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Thermolysis of *N*-Unsaturated Alkyl-β-ketoamides. An Easy Access to Spirolactams.

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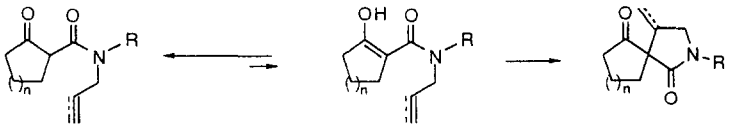
Abstract: A facile access to spirolactams based on the thermal rearrangement of *N,N*-unsaturated dialkyl- and of *N*-unsaturated alkyl-*N*-alkyl-β-ketoamides is presented. © 1997 Elsevier Science Ltd.

Upon heating, ε-ethylenic ketones are isomerized into cyclopentylketones in nearly quantitative yields through intramolecular oxa-ene reactions [1-3]. Similar isomerizations occur also with α-ethylenic ketones that bear another ε-or ξ-double bond [4-7], with ε-acetylenic ketones [10-13] or with ε-ethylenic aldehydes [8-11]. Applications of these reactions to the synthesis of hydrindanes [12-13], decalones [14], perhydropentalenones [14], steroids [15-19], bicyclo[n.m.1]alkan-2-ones [17-18], tricyclic systems [19] or spirocyclic skeletons [20-22] have been reported. Heterocyclic skeletons such as pyrrolidines [23-24], γ-lactones and γ-lactams [25] have also been prepared through intramolecular ene-reactions.

Azaspiranic compounds of type **C** are appropriate building blocks for the synthesis of natural products such as sibirine, nitramine, isonitramine, spirostaphylotrichin. Since β-ketoamides [26] of type **A** are equilibrated with the corresponding enols of type **B**, the *N*-unsaturated alkyl group could behave as an "enophile" on one side, and the enol group as an "ene" on the other side. Herein, we would like to report that the thermolysis of *N,N*-unsaturated dialkyl-β-ketoamides and *N*-unsaturated alkyl-*N*-alkyl-β-ketoamides of type **A** realizes an efficient method to produce azaspiranic compounds of type **C** [27].



A **B** **C**

Our results are summarized in Tables I and II.

The thermolysis of *N,N*-unsaturated dialkyl-β-ketoamides and *N*-unsaturated alkyl-*N*-alkyl-β-ketoamides led to spirolactams in moderate to good yields. In all cases the diastereoselectivity was satisfactory. In the case of *N,N*-diallyl-β-ketoamides **1**, the reaction required heating to 230°C (neat) for 2 h and gave a 9:1 mixture of the two diastereoisomeric spirolactams **11a** and **11b** that were isolated in

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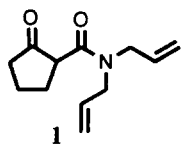
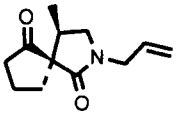
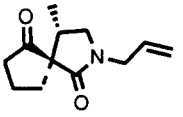
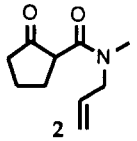
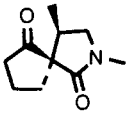
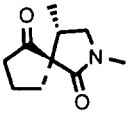
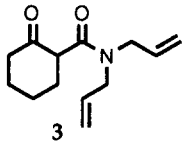
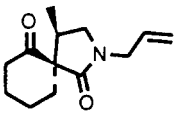
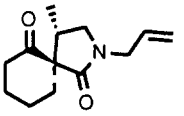
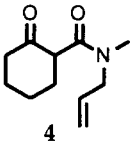
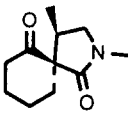
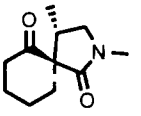
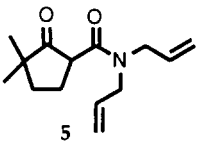
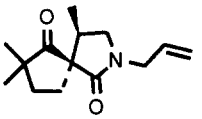
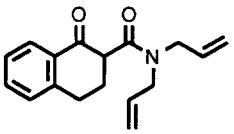
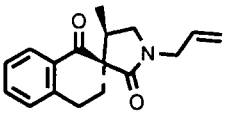
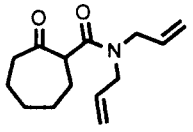
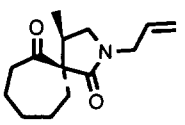
23% yield. The thermolysis of *N*-methyl-*N*-allyl-β-ketoamide **2** furnished a 9:1 mixture of the corresponding spirolactams **12a** and **12b** (15%).

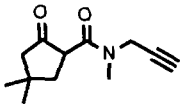
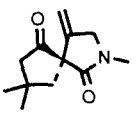
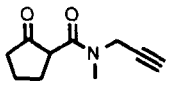
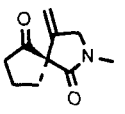
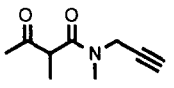
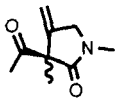
Table I: Thermolysis of *N*-alkyl, *N*-allyl β-ketoamides of type **A**

β-Ketoamides	t°C (h)	Spirolactams		Yield (a/b)*
 **1**	230 (2.0)	 **11a**	 **11b**	23% (90/10)
 **2**	230 (2.5)	 **12a**	 **12b**	15% (90/10)
 **3**	230 (2.0)	 **13a**	 **13b**	68% (95/5)
 **4**	230 (2.0)	 **14a**	 **14b**	60% (90/10)
 **5**	310 (2.0)	 **15**		27%
 **6**	230 (2.0)	 **16**		71%
 **7**	230 (2.0)	 **17**		75%

