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A new procedure to obtain ε-caprolactam catalyzed by a guanidinium salt†

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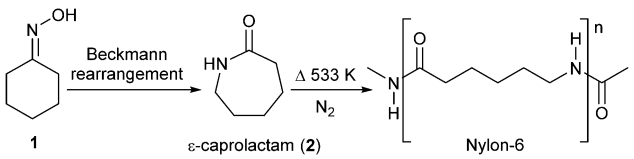
A new procedure to prepare ε-caprolactam by the Beckmann rearrangement of cyclohexanone oxime is described. Treatment of the oxime with the novel salt cyanoguanidinium tosylate affords ε-caprolactam without the need of any other promoter.

Introduction

The Beckmann rearrangement is among the most classical and popular reactions in organic chemistry. It allows the transformation of oximes into the corresponding amides.[1] Its interest in industry is very high because it is the main method employed to obtain ε-caprolactam (**2**) from cyclohexanone oxime (**1**, Scheme 1).[1] ε-Caprolactam is the precursor used in the synthesis of the fiber Nylon 6, a synthetic polyamide of great interest to the textile industry for polymers and material science development. It is widely used for the production of carpets, hoses, ropes, toothbrushes or clothing due to its excellent properties such as high tensile strength, elasticity and lustre, and high resistance to abrasion and to acids and bases.[2]

The enormous interest of ε-caprolactam is reflected in its global production, which exceeded 4.0 million tonnes (Mt) in 2012, with a market price of 2000–2500 $ per ton;[3] and in the growth of its worldwide demand, expected to reach 8.1% CAGR in the period 2016–2022, which is related to the overall growth of nylon 6 demand.[4]

The traditional procedure employed at industrial level to obtain ε-caprolactam (**2**) from cyclohexanone oxime (**1**), requires the use of high reaction temperatures (90–130 °C) and a strongly acidic medium (fuming sulfuric acid).[5] The release of ε-caprolactam is then achieved after neutralization with NH_3, which produces ammonium sulfate (between 1.8 and 5 kg per kg of ε-caprolactam) and demands the employment of organic solvents for product purification.[6] This procedure is hindered by serious environmental and cost issues related with corrosion and the production of such large amounts of by-products. Therefore, there is a need for milder synthetic approaches and many alternative methods have been studied.



Scheme 1 Industrial production of Nylon 6 from cyclohexanone oxime (**1**).

The employment of solid catalysts combined with vapor phase has yielded good results. Nevertheless, these methods require the use of high temperatures (250–300 °C), leading to catalyst deactivation and a huge energy consumption.[7–9] The use of supercritical water produces good selectivity but low conversion rates of cyclohexanone oxime (30%), which makes it unpractical at industrial level.[10] The use of organic solvents and catalysts as sulfamic acid, antimonium salts, oxalic acid, metaboric acid or chlorosulfonic acid have yielded good results in conversion and selectivity.[11,12] However, the need of acids neutralization and the subsequent formation of salts, makes the isolation of ε-caprolactam highly problematic decreasing the reaction yield. In a similar fashion, the use of organo-catalysts as 2,4,6-trichloro-1,3,5-triazine also gave good conversion and selectivity, but the difficulties in the product separation and the need of reactivating the catalysts reduce its industrial implementation.[13]

The Beckmann rearrangement of cyclohexanone oxime has been also studied employing simple ionic liquids in the presence of Lewis acids,[14–19] acyl or sulfonyl chlorides,[20–22] organocatalysts,[23] or functionalized ionic liquids that act as solvents/catalysts.[24–30] However, the ionic liquids can require anhydrous reaction conditions under an inert atmosphere and present serious

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† Electronic supplementary information (ESI) available: Synthetic experimental details, NMR spectra, X-ray diffraction data. CCDC 1557334. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7nj03443a

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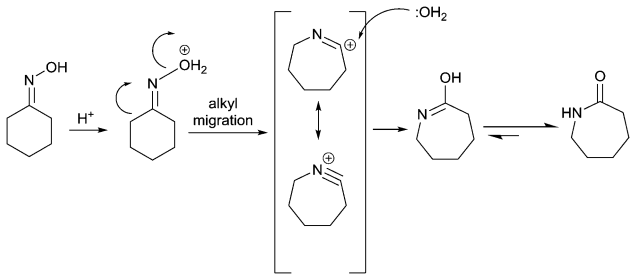
complications to extract the ε-caprolactam from the reaction medium and therefore for its reuse.

