A FACILE ROUTE TO POLYSUBSTITUTED 2-HYDROXY-3-NITRO-CYCLOPENTANONES VIA A LINEAR α-KETOENAMINE

F.Felluga, P.Nitti, G.Pitacco, and E.Valentin Dipartimento di Scienze Chimiche, Università, Piazzale Europa 1, 34127 Trieste, Italy

Abstract - The morpholino monoenamine of diacetyl has been synthesized and reacted with conjugated nitroolefins to give functionalized cyclopentanone derivatives, after hydrolysis of the isolated enamine intermediates.

The importance of nitroalkenes in organic synthesis is well known, as underlined in some reviews on this subject.^{1,2} Of particular interest in this context is the obtainment of carbocyclic and heterocyclic compounds starting from conjugated nitroalkenes with enamines as counterparts,^{3,4} especially when these latter systems are functionalized by the presence of particular substituents, such as for instance a carbonyl group.

As an extension of our studies of the reactivity of conjugated nitroolefins with cyclic α -ketoenamines, ⁵ we have undertaken the study of linear α -ketoenamines, starting from the simplest possible one, that is 3-(4-morpholinyl)-3-buten-2-one (1) (Scheme 1) $|\nu_{max}|$ (CCl₄), cm⁻¹: 3100, 1688, 1595, 1120; λ_{max}^{EtOH} 206.7 (lg ϵ 3.69), 285.6 (lg ϵ 3.24); ¹H NMR (CDCl₃), δ : 5.2 (d, J 2.0 Hz, 1 H, C=CH), 4.8 (d, J 2.0 Hz, 1 H, C=CH), 3.8 (m, 4 H, (CH₂)₂O), 2.8 (m, 4 H, (CH₂)₂N), 2.4 (s, 3 H, Me); ¹³C NMR (CDCl₃), δ : 197.7 (s), 155.1 (s), 100.1 (t), 65.6 (2 t), 48.8 (2 t7, 26.6 ppm (q); M⁺ 155.09431 (155.09462) |.⁶ This α -ketoenamine is likely to be in *s-cis* conformation, as shown by both the difference in frequency between the carbonyl and the double bond stretching absorptions and their relative intensities.⁷

The α -ketoenamine (1) has been prepared by a slightly modified version of the White and Weingarten method,^{8,9} in which the excess of morpholine has been substituted for triethylamine. The classic method in fact would have led to the diendiamine 2,3-(4,4-dimorpholinyl)-1,3-butadiene, already known.¹⁰

The reactions of this substrate with the linear conjugated nitroolefins 2a-c (Scheme 1) were carried out in the absence of solvent, as it is usual for α -ketoenamines, otherwise the reaction does not proceed.⁵

The corresponding cyclopentenyl morpholino derivatives 5a-c were separated in 95%, 95%, and 90% yields respectively, each as a single diastereoisomer. Their formation is evidently a consequence of a |3 + 2| carbocyclization reaction,¹¹ proceeding first through the dipolar intermediate 3 and later through the betaine-type intermediate 4.

Hydrolyses of the five-membered ring enamines 5a-c furnished the corresponding 2-hydroxy-3-nitro-cyclopentanone derivatives 6a-c respectively, also as

푸포 Ξ. Ŕ N02 + N02 5 ິ ເບິ Ć \bigcirc R2 R² <mark>ہ</mark>' ġ н**3**0•





ΓĊ.

ŕ



R2

, N O S N



(1)

ò

R ²	Ξ	ЧЧ	Me
R1	ď	Me	ፈ
<i></i>	σ	р	υ

ድ

R2/

Ś



O

(9)

Scheme 1

single diastereoisomers, the yields varying from 85% to 90%.

In one case, namely with the enamine 5b, the cyclization reaction was found to be reversible. A retro nitro-aldol condensation in fact occurred slowly in solution and even in the solid state at room temperature, to give the corresponding Michael-type adduct 7, which was a product of kinetic formation and isomerized slowly into its double bond isomer 8, in acidic medium (Scheme 2). Each isomer was a pair of diastereoisomers for the configuration of the nitromethine carbon atom. Hydrolysis of the mixture led to the corresponding hexane-2,3-dione derivative 9, also as a pair of diastereoisomers.



