, CH_3); 1.10 (s, 3H, CH_3); 1.17 (s, 3H, CH_3); 2.60 (s, 2H, CH_2CO); 2.94, 3.89 (dd, 2H, J = 12, CH_2N); 3.53 (s, 1H, OH); 7.03–7.43 (m, 5H, H$_{arom}$)	169.1	71.8
11d	7	–	60	130–132 (ethanol)	$C_{15}H_{21}NO_2$ (247.3)	3260	1615	0.93 (s, 6H, 2CH_3); 1.20 (s, 3H, CH_3); 2.30 (br s, 1H, OH); 2.57 (s, 2H, CH_2CO); 2.64, 3.39 (dd, 2H, J = 12, CH_2N); 4.38 and 4.78 (dd, 2H, J = 14, $C\underline{H}_2C_6H_5$); 7.23 (s, 5H$_{arom}$)		
11e	24	30	45[g]	175–176[h] (AcOEt/ hexane)	$C_{20}H_{23}NO_2$ (309.4)	3460	1630[h]	0.80 (s, 3H, CH_3); 1.10 (d, 3H, J = 7, $CHC\underline{H}_3$); 1.17 (s, 3H, CH_3); 2.37 (s, 1H, OH); 3.01, 4.19 (dd, 2H, J = 12, CH_2); 3.43 (q, 1H, J = 7, $C\underline{H}CH_3$); 7.17–7.57 (m, 10H$_{arom}$)[h]		
11f	6	9	72[g]	113–115[h] (AcOEt/ hexane)	$C_{15}H_{21}NO_2$ (247.3)	3415	1625[h]	1.07 (s, 3H, CH_3); 1.20 (s, 3H, CH_3); 1.27 (s, 3H, CH_3); 1.37 (d, 3H, J = 7, $CHC\underline{H}_3$); 1.60 (s, 1H, OH); 2.60 (q, 1H, J = 7, $C\underline{H}CH_3$); 2.91, 3.99 (dd, 2H, J = 12, CH_2); 7.10–7.47 (m, 5H$_{arom}$)[h]		
11g	15	4.5	75	158–160 (AcOEt/ hexane)	$C_{16}H_{23}NO_2$ (261.4)	3440	1630	1.03 (s, 3H, CH_3); 1.23, 1.27, 1.33, 1.37 (s, s, s, s, 12H, 4CH_3); 1.73 (s, 1H, OH); 2.91, 4.02 (dd, 2H, J = 12, CH_2); 7.03–7.43 (m, 5H$_{arom}$)		

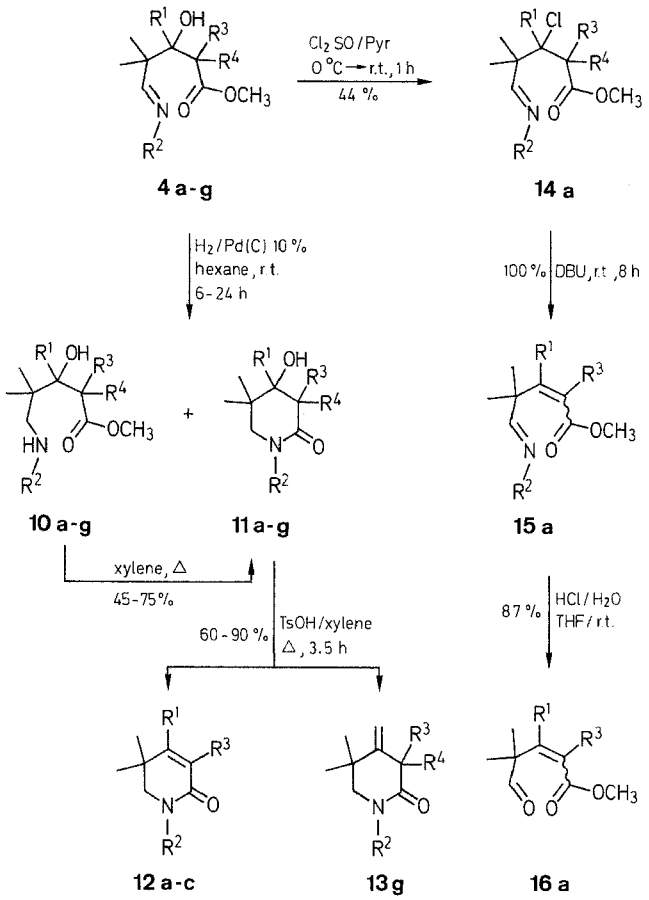
[a] Yield of isolated product **11** based on **4**.
[b] Uncorrected, measured with a Büchi apparatus.
[c] Satisfactory microanalyses obtained: C ±0.30, H ±0.30, N ±0.08.
[d] Recorded on a Perkin Elmer 781 Infrared spectrophotometer.
[e] Recorded on a Varian T-60 A spectrometer. DMSO-d_6 for **11a** and $CDCl_3$ for the other compounds.
[f] Recorded on a Varian FT-80 A spectrometer. DMSO-d_6 for **11a** and $CDCl_3$ for the other compounds.
[g] Mixture of diastereoisomer in the ratios 55 : 45 for **11e** and 75 : 25 for **11f**.
[h] Data for the major diastereoisomer.