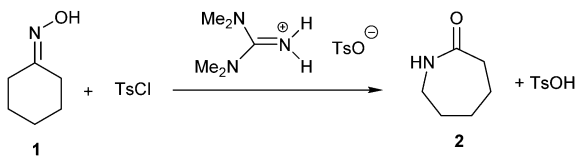
Alternative routes for the production of ε-caprolactam from renewable sources such as 1,3-butadiene, lysine of adipic acid have been also studied. However, these routes are hindered by the low overall yields or the high prices of the starting compounds.[6] Although many procedures for the transformation of the cyclohexanone oxime into ε-caprolactam have been developed, still there is a lack of mild reaction conditions at industrial scale that allow a clean and simple extraction of the ε-caprolactam.

The mechanism of the Beckmann rearrangement under acidic conditions has been widely studied (Scheme 2). The consensus is that the acid converts the hydroxyl group of the oxime into a good leaving group, and an alkyl group migrates to the nitrogen as water departs; a nitrilium cation is then formed and trapped by water to give an amide.[31,32] Nevertheless, the introduction of another good leaving group on the N, as a tosylate, can also cause the alkyl group migration. Also, an intramolecular mechanism involving radical intermediates has been recently proposed.[33]

In a previous work on the Beckmann rearrangement of cyclohexanone oxime, we carried out the reaction by treatment of the oxime with *p*-toluenesulfonyl chloride (TsCl) using 1,1,3,3-tetramethylguanidinium tosylate as promoter (Scheme 3).[34,35] Knowing the high capacity to form hydrogen bonds of guanidinium cations,[36] the catalytic effect of the guanidinium salt can be explained by the hydrogen bonds that the cation can form with the sulfonic group, promoting both tosylation and TsOH leaving (Fig. 1a and b). This procedure allowed the obtention of pure ε-caprolactam with good yield and under mild conditions (60 °C). However, it required the use of tosyl chloride and big quantities of pollutant organic solvents; in addition, it produced *p*-toluenesulfonic acid as a non-desired by-product.



Scheme 2 Mechanism of the Beckman rearrangement of cyclohexanone oxime to produce ε-caprolactam.



Scheme 3 Beckmann rearrangement of cyclohexanone oxime with by treatment with TsCl in the presence of 1,1,3,3 tetramethylguanidinium tosylate.[34]

