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Photoreduction of α-Ketoamides; Cyclization of Unsaturated Captodative Radicals

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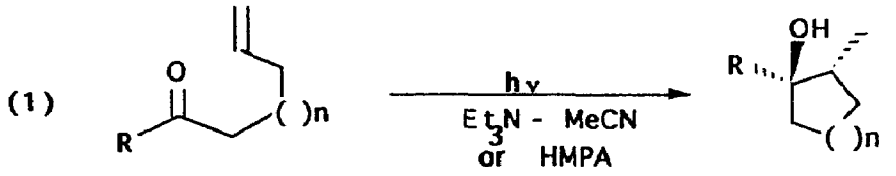
Abstract : When N-allyl α-ketoamides are irradiated in the presence of t-amines, a reductive photocyclization to hydroxypyrrolidones is observed. The reaction involves cyclization of an unsaturated captodative radical

***Key Words** : Photoreduction, α-ketoamides, cyclization, captodative radicals.*

The photoreductive cyclization of δ, ε-unsaturated ketones in the presence of tertiary amines or HMPA is a very efficient process for the preparation of substituted cyclopentanols (equation 1).[1]



This stereoselective reaction, which is carried out under mild conditions, can be applied to the total synthesis of polycyclic and heterocyclic natural products.[2] In connection with our interest in the synthesis of functionalized pyrrolidines, we have investigated the photoreactivity of N-allyl and N-propargyl-α-ketoamides in the presence of tertiary amines. The intramolecular photoreaction of α-ketoamides has already been shown to produce β-lactams by a Norrish type II process [3] when other cyclization processes become competitive in polar solvents.[4] We anticipated that a photoreduction process involving an intermediate captodative radical [5] might lead to an intramolecular addition to an unsaturated group although no cyclized product could be isolated from allylbenzoylformates when irradiated in HMPA (equation 2).[6]

Here, we report that irradiation of unsaturated α-ketoamides leads to 5-membered ring derivatives under photoreductive conditions.

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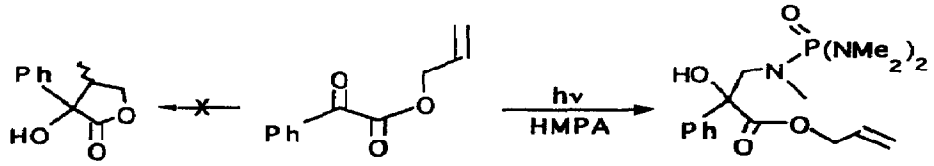
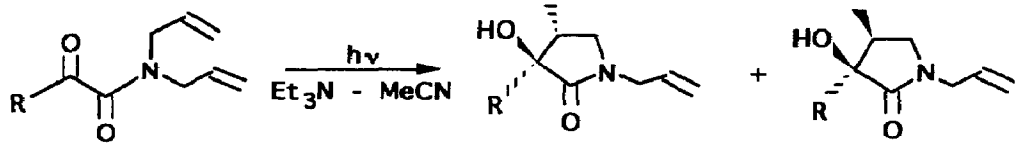
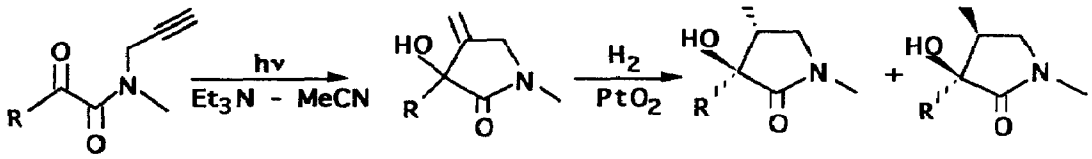
(2) 

When solutions of α-ketoamides 1 or 2 and triethylamine were irradiated in acetonitrile (10^{-2}M) at 254 nm, the hydroxypyrrolidones **4-6** were isolated in low yields from the complex reaction mixture (equation 3). Similar results are obtained when the irradiation was carried out in HMPA and Et_3N (10 equivalents).

(3) 

1	R = CH_3	4	7%	5	4%
2	C_2H_5	6	11%	-	
3	H	7	30%	-	

When the irradiation of aldehyde 3 was carried out under similar conditions, **7** was isolated as the only butyrolactam. Similarly, the propargyl ketoamide **8** led to the lactam **9** (50%). The stereochemistry of the lactams **4** and **5** was established by comparison of their NMR spectra [7] with those of the lactams **10** and **11** obtained stereoselectively by hydrogenation of the allylic alcohol **9**.[8]

(4) 

The behaviour of the benzoylformamide **12** under photoreductive conditions depends on the nature of the reducing agent (equation 5, Table). In pure HMPA the benzylic alcohol **13** and the β-lactam **15** arising from a γ-hydrogen abstraction process, could be isolated. No γ-lactam could be detected under these conditions.