* Determined by ^{1}H NMR spectra

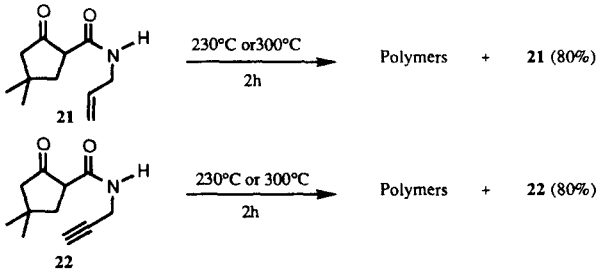
The yields were better for the pyrolysis of *N,N*-dialkyl-β-ketoamides **3** and **4** (230°C, 2 h) which afforded mixtures of the corresponding spirolactams **13a/13b** (67%) and **14a/14b** (57%), respectively. The diastereoselectivity was good as the product ratio for **13a/13b** and **14a/14b** was 95/5 and 90/10, respectively. Interestingly, the diastereoselectivity was complete in the cases of the thermolysis of *N,N*-dialkyl-β-ketoamides **5**, **6** and **7** that produced **15** (27%), **16** (71%) and **17** (75%) respectively. The pyrolysis of *N*-methyl-*N*-propargyl-β-ketoamides **8**, **9** and **10** yielded the corresponding ene-products **18** (67%), **19** (72%) and **20** (45%) respectively.

Table II: Thermolysis of *N*-alkyl-*N*-propargyl-β-ketoamides of type **A**

β-Ketoamides	t°C (h)	Spirolactams	Yield(%)
 **8**	230 (3.0) or 300 (2.0)	 **18**	67%
 **9**	230 (3.0) or 300 (2.0)	 **19**	72%
 **10**	230 (3.0) or 300 (2.0)	 **20**	45%

Surprisingly, when *N*-unsaturated alkyl-β-ketoamides **21** and **22** were thermolyzed at 230°C or at 300°C, no products of ene-reaction were observed and most of the starting materials were recovered (Scheme I).

Scheme I: Thermolysis of *N*-unsaturated alkyl-β-ketoamides



21 **22**

The relative configurations of the azaspiranic compounds were deduced from their ^{1}H NMR spectra and confirmed by single cristal X-ray diffraction of the spirolactams obtained [28]. The ^{1}H NMR spectra of the major isomers (the methyl and the carbonyl group of the ketone which are *cis*, with respect to the

lactam ring) showed, for the methyl group of protons, doublets that were slightly shielded compared with the methyl group of protons signals of the corresponding *trans* isomers (see Table III).

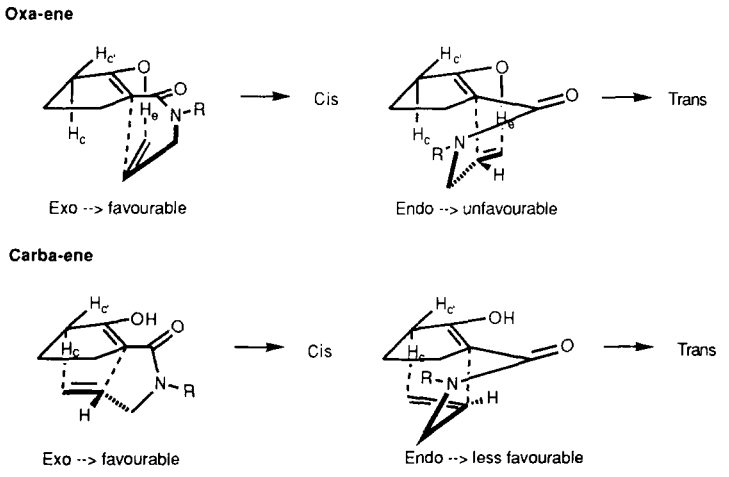
Table III: Chemical shifts of the methyl groups of protons at C-4 (in ppm) for compounds **a** and **b**

Compounds	*cis* isomer **a**	*trans* isomer **b**
11	1.02	1.09
12	1.01	1.05
13	0.99	1.09
14	0.98	1.15
15	1.02	-
16	0.98	-
17	1.10	-

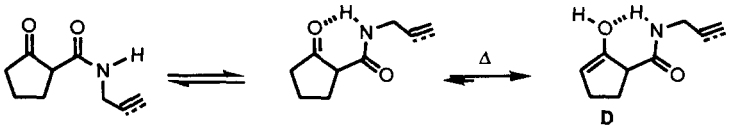
Two possible pathways can take place in the rearrangements reported in this work. On one hand, the carbon-carbon bond formation occurs concomittantly with the hydrogen atom transfer H_C (α to the ketone moiety) (intramolecular carba-ene reaction). On the other hand, the hydrogen H_e from the enol, is transfered to the double bond (intramolecular oxa-ene reaction). In both cases, the nitrogen lone pair can be oriented in the *exo* or *endo* position with respect to the cycloalkane ring (Scheme II).

With β-ketoamides **5** and **6** which do not possess hydrogen atom at the α' position of the ketone, only the oxa-ene reaction is possible and the cyclization generate *cis* lactams only, in agreement with a favoured *exo* transition state. Alternatively compounds **1**, **2**, **3**, **4** and **7** that possess hydrogen atoms in the α' position led to the major *cis* products that may arise either from an oxa-ene or from a carba-ene reaction. In both cases, *exo* transition states must be preferred. The minor *trans* products must therefore arise from *endo* oriented transition states.

Scheme II: Possible transition states of the ene-reaction



The thermolysis of *N*-unsaturated alkyl-β-ketoamides **21** and **22** did not produce spirolactams. This is probably due to the formation of enols of type **D**, the structure of which prevents H_c or H_e hydrogen transfer to the unsaturation moiety.