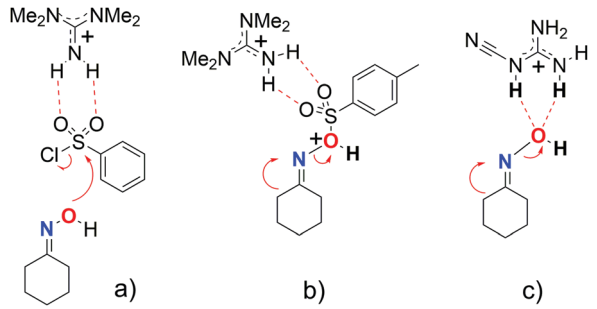


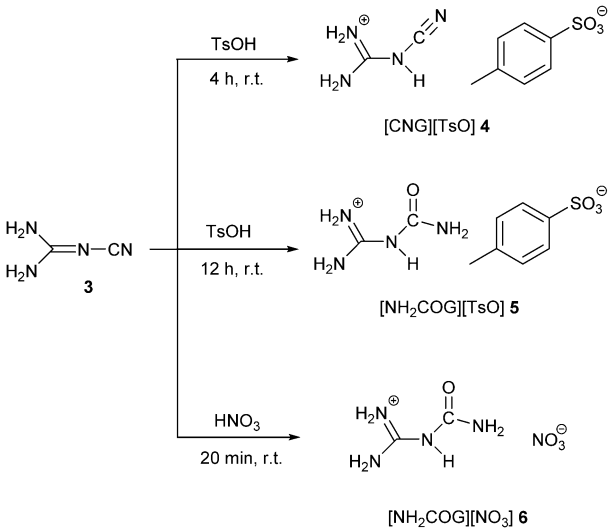
Fig. 1 Catalytic effect of 1,1,3,3 tetramethylguanidinium cation on the Beckmann rearrangement of cyclohexanone oxime: (a) tosylation, (b) rearrangement and TsOH leaving; (c) catalytic effect of [CNG][TsO].

In order to improve the previous result, the possibility of introducing an electron withdrawing group on the guanidinium cation that would increase its acidic character and so its catalytic effect, was considered. The electron withdrawing group selected was the cyano (CN).

Results and discussion

N-Cyanoguanidinium *p*-toluenesulfonate, [CNG][TsO] (**4**), was synthesized by treatment of *N*-cyanoguanidine (**3**) with *p*-toluenesulfonic acid (Scheme 4). When the reaction was performed at room temperature for 4 hours, [CNG][TsO] (**4**) was obtained with high yield and purity. However, longer reaction times led to the hydrolysis of the cyano group, to afford the corresponding amide derivative *N*-carbamoylguanidinium *p*-toluenesulfonate, [NH_2COG][TsO] (**5**). It was observed that after 12 hours the cyanoguanidinium salt is completely hydrolysed, which was confirmed by ^{13}C NMR and Mass spectrometry (Fig. S5 and S6, ESI†). The salt [NH_2COG][TsO] (**5**) is reported in this work for the first time.

In order to investigate the effect of the anion in the reaction, *N*-carbamoylguanidinium nitrate [NH_2COG][NO_3] (**6**),[37] was



Scheme 4 Synthesis of the *N*-cyanoguanidinium and *N*-carbamoylguanidinium salts.

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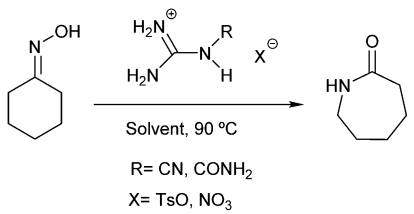
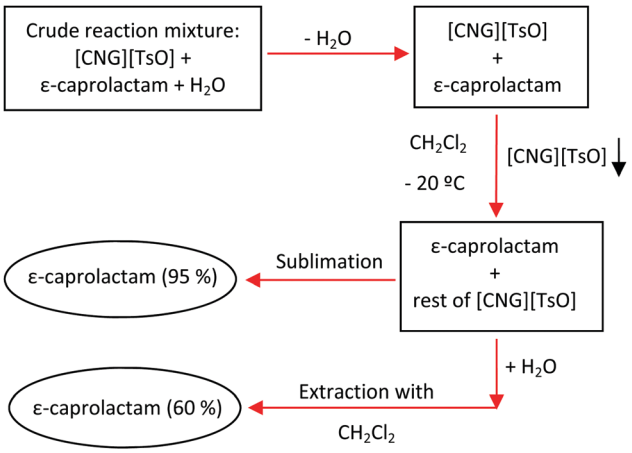
prepared by treatment of *N*-cyanoguanidine with nitric acid. The desired product was obtained as a solid in high yield.

