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N-NITROSATION AND N-NITRATION OF LACTAMS. FROM MACROLACTAMS TO MACROLACTONES

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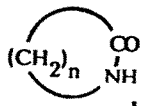
Abstract. N-Nitroso and N-nitro derivatives of lactams, from 2-pyrrolidinone to 15-pentadecanelactam, have been characterised by ^1H NMR, ^{13}C NMR, and IR spectroscopy. The conversion of these nitrosolactams and nitrolactams to lactones has been systematically (re)investigated.

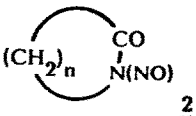
It is known that the decomposition of nitrosoamides can afford esters.[1] The mechanism of this reaction was studied by Huisgen et al.,[2] Hey et al.,[3] and White et al.[4,5] A similar mechanism was proposed for the thermal decomposition of nitroamides to esters and N_2O.[5] The decomposition of a few nitrosolactams was reported in the fifties,[6] and some authors[7] took advantage, more recently, of this reaction to convert seven-membered lactam rings (contained in a steroid, triterpenoid, or heterocyclic system) into lactones.

Our interest in the chemistry of nitrosoamides and nitroamides,[8] including polynitrosated[9] and polynitrated peptides, led us to review the lactam-to-lactone transformation just mentioned. To our knowledge, the only systematic report is that of Huisgen and Reinertshofer,[6] who studied the effect of the ring size on the rearrangement rate of nitrosolactams (from *N*-nitroso-2-pyrrolidinone to *N*-nitroso-10-decanelactam) by measuring the nitrogen evolved, as well as the reaction products arising from heating of these nitrosolactams in benzene or benzene derivatives; according to these authors, polyesters were mainly obtained in most cases, except for *N*-nitroso-2-pyrrolidinone and *N*-nitroso-2-piperidone.

Starting from a larger set of lactams (1), we have investigated the decomposition reaction of nitrosolactams 2 and nitrolactams 3 under different conditions. Furthermore, the corresponding lactams, nitrosolactams, and nitrolactams have been characterised by current spectroscopic techniques.



1, n=3-14



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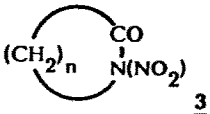

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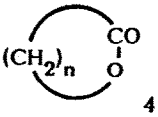

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Most lactams used in this work have been obtained from the corresponding cyclic ketones via the Beckmann rearrangement of their oximes. Cyclodecanone was prepared from cycloundecanone, which we had obtained from commercial cyclododecanone; also by a ring-contraction process, we prepared cyclotetradecanone from cyclopentadecanone.[10,11] On the other hand, cyclotridecanone was synthesised by ring enlargement using the method of Taguchi et al.[12] (treatment with CH_2Br_2 and lithium dicyclohexylamide, followed by isolation of the alcohol and addition of an excess of BuLi); other attempted routes were much less successful.[11]

Lactams **1** were submitted to quite standard nitrosation conditions (N_2O_4/NaAcO, in CH_2Cl_2 at -10 °C for ca. 1 h)[13] and nitration conditions (HNO_3/Ac_2O in cold, for 15 h to 72 h)[14] to afford nitrosolactams **2** and nitrolactams **3**, respectively (see **Table I**). *N*-Nitroso-8-octanelactam (**2**, **n=7**) could not be isolated, as reported,[6] since during the preparation and workup, even at 0 °C, it decomposed spontaneously to give mainly **4**, **n=7**. A similar fact took place with the corresponding nitro derivative (**3**, **n=7**). In general, the results shown in **Table I** were expected: macrolactams, if not all lactams, should behave almost like open-chain carboxamides, for which the nitration yields are usually lower than the nitrosation ones.[8,15,16]

Table I. Yields of N-Nitrosation and N-Nitration of Lactams **1** under Standard Conditions

	n =	3	4	5	6	7	8	9	10	11	12	13	14
1 → **2**		100%	100%	100%	100%	-[a]	30%[b]	92%[b]	94%[b]	95%[b]	90%[b]	90%[b]	100%
1 → **3**		80%	73%	70%	45%	-[a]	50%[c]	40%	52%	67%	45%	50%	75%

[a] It decomposed, with bubbles, even at 0 °C. [b] 100% using pyridine instead of NaAcO. [c] After 9 days of reaction at 0 °C.

