Intramolecular Thermal Oxidoreduction of *N*-(2-Hydroxypropyl)- β -enaminoesters: Synthesis of *N*-(Acetonyl)- β -enaminoaldehydes and 2-Acetylpyrroles

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Flow pyrolysis of the β -enaminoesters (1) provides the enaminoaldehydes (2), resulting from intramolecular oxidoreduction, and the acetylpyrroles (3); their relative yields depend on the temperature range.

During the course of our studies on the use of flow pyrolytic methods in heterocycle synthesis, we have investigated the thermal behaviour of β -enaminoesters and discovered that the products obtained are highly dependent on the nature of the substituents.¹ Herein, we report that *N*-(2-hydroxypropyl)- β -enaminoesters (1) undergo a [1,4] elimination of methanol, affording in one step from readily available precursors *N*-(acetonyl)- β -enaminoaldehydes (2) and 2-acetylpyrroles (3) (Scheme 1). To our knowledge the formation of the products (2), which may prove to be useful building blocks in synthesis,² represents a new thermal intramolecular oxidoreduction reaction of alcohol and ester groups to ketone and aldehyde groups, respectively.

The required enaminoesters (1a—c) were prepared in one step either by Michael addition of prop-2-ynylic esters with 1-aminopropan-2-ol for (1a),³ or by condensation of β -ketoesters with the same amino-alcohol for (1b, and c). The aromatic compound (1d)⁴ was synthesised by aminolysis of propene oxide with the aluminium derivative of methyl anthranilate.⁵

Flow pyrolysis⁶ of compounds (**1a**—c) in the temperature range 330—420 °C and at 15 mmHg converted them into a mixture (45—76% overall yields) of β -enaminoaldehydes (**2a**—c) and acetylpyrroles (**3a**—c) (Table 1). Pure samples were quantitatively separated by flash chromatography of the crude products.⁷ It is noteworthy that at lower temperatures (*ca.* 330—350 °C) the enaminoaldehydes (**2a**—c) are the major products; the relative yields (**3**)/(**2**) increase with temperature. Moreover, pyrolysis of the aromatic derivative (**1d**) took place only at a much higher temperature and the yield was very low.

Compounds (3) were characterized by spectral and analytical data and, when appropriate, by comparison with literature data. The structures of the new dicarbonyl derivatives (2) were established by i.r. and ¹H n.m.r. spectroscopy.† It appears that the configuration of the double bond is exclusively E in (2a) and predominantly Z in (2b) (Z : E 65 : 35); the arguments in favour of the Z and E stereochemistry are based on the values of the ³J coupling constants of the aldehydic protons (Z : J 3 Hz; E : J 8 Hz). It is likely that owing to the low energy barriers for thermal isomerization in closely related systems,⁸ the percentages reflect the thermodynamic stabilities of these species.

The mechanism (Scheme 2) by which we envisage the conversion $(1) \rightarrow (2) + (3)$ involves initial [1,4] elimination of

[†] Selected spectroscopic data (¹H n.m.r. chemical shifts from Me₄Si and coupling constants in Hz): compound (**2a**), ¹H n.m.r. δ (CDCl₃) 2.18 (3H, s, COMe), 3.98 (2H, d, CH₂CO), 5.17 (1H, dd, 2-H), 7.25 (1H, dd, 3-H), and 9.15 (1H, d, CHO); $J_{1,2}$ 8, $J_{2,3}$ 13.5; v_{CO} : 1715s and 1610s cm⁻¹; (*E*)-(**2b**), ¹H n.m.r. δ (CDCl₃) 1.90 (3H, s, 3-Me), 2.30 (3H, s, COMe), 3.95 (2H, d, CH₂CO), 5.01 (1H, s, 2-H), and 9.60 (1H, d, CHO); $J_{1,2}$ 8; (*Z*)-(**2b**), ¹H n.m.r. δ (CDCl₃) 1.90 (3H, s, 3-Me), 2.30 (3H, s, COMe), 4.20 (2H, d, CH₂CO), 5.05 (1H, s, 2-H), and 9.61 (1H, d, CHO); $J_{1,2}$ 3.



Scheme 2

methanol from (1) producing the iminoketene (4). It is likely that this is the rate-determining step, explaining the much higher temperature needed for (1d), since in this step aromaticity is lost in (4d). From (4), a sequence of signatropic shifts as suggested earlier and recently demonstrated unambiguously by deuterium labelling⁹ would give the enols (6) and then the tautomerization products (2). This last reaction

Table 1. Yields of (2) and (3) as a function of temperature with toluene as solvent.^a

Starting	Temp.	% Yield of products	
material	/°Ĉ	(2)	(3)
(1 a)	350	39	23
(1a)	410	14	45
(1b)	330	47	9
(1b)	415		51
(1c)	360	61	15
(1c)	420		46
(1d)	600	14	14

^a The normal conditions involved dropwise flow pyrolysis through a hot vertical Pyrex tube (2 × 60 cm) filled with Pyrex balls. ^b Yields are based on products isolated by flash chromatography using pentane–ethyl acetate as eluant.

competes with an intramolecular ene reaction leading to (7) and finally (3).¹⁰ That (3) is the product of intramolecular crotonization of (2) was further demonstrated by flow pyrolysis of (2).

In summary, a pyrolytic method for the synthesis of highly functionalized synthons (2) starting from easily accessible enaminoesters (1) has been developed; under more forcing conditions 2-acetylpyrroles (3) were isolated in good yields. This new method of access to pyrrole derivatives from alicyclic compounds is comparable both in yield and practicability with the Hantzsch and Knorr methodology.¹¹

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References

- 1 A. Maujcan, G. Marcy, and J. Chuche, *Tetrahedron Lett.*, 1980, **21**, 519; *J. Chem. Soc., Chem. Commun.*, 1980, 92.
- 2 L. F. Tietze, A. Bergmann, and L. Brüggeman, *Tetrahedron Lett.*, 1983, 24, 3759.
- 3 R. Huisgen, K. Herbig, A. Siegl, and H. Huber, Chem. Ber., 1966, 99, 2526.
- 4 C. Pale-Grosdemange and J. Chuche, unpublished results.
- 5 L. E. Overman and L. A. Flippin, *Tetrahedron Lett.*, 1981, **22**, 195.
- 6 R. F. C. Brown, 'Pyrolytic Methods in Organic Chemistry,' Academic Press, New York, 1980, p. 23.
- 7 W. C. Still, M. Khan, and A. Mitra, J. Org. Chem., 1978, 43, 2923.
- 8 Y. Shvo and I. Belsky, Tetrahedron, 1969, 25, 4649.
- 9 H. J. Gordon, J. C. Martin, and H. McNab, J. Chem. Soc., Chem. Commun., 1983, 957.
- 10 J. M. Conia and P. Le Perchec, Synthesis, 1975, 1.
- 11 R. A. Jones and P. Bean, 'The Chemistry of Pyrroles,' Academic Press, New York, 1977, p. 51.