The catalytic effect of the synthesized guanidinium salts **4–6** on the Beckmann rearrangement of cyclohexanone oxime (**1**), was started by treatment of the oxime with cyanoguanidinium *p*-toluenesulfonate [CNG][TsO] (**4**) without any other promoter. Different reaction solvents and conditions (concentrations and temperature) were tried (Scheme 5 and Table 1). When the reaction was carried out in H_2O, ε-caprolactam was always obtained as the only product. The reaction time was too long (60 h) when only 1 eq. of the salt was employed heating at 90 °C (entry 1). But when 2 eq. were used, the reaction was finished in 3 h heating at the same temperature (entry 2), and in only 45 min heating at 90 °C (entries 3 and 4). The work up procedure and product isolation are summarized in Scheme 6. Once the reaction was completed, water was eliminated by heating under reduced pressure; CH_2Cl_2 was then added and the mixture was allowed to cool at −20 °C overnight. A precipitate corresponding to the cyanoguanidinium salt was formed and filtered; the solvent was evaporated and ε-caprolactam was obtained with some rest of the guanidinium salt. Two different approaches were followed for the ε-caprolactam purification: liquid–liquid extraction and sublimation. Liquid–liquid extraction (LLE) was performed by the addition of water to dissolve the rests of the salt and later extraction with CH_2Cl_2; because ε-caprolactam is also soluble in water, only a 60% yield was attained. On the other hand, sublimation at 120 °C under a reduced pressure of 2×10^{-1} Pa allowed to obtain pure ε-caprolactam with a 95% yield. ε-caprolactam was completely characterized in agreement with the literature data.[38]

The solvent effect on the reaction was also studied by employing MeOH and DMF instead of water. Surprisingly, the reaction did not evolved when MeOH was employed, whereas with DMF the reaction proceeded slower than with water (Table 1, entries 5 and 6).



Scheme 5 Beckmann rearrangement of cyclohexanone oxime by treatment with the synthesized guanidinium salts **4–6**.



Scheme 6 Work up procedure and product isolation.

The proposed mechanism for the catalytic effect of [CNG][TsO] involves hydrogen bonding interaction with the hydroxyl group of the oxime, which is turned into a good leaving group, causing the alkyl group migration (Fig. 1c).

The other synthesized guanidinium salts, *N*-carbamoylguanidinium *p*-toluenesulfonate, [NH_2COG][TsO] (**5**) and *N*-carbamoylguanidinium nitrate [NH_2COG][NO_3] (**6**), were also tested in the synthesis of ε-caprolactam from cyclohexanone oxime. However, none of them allowed obtaining of the desired product. After heating cyclohexanone oxime with 2 eq. of these salts at 90 °C in water for more than 40 h, no reaction product was observed. This could be explained by the deactivation of the hydrogen bonding donor character of the *N*-carbamoyl cation due to the strong intramolecular NH···O hydrogen bond that is formed between one NH group as donor and the carbonyl oxygen as acceptor. This was confirmed by X-ray diffraction of a single crystal.‡

Due to the partial double character of each C–N bond of the guanidinium core, all atoms of the guanidinium cation are located in the same plane (Fig. 2 and 3). As expected, the shortest hydrogen bond appears between the oxygen of the carbonyl O(1) and one of the hydrogens located in N(3) with a length of 2.00(3) Å (Table S3, ESI†).

Table 1 Beckmann rearrangement of the cyclohexanone oxime by treatment with [CNG][TsO]. Effect of solvent and [CNG][TsO] concentration over the reaction time and yield

Entry	Solvent	[CNG][TsO] (eq.)	*t* (h)	*T* (°C)	Purification method	Yield (%)
1	H_2O	1	60	90	LLE	62
2	H_2O	2	3	60	LLE	60
3	H_2O	2	0.75	90	LLE	60
4	H_2O	2	0.75	90	Sublimation	95
5	MeOH	2	40	90	LLE	—
6	DMF	2	6	90	LLE	63

‡ Crystallographic data were collected at room temperature using a Bruker Smart 6000 CCD detector and Cu-Kα radiation (λ = 1.54178 Å) generated by a Incoatec microfocus source equipped with Incoatec Quazar MX optics. The software APEX2 was used for collecting frames of data, indexing reflections, and the determination of lattice parameters, SAINT for integration of intensity of reflections, and SADABS for scaling and empirical absorption correction. The structures were solved by dual-space methods using the program SHELXT. All non-hydrogen atoms were refined with anisotropic thermal parameters by full-matrix least-squares calculations on *F* using the program SHELXL-2014. Hydrogen atoms were inserted at calculated positions and constrained with isotropic thermal parameters except for the hydrogen atoms of the NH and NH_2 groups, which were located from a Fourier-difference map and refined isotropically. Drawings were produced with PLATON.