D

In conclusion, the thermolysis of β-ketoamides realizes a simple and efficient method for the preparation of spirolactams that can arise from either from oxa-ene or carba-ene reactions.

EXPERIMENTAL PART

General methods: All experiments were run under an Ar atmosphere. ^1H NMR and ^{13}C NMR spectra were obtained with a Bruker AC 300 instrument at 300 MHz and 75 MHz respectively, in $CDCl_3$ (Me_4Si as internal standard). IR spectra were recorded on a Perkin-Elmer Infracord 137 spectrometer. Mass spectra were run on a Hewlett-Packard (EI mode at 70 eV).
Flash chromatography was accomplished with Merck Silicagel 0.043-0.063 mm.
Acetonitrile, toluene, amines were distilled from CaH_2.

Synthesis of β-ketoamides

Photochemical synthesis

To a solution of 2-diazo-1,3-dione (3 mmol, 1 eq) in acetonitrile (60 mL) was added the amine (6 mmol, 2eq). The solution was irradiated for 2 h at 254 nm in 3 quartz tubes (ø = 1cm). After evaporation of the solvent, the product was purified by flash chromatography using petroleum ether/ethyl acetate as the eluent (PE/EtOAc).

N,N-*Diallyl-2-oxocyclopentane-1-carboxamide* **1**: R_f: 0.40 (PE/EtOAc: 70/30). Yield: 95%. IR: 1735; 1630; 1470; 1445; 1415; 990; 920 cm^{-1}. ^1H RMN: δ 1.77-2.55 (m, 6H); 3.42 (t, *J* = 8.5 Hz, 1H); 3.70 (m, 1H) ; 3.78-3.88 (m, 1H); 4.25-4.36 (m, 2H); 5.11-5.25 (m, 4H); 5.68-5.90 (m, 2H). ^{13}C NMR: δ 20.64 (t); 29.19 (t); 38.16 (t); 47.80 (t); 48.92 (t); 51.61 (d); 116.04 (d); 116.48 (t); 132.41 (d); 132.97 (d); 166.62 (s); 214.13 (s). MS: *m/z* 207 (M^+,30); 186 (29); 152 (26); 111 (42); 97 (47); 96 (100); 83 (38); 70 (46). Anal. Calcd. for $C_{12}H_{17}O_2N$: C, 69.53; H, 8.27; N, 6.76. Found: C, 69.56; H, 8.30; N, 6.80.

N-*Allyl*-N-*methyl-2-oxocyclopentane-1-carboxamide* **2**: R_f: 0.30 (PE/EtOAc: 70/30). Yield: 95% (two rotamers. ^1H NMR ratio: 1.1/1). IR: 1735; 1640; 1470; 1400; 1270; 1200; 1150; 1100; 920 cm^{-1}. ^1H NMR. Major rotamer: δ 2.95 (s, 3H); 3.38 (t, *J* = 8.5 Hz, 1H); Minor rotamer: δ 3.09 (s, 3H); 3.50 (t, *J* = 8.5 Hz, 1H); For both rotamers: δ 1.79-1.95 (m, 1H); 2.10-2.35 (m,4H); 2.50-2.60 (m, 1H); 3.78-4.35 (m, 2H); 5.10-5.25 (m, 2H); 5.68-5.90 (m, 1H). ^{13}C NMR. Major rotamer: δ 21.69 (t); 27.87 (t); 35.87 (q); 39.21 (t); 52.48 (d); 52.93 (t); 117.70 (t); 133.24 (d); 169.18 (s); 214.15 (s); Minor rotamer: δ 21.65 (t); 28.31 (t); 34.69 (q); 39.24 (t); 51.06 (t); 52.76 (d); 117.22(t); 133.58 (d); 169.66 (s); 213.75 (s). MS: *m/z* 181 (M^+,12); 166 (9); 153 (8); 126 (25); 111 (20); 98 (15); 83 (15); 70 (100); 55 (55).

N-*Methyl*-N-*propargyl-2-oxocyclopentane-1-carboxamide* **9**: R_f: 0.32 (PE/EtOAc: 55/45). Yield: 76% (two rotamers. ^1H NMR ratio 1.6/1). IR: 3300; 1735; 1630; 1460; 1400; 1370; 1340; 1285; 1145; 1100 cm^{-1}. ^1H NMR. Major rotamer: δ 3.21 (s, 3H); Minor rotamer: δ 3.03 (s, 3H); For both rotamers: δ 1.78-2.61 (m, 6H); 2.22 (t, J = 2.5 Hz, 1H); 3.45-3.58 (m, 1H); 3.86-4.70 (m, 2H). ^{13}C NMR. Major rotamer: δ 21.07 (t); 27.32 (t); 35.00 (q); 36.88 (t); 38.75 (t); 52.07 (d); 72.09 (d); 103.57 (s); 168.58 (s); 214.17 (s). Minor rotamer: δ 21.07 (t); 27.43 (t); 34.06 (q); 38.67 (t); 39.71 (t); 52.18 (d); 72.99 (d); 103.57 (s); 168.58 (s); 214.17 (s); MS: *m/z* 179 (M^+, 28); 124 (28); 87 (23); 85 (37); 68 (100); 55 (33). Anal. Calcd. for $C_{10}H_{13}NO_2$: C, 67.01; H, 7.31; N, 7.82. Found: C, 66.72; H, 7.37; N, 7.83.