For most nitrosolactams, smooth heating of dilute solutions of **2** in anhydrous CCl_4 for 6 h afforded substantial yields of lactones **4**, as shown by MS, 200 MHz ^1H NMR, 50.3 MHz ^{13}C NMR, and chromatographic comparison with authentic samples prepared by means of the Baeyer-Villiger oxidation of the appropriate ketones. For *N*-nitroso-7-heptanelactam (**2**, **n=6**) and *N*-nitroso-6-hexanelactam (**2**, **n=5**) stirring of the solution at r.t. was sufficient. As mentioned above, **2**, **n=7**, gave directly **4**, **n=7**, below 0 °C. In sharp contrast, *N*-nitroso-2-pyrrolidinone (**2**, **n=3**) was recovered unchanged after refluxing either in CCl_4 or toluene for 3 days. *N*-Nitroso-2-piperidone (**2**, **n=4**) underwent partial denitrosation in refluxing CCl_4 but no conversion to lactone at all. The yields of **4** for all the series are collected in the first row of **Table II**. In addition, some minor impurities were detected in the crude products and were sometimes isolated as well. Thus, in all the cases small amounts of unsaturated carboxylic acids were clearly observed in the ^1H and ^{13}C NMR spectra of the residues. Furthermore, for the larger members of the series, the spectra of the crudes showed duplicate signals. Separation of these mixtures by flash chromatography afforded first the monolactones and then the products that caused these additional peaks; these products appeared to be the corresponding diolides, as shown by MS and mp comparison with literature data.

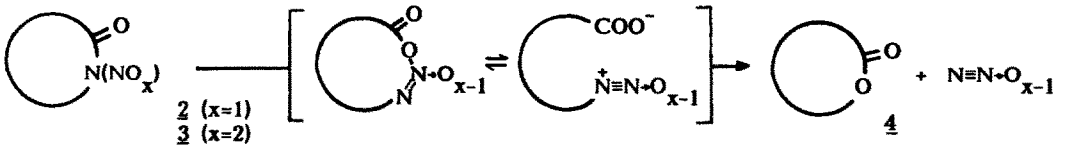


Table II. Yields of Lactones **4**, in Refluxing CCl_4 (unless otherwise Indicated) for 6 h (**2** → **4**) or 12 h (**3** → **4**)

	n =	3	4	5	6	7	8	9	10	11	12	13	14
2 → **4**		0%	0%	82%[a]	80%[a]	75%[b]	85%[c]	80%	82%	72%	78%	80%	76%
3 → **4**		0%	0%	0%[d]	82%[a]	73%[b]	85%	88%	84%	78%	85%	85%	80%

[a] At r.t. [b] Overall yields for nitrosation/nitration and rearrangement. [c] At 40 °C. [d] 84% in refluxing chlorobenzene.

As far as the transformation of nitrolactams **3** into lactones **4** is concerned, we proceeded as with the nitrosoamides, with similar results (see the second row of **Table II**), although longer reaction times were usually needed. The main impurities observed in the ^{13}C NMR spectra of the reaction residues were again

unsaturated carboxylic acids and, for the bigger rings, the diolides. On the other hand, *N*-nitro-2-pyrrolidinone (**3**, **n=3**) and *N*-nitro-2-piperidone (**3**, **n=4**) did not react at all.

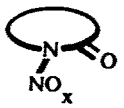
The most significant features of ^{1}H NMR, ^{13}C NMR, and IR spectra of **2** and **3** are summarised in **Table III**. For the sake of comparison, as well as to gain insight into possible configurational or conformational changes, spectral data of the parent lactams are included.