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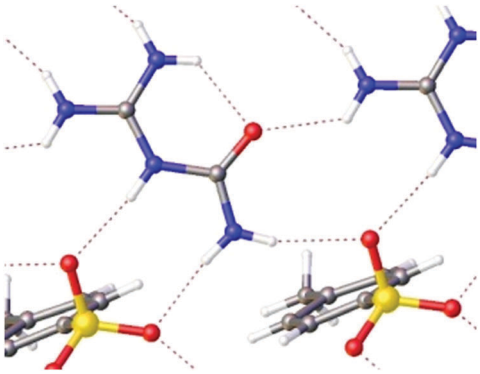

Fig. 2 Representation of 2D supramolecular architecture of [NH_2COG][TsO] (**5**) by hydrogen bonding interactions. Colour code: O, red; N, blue; C, grey; S, yellow; C, grey.

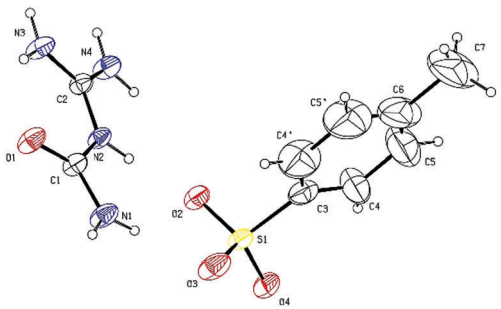

Fig. 3 X-ray structure of [NH_2COG][TsO] (**5**). Selected bond lengths (Å) and angles (°) are: C(1)–O(1) 1.216(3); C(1)–N(1) 1.322(4); C(1)–N(2) 1.396(3); N(1)–H(1A) 0.840(18); N(1)–H(1B) 0.855(19); C(2)–N(3) 1.304(3); C(2)–N(4) 1.315(4); C(2)–N(2) 1.347(3); N(2)–H(2) 0.862(18); N(3)–H(3A) 0.865(19); N(3)–H(3B) 0.855(18); N(4)–H(4A) 0.849(18); N(4)–H(4B) 0.860(18); S(1)–O(4) 1.426(2); S(1)–O(3) 1.443(2); S(1)–O(2) 1.452(2); S(1)–C(3) 1.749(3); C(4)–C(3) 1.3900(X).

Conclusion

In summary, we have developed a new procedure to synthesize ε-caprolactam by using a novel salt, cyanoguanidinium *p*-toluenesulfonate, which is able to catalyze the Beckmann rearrangement of cyclohexanone oxime without the need of any other promoter. High reaction temperatures and toxic solvents are avoided; the catalyst is not corrosive and is easy to prepare.