N-*Methyl-N-propargyl-3-methyl-2-oxobutanamide* **10**: R_f: 0.40 (PE/EtOAc: 50/50). Yield: 64 % (two rotamers. 1H NMR ratio 2/1).IR: 3300; 1725; 1645; 1470; 1455; 1400; 1360; 1120; 1065 cm^{-1}. ^1H NMR. Major rotamer: δ 1.37 (d, J = 7 Hz, 3H); 2.17 (s, 3H); 2.29 (t, J = 2,5 Hz, 1H); 3.13 (s, 3H); 3.70 (q, J = 7 Hz, 1H); 4.20-4.32 (m, 2H); Minor rotamer: δ 1.39 (d, J = 7 Hz, 3H); 2.18 (s, 3H); 2.42 (t, J = 2.5 Hz, 1H); 3.05 (s, 3H); 3.75 (q, J = 7 Hz, 1H); 4.03-4.24 (m, 2H). ^{13}C NMR. Major rotamer: δ 13.13 (q); 26.94 (q); 34.49 (q); 36.44 (t); 51.46 (d); 71.95 (d); 78.03 (s),;169.80 (s); 204.47 (s); Minor rotamer: δ 13.36 (q); 27.08 (q); 33.56 (q); 39.51 (t); 51.46 (d); 73.13 (d); 78.03 (s); 170.06 (s); 204.47 (s). MS: *m/z* 167 (M^+, 2); 125 (13); 124 (53); 110 (15); 60 (15); 59 (15); 58 (100); 55 (18). Anal. Calcd. for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.56; H, 8.08; N, 8.45.

N-*Allyl-4,4-dimethyl-2-oxocyclopentane-1-carboxamide* **21**: R_f: 0.45 (EP/EtOAc: 85/15). Yield: 71%. IR (CCl_4): 3390 (large); 1735; 1685; 1660; 1520; 1460; 1410; 1370; 1280; 1135; 990; 925 cm^{-1}. ^1H NMR: δ 1.06 (s, 3H); 1.17 (s, 3H); 2.00-2.45 (m, 4H); 3.20 (t, J = 9 Hz, 1H); 3.82-3.93 (m, 2H); 5.07-5.21 (m, 2H); 5.72-5.88 (m, 1H); 6.65 (s, 1H). ^{13}C NMR: δ 27.89 (q); 28.83 (q); 34.08 (s); 39.37 (t); 42.02 (t); 53.66 (t); 53.81 (d); 116.21 (t); 134.05 (d); 166.89 (s); 216.10 (s). MS: *m/z* 195 (M^+, 16); 180 (17); 139 (16); 112 (90); 97 (25); 58 (55); 57 (62); 56 (100); 55 (46). Anal. Calcd. for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.77; N, 7.17. Found C, 67.58; H, 8.65; N, 7.11.

N-*Propargyl-4,4-dimethyl-2-oxocyclopentane-1-carboxamide* **22**: R_f: 0.31 (EP/EtOAc: 80/20). Yield: 68%. mp: 85-87°C. IR: 3370 (large); 3300; 1725; 1660; 1510; 1460; 1400; 1370; 1280; 1130 cm^{-1}. ^1H NMR: δ 1.04 (s, 3H); 1.15 (s, 3H); 2.00-2.35 (m, 5H); 3.20 (t, J = 9.5 Hz, 1H); 3.92-4.12 (m, 2H); 7.05 (s, 1H). ^{13}C NMR: δ 27.86 (q); 28.85 (q); 29.32 (t); 34.08 (s); 39.22 (t); 53.61 (t); 53.66 (d); 71.59 (d); 79.48 (s); 166.85 (s); 215.90 (s). MS: *m/z* 193 (M^+, 12); 178 (22); 123 (10); 114 (9); 113 (100); 100 (11); 56 (23); 55 (32); 54 (18). Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.36; H, 7.82; N, 7.25. Found: C, 68.17; H, 7.71; N, 7.21.

Chemical synthesis

To a solution of a β-ketoester (1.8 mmol, 1 eq) in toluene (20 mL) was added the amine (3.5 mmol, 2 eq) and a catalytic amount of DMAP. The reaction media was stirred under reflux for 15 h. The toluene was evaporated under reduced pression and the crude reaction mixture was purified by flash chromatography.

N,N-*Diallyl-2-oxocyclohexane-1-carboxamide* **3**: R_f: 0.39 (PE/EtOAc: 70/30). Yield: 90%. IR: 1695; 1625; 1440; 1280; 1175; 1120; 990 cm^{-1}. ^1H NMR: δ 1.50-1.60 (m, 2H); 1.63-2.05 (m, 3H); 2.05-2.35 (m, 2H); 2.44-2.55 (m, 1H); 3.40-3.50 (m, 1H); 3.60-3.80 (m, 3H); 4.15-4.25 (m, 1H); 5.00-5.20 (m, 4H); 5.60-5.80 (m, 2H). ^{13}C NMR: δ 23.42 (t); 26.60 (t); 30.27 (t); 41.73 (t); 47.86 (t); 49.13 (t); 54.24 (d); 116.33 (t); 116.74 (t); 132.66 (d); 133.27 (d); 169.54 (s); 207.24 (s). MS: *m/z* 221 (M^+, 30); 180 (23); 125 (49); 124 (40); 98 (33); 96 (100); 82 (45); 70 (65). Anal. Calcd. for $C_{13}H_{19}NO_2$: C, 70.55; H, 8.65; N, 6.33. Found: C, 70.34; H, 8.7; N, 6.26.