Table 4. Substituted δ-Lactams **12** and **13** Prepared

Product	Yield[a] (%)	mp (°C)[b] (solvent)	Molecular Formula[c]	IR, ν(cm^{-1})[d] NC=O	IR, ν(cm^{-1})[d] C=C	^{1}H-NMR ($CDCl_3$/TMS)[e] δ	^{13}C-NMR ($CDCl_3$/TMS)[f] $\delta_{C=O}$
12a	71	130–131 (EtOH)	$C_{19}H_{19}NO$ (277.4)	1660	1610	1.27 (s, 6H, 2CH_3); 3.67 (s, 2H, CH_2); 5.90 (s, 1H, CH=C); 7.10–7.43 (m, 10H$_{arom}$)	163.6
12b	90	oil	$C_{20}H_{21}NO$ (291.4)	1660	1610	1.07 (s, 6H, 2CH_3); 3.13 (s, 2H, C–CH_2N); 4.67 (s, 2H, N$C\underline{H}_2C_6H_5$); 5.83 (s, 1H, CH=C); 7.00–7.47 (m, 10H$_{arom}$)	
12c	60	104–106 (AcOEt/ hexane)	$C_{14}H_{17}NO$ (215.3)	1660	1620	1.17 (s, 6H, 2CH_3); 1.87 (d, 3H, J = 1.5, CH=C–$C\underline{H}_3$); 3.53 (s, 2H, CH_2); 5.77 (q, 1H, J = 1.5 Hz, $C\underline{H}$=C–CH_3); 7.20–7.40 (m, 5H$_{arom}$)	163.8
13g	85	84–86 (EtOH/H_2O)	$C_{16}H_{21}NO$ (243.3)	1650	1625	1.23 (s, 6H, 2CH_3); 1.47 (s, 6H, 2CH_3); 3.47 (s, 2H, CH_2N); 5.07 (s, 2H, =CH_2); 7.07–7.37 (m, 5H$_{arom}$)	174.6

[a] Yield of isolated products **12** and **13** based on **11**.
[b] Uncorrected, measured with a Büchi apparatus.
[c] Satisfactory microanalyses obtained: C ±0.28, H ±0.30, N ±0.12.
[d] Recorded on a Perkin Elmer 781 Infrared spectrophotometer. Liquid film for **12b** and KBr for the other compounds.
[e] Obtained on a Varian T-60 A spectrometer.
[f] Obtained on a Varian FT-80 A spectrometer.

conditions. Thus, reaction in different acidic and basic media, reduction with complexes hydrides, etc., have been unsuccessful, affording in every case intractable mixtures. Also, when heated in different solvents compounds **4** undergo easy thermal ene-type fragmentations affording compounds **6** and **8**. This behavior must be a consequence of the β-hydroxyimino structure present in **4**. Nevertheless, some reactions of compounds **4** could be achieved (Scheme **C**). Catalytic reduction of **4** with hydrogen is carried out in hexane at room temperature in the presence of palladium/charcoal (10%) catalyst. Compound **4d** was reductively cyclized to δ-lactam **11d** exclusively. In the remaining cases, mixtures of **10** and **11** resulted. When these crude mixtures were refluxed in xylene, 3-hydroxy-5-alkanelactams **11** were the only products obtained. Further, treatment of compounds **11a–c** with *p*-toluenesulfonic acid in refluxing xylene gave dihidropyridones **12a–c** whilst from compound **11g** the 3-methylene-5-alkanelactam **13g** was obtained.



10–16	R^1	R^2	R^3	R^4
a	C_6H_5	C_6H_5	H	H
b	C_6H_5	$C_6H_5CH_2$	H	H
c	CH_3	C_6H_5	H	H
d	CH_3	$C_6H_5CH_2$	H	H
e	C_6H_5	C_6H_5	CH_3	H
f	CH_3	C_6H_5	CH_3	H
g	CH_3	C_6H_5	CH_3	CH_3

Scheme **C**

On the other hand, when **4a** was treated with thionyl chloride in pyridine at 0 °C, the 3-chloro-5-iminoalkanoic ester **14a** was obtained as the main product (44%) along with the 5-oxo-2-alkenoic ester **16a** as by-product. Dehydrohalogenation of **14a** with triethylamine was unsuccessful, giving a complex mixture of products. However, reaction with an equimolecular amount of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in chloroform proceeds satisfactorily to give the 5-imino-2-alkenoic ester **15a** in nearly quantitative yield, as one diastereoisomer of undetermined configuration. Finally, hydrolysis of **15a** with dilute hydrochloric acid in tetrahydrofuran furnished **16a** quantitatively.