Experimental section

See ESI.†

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

1 M. Linares, C. Vargas, A. García, C. Ochoa-Hernández, J. Čejka, R. A. García-Muñoz and D. P. Serrano, *Catal. Sci. Technol.*, 2017, **7**, 181.
2 T. M. Ting, M. M. Nasef and K. Hasim, *Radiat. Phys. Chem.*, 2015, **109**, 55.
3 J. Han, *ACS Sustainable Chem. Eng.*, 2017, **5**, 1892.
4 Global caprolactam Market Research Report, https://www.marketresearchfuture.com/reports/caprolactam-market-2255, accessed March 2017.
5 G. Dahlhoff, J. P. M. Niederer and W. F. Hoelderich, *Catal. Rev.*, 2001, **43**, 381.
6 R. Beerthuis, G. Rothenberg and N. R. Shiju, *Green Chem.*, 2015, **17**, 1341.
7 T. Takahashi, T. Kai and E. Nakao, *Appl. Catal., A*, 2004, **262**, 137.
8 M. J. Climent, A. Corma and S. Iborra, *J. Mol. Catal.*, 2005, **233**, 308.
9 M. Anilkumar and W. F. Hoelderich, *Appl. Catal., B*, 2015, **165**, 87.
10 M. Boero, T. Ikeshoji, C. C. Liew, K. Terakura and M. Parrinello, *J. Am. Chem. Soc.*, 2004, **126**, 6280.
11 D. Li, F. Shi, S. Guo and Y. Deng, *Tetrahedron Lett.*, 2005, **46**, 671.
12 J. Zhang, Y. Lu, K. Wang and G. Luo, *Ind. Eng. Chem. Res.*, 2013, **52**, 6377.
13 A. S. Deshpande, S. N. Chamle, M. V. Yadav and A. D. Sagar, *Int. J. Res. Chem. Environ.*, 2014, **4**, 93.
14 R. X. Ren, L. D. Zueva and W. Ou, *Tetrahedron Lett.*, 2001, **42**, 8441.
15 J. Peng and Y. Deng, *Tetrahedron Lett.*, 2001, **42**, 403.
16 S. Guo, *et al.*, *Catal. Commun.*, 2005, **6**, 225.
17 K. Elango, R. Srirambalaji and G. Anantharaman, *Tetrahedron Lett.*, 2007, **48**, 9059.
18 A. Zicmanis, S. Katkevica and P. Mekss, *Catal. Commun.*, 2009, **10**, 614.
19 Z. Li, Q. Yang, X. Qi, Y. Xu, D. Zhang, Y. Wang and X. Zhao, *Chem. Commun.*, 2015, **51**, 1930.
20 H.-J. Pi, J.-D. Dong, N. An, W. Du and W.-P. Deng, *Tetrahedron*, 2009, **65**, 7790.
21 D. Y. Du, *CN Pat.*, 1919833, 2007.
22 N. An, B.-X. Tian, H.-J. Pi, L. A. Erikson and W.-P. Deng, *J. Org. Chem.*, 2013, **78**, 4297.
23 A. Maia, D. C. M. Albanese and D. Landini, *Tetrahedron*, 2012, **68**, 1947.
24 Z. Du, Z. Li, Y. Gu, J. Zhang and Y. Deng, *J. Mol. Catal.*, 2005, **237**, 80.
25 J. Gui, Y. Deng, Z. Hu and Z. Sun, *Tetrahedron Lett.*, 2004, **45**, 2681.
26 W. Bonrath, J. M. Leveque, V. Ragaini and R. Turgis, *WO Pat.*, 145312, 2008.

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27 S. Guo, Z. Du, S. Zhang, D. Li, Z. Li and Y. Deng, *Green Chem.*, 2006, **8**, 296.
28 D. Y. Du, *CN Pat.*, 1919834, 2007.
29 D. Mao, Z. Long, Y. Zhou, J. Li, X. Wang and J. Wang, *RSC Adv.*, 2014, **4**, 15635.
30 R. Kore and R. Srivastava, *J. Mol. Catal. A: Chem.*, 2013, **376**, 90.
31 R. Kumar, S. Shah, J. Bahadur, Y. B. Melnichenko, D. Sen, S. Mazumder, C. P. Vinod and B. Chowdhury, *Microporous Mesoporous Mater.*, 2016, **234**, 293.
32 H. Yamamoto, M. Komeda, A. Ozaki, M. Sumimoto, K. Hori and T. Sugimoto, *Int. J. Org. Chem.*, 2015, **5**, 147.
33 P. S. Mahajan, V. T. Humne, S. D. Tanpure and S. B. Mhaske, *Org. Lett.*, 2016, **18**, 3450.
34 M. Vilas and E. Tojo, *Tetrahedron Lett.*, 2010, **51**, 4125.
35 X. Fu and C.-H. Tan, *Chem. Commun.*, 2011, **47**, 8210.
36 E. Tojo and M. Vilas, *ES Pat.*, 2359819, 2011.
37 T. M. Klapötke and C. M. Sabaté, *Heteroat. Chem.*, 2008, **19**, 301.
38 Y. Izumi, S. Sato and K. Urabe, *Chem. Lett.*, 1983, 1649.