Table III. Summary of Spectral Data of **1-3**

	n =	3	4	5	6	8	9	10	11	12	13	14
	1	2.31	2.30	2.47	2.43	2.25	2.22	2.23	2.20	2.22	2.23	2.18
$\delta(CH_2CO)$	**2**	2.82	2.86	2.89	2.86	3.15	3.17	3.10	3.20	3.17	3.21	3.20
	3	2.66	2.68	2.71	2.65	3.13	3.06	3.05	3.02	3.00	2.99	2.96
	1	3.41	3.30	3.21	3.34	3.34	3.32	3.25	3.29	3.31	3.32	3.32
$\delta(CONCH_2)$	**2**	3.70	3.59	3.84	3.89	3.87	3.83	3.83	3.85	3.83	3.87	3.89
	3	4.03	4.15	4.21	4.23	4.34	4.16	4.28	4.23	4.22	4.20	4.19
	1	179.7	172.9	179.6	178.1	174.3	174.2	173.7	173.6	173.1	173.9	173.3
$\delta(CO)$	**2**	173.3	170.1	174.7	-[a]	180.0	179.6	178.2	178.2	177.9	177.7	177.7
	3	167.8	167.2	170.5	172.1	176.0	174.7	174.3	173.2	173.2	173.1	173.5
	1	30.4	31.5	36.8	32.1	37.6	37.6	36.4	36.9	36.2	36.5	36.7
$\delta(CH_2CO)$	**2**	30.8	33.9	37.8	-[a]	36.7	35.6	35.2	34.8	34.5	34.1	34.0
	3	30.9	35.3	37.9	36.4	39.1	37.4	38.3	37.9	37.7	37.6	37.9
	1	42.5	42.1	42.8	41.7	40.6	39.7	39.4	39.1	38.1	38.9	39.0
$\delta(CONCH_2)$	**2**	42.7	43.5	38.9	-[a]	38.6	39.1	37.4	38.4	38.5	38.6	38.4
	3	47.7	51.1	49.6	48.4	48.5	46.7	47.9	47.0	46.8	46.7	47.0
	1	1680	1660	1650	1650	1630	1640	1640	1640	1650	1640	1640
$\tilde{\nu}_{CO}$	**2**	1765	1730	1735	1730	1725	1730	1730	1730	1730	1720	1725
	3	1775	1735	1740	1720	1720	1720	1720	1730	1730	1720	1725

[a] The sample decomposes.

Some points of **Table III** are worthy of mention: (i) in comparing the $\delta(CH_2CO)$ values for **1-3**, it is seen that a close parallelism does exist for **n=3-6** (nitrosation shifts these protons 0.4-0.6 ppm downfield and nitration shifts them only 0.2-0.4 ppm downfield); the relationship among **1-3** with **n=8-14** is also evident, but the changes are larger than those observed for **n=3-6** (nitrosation of the larger rings moves such protons ca. 1 ppm to lower field and nitration ca. 0.8 ppm also to lower field); (ii) analogous differences are detected for the chemical shifts of the carbonyl carbon atoms, since for **n=3-6** the $\delta(CO)$ values are shifted to higher field after nitrosation and even more after nitration, whereas for **n=8-14** the $\delta(CO)$ values are shifted 5-6 ppm to lower field after nitrosation but do not practically change after nitration. It is obvious that for **n=3-6** the nitrosolactams and nitrolactams must be cis (see **5**), like their parent lactams. On the other hand, comparison of the δH and δC changes, due to the nitrosation and nitration, observed for **n=8-14** with those reported for acyclic amides[8,9] indicates that the carbonyl oxygen and NO_X group are trans (see **6**). Thus, the borderline between the two different sets of lactams is very likely 8-octanelactam (**n=7**), which "curiously" affords only rearranged products when its nitrosation and nitration are attempted. Molecular models of **1-3**, **n=7**, show that, owing to the size of the ring, the preferred conformation of the nitrosoamide and nitroamide (with a OCCN dihedral angle larger than for **n=6** but no so close to 180° as for **n=8-9**) is especially prone to rearrange.[17]



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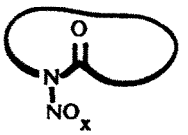

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In conclusion, in spite of the unstability of many nitrosoamides and nitroamides, the spectroscopic properties of most nitrosolactams and nitrolactams have been obtained and compared, affording relevant insight into their stereochemistry. Furthermore, is is clear that nitrosation of lactams, which can be performed rapidly and quantitatively, constitutes a good route to medium-sized and large-sized lactones.[18] In this connection, the route through the nitro derivatives is at present less promising.

