

$\alpha$ -NITROSTYRENE. FIRST REACTIONS WITH ENAMINES

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**Abstract:** The reactivity of the title nitroolefin towards conformationally locked enamines is examined. A comparison with its isomer  $\beta$ -nitrostyrene is also made.

In spite of the interest in the nitroolefins as reagents in the formation of nitroalkylated compounds,<sup>2,3</sup> no data are reported in the literature about the reactivity of  $\alpha$ -nitrostyrene,<sup>4</sup> whereas the electrophilic behaviour of its structural isomer  $\beta$ -nitrostyrene, in particular with enamines, is well known.<sup>5-11</sup>

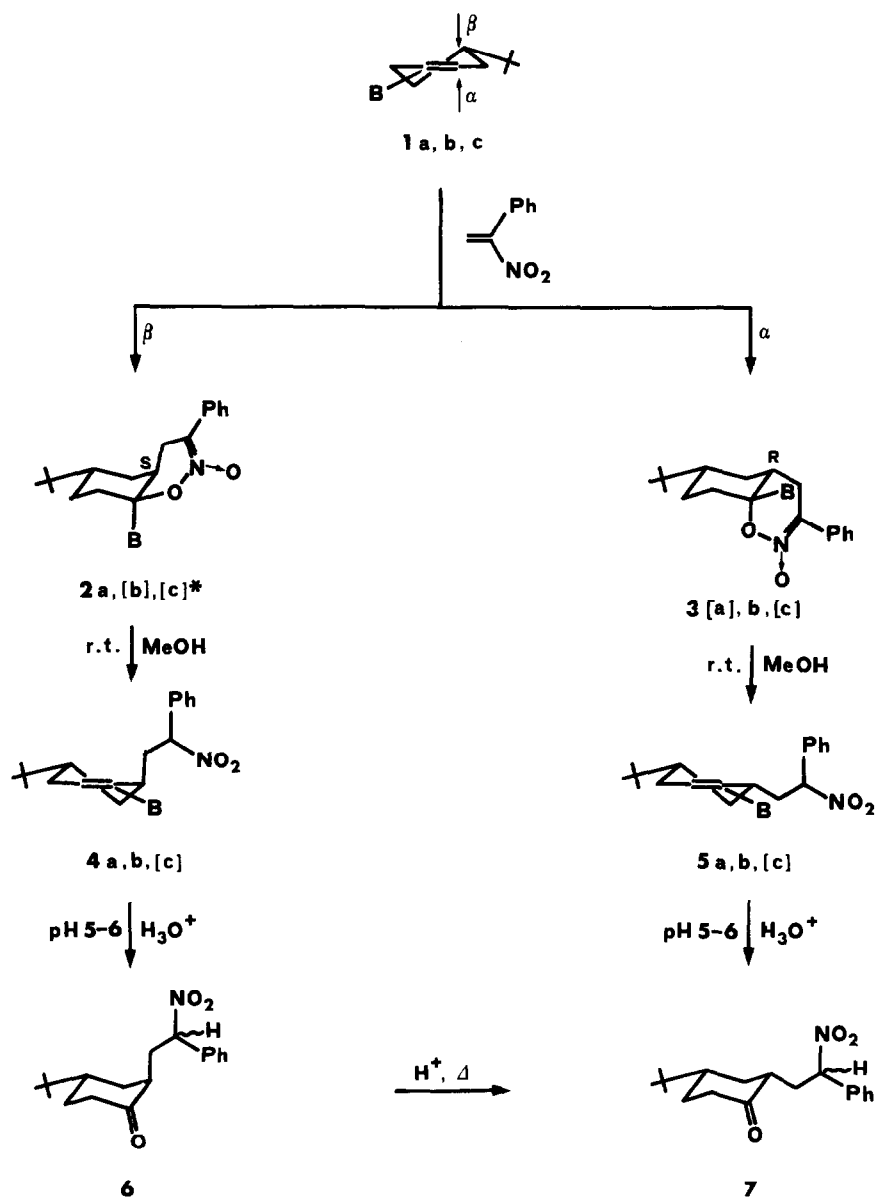
We have reacted the title olefin with anancomeric<sup>12</sup> enamine systems,<sup>13</sup> such as (1), in order to compare the reactivity of the two isomers and their possible interconversion under our reaction conditions (Scheme).<sup>14</sup>

$\alpha$ - and  $\beta$ -nitrostyrene have different degrees of stereoselectivity in their reaction with enamines. While the latter reacts with (1) only by a  $\beta$  approach,<sup>15</sup> the former shows a lower degree of stereoselectivity. The ratio of  $\alpha$  to  $\beta$  attack varies from 1:3 for the morpholino derivative (1a) to 1:4 for the piperidino (1b) and pyrrolidino (1c) ones. Furthermore, in contrast to  $\beta$ -nitrostyrene, which gives nitroalkylated enamines in almost all reactions,<sup>6-8,10</sup>  $\alpha$ -nitrostyrene leads to the formation of 1,2-oxazine N-oxide derivatives as the products of kinetic control. The relatively low stereoselectivity in the attack results in the formation of two diastereoisomeric heterocycles (2) and (3). Both are assigned the cis fusion between the rings, although this is obvious only for (2), in which the newly formed C-C bond is in the axial position. The configuration around C-4a in (2) can be inferred from the hydrolysis, carried out under mild acidic conditions, of enamines (4), derived from (2) by ring fission. Since the resulting ketones (6) (they form a pair of diastereoisomers) undergo rapid equilibration into a new pair of diastereoisomers (7), the nitroalkyl group must be axial in (6), as well as in enamines (4), and the configuration around C-4a in (2) must be S,<sup>17</sup> as depicted in the Scheme.