The mechanism of this ring fission however seems unlikely to be a simple retro-Henry condensation, as the same opening was not observed for the corresponding ketone 6b, which on the contrary is stable in both mild acidic and basic media. Therefore a participation of the amine component in the opening of the enamine 5b should be envisaged.

The main physical and spectroscopic data of the carbocyclic products are summarized in the Table. The analytical data are in accordance with the given structures.

Scheme 2

			Table
	m.p. ⁰C	IR (nujol), v, cm ⁻¹	¹ H NMR (80 MHz, CDCl ₃) δ , ppm
5a	137-138	3520,1625,	7.4 (m, 5 H, Ph), 4.7 (bs, 2 H, CHPh, CHNO ₂), 4.4
		1540,1110	(d, J 1.0 Hz, 1 H, C=CH), 1.7 (bs, 1 H, OH), 1.5 (s,
			3 H, Me)
5b	109-110	3540,1630	7.5 (m, 5 H, Ph), 4.3 (d, J 1.5 Hz, 1 H, C=CH), 1.1
		1530,1110	(d, J 7.0 Hz, 3 H, Me), 1.0 (s, 3 H, Me)
5c 1	156-157	3340,1620	7.3 (m, 5 H, Ph), 5.0 (d, J 2.0 Hz, 1 H, CHNO ₂), 4.3
		1520,1105	(d, J 2.0 Hz, 1 H, CHPh), 2.3 (bs, 1 H, OH), 1.8 (s,
			3 H, Me), 1.4 (s, 3 H, Me)
6a	161-163	3410,1755	7.2 (m, 5 H, Ph), 4.9 (d, J 9.0 Hz, 1 H, CHNO ₂), 4.3
		1545	(dd, J ₃₄ 9.0 Hz, J _{AX} 8.6 Hz, J _{BX} 10.4 Hz, 1 H, CHPh),
			3.3, 2.7 (dq, J_{AB} 20.0 Hz, J_{AX} 8.6 Hz, J_{BX} 10.4 Hz,
			CH ₂ CO, 2.7 (bs, OH), 1.5 (s, 3 H, Me)
6Ъ	172-173	3470,1755,	7.3 (m, 5 H, Ph), 3.3 (m, 2 H, CHMe, OH), 2.6 (dq,
		1535	2 H, CH ₂ CO), 1.2 (d, J 7.0 Hz, 3 H, Me), 0.9 (s, 3 H,
			Me)
6c	196-197	3340,1760,	7.3 (m, 5 H, Ph), 3.6 (dd, J _{AX} 12.0 Hz, J _{BX} 8.0 Hz,
		1535	1 H, CHPh), 3.1, 2.9 (dq, J_{AB} 20.0 Hz, J_{AX} 12.0 Hz,
			J _{BY} 8.0 Hz, 2 H, CH ₂ CO), 1.6 (s, 3 H, Me), 1.4 (s,
			3 H, Me)

Acknowledgment - The Ministry of Education (Fund 60%) and the CNR are thanked for financial support.

Footnotes and References

- 1. D.Seebach, E.W.Colvin, P.Lehr, and T.Weller, Chimia 33, 1 (1979).
- 2. A.G.M.Barrett and G.G.Graboski, Chem. Revs 86, 751 (1986).
- 3. P.W.Hickmott, Tetrahedron 38, 1975, 3363 (1982).
- 4. G.Pitacco and E.Valentin, in The Chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives, Suppl. F, Ed. S.Patai, Wiley-Interscience, N.Y., 1982.
- 5. F.Asaro, G.Pitacco and E.Valentin, Tetrahedron 43, 3279 (1987).
- 6. The α -ketoenamine must be used just as it is, as any attempt to purify it leads to tars.
- 7. R.L.Erskine and E.S.Waight, J.Chem.Soc., 3425 (1960).
- 8. W.White and H.Weingarten, J.Org.Chem. 32, 213 (1967).
- 9. R.Carlson, A.Nilson, and M.Strömquist, Acta Chem. Scand. B37, 7 (1983).
- 10. S.Baroni, E.Rivera, R.Stradi, and M.L.Saccarello, Tetrahedron Lett. 21, 889 (1980).
- 11. D.Pocar, P.Trimarco, R.Destro, E.Ortoleva, and M.Ballabio, Tetrahedron 40, 3579 (1984).

(Received in UK 20 June 1988)