EXPERIMENTAL

The NMR spectra were obtained in deuteriochloroform on Varian XL-200 and Hitachi-Perkin-Elmer R-24B spectrometers; chemical shifts are reported in ppm with respect to internal tetramethylsilane in all the cases, and *J* values are given in hertz. The IR spectra were recorded as films or in chloroform solutions with a Perkin-Elmer 681 instrument; only the most significant absorptions (in cm-1) are listed. Mass spectra were recorded on a Hewlett-Packard 5988A spectrometer. GC analyses were performed on a Hewlett-Packard 5710A (3% SE-52 on chromosorb). Melting points were determined on a Kofler apparatus and are uncorrected. Elemental analyses were performed with a Perkin-Elmer 240 analyser, at the Instituto de Química Orgánica Biológica, CSIC, Barcelona. The lactams used in this work were known[19] and have been prepared from the corresponding cyclic ketones through their oximes, with the exceptions of 6-caprolactam and 2-pyrrolidinone that are available commercial products.

N-Nitrosolactams. Lactams **1**, in amounts of 100-400 mg, were dissolved in 50-100 ml of dichloromethane and 1.0-1.5 g of anhydrous sodium acetate were added.[13] Through the stirred suspension, maintained at -10 °C, a stream of nitrogen dioxide[8] was bubbled with the aid of an air stream for ca. 1 h. After the usual workup,[8] pure yellow oils, generally in excellent yields, were obtained (see **Table I**). One hundred mg of lactams **1**, **n=8-13**, were also nitrosated in 50 ml of dichloromethane and 10 ml of pyridine; then, dichloromethane was added and the usual workup was followed, quantitative yields of **2**, **n=8-13**, being obtained.