N-*Allyl*-N-*methyl-2-oxocyclohexane-1-carboxamide* **4**: R_f: 0.30 (PE/EtOAc: 70/30). Yield: 95% (two rotamers. ^1H NMR ratio 1.1/1). IR: 1710; 1640; 1480; 1450; 1405; 1350; 1290; 1130; 925 cm^{-1}. ^1H NMR. Major rotamer: δ 2.88 (s, 3H); Minor rotamer: δ 2.97 (s, 3H); For both rotamers: δ 1.68-1.90 (m, 2H); 1.90-2.40 (m, 5H); 2.50-2.59 (m, 1H); 3.48-3.65 (m, 1H); 3.70-4.17 (m, 2H); 5.10-5.20 (m, 2H); 5.70-5.85 (m, 1H). ^{13}C NMR. Major rotamer: δ 24.26 (t); 27.62 (t); 30.90 (t); 35.42 (q); 42.66 (t); 50.93 (t); 54.93 (d); 117.68 (t); 133.37 (d); 170.00 (s); 207.93 (s); Minor rotamer: δ 24.16 (t); 27.78 (t); 31.18 (t); 35.42 (q); 42.52 (t); 52.85 (t); 55.29 (d); 117.32 (t); 133.64 (d); 170.41 (s); 208.27 (s). MS: *m/z* 195 (M^+, 15); 180 (10); 167 (17); 154 (15); 126 (20); 98 (30); 70 (100); 55 (30).

N,N-*Diallyl-5,5-dimethyl-2-oxocyclopentane-1-carboxamide* **5**: R_f: 0.42 (PE/EtOAc: 70/30). Yield: 77%. IR: 1730; 1630; 1430; 1220; 1050 cm^{-1}. ^1H NMR: δ 1.08 (s, 3H); 1.09 (s, 3H); 1.70-1.80 (m, 1H); 1.95-2.10 (m, 2H); 2.45-2.55 (m, 1H); 3.50 (t, J = 8.9 Hz, 1H); 3.60-3.90 (m, 2H); 4.30-4.50 (m, 2H); 5.10-5.25 (m, 4H); 5.65-5.90 (m, 2H). ^{13}C NMR: δ 23.44 (q); 23.46 (t); 24.09 (q); 36.56 (t); 44.57 (s); 48.24 (t); 49.34 (t); 51.47 (d); 116.35 (t); 116.83 (t); 132.70 (d); 133.32 (d); 169.18 (s); 218.13 (s). MS: *m/z* 235 (M^+, 7%); 152 (27); 132 (22); 96 (100). Anal. Calcd. for $C_{14}H_{21}NO_2$: C, 71.45; H, 8.99; N, 3.29. Found: C, 71.49; H, 9.1; N, 3.32.

N,N-*Diallyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxamide* **6**: R_f: 0.28 (PE/EtOAc: 95/05). Yield: 88%. IR: 1680; 1640; 1600; 1450; 1410; 1350; 1300; 1220; 1190; 990; 920 cm^{-1}. ^1H NMR: δ 2.18-2.28 (m, 1H); 2.52-2.68 (m, 1H); 2.92-3.15 (m, 2H); 3.67-3.90 (m, 3H); 4.12 (m, 1H); 4.40 (m, 1H); 5.12-5.40 (m, 4H); 5.78-5.95 (m, 2H); 7.50 (m, 1H); 8.00 (m, 1H). ^{13}C NMR: δ 27.31 (t); 29.02 (t); 48.87 (t); 50.12 (d); 116.99 (t); 117.71 (t); 127.42 (d); 128.23 (d); 129.45 (d); 132.73 (s); 133.45 (d); 134.27 (d); 134.42 (d); 144.78 (s); 170.90 (s); 195.22 (s). MS: *m/z* 269 (M^+, 12); 228 (15); 173 (15); 145 (50); 115 (40); 96 (100); 91 (20); 56 (35). Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.75; H, 7.11; N, 5.20. Found: C, 75.85; H, 7.20; N, 5.27.

N,N-*Diallyl-2-oxocycloheptane-1-carboxamide* **7**: R_f: 0.25 (PE/EtOAc: 80/20). Yield: 71%. IR: 1700; 1630; 1440; 1410; 1340; 1230; 1210; 990 cm^{-1}. ^1H NMR: δ 1.10-1.60 (m, 3H); 1.80-2.20 (m, 5H); 2.45-2.55 (m, 1H); 2.80-2.90 (m, 1H); 3.60 (dd, J = 5.0 and 14.0 Hz, 1H); 3.70-3.85 (m, 2H); 4.10-4.18 (m, 2H); 5.10-5.25 (m, 4H); 5.70-5.90 (m, 2H). ^{13}C NMR: δ 26.22 (t), 28.53 (t); 28.94 (t); 30.99 (2t); 43.52 (t); 48.83 (t); 50.06 (t); 57.47 (d); 117.27 (t); 117.78 (t); 133.48(d); 133.82 (d); 164.98 (s); 215.30 (s). MS: *m/z* 235 (M^+, 10); 194 (15); 152 (12); 139 (20); 124 (21); 111 (5); 96 (100); 82 (22); 70 (18); 56 (70).

N-*Methyl*-N-*propargyl-4,4-dimethyl-2-oxocyclopentane-1-carboxamide* **8**: R_f: 0.57 (PE/EtOAc: 60/40). Yield: 94% (two rotamers. ^1H NMR ratio 1.6/1). IR: 3300; 1745; 1645; 1450; 1400; 1375; 1350; 1290; 1110 cm^{-1}. ^1H NMR. Major rotamer: δ 1.00 (s, 3H); 3.21 (s, 3H); 3.21 (s, 3H); Minor rotamer: δ 1.01 (s, 3H); 1.18 (s, 3H); 3.04 (s, 3H); For both rotamers: δ 1.92-2.52 (m, 5H); 3.66-3.80 (m, 1H); 3.87-4.67 (m, 2H). ^{13}C NMR. Major rotamer: δ 27.93 (q); 28.88 (q); 34.74 (q); 36.68 (s); 40.44 (t); 51.27 (d); 53.29 (t); 53.31 (t); 71.86 (d); 78.43 (s); 168.33 (s); 213.10 (s); Minor rotamer: δ 27.93 (q); 28.88 (q); 33.88 (q); 34.07 (s); 39.45 (t); 51.20 (d); 53.29 (t); 53.31 (t); 72.81 (d); 78.38 (s); 167.92 (s); 213.50 (s). MS: *m/z* 207 (M^+, 14); 124 (56); 123 (14); 70 (17); 69 (18); 68 (100); 55 (33). Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.26; N, 6.75. Found: C, 69.62; H, 8.23; N, 6.76.