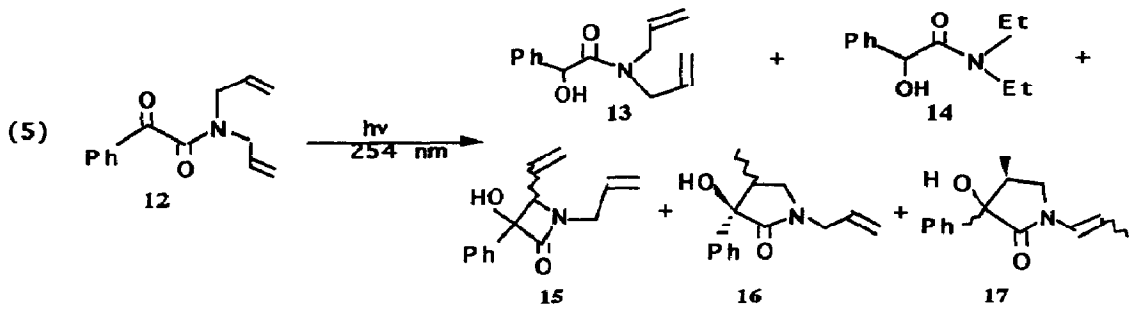
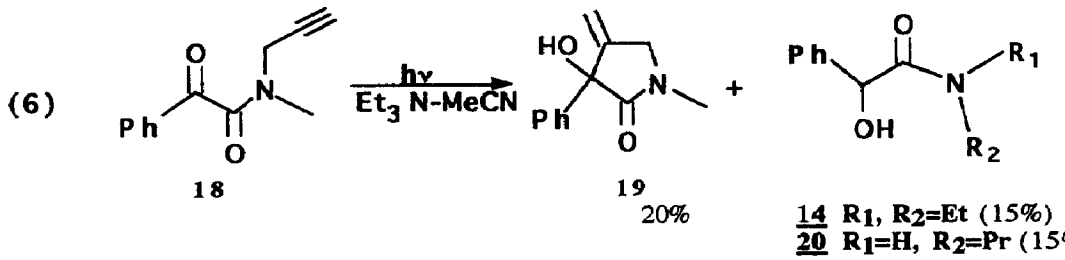
(5) 

Table : Yields (%) of the products isolated from the irradiation of **12** at 254 nm.

Solvent	13	14	15	16	17
HMPA	18%	-	30%	-	-
Et_3N-MeCN	-	20	22	20	10
Et_3N-HMPA	-	20	7	25	-

When the irradiation of **12** was conducted in the presence of triethylamine, the benzylic alcohol **14** was preferred to **13**, and the γ-lactam **16** was preferred to the β-lactam **15** when the photolysis was carried out in a solution of triethylamine in HMPA (10^{-2}.M).

The photolysis of the propargylamide **18** in a solution of Et_3N (10 equivalents) in MeCN led to a mixture of the γ-lactam **19** and the benzylic alcohol **14**.



18 **19** 20%

14 R_1, R_2=Et (15%)
20 R_1=H, R_2=Pr (15%)

Production of γ-lactams by photolysis of α-ketoamides in a reducing medium contrasts with the results described for α-ketoesters and is in agreement with recent results on the ring closure of α-alkoxyester free radicals [5c]. γ-Lactams could result from an intermolecular electron transfer from the reducing agent to the excited carbonyl group and consequently from an anion radical intermediate. The replacement of an alkyl group by a phenyl substituent on the α-oxoamide stabilizes the α-hydroxyamide free radical intermediate by delocalisation and allows competitive processes to occur. Formation of products **15** derived from a Norrish type II process and benzylic alcohols **13** or **14** now compete with γ-lactam production. The formation of benzylic alcohol **14** might be due to diethylamine present in very small amounts in the triethylamine used and its addition to the hydroxyketene expected from the Norrish type II elimination of **12**. To test this hypothesis we carried out the irradiation of **12** in a mixture of triethylamine and acetonitrile in the presence of n-propylamine. Besides **15** and **17** we now isolated the N-methyl, N-propyl mandelamide **20** (15%) rather than the corresponding diethylamide **14**.

REFERENCES

1 a) Belotti, D.; Cossy, J.; Pete, J.P. and Portella, C. *Tetrahedron Lett.* **1985**, *26*, 4591-4594
b) Belotti, D.; Cossy, J.; Pete, J.P. and Portella, C. *J. Org. Chem.* **1986**, *51*, 4196-4200
c) Belotti, D.; Cossy, J. and Pete, J.P. *Tetrahedron Lett.* **1987**, *28*, 4545-4546
d) Belotti, D.; Cossy, J. and Pete, J.P. *Tetrahedron Lett.* **1989**, *30*, 7361-7364.

2 a) Cossy, J.; Belotti, D. and Pete, J.P.*Tetrahedron Lett.* **1987**, *28*, 4547-4550
b) Cossy, J.; Belotti, D. and Pete, J.P. *Tetrahedron* **1990**, *46*, 1859-1870
c) Cossy, J.and Belotti, D. *Tetrahedron Lett.* **1988**, *29*, 6113-6114
d) Cossy, J.*Tetrahedron Lett.* **1989**, *30*, 4113-4116.