N-Nitroso-2-pyrrolidinone or *N*-nitroso-4-butyrolactam (**2**, **n=3**): yellow oil;[6] ^{1}H NMR δ 2.19 (m, 2H), 2.82 (t, 7.9, 2H), 3.70 (m, 2H); ^{13}C NMR δ 15.8, 30.8, 42.7, 173.3; IR 1765, 1490; MS 114 (M^+). *N*-Nitroso-2-piperidone (**2**, **n=4**): yellow oil;[6] ^{1}H NMR δ 1.8-2.0 (m, 4H), 2.86 (m, 2H), 3.59 (m, 2H); ^{13}C NMR δ 20.1, 21.4, 33.9, 43.5, 170.1; IR 1730, 1500; MS 128 (M^+). *N*-Nitroso-6-caprolactam (**2**, **n=5**): yellow oil;[6] ^{1}H NMR δ 1.0-2.0 (m, 6H), 2.89 (m, 2H), 3.84 (m, 2H); ^{13}C NMR δ 23.6, 27.6, 28.3, 37.8, 38.9, 174.7; IR 1735, 1500;[8] MS 142 (M^+). *N*-Nitroso-7-heptanelactam (**2**, **n=6**): yellow oil;[6] ^{1}H NMR δ 1.3-2.1 (m, 8H), 2.86 (m, 2H), 3.89 (m, 2H); IR 1730, 1500. *N*-Nitroso-9-nonanelactam (**2**, **n=8**): yellow oil;[6] ^{1}H NMR δ 0.8-2.0 (m, 12H), 3.15 (m, 2H), 3.87 (m, 2H); ^{13}C NMR δ 22.1-24.5 (six peaks), 36.7, 38.6, 180.0; IR 1725, 1490. *N*-Nitroso-10-decanelactam (**2**, **n=9**): yellow oil;[6] ^{1}H NMR δ 1.0–2.0 (m, 14H), 3.17 (m, 2H), 3.83 (m, 2H); ^{13}C NMR δ 23.2-25.9 (seven peaks), 35.6, 39.1, 179.6; IR 1730, 1500. *N*-Nitroso-11-undecanelactam (**2**, **n=10**): yellow oil; ^{1}H NMR δ 1.0–2.0 (m, 16H), 3.10 (m, 2H), 3.83 (m, 2H); ^{13}C NMR δ 22.6-25.6 (eight peaks), 35.2, 37.4, 178.2; IR 1730, 1510. *N*-Nitroso-12-dodecanelactam (**2**, **n=11**): yellow oil; ^{1}H NMR δ 1.0-2.1 (m, 18H), 3.20 (m, 2H), 3.85 (t, 6.5, 2H); ^{13}C NMR δ 24.2-26.6 (nine peaks), 34.8, 38.4, 178.2; IR 1730, 1500;[8] MS(CI) 227 ($M+1^+$). *Anal.* Calcd for $C_{12}H_{22}N_2O_2$: C, 63.68; H, 9.80; N, 12.38. Found: C, 63.48; H, 9.81; N, 12.05. *N*-Nitroso-13-tridecanelactam (**2**, **n=12**): yellow oil; ^{1}H NMR δ 0.9-1.9 (m, 20H), 3.17 (m, 2H), 3.83 (m, 2H); ^{13}C NMR δ 24.5-27.2 (ten peaks), 34.5, 38.5, 177.9; IR 1730, 1510. *N*-Nitroso-14-tetradecanelactam (**2**, **n=13**): yellow oil; ^{1}H NMR δ 1.0-1.9 (m, 22H), 3.21 (m, 2H), 3.87 (m, 2H); ^{13}C NMR δ 24.7-27.4 (eleven peaks), 34.1, 38.6, 177.7; IR 1720, 1510. *Anal.* Calcd for $C_{14}H_{26}N_2O_2$: C, 66.11; H, 10.30; N, 11.01. Found: C, 65.85; H, 9.97; N, 11.00. *N*-Nitroso-15-pentadecanelactam (**2**, **n=14**): yellow oil; ^{1}H NMR δ 1.0-1.9 (m, 24H), 3.20 (t, 6.5, 2H), 3.89 (t, 6.5, 2H); ^{13}C NMR δ 24.8-27.6 (twelve peaks), 34.0, 38.4, 177.7; IR 1725, 1510; MS 268 (M^+). *Anal.* Calcd for $C_{15}H_{28}N_2O_2$: C, 67.13; H, 10.52; N, 10.44. Found: C, 66.96; H, 10.85; N, 10.25.

N-Nitrolactams. Lactams **1**, in amounts of 100-300 mg, were added to stirred solutions of 4 ml of acetic anhydride and 2 ml of nitric acid at -15 °C.[14] Then, the reactions were maintained at 0 °C for 15 h to 72 h (depending on the case). After pouring the final solutions in 50 ml of cold water, the organic products were extracted with dichloromethane. The extracts were washed with aqueous sodium hydrogencarbonate and water, dried over anhydrous sodium sulphate, and evaporated in vacuo to afford mixtures of the starting amides and nitro derivatives, which were separated by flash chromatography (silica gel, dichloromethane). Nitrolactams are colourless oils or solids of low melting point.

