



Pergamon

Tetrahedron Letters 41 (2000) 7235–7237

TETRAHEDRON
LETTERS

An environment-friendly Beckmann rearrangement: the diazotisation of ketoxime carbamates

R. Anilkumar and Sosale Chandrasekhar*

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India

Received 7 July 2000; accepted 20 July 2000

Abstract

The titled reaction was effected with *iso*-amyl nitrite or sodium nitrite, both in conc. H₂SO₄ at 0–25°C in excellent yields (55–98%). Apart from the mild temperatures employed, organic solvents and reagents can be avoided, and the by-products are CO₂ and N₂, so the conditions are environment-friendly. © 2000 Elsevier Science Ltd. All rights reserved.

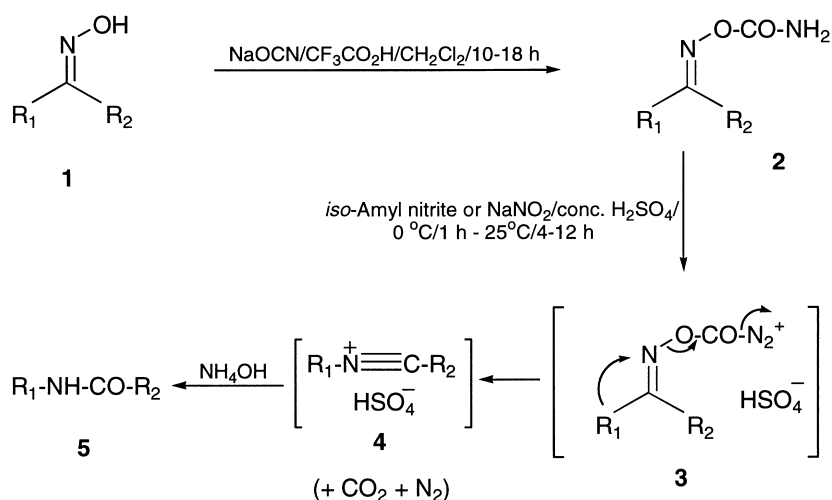
Keywords: Beckmann rearrangement; environment-friendly; oxime carbamates.

The historic Beckmann rearrangement has retained its practical importance to this day, with improved variants and ever milder conditions still being sought.¹ We have previously reported² the BF₃ induced Beckmann rearrangement of oxime carbonates, and herein report our results on the transformation of ketoxime carbamates.

In principle, the Beckmann rearrangement can be induced in the oxime carbamates **2** by the diazotisation of the carbamate amine function: the resulting diazonium compound **3** is expected to be unstable and to fragment with loss of carbon dioxide and nitrogen (Scheme 1), thus ‘triggering’ the migration of an alkyl or aryl group of the oxime moiety; the resulting nitrilium species **4** is hydrated to the final amide or lactam product **5** in the usual way. Although oxime carbamates were being prepared as early as in 1906, their structure had been misassigned as an oxaziridine and as a nitron;^{3–6} Exner and Horák⁵ suggested the correct structure in 1959, which has been confirmed by recent spectroscopic work.⁶ The oxime carbamates are readily prepared by the reaction of the corresponding oxime **1** with an excess of sodium cyanate, in the presence of a strong acid in an organic solvent^{3,4} (trifluoroacetic acid in dichloromethane in the present study); the direct preparation^{3,4} from the carbonyl compound is far less satisfactory.

The diazotisation of benzophenone oxime carbamate **2a** under a variety of aqueous and non-aqueous conditions, was explored in the present study. The diazotising agent was generally *iso*-amyl nitrite in the presence of sulphuric acid, trifluoroacetic acid, *p*-toluenesulphonic acid or boron trifluoride etherate, in dioxane, THF or water as appropriate at 0°C. Thereafter, the

* Corresponding author. Fax: +91-80 3600 529; e-mail: sosale@orgchem.iisc.ernet.in



Scheme 1.

reaction mixture needed to be stirred at 25 °C for several hours—which presumably facilitated the decomposition of **3**—to effect the rearrangement. Although the formation of the expected benzanilide **5a** was observed under many of the above conditions, the yields were variable, with benzophenone as a by-product. The best conditions were determined to be concentrated sulphuric acid (12–14 equiv.) at 0 °C, with either *iso*-amyl nitrite or sodium nitrite as the diazotising agent, followed by stirring at 25 °C for 6 h.† (A control experiment confirmed that the diazotising agent was necessary.) The scope of the reaction was also determined to be wide, as seen in Table 1.