Thermolysis of compounds 1-10, 21, 22.

Compounds **1-10, 21, 22** were thermolyzed neat under an argon atmosphere.

2-Allyl-4-methyl-2-azaspiro[4.4]nonane-1,6-dione ***11***: The two diastereoisomers **11a** and **11b** were obtained in a ratio 90/10 (determined by ^1H NMR) and could not be separated by flash chromatography. For both isomers: Rf: 0.35 (PE/EtOAc: 70/30). Yield 23%. IR: 1740; 1690; 1480; 1430; 1410; 1270; 1140; 920 cm^{-1}. MS: *m/z* 207 (M^+, 37); 152 (100); 97 (30); 89 (18); 65 (13); 59 (10). Anal. Calcd.for $C_{12}H_{17}O_2N$: C, 69.53; H, 8.27; N, 6.76. Found: C, 69.58; H, 8.37; N, 6.82. Isomer **11a**: ^1H NMR: δ 1.02 (d, *J* = 7.0 Hz, 3H); 2.85 (dd, *J* = 9.4 and 4.3 Hz, 1H); 3.69 (dd, *J* = 9.4 and 8.2 Hz, 1H); 1.80-2.05 (m, 2H); 2.15-2.45 (m, 4H), 2.62 (m, 1H); 3.80-4.00 (m, 2H); 5.10-5.25 (m, 2H); 5.64-5.80 (m, 1H). ^{13}C NMR: δ 15.54 (q); 19.36 (t); 27.95 (t); 32.89 (d); 37.58 (t); 45.15 (t); 51.89 (t); 61.99 (s); 117.66 (t); 131.98 (d); 173.08 (s); 216.57 (s). Isomer **11b**: ^1H NMR: δ 1.09 (d, *J* = 7.0 Hz, 3H); 1.85-2.00 (m, 2H); 2.10-2.45 (m, 4H); 2.60 (m, 1H); 3.20-3.38 (m, 2H); 3.82-4.00 (m, 2H); 5.20 (m, 2H); 5.67-5.80 (m, 1H). ^{13}C NMR: δ 12.36 (q); 20.17 (t); 32.30 (t); 38.30 (d); 39.60 (d); 45.27 (t); 51.20 (t); 62.05 (s); 117.40 (t); 131.98 (d); 173.08 (s); 216.57 (s).

2,4-Dimethyl-2-azaspiro[4.4]nonane-1,6-dione ***12***: The two diastereoisomers **12a** and **12b** were obtained in a ratio 90/10 (determined by ^1H NMR) and could not be separated by flash chromatography. For both isomers: Rf: 0.25 (PE/EtOAc: 70/30). Yield: 15%. IR: 1730; 1675; 1490; 1430; 1400; 1340; 1270; 1200; 1150 cm^{-1}. MS: *m/z* 181 (M^+, 68); 166 (20); 140 (17); 126 (100); 111 (20); 98 (20); 71 (42); 70 (38); 55 (20). Anal. Calcd. for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.72. Found: C, 66.37; H, 8.37; N, 7.71. Isomer **12a**: ^1H NMR: δ 1.01 (d, *J* = 7.0 Hz, 3H); 1.84-2.06 (m, 2H); 2.10-2.42 (m, 4H); 2.52-2.62 (m, 1H); 2.85 (s, 3H); 3.30 (m, 2H).^{13}C NMR: δ 15.65 (q); 19.50 (t); 28.02 (t); 29.89 (q); 33.02 (d); 37.70 (t); 54.68 (t); 62.51 (s); 173.90 (s); 216.05 (s). Isomer **12b**: ^1H NMR: δ 1.05 (d, *J* = 7.0 Hz, 3H); 1.90 (m, 2H); 2.10-2.40 (m, 4H); 2.55 (m, 1H); 2.87 (m, 3H); 3.20-3.30 (m, 2H). ^{13}C NMR: δ 13.23 (q); 20.96 (t); 30.53 (q); 32.92 (t); 39.06 (d); 40.32 (t); 54.44 (t); 62.45 (s); 174.04 (s); 217.15 (s).