N-Nitro-2-pyrrolidinone (**3**, **n=3**): mp 54-56 °C (lit.[20] 55.5 °C); ^{1}H NMR δ 2.06 (m, 2H), 2.66 (m, 2H), 4.03 (t, 7.1, 2H); ^{13}C NMR δ 14.7, 30.9, 47.7, 167.8; IR 1775, 1575, 1275; MS 130 (M^+). *N*-Nitro-2-piperidone (**3**, **n=4**): mp 30-32 °C (lit.[15] 29.5-32.5 °C); ^{1}H NMR δ 1.8-2.1 (m, 4H), 2.68 (t, 6.5, 2H), 4.15 (t, 5.0, 2H); ^{13}C NMR δ 21.1, 23.3, 35.3, 51.1, 167.2; IR 1735, 1565, 1280; MS 144 (M^+). *N*-Nitro-6-caprolactam (**3**, **n=5**): mp 26-28 °C; ^{1}H NMR δ 1.5-1.9 (m, 6H), 2.71 (m, 2H), 4.21 (m, 2H); ^{13}C NMR δ 23.0, 27.5, 28.8, 37.9, 49.6, 170.5; IR 1740, 1590, 1280;[8] MS 158 (M^+). *Anal.* Calcd for $C_6H_{10}N_2O_3$: C, 45.57; H, 6.37; N, 17.71. Found: C, 45.76; H, 6.38: N, 17.84. *N*-Nitro-7-heptanelactam (**3**, **n=6**): oil; ^{1}H NMR δ 1.5-1.9 (m, 8H), 2.65 (m, 2H), 4.23 (t, 6.0, 2H); ^{13}C NMR δ 23.6, 26.0, 28.7, 28.8, 36.4, 48.4, 172.1; IR 1720, 1580, 1280. *N*-Nitro-9-nonanelactam (**3**, **n=8**): oil; ^{1}H NMR δ 1.3-2.0 (m, 12H), 3.13 (m, 2H), 4.34 (t, 5.6, 2H); ^{13}C NMR δ 22.8-25.1 (six peaks), 39.1, 48.5, 176.0; IR 1720, 1565, 1290. *N*-Nitro-10-decanelactam (**3**, **n=9**): oil; ^{1}H NMR δ 1.2-1.9 (m, 14H), 3.06 (m, 2H), 4.16 (t, 5.8, 2H); ^{13}C NMR δ 22.0-24.9 (seven peaks), 37.4, 46.7, 174.7; IR 1720, 1565, 1290. *N*-Nitro-11-undecanelactam (**3**, **n=10**): oil; ^{1}H NMR δ 1.2-1.8 (m, 16H), 3.05 (m, 2H), 4.28 (m, 2H); ^{13}C NMR δ 23.8-26.5 (eight peaks), 38.3, 47.9, 174.3; IR 1720, 1565, 1290. *Anal.* Calcd for C11H20N2O3: C, 57.87; H, 8.83; N, 12.27. Found: C, 58.01; H, 8.95; N, 12.01. *N*-Nitro-12-dodecanelactam (**3**, **n=11**): mp 20 °C; ^{1}H NMR δ 1.2-1.8 (m, 18H); 3.02 (m, 2H), 4.23 (m, 2H); ^{13}C NMR δ 24.0-26.8 (nine peaks), 37.9, 47.0, 173.2; IR 1730, 1560, 1290; MS(CI) 243 ($M+1^+$). *Anal.* Calcd for $C_{12}H_{22}N_2O_3$: C, 59.48; H, 9.15; N, 11.56. Found: C, 59.19; H, 9.18; N, 11.56.[8] *N*-Nitro-13-tridecanelactam (**3**, **n=12**): mp 30-32 °C; ^{1}H NMR δ 1.2-1.9 (m, 20H), 3.00 (m, 2H), 4.22 (m, 2H); ^{13}C NMR δ 24.0-27.2 (ten peaks), 37.7, 46.8, 173.2; IR 1730, 1560, 1290. *Anal.* Calcd for $C_{13}H_{24}N_2O_3$: C, 60.91; H, 9.44; N, 10.93. Found: C, 61.13; H, 9.50; N, 10.68. *N*-Nitro-14-tetradecanelactam (**3**, **n=13**): mp 38-39 °C; ^{1}H NMR δ 1.2-1.8 (m, 22H), 2.99 (m, 2H), 4.20 (t, 6.0, 2H); ^{13}C NMR δ 24.1-27.5 (eleven peaks), 37.6, 46.7, 173.1; IR 1720, 1570, 1290; MS(CI) 271 ($M+1^+$). *Anal.* Calcd for $C_{14}H_{26}N_2O_3$: C, 62.20; H, 9.69; N, 10.36. Found: C, 61.90; H, 9.45; N, 10.10. *N*-Nitro-15-pentadecanelactam (**3**, **n=14**): oil; ^{1}H NMR δ 1.2-1.7 (m, 24H), 2.96 (t, 6.4, 2H), 4.19 (t, 6.4, 2H); ^{13}C NMR δ 24.3-27.7 (twelve peaks), 37.9, 47.0, 173.5; IR 1725, 1570, 1290. *Anal.* Calcd for $C_{15}H_{28}N_2O_3$: C, 63.35; H, 9.92; N, 9.85. Found: C, 63.12; H, 9.87; N, 9.43.