N-Substituted 2-Acyl-2-methylpropanimines 2; General Procedure:
To a mixture of the 3-oxoalkanal **1** (35 mmol) and anhydrous $MgSO_4$ (3 g) in dry Et_2O (200 mL) under N_2 is added dropwise a solution of the primary amine (35 mmol) in Et_2O (100 mL). After stirring for 1 h at room temperature, the mixture is filtered and the solvent is evaporated under reduced pressure. The residual product is distilled *in vacuo* to give the β-iminoketone **2** (Table 1). Compounds **2** should be kept under an inert atmosphere at low temperature (– 20 °C) to avoid decomposition.

3-Hydroxy-5-iminoalkanoic Esters 4; General procedure:
In a dried, N_2-filled, round-bottomed flask fitted with stirrer and addition funnel, a solution of lithium diisopropylamide (22 mmol for **4a–d** and 45 mmol for **4e–g**) is prepared by adding, at – 78 °C, butyllithium (13.7 mL for **4a–d** and 28.1 mL for **4e–g**, 1.6 M solution in hexane, Aldrich) to a solution of dry diisopropylamine (2.22 g, 22 mmol for **4a–d** and 4.54 g, 45 mmol for **4e–g**) in anhydrous THF (22 mL for **4a–d** and 45 mL for **4e–g**). The mixture is warmed to – 15 °C to 0 °C, and stirred for 15 min. This solution is cooled at – 78 °C, a solution of the ester (22 mmol for **4a–d** and 45 mmol for **4e–g**) in THF (7 mL for **4a–d** and 15 mL for **4e–g**) is added dropwise, and the mixture is stirred for 15 min at – 78 °C. Then, a solution of the β-iminoketone **2** (10 mmol) in THF (20 mL) is added dropwise and the mixture is stirred for 3 min (1 h for **4g**) at – 78 °C. Finally, the mixture is quenched with H_2O (25 mL). Ether (100 mL) is added and the organic phase is separated, washed with H_2O (2 × 20 mL) and brine (20 mL), dried ($MgSO_4$), evaporated under reduced pressure. The crude, oily products are of sufficient purity (determined by ^{1}H-NMR) and are used as such in the next step (Table 2). All compounds **4** decompose upon attempted chromatography. Only compounds **4a** and **4e** were solids, which could be recrystallized, with appreciable decomposition, from cold EtOH.

3-Hydroxy-5-alkanelactams 11; General Procedure:
A solution of the ester **4** (4 mmol) in hexane (60 mL) is hydrogenated in presence of Pd-C (10%, 0.32 g) in a Parr-type apparatus at room temperature at an initial pressure of 40 psi (2.8 atm). When no more hydrogen is absorbed (6–24 h) the catalyst is filtered off and the solvent evaporated under reduced pressure. The crude product (a mixture of **10** and **11**, except for the conversion of **4d** which gives only **11d**), is used in the next step without further purification. If purification is desired, a solution of the crude product in xylene (20 mL) is refluxed for 4.5–30 h. The solvent is evaporated, and the residue is recrystallized from an appropriate solvent (Table 3).

2-Alkene-5-lactams 12 and 3-Methylene-5-alkanelactams 13; General Procedure:
In a flask equipped with a Dean-Stark device for azeotropic distillation of water and a reflux condenser, the lactam **11** (2 mmol) is dissolved in xylene (40 mL) and a trace of *p*-toluenesulphonic acid is added. Enough xylene is added into the Dean-Stark device to avoid loss of solvent from the reaction mixture. Reflux is maintained for 3.5 h. Finally, the mixture is washed with 5% aqueous NaOH (2 × 10 mL) and H_2O (10 mL); the extract is dried ($MgSO_4$) and evaporated. The crude products **12b** and **13g**, which were found to contain some minor isomeric by-products, are purified by column chromatography [silica gel, *n*-hexane/EtOAc (4:1 for **12b** and 9.5:0.5 for **13g**) as eluent]. In the remaining cases, recrystallization of the residue furnishes the lactams **12** (Table 4).

