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A NEW RING TRANSFORMATION : SYNTHESIS OF 5,5-DIMETHYL-3-OXO-1-PYRROLINE 1-OXIDES FROM 6,6-DIMETHYL-4-OXO-5,6-DIHYDRO-1,2,*4H*-OXAZINES

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Abstract : The nitrosation of some γ,δ-unsaturated β-diketo compounds affords the 3-substituted 4-oxo-5,6-dihydro-1,2,*4H*-oxazines. These compounds are converted to the isomeric 3-oxo-1-pyrroline 1-oxides by a facile thermal rearrangement.

In connection with our study of γ,δ-unsaturated β-ketoesters[1,2], we have explored their nitrosation. We report here the preparation of 4-oxo-5,6-dihydro-1,2,*4H*-oxazine derivatives. We have observed one unusual transformation of this novel heterocyclic system into the isomeric 3-oxo-1-pyrroline 1-oxides. No evidence of this type of ring contraction was found in the literature[3].

It is well known that the nitrosation of β-diketo compounds leads to the α-hydroxyimino derivatives[4a]. Treatment of substances 1 with nitrous acid affords a material constituted by either the 4-oxo-5,6-dihydro-1,2,*4H*-oxazine 3, or a mixture of 3 and the oxime 2 (presumably in the anti-configuration with respect to the double bond), depending on the X substituent, as shown by the ^{1}H-NMR spectra[5]:

2 : 3 ratio a, 0 : 100 b, 90 : 10 c, 36 : 64

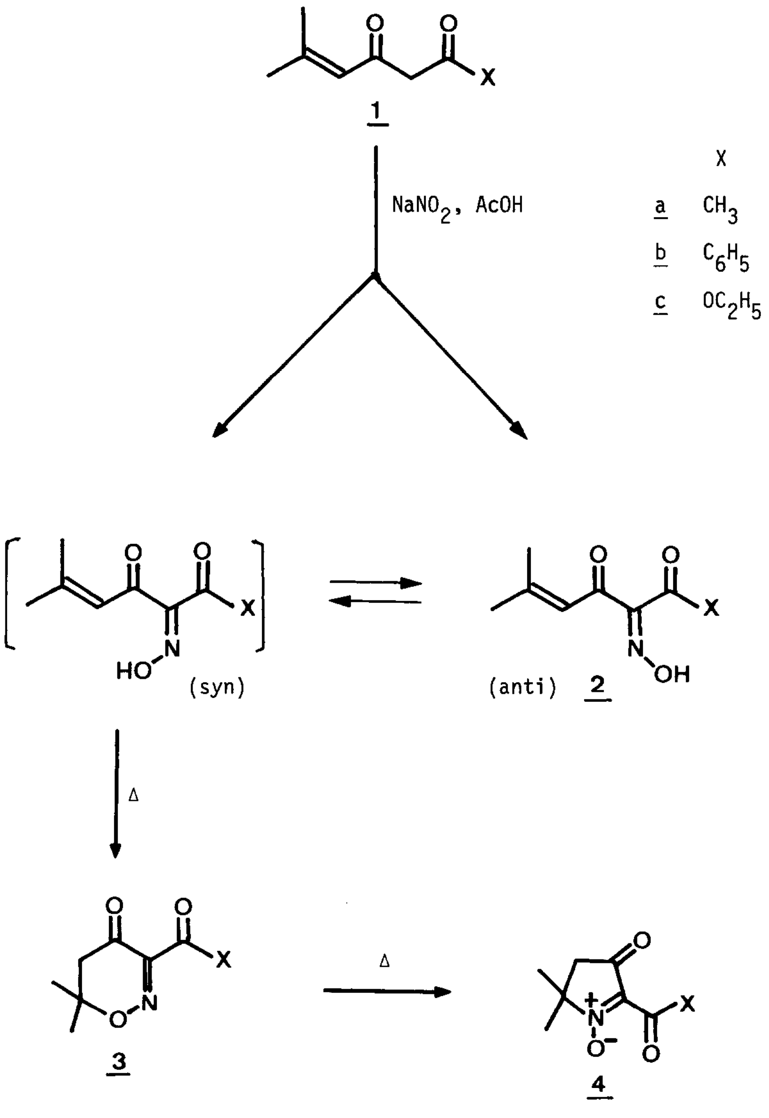
The 2 : 3 ratio may reflect the distribution of the anti and syn forms of the oximes, the ring closure taking place only when the hydroxyl group is syn to the double bond. When the reaction mixture is refluxed in xylene for 15 minutes, the oximes 2b and 2c are converted to the oxazines 3b and 3c, via a facile anti-syn isomerization[6].