2-Allyl-4-methyl-2-azaspiro[4.5]decane-1,6-dione ***13***: The two diastereoisomers **13a/13b** were separated by flash chromatography. The ratio of the two isomers was 95/5 (determined by ^1H NMR). Isomer **13a**. Rf: 0.60 (PE/EtOAc: 70/30). Yield: 62%. IR: 1700; 1675; 1495; 1455; 1420; 1255; 1225; 1125 cm^{-1}. ^1H NMR: δ 0.99 (d, *J* = 7.0 Hz, 3H), 1.63-1.79 (m, 3H); 1.95-2.14 (m, 2H); 2.17-2.30 (m, 1H); 2.38-2.50 (m, 1H); 2.83 (dd, *J* = 9.5 and 7.0 Hz, 1H); 2.96-3.10 (m, 2H); 3.35 (dd, *J* = 9.5 and 7.0 Hz, 1H); 3.83-3.93 (m, 2H); 5.13-5.21 (m, 2H); 5.63-5.87 (m, 1H). ^{13}C NMR: δ 13.47 (q); 20.61 (t); 26.76 (t); 30.19 (t); 31.56 (d); 40.30 (t); 45.31 (t); 50.46 (t); 61.50 (t); 117.87 (t); 132.06 (d); 172.46 (s); 20.37 (s). MS: *m/z* 221 (M^+, 37); 193 (25); 165 (30); 152 (100); 97 (30); 89 (18); 65 (13). Anal. Calcd. for $C_{13}H_{19}NO_2$: C, 70.55; H, 8.65; N, 6.33. Found: C, 70.50; H, 8.80; N, 6.39. Isomer **13b**. Rf: 0.35 (PE/EtOAc: 70/30). Yield: 6.5%. IR: 1700; 1675; 1495; 1455; 1420; 1255; 1225; 1125 cm^{-1}. ^1H NMR: δ 1.09 (d, *J* = 7.0 Hz, 3H); 1.54-1.92 (m, 4H); 2.00-2.28 (m, 4H); 2.40-2.60 (m, 1H); 3.00-3.27 (m, 2H); 3.70-3.93 (m, 2H); 4.98-5.25 (m, 2H); 5.52-5.78 (m, 1H). ^{13}C NMR: δ 13.82 (q); 20.91 (t); 24.31 (t); 34.23 (t); 39.27 (d); 41.48 (t); 45.18 (t); 51.28 (t); 61.63 (s); 117.44 (t); 131.96 (d); 173.58 (s); 208.64 (s). MS: *m/z* 221 (M^+, 37); 193 (25); 165 (30); 152 (100); 97 (30); 89 (18).

2,4-Dimethyl-2-azaspiro[4.5]decane-1,6-dione ***14***: **14a** and **14b** were separated by flash chromatography. The ratio of the two isomers was 90/10 (determined by ^1H NMR). Isomer **14a**. Rf: 0.55 (PE/EtOAc: 70/30). Yield: 6%. IR: 1700; 1675; 1490; 1430; 1400; 1270; 1200 cm^{-1}. ^1H NMR: δ 0.98 (d, *J* = 7.0 Hz, 3H); 1.60-1.75 (m, 3H); 1.90-2.30 (m, 4H); 2.35-2.42 (m, 1H); 2.83 (s, 3H); 2.90-3.10 (m, 2H); 3.30 (m, 1H). ^{13}C NMR: δ 13.65 (q); 20.74 (t); 26.87 (t); 29.65 (d); 29.97 (t); 31.59 (q); 40.41 (t); 53.35 (t); 61.36 (s); 172.84 (s); 208.54 (s). MS: *m/z* 195 (M^+, 50); 181 (8); 167 (14); 152 (16); 139 (24); 126 (35); 110 (10); 71 (100). Anal. Calcd. for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.77; N, 7.17. Found: C, 67.72; H, 8.83; N, 7.27. Isomer **14b**. Rf: 0.29 (PE/EtOAc: 70/30). Yield: 54%. IR: 1700; 1675; 1490; 1430; 1400; 1270; 1200 cm^{-1}. ^1H NMR: δ 1.15 (d, *J* = 7.0 Hz, 3H); 1.62-1.98 (m, 4H); 2.08-2.33 (m, 4H); 2.50-2.65 (m, 1H); 2.85 (s, 3H); 3.33 (dd, *J* = 6.9 and 6.9 Hz, 1H); 3.62 (dd, *J* = 6.9 and 1.2 Hz, 1H). ^{13}C NMR: δ 14.02 (q); 21.07 (t); 24.51 (t); 29.87 (q); 34.43 (t); 39.39

(d); 41.69 (t); 54.07 (t); 61.57 (s); 173.97 (s); 209.01 (s). MS: *m/z* 195 (M^+, 50); 181 (8); 167 (14); 152 (16); 110 (10); 71 (100).

2-Allyl-4,7,7-trimethyl-2-azaspiro[4.4]nonane-1,6-dione ***15***: Rf: 0.32 (PE/EtOAc: 50/50). Yield: 27%. IR: 1740; 1697; 1480; 1430; 1270 cm^{-1}. ^1H NMR: δ 1.03 (d, *J* = 5.5 Hz, 3H); 1.08 (s, 3H); 1.10 (s, 3H); 1.70-1.85 (m, 1H); 1.95-2.15 (m, 2H); 2.30-2.40 (m, 1H); 2.43-2.60 (m, 1H); 3.20 (dd, *J* = 9.0 and 8.3 Hz, 1H); 3.35 (dd, *J* = 9.8 et 9.3 Hz, 1H); 3.90-4.05 (m, 2H); 5.10-5.25 (m, 2H); 5.65-5.80 (m, 1H). ^{13}C NMR: δ 12.90 (q); 22.77 (q); 23.65 (q); 28.70 (t); 36.02 (t); 38.82 (t); 45.87 (s); 46.56 (s); 51.15 (t); 62.66 (d); 117.48 (t); 133.19 (d); 173.34(s); 220.27 (s). MS: *m/z* 235 (M^+, 90); 220 (40); 153 (40); 152 (100); 100 (56); 84 (35).