Methyl 3-Chloro-4,4-dimethyl-3-phenyl-5-phenyliminopentanoate (14a):
Thionyl chloride (0.1 mL, 1.4 mmol) is added dropwise to a stirred solution of ester **4a** (0.34 g, 1 mmol) in pyridine (1.5 mL) at 0 °C, and stirring is continued at 0 °C for 10 min and at room temperature for 50 min. Then, the mixture is quenched with ice water (50 mL) and extracted with Et_2O (3 × 25 mL) and with $CHCl_3$ (3 × 25 mL). Each

organic phase is washed separately with aqueous 0.5 N NaOH (2 × 10 mL), with aqueous 3 N HCl (2 × 10 mL), and with saturated $NaHCO_3$ solution (2 × 10 mL). The Et_2O and $CHCl_3$ phases are then separately dried ($MgSO_4$) and evaporated. The residue from the Et_2O phase is recrystallized from EtOH giving colorless **14a**; yield: 0.15 g (44%); mp 100–101 °C (EtOH).

$C_{20}H_{22}ClNO_2$	calc.	C 69.86	H 6.45	Cl 10.31	N 4.07
(343.9)	found	69.79	6.57	10.61	4.07

MS: m/z = 309 ($M^+ + 1$, 32%); 308 (M^+, 100); 197 (15); 155 (27); 147 (23); 146 (29); 104 (22); 101 (19); 100 (15); 77 (29).

IR (KBr): ν = 1725 (C=O); 1635 (C=N) cm^{-1}.

^{1}H-NMR ($CDCl_3$): δ = 1.30 (s, 6H, $2CH_3$); 3.38, 3.76 (dd, 2H, J = 16 Hz, CH_2); 3.53 (s, 3H, OCH_3); 6.83–7.60 (m, 10 H_{arom}); 7.80 (s, 1H, CH=N).

The residue from the $CHCl_3$ phase is purified by column chromatography (silica gel, *n*-hexane/EtOAc, 8:2) to give **16a** as a colorless oil; yield: 0.04 g (26%).

Methyl 4,4-Dimethyl-5-oxo-3-phenyl-2-pentenoate (16a):

Methyl 4,4-Dimethyl-3-phenyl-5-phenylimino-2-pentenoate **(15a)**: To a stirred solution of ester **14a** (0.22 g, 0.64 mmol) in $CHCl_3$ (2.2 mL) is added dropwise DBU (0.64 mmol) at 0 °C. The mixture is stirred at room temperature for 8 h. Then, $CHCl_3$ (30 mL) is added and the organic phase is washed with H_2O (4 × 10 mL), dried ($MgSO_4$), and evaporated under reduced pressure to give **15a** as a yellowish viscous oil pure by ^{1}H-NMR; yield: 0.2 g (~ 100%). This compound decomposes upon attempted chromatography and should be kept under an inert atmosphere at −20 °C to avoid decomposition.

IR ($CHCl_3$): ν = : 1725 (C=O); 1635 (C=N and C=C) cm^{-1}.

^{1}H-NMR ($CDCl_3$): δ = 1.37 (s, 6H, $2CH_3$); 3.43 (s, 3H, OCH_3); 6.07 (s, 1H, CH=C); 6.80–7.47 (m, 10H, H_{arom}); 7.70 (s, 1H, CH=N).

^{13}C-NMR ($CDCl_3$): δ = 168.3, 165.6 (C=O and C=N).

Methyl 4,4-Dimethyl-5-oxo-3-phenyl-2-pentenoate **(16a)**:

To a stirred solution of the crude product **15a** (~ 0.17 g, ~ 0.55 mmol) in THF (4 mL) is added 1 N HCl(H_2O) (7 mL). The mixture is stirred at room temperature for 2 h, then quenched with H_2O (7 mL), and extracted with Et_2O (3 × 15 mL). The combined extracts are washed with 5% aqueous $NaHCO_3$ (2 × 10 mL) and brine (10 mL), then dried ($MgSO_4$), and evaporated. The residue is purified by column chromatography (silica gel, *n*-hexane/EtOAc, 8:2) to give **16a** as a colorless viscous oil; yield: 0.13 g (87% based on **14a**).

$C_{14}H_{16}O_3$	calc.	C 72.39	H 6.94
(232.3)	found	72.48	6.99

MS: m/z = 232 (M^+, 1%); 203 (97); 172 (85); 171 (46); 170 (66); 156 (27); 144 (59); 142 (74); 128 (70); 127 (100); 114 (35); 104 (42); 90 (46); 76 (34); 42 (34).

IR (liquid): ν = 1730 (HC=O) and OC=O); 1635 (C=C) cm^{-1}.

^{1}H-NMR ($CDCl_3$): δ = 1.20 (s, 6H, $2CH_3$); 3.47 (s, 3H, OCH_3); 5.97 (s, 1H, CH=C); 6.83–7.40 (m, 5H, H_{arom}); 9.60 (s, 1H, CH=O).

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