A related method for the Beckmann rearrangement, via the diazotisation of ketone hydrazones⁷ under similar conditions to the above, must be mentioned. However, the above hydrazones were apparently unstable to geometrical isomerisation under the reaction conditions,⁷ which clearly limits the scope of the method. In the present methodology, such isomerisation is apparently not a problem, as seen in the reactions of the three unsymmetrical ketoxime carbamates **2e–2g**, each of which furnished only one of the two possible rearrangement products (**5e–5g**, respectively, Table 1) in excellent yields. (A recent report⁸ on the conversion of aldoximes to nitriles via the *O*-phenylcarbamoyl derivatives is of some relevance to the present work and also bears mention.)

In the present method—apart from the mild temperatures employed—the rearrangement step per se possesses two important advantages: (i) no organic reagent or solvent is employed (when sodium nitrite is the diazotising agent); and (ii) the only by-products are the relatively harmless gases nitrogen and carbon dioxide (apart from sodium sulphate and ammonium sulphate). Thus, the conditions are environment-friendly and would be valuable for scale-up. Further work is planned.

† Typical procedure for the rearrangement: Conc. H₂SO₄ (7 mmol) at 0 °C was stirred and treated portion-wise with either NaNO₂ (2.5 mmol) or *iso*-amyl nitrite (5 mmol), followed by the oxime carbamate **2** (0.5 mmol) portion-wise over 0.5 h. After another 0.5 h at 0 °C, the mixture was stirred at 25 °C for the specified time, and poured into cold NH₄OH (5 ml). The amide/lactam **5** was generally filtered off, recrystallised and characterised by mp comparison with reported values; **5c** and **5e** were isolated via ether extraction and characterised spectroscopically. The ketoxime carbamates **2** were prepared and characterised spectroscopically and by mp comparison,^{3–6} with the new ones furnishing satisfactory elemental analysis for C, H and N.

Table 1

The preparation of the oxime carbamates **2** and their Beckmann rearrangement to the amides/lactams **5**: yields and the duration of the rearrangement

2	R ₁	R ₂	% Yield	Time (h) ^a	5	% Yield
a	Ph	Ph	85	6	a	98
b	PhCH ₂	PhCH ₂	92	4	b	73
c	Et	Et	83	8	c	55
d	<i>p</i> -Cl- C ₆ H ₄	<i>p</i> -Cl- C ₆ H ₄	91	6	d	98
e	Ph(CH ₂) ₂	Me	89	12	e	66
f	Ph	Me	94	9	f	82
g ^b	MeO-C ₆ H ₃ -(CH ₂) ₃		86	8	g ^c	74
h ^d	-(CH ₂) ₅ -		86	5	h ^e	56
i ^f	C ₆ H ₁₀ -(CH ₂) ₂		78	6	i ^g	87

^aFor the rearrangement; ^bfrom 6-methoxy- α -tetralone oxime; ^c1,2,3,4-tetrahydro-7-methoxy-5*H*-benzazepin-2-one; ^dfrom cyclohexanone oxime; ^ecaprolactam; ^ffrom β -decalone oxime; ^ginseparable mixture of the corresponding lactams (the original oxime stereochemistry not defined).

Acknowledgements

UGC and CSIR (N. Delhi) are thanked for generous financial support.

References

1. Maruoka, K.; Yamamoto, H. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I.; Winterfeld, E., Eds.; Pergamon Press: Oxford, 1991; Vol. 6, pp. 763–775, and references cited therein.
2. Anilkumar, R.; Chandrasekhar, S. *Tetrahedron Lett.* **2000**, *41*, 5427–5429.
3. Loev, B.; Kormendy, M. F. *J. Org. Chem.* **1963**, *28*, 3421–3426, and references cited therein.
4. Dalton, D. R.; Foley, H. G. *J. Org. Chem.* **1973**, *38*, 4200–4203, and references cited therein.
5. Exner, O.; Horák, M. *Collect. Czech. Chem. Commun.* **1959**, *24*, 2992–3001.
6. Wazeer, M. I. M.; Ali, Sk. A.; Arab, M. *Magn. Reson. Chem.* **1989**, *27*, 1102–1104, and reference cited therein.
7. Pearson, D. E.; Carter, K. N.; Greer, C. M. *J. Am. Chem. Soc.* **1953**, *75*, 5905–5908.
8. Coskun, N.; Arikan, N. *Tetrahedron* **1999**, *55*, 11943–11948.