3 a) Äkermark,B.; Johansson, N.G.and Sjöberg, B.*Tetrahedron Lett.* **1969**, *10*, 371-372
b) Henery-Logan, K.R. and Chen, C.G. *Tetrahedron Lett.* **1973**, *14*, 1103-1104
c) Aoyama, H.; Sakamato, M. and Omote, Y.*J.C.S. Chem. Comm.* **1982**, 119-120.

4 a) Aoyama, H.; Sakamato, M. and Omote, Y. *J.C.S. Perkin Trans.* I **1981**, 1357-1359
b) Shima, K.; Tanabe, K.; Furukawa, S.; Saïto, J. and Shirakashi, K. *Bull. Chem. Soc. Jap.* **1984**, *57*, 1515-1517.

5 a) Viehe, H.G.; Janouzek, Z. and Merenyi, R. *Acc. Chem. Res.* **1985**, *18*, 148-154
b) Viehe, H.G.; Merenyi, R ;.Stella, L. and Janouzek, Z. *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 917-932
c) Lolkema, L.D.M.; Hiemstra, H.; Ghouch, A.A.A. and Speckamp, W.N. *Tetrahedron Lett.* **1991**, *32*, 1491-1494 and references therein
d) Baldwin, J.E.; Adlington, R.M.; Lowe, C.; O'Neil, A.; Sanders, G.L.; Schofield, C.J. and Sweeney, J.B. *J.C.S. Chem. Comm.* **1988**, 1030-1031.

6 Kohmoto, S.; Kreker, T.; Yamamoto, M. and Yamada, K. *Bull. Chem. Soc. Jap.* **1990**, *63*, 3698-3700.

7 Selected NMR data δ (ppm) in $CDCl_3$. **4** : ^1H NMR : δ 1.09 (d, 3H, J=7 Hz), 1.20 (s, 3H), 1.85 (sl, 1H), 2.38 (m, 1H), 2.78 (dd, 1H, J=9.5and 9.4 Hz, 3.33 (dd, 1H, J=9.5 and 8 Hz), 3.87-4.05 (m, 2H), 5.14-5.24 (m, 2H), 5.64-5;78 (m, 1H); ^{13}C NMR: δ 11.60 (q), 18.83 (q), 39.14 (t), 45.37 (t), 49.50 (d), 76.09 (s), 118.28 (t), 131.81 (d), 177.26 (s). **5** : ^1H NMR : δ 1.08 (d, 3H, J=7 Hz), 1.37 (s, 3H), 1.83 (sl, 1H), 2.15 (m, 1H), 2.97 (dd, 1H, J=9.7 and 5.7 Hz), 3.33 (dd, 1H, J=9.7 and 7 Hz), 3.8-4.05 (m, 2H), 5.14-5.24 (m, 2H), 5.64-5.78 (m, 1H); ^{13}C NMR : δ 12.11 (q), 23.48 (q), 38.18 (t), 45.40 (t), 50.90 (t), 77.19 (s), 118.18 (t), 131.84 (d), 177.0 (s). **9**: ^1H NMR : δ 1.25 (s, 1H), 1.45 (s, 3H), 2.95 (s, 3H), 3.93 (dt, 1H, J_1=14, J_2=1.9 Hz), 4.0 (dt, 1H, J_1=14, J_2=1.9 Hz), 5.20 (t, 1H, J=1.9 Hz), 5.47 (t, 1H, J=1.9 Hz); ^{13}C NMR : δ 25.60 (q), 29.62 (q), 51.47 (t), 73.71 (s), 109.69 (t), 144.94 (s), 175.52 (s). **16a** : ^1H NMR : δ 1.08 (d, 3H, J=7.1 Hz), 1.72 (sl, 1H), 2.37-2.48 (m, 1H), 3.07 (dd, 1H, J=9.8 and 6.7 Hz), 3.37 (dd, 1H, J=9.8 and 7 Hz), 3.93-4.03 (m, 2H), 5.18-5.29 (m, 2H), 5.68-5.86 (m, 1H), 7.20-7.40 (m, 5H); ^{13}C NMR : δ 11.35 (q), 40.83 (t), 45.72 (t), 50.89 (d), 80.28 (s), 118.45 (t), 125.58 (d), 126.96 (d), 127.70 (d), 128.31 (d), 131.94 (d), 142.27 (s), 174.79 (s). **16b** : ^1H NMR : δ 0.67 (d, 3H, J=6.7 Hz), 1.28 (sl, 1H), 2.6-2.7 (m, 1H), 2.86 (dd, 1H, J=9.8 and 9.4 Hz), 3.39 (dd, 1H, J=9.4 and 8.6 Hz), 4.05 (d, 2H, J=6.3 Hz), 5.25-5.38 (m, 2H), 5.8-5.95 (m, 1H), 7.2-7.4 (m, 5H); ^{13}C NMR : δ 12.96 (q), 40.48 (d), 45.66 (t), 49.77 (t), 81.22 (s), 118.60 (t), 125.56 (d), 127.72 (d), 128.23 (d), 131.69 (d), 138.83 (s), 175.62 (s).

8 Mitsui, S.; Hebiguchi, K. and Saito, H. *Chem. and Ind.* **1967**, 1746-1747 and references therein.

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