Lactones. *N*-Nitrosolactams **2**, **n=9-14**, in amounts of ca. 100 mg, were refluxed in 100 ml of anhydrous carbon tetrachloride for 6 h; then, the solvent was removed to afford the crude lactones, which were separated from unsaturated acids and lactone dimers by flash chromatography on silica gel (hexane/ethyl acetate 9:1). Alternatively, 100 mg of nitrosolactams **2** in ca. 30 ml of carbon tetrachloride were added dropwise (5 h) to 100 ml of refluxing carbon tetrachloride; heating was maintained for a further hour, the solvent was eliminated, and the lactones were purified as above. (In general, the monomer/dimer ratio increased from 3:1 or 2:1, depending on the case, to about 5:1 or 4:1, when the addition was performed dropwise, under higher dilution conditions. **Table II** shows the yields of the pure monomers under these last conditions.)

Solutions of 100 mg of **2**, **n=6**, and **2**, **n=5**, in 100 ml of carbon tetrachloride were stirred at r.t. for 4-6 h, whereas similar solutions of **2**, **n=8**, were heated at 40 °C for ca. 6 h. Separation of the desired lactones from small amounts of unsaturated acids was performed by filtration through a short column of silica gel, with dichloromethane as the eluent.

All the lactones obtained in this way are known compounds.[21] Physical data, IR spectra (band at 1745-1730 cm^{-1}), and NMR spectra (CH_2OCO at δ 4.0±0.1, CH_2OCO at δ 64.3±0.3, and COO at δ 174.0±0.5) agree with those reported or expected. In some cases (6-hexanolide, 12-dodecanolide, and 15-pentadecanolide), reaction samples were compared by GC and TLC with the lactones arising from the Baeyer-Villiger oxidation of cyclohexanone, cyclododecanone, and cyclopentadecanone, respectively, with the expected result. Apart from the mass spectra, lactone dimers can be distinguished from monomers by NMR, as the dimer CH_2OCO signals

appear 0.10 ppm at higher field, their CH_2OCO signals are shifted 0.3±0.1 ppm at higher field as well, and their COO peaks ca. 0.2 ppm at higher field too. Physical data for dimers also agree with those found in the literature.[22]

N-Nitrolactams **3, n=8-14**, in amounts of ca. 100 mg, were heated for 12 h in 100 ml of anhydrous carbon tetrachloride. Alternatively, the same amounts were added dropwise (10-12 h) to the refluxing solvent. Workup as above gave the corresponding lactones in good yields, as shown in **Table II** (yields given under the last conditions, in which the monomer/dimer ratios were slightly higher). Solutions of 100 mg of **3, n=6**, in 100 ml of carbon tetrachloride were left to decompose at r.t., overnight. Compound **3, n=5**, required an overnight reflux in chlorobenzene. Compounds **3, n=3**, and **3, n=4**, were recovered unchanged after heating in carbon tetrachloride for several days or in toluene for 3 days.