1'-Allyl-4'-methylspiro[1,2,3,4-tetrahydronaphthalene-2,3'-pyrrolidine]-1,2'-dione **16**: Rf: 0.32 (PE/EtOAc: 70/30). Yield: 71%. IR: 1730; 1690; 1660; 1600; 1480; 1440; 1355; 1280; 1268; 1220; 920 cm^{-1}. ^1H NMR: δ 0.98 (d, *J* = 7.0 Hz, 3H); 2.05 (m, 1H); 2.50 (m, 1H); 2.80 (m, 1H); 3.00-3.40 (m, 4H); 3.90-4.10 (m, 2H); 5.20-5.35 (m, 2H); 5.80 (m, 1H); 7.30 (m, 2H); 7.50 (m, 1H); 8.05 (m, 1H). ^{13}C NMR: δ 14.52 (q); 25.32 (t); 31.71 (t); 38.50 (d); 45.43 (t); 51.77 (t); 58.81 (s); 117.66 (t); 126.63 (d); 127.32 (d); 128.46 (d); 139.19 (d); 132.51 (s); 133.71 (d); 143.67 (s); 174.20 (s); 196.40 (s). MS: *m/z* 269 (M^+, 100); 252 (39); 226 (15); 200 (10); 185 (15); 173 (60); 170 (45); 115 (35); 97 (80); 90 (50). Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 77.81; H, 7.11; N, 5.20. Found: C, 77.81; H, 7.15; N, 5.27.

2-Allyl-4-methyl-2-azaspiro[4.6]undecane-1,6-dione ***17***: Rf: 0.32 (PE/EtOAc 70/30). Yield: 75%. IR: 1735; 1680; 1642; 1475; 1430; 1355; 1310; 1260; 1165 cm^{-1}. ^1H NMR: δ 1.10 (d, *J* = 7.0 Hz, 3H); 1.50-1.60 (m, 2H); 1.72-1.85 (m, 4H); 2.10-2.30 (m, 3H); 2.52-2.62 (m, 2H); 3.07 (dd, *J* = 10.0 and 10.0 Hz, 1H); 3.23 (dd, *J* = 10.0 and 8.0 Hz, 1H); 3.90 (m, 2H); 5.25 (m, 2H); 5.68-5.82 (m, 1H). ^{13}C NMR: δ 13.22 (q); 24.57 (t); 25.60 (t); 30.92 (t); 34.16 (t); 39.95 (d); 44.76 (t); 45.20 (t); 50.98 (t); 63.42 (s); 117.52 (t); 132.24 (d); 174.78 (s); 212.19 (s). MS: *m/z* 235 (M^+, 90); 220 (15); 207 (20); 192 (30); 181 (50); 166 (40); 152 (100); 139 (45); 124 (30); 97 (83). Anal. Calcd. for $C_{14}H_{21}NO_2$: C, 71.45; H, 8.99; N, 5.95. Found: C, 71.57; H, 9.09; N, 5.92.

2,8,8-Trimethyl-4-methylene-2-azaspiro[4.4]nonane-1,6-dione ***18***: Rf: 0.33 (PE/EtOAc: 60/40). Yield: 67%. IR: 1740; 1690; 1660; 1430; 1410; 1150 cm^{-1}. ^1H NMR: δ 1.15 (s, 3H); 1,25 (s, 3H); 1.90 (d, *J* = 14.0 Hz, 1H); 2.35 (m, 2H); 2.55 (d, *J* = 14.0 Hz, 1H); 2.95 (s, 3H); 3.85 (dt, *J* = 13.5 and 2.0 Hz, 1H); 4.28 (dt, *J* = 13.5 and 2.1 Hz, 1H); 5.10 (t, *J* = 2.0 Hz, H).5.17 (t, 2.0 Hz, 1H). ^{13}C NMR: δ 28.87 (q); 29.60 (q); 29.69 (q); 33.11 (t); 45.71 (t); 53.08 (t); 53.67 (s); 65.08 (s); 107.91 (t); 144.25 (s); 171.82 (s); 211.97 (s). MS: *m/z* 207 (M^+, 20); 125 (9); 124 (100); 107 (8); 81 (8); 77 (10). Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.53; H, 8.27; N, 6.76. Found: C, 69.61; H, 8.42; N, 6.88.

N-*Methyl-4-methylene-2-azaspiro[4.4]nonane-1,6-dione* ***19***: Rf: 0.44 (EP/AcOEt: 80/20). Yield: 60%. IR: 1730; 1680; 1650; 1485; 1425; 1400; 1310; 1280; 1135; 1070; 890 cm^{-1}. ^1H NMR: δ 1.95-2.70 (m, 6H); 2.90 (s, 3H); 3.80-3.97 (m, 1H); 4.10-4.23 (m, 1H); 5.05 (d, 1H, *J* = 2 Hz); 5.12 (d, 1H, *J* = 2 Hz). ^{13}C NMR: δ 20.13 (t); 29.57 (q); 32.83 (t); 37.82 (t); 53.49 (t); 63.24 (s); 108.04 (t); 143.81 (s); 172.06 (s); 213.96 (s). MS: *m/z* 180 (M+1, 11); 179 (M^+, 39); 151 (24); 150 (24); 138 (20); 124 (100); 87 (59); 85 (91); 53 (20). Anal. Calcd. for $C_{10}H_{13}NO_2$: C, 67.01; H, 7.31; N, 7.82. Found: C, 66.86; H, 7.48; N, 7.86.

3-Acetyl-1,3-dimethyl-4-methylenepyrrolidin-2-one ***20***: Rf: 0.26 (EP/AcOEt: 55/45). Yield: 40%. IR: 1710; 1650; 1460; 1435; 1400; 1350; 1285; 1130; 1080; 1060; 900 cm^{-1} ^1H NMR: δ 1.44 (s, 3H); 2.15 (s, 3H); 3.00 (s, 3H); 4.05-4.21 (m, 2H); 5.06-5.25 (m, 2H). ^{13}C NMR: δ 19.42 (q); 25.76 (q); 29.47 (q); 52.92 (t); 62.00 (s); 110.62 (t); 142.29 (s); 173.18 (s); 202.20 (s). MS: *m/z* 168 (M+1, 14); 167 (M^+, 0.25); 139 (36); 125 (86); 124 (100); 110 (23); 53 (17). Anal. Calcd. for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.16; H, 7.80; N, 8.42.

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