Opening of (3), followed by hydrolysis under the same conditions as above, furnishes the already mentioned ketones (7), thus proving that the configuration around C-4a in (3) is R. However in this case the fusion between the rings might be either cis or trans, since the mechanism is most likely non-concerted. The heterocycles (3) have been tentatively assigned the cis fusion, by analogy with a six-membered heterocyclic system derived from 4a-methyl-trans-2-decalone enamine and phenyl vinyl ketone, as both systems are formed by an  $\alpha$  attack of the

olefin onto the respective substrates.<sup>8</sup>

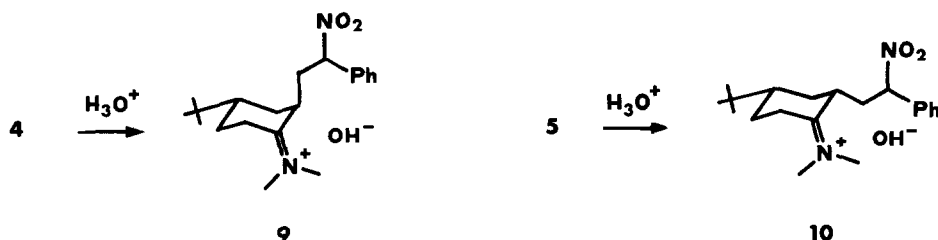
SCHEME



\*Compounds in brackets have not been isolated.

a: B = morpholin-4-yl; b: B = piperidin-1-yl; c: B = pyrrolidin-1-yl

As expected, hydrolyses of (5a) and (5b) are slower than those of (4a) and (4b), under the same conditions. This is related to the higher energy of the immonium intermediates (10), with respect to the analogs (9), owing to the  $A^{1,3}$  strains<sup>18</sup> between the base and the nitroalkyl side-chain.



The pyrrolidino derivatives could not be isolated either as 1,2-oxazine N-oxides (2c) and (3c), or as enamine adducts (4c) and (5c), owing to the great instability of (2c) and (3c) and to the hydrolytic lability of (4c) and (5c). However their corresponding hydrolysis products were isolated and identified as a mixture of (6) and (7) in ratio 4:1, thus demonstrating that also the ratio of  $\beta$  to  $\alpha$  attack is 4:1.

Finally, no equilibration between  $\alpha$  and  $\beta$ -nitrostyrene has been observed under our reactions conditions,<sup>14</sup> probably because of the lack of reactivity of the enamine nitrogen, when compared with that of saturated tertiary amines, such as triethylamine, which is known<sup>4</sup> to induce isomerization.

Some physical and spectroscopic data for the compounds are reported in the Table.

TABLE

Entry	m.p. °C	IR(nujol), $cm^{-1}$				$^1H$ -NMR( $CDCl_3$ ), $\delta$			
		C=O	N=C=C	Ph-C=N <sup>+</sup>	NO <sub>2</sub>	Ph	CHNO <sub>2</sub>	C=CH	Bu <sup>t</sup>
(2a)	66-8			1600, 1576 1564		a			
(3b)	110-1			1600, 1570 1560		7.82, 7.18 <sup>b</sup>			0.96(s)
(4a)	116-8		1652		1540	7.25	5.70(t)	4.65(dd)	0.85(s)
(4b)	106-8		1652		1545	7.21	5.77(m)	4.62(bs)	0.90(s)
(5a)	125-6		1642		1540	7.25	5.50(dd)	4.75(m)	0.88(s)
(5b)	112-3		1640		1540	7.15	5.34(dd)	4.61(m)	0.87(s)
(6) <sup>c</sup>	57-9	1710			1545	7.20	5.8-5.3		0.88(s), 0.85(s)
(7) <sup>c</sup>	62-4	1708			1545	7.4-7.1	5.8-5.4		0.88(s), 0.83(s)
(7) <sup>d</sup>	79-80	1708			1545	7.27	5.61(m)		0.88(s)

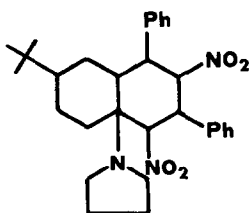
<sup>a</sup>The compound rapidly opens to (4a); <sup>b</sup><sub>o</sub>- and <sub>m</sub>- + <sub>p</sub>-aromatic protons respectively;

<sup>c</sup>mixture of diastereoisomers; <sup>d</sup> the thermodynamically more stable diastereoisomer.

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# REFERENCES AND NOTES

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- <sup>13</sup>Also mobile systems such as aminocyclopentenes and aminocyclohexenes react with  $\alpha$ -nitrostyrene to give [4+2] cycloaddition products and nitroalkylated enamines. However they are unstable and undergo easy hydrolysis to the corresponding  $\gamma$ -nitroketones.
- <sup>14</sup>Dry ether, 0-5°C, 24 h, quantitative yield.
- <sup>15</sup> $\beta$ -Nitrostyrene reacts with (1) leading to the corresponding nitroalkylated enamines in cis configuration with high stereoselectivity (>90%). The reaction of (1c) however is complicated by the formation of a decaline system, i.e. (8), as a consequence of a double addition of the nitroolefin onto (1c).<sup>16</sup>



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