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References and footnotes

1. Chancel, M. F. *Bull. Soc. Chim. Fr.* **1895**, *13*, 125. Pechmann, H. v. *Ber.* **1898**, *31*, 2640.
2. Huisgen, R.; Horeld, G. *Liebigs Ann. Chem.* **1948**, *567*, 137. Huisgen, R.; Krause, L. *Ibid.* **1951**, *574*, 157. Huisgen, R.; Reimlinger, H. *Ibid.* **1956**, *599*, 183.
3. Hey, D. H.; Stuart-Webb, J.; Williams, G. H. *J. Chem. Soc.* **1952**, 4657.
4. White, E. H. *J. Am. Chem. Soc.* **1955**, *77*, 6011 and 6014. White, E. H.; Aufdermarsh, C. A. *Ibid.* **1961**, *83*, 1174 and 1179. Also see references therein.
5. For reviews, see: White, E. H.; Woodcock, D. J. In *The Chemistry of the Amino Group*; Patai, S.; Ed.; Wiley: New York, 1968. Lobl, T. J. *J. Chem. Ed.* **1972**, *49*, 730. Challis, B. C.; Challis, J. A.. In *Comprehensive Organic Chemistry*, Vol. 2; Barton, D. H. R.; Ollis, W. D., Eds.; Pergamon Press: Oxford, 1979. For a related work, see: Cooley, J. H.; Stone, D. M.; Oguri, H. *J. Org. Chem.* **1977**, *42*, 3096.
6. Huisgen, R.; Reinertshofer, J. *Liebigs Ann. Chem.* **1952**, *575*, 174 and 197. Nischk, G.; Müller, E. *Ibid.* **1952**, *576*, 232. Heyns, K.; Woyrsch, O. F. *Chem. Ber.* **1953**, *86*, 76.
7. Bladon, P.; McMeekin, W. *J. Chem. Soc.* **1961**, 3504. Stevenson, R. *J. Org. Chem.* **1963**, *28*, 188. Uskokovic, M.; Gutzwiller, J.; Henderson, T. *J. Am. Chem. Soc.* **1970**, *92*, 203.
8. Garcia, J.; González, J.; Segura, R.; Urpí, F.; Vilarrasa, J. *J. Org. Chem.* **1984**, *49*, 3322.
9. Garcia, J.; González, J.; Segura, R.; Vilarrasa, J. *Tetrahedron* **1984**, *40*, 3121.
10. Hoffmann, H. M. R.; Vinter, J. G. *J. Org. Chem.* **1971**, *39*, 3921. Garbisch, E. W.; Wohllebe, J. *Org. Synth.* **1959**, *56*, 107; *J. Chem. Soc., Chem. Commun.* **1968**, 306; *J. Org. Chem.* **1968**, *33*, 2157. Schank, K.; Eistert, B. *Chem. Ber.* **1965**, *98*, 650.
11. Torra, N.; Graduation Thesis; Universitat de Barcelona: 1985.
12. Taguchi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 3010 and 6510; *Bull. Soc. Chim. Jpn.* **1977**, *50*, 1588 and 1592.
13. White, E. H. *J. Am. Chem. Soc.* 1955, *77*, 6008. Also see reference 8.
14. Campbell, R.; Peterson, C. J. *J. Org. Chem.* **1963**, *28*, 2294. Also see reference 8.
15. White, E. H.; Grisley, D. W. *J. Am. Chem. Soc.* **1961**, *83*, 1191. White, E. H.; Chen, M. C.; Dolak, L. A. *J. Org. Chem.* **1966**, *31*, 3038.
16. Although not included in **Table I**, the lactam arising from dihydrocivetone (**1, n=16**) was nitrosated and nitrated in 94% and 44% yields, respectively. This ring is large enough to assume that the lactam group can react as an acyclic amide.
17. For a very recent outlook on the subject, see: White, E. H.; Lim, H. M. *J. Org. Chem.* **1987**, *52*, 2162.
18. We are applying this reaction to the synthesis of some natural macrolides. For a related communication, see: Bartra, M.; Bou, V.; Garcia, J.; Urpí, F.; Vilarrasa, J. *J. Chem. Soc., Chem. Commun.* **1988**, 270.
19. Ruzicka, L.; Kobelt, M.; Häfliger, O.; Prelog, V. *Helv. Chim. Acta* **1949**, *32*, 544.
20. Copburn, M. D.; Ungnade, H. E. *J. Heterocycl. Chem.* **1965**, *2*, 308.
21. Huisgen, R.; Ott, H. *Tetrahedron* **1959**, *6*, 253, and references therein.
22. Corey, E. J.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1974**, *96*, 5614. Mohanraj, S.; Ford, W. T. *J. Org. Chem.* **1985**, *50*, 1616.