On heating in xylene for a few hours, the oxazines 3 are converted, in fair yields, into isomers, which are formulated as 3-oxo-1-pyrroline 1-oxides 4 on the basis of the following evidence :

- The melting point and spectral data for 2-benzoyl-5,5-dimethyl-3-oxo-1-pyrroline 1-oxide 4b are in good agreement with those reported by Black and Boscacci[7a] who synthetized this compound from 5,5-dimethyl-1-pyrroline 1-oxide.

- The infrared spectrum of substances 3 exhibits a strong band at 960-970 cm^{-1} (N-O), while substances 4 possess a strong band at 1525-1545 cm^{-1} (C=$\overset{+}{N}$-O$^-$). The pyrroline oxides 4 absorb around 262-283 nm, in agreement with the literature values[7].

- In the ^{13}C-NMR spectra (see table 2), the resonance of the C=N carbon atom lies in the region 149-154 ppm for the oxazines 3, whereas it appears at higher field (134-140 ppm) for the 1-pyrroline 1-oxides 4, well within the range expected for a nitrone[8].



	X
a	CH_3
b	C_6H_5
c	OC_2H_5

Reversion to the starting oximes during the thermal rearrangement was not detected, according to Baldwin's vectorial rules[9]. The 5-endo-trigonal process involving the formation of the nitrones from the oximes is much less favorable than the 6-endo-trigonal process. Thus, the nitrone formation from the oxazine may be visualized either by a concerted [1,2] sigmatropic rearrangement or by a homolysis-recombination mechanism. Only a limited number of 3-oxo-1-pyrroline 1-oxides have been reported in the literature[7], and all bear two methyl groups at the 5-position. We believe that this gem disubstitution is important for the stability of these heterocycles. Attempts to induce the thermal isomerization of the 3-acetyl-6-methyl-4-oxo-5,6-dihydro-1,2,*4H*-oxazine[10] resulted in extensive polymerization. The mechanistic details of this rearrangement are in progress.

Table 1 - Physical constants and spectral data of compounds 3 and 4

Compound	Refluxing time in xylene (h)	Yield[a] %	MP[b] °C	^{1}H-NMR (δ, acetone-d_6)		I.R. ν cm^{-1}	U.V. (C_2H_5OH) λ nm (ε)
				$(CH_3)_2$ (s)	CH_2 (s)		
3a	0	54	oil	1.45	2.78	1745,1715^{sh}, 965[c]	248 (4000), 270^{sh} (2500)
3b	0.25	58	40	1.55	2.96	1740,1695, 960[c]	253 (12300)
3c	0.25	52	oil	1.47	2.86	1760,1725, 970[c]	242 (3600), 270^{sh} (2500)
4a	4	44	98	1.59	2.89	1745,1675, 1530[d]	283 (13800)
4b	12	44	145[e]	1.71	3.09	1725^{sh},1660, 1545[d]	262 (15500)
4c	12	56	117	1.59	2.93	1740^{sh},1730, 1715^{sh},1525[d]	275 (14200)

a) Isolated yield of pure material : compound 4b by single filtration after cooling; compounds 3 and 4 by column chromatography, using hexane / ethyl acetate (1:1 for 3a and 3b ; 7:3 for 3c) or ethyl acetate (for 4a and 4c) as eluent.

b) All products gave satisfactory elemental analyses

c) CCl_4 solution

d) KBr disc.

e) Lit. mp 145°C [7a].

Table 2 - Pertinent ^{13}C-NMR chemical shifts (δ, DMSO-d_6) for compounds 3 and 4

Compound	X-C=O	C=N	C=O	CH_2	C-O or C=N
3a	194.3	151.4	184.9[a]	46.2	86.3
3b	189.2	153.8	185.8[a]	45.9	85.3
3c	161.5	149.4	183.9	45.8	85.8
4a	189.6	138.0	195.0[a]	48.1	76.9
4b	187.0	139.8	194.6[a]	48.9	77.4
4c	158.6	134.0	193.2	48.2	77.6

a) In the coupled spectrum, the carbon resonance appears as a triplet (^2J = 7 Hz).

Experimental : The nitrosation is carried out in a manner parallel to the literature[4b]. A solution of sodium nitrite (1.63 g, 23.6 mmol) in 4.5 ml of water is added with stirring to a solution of compound 1 (20 mmol) in glacial acetic acid (10 ml), the temperature being kept under 10°C. The reaction mixture is stirred for further 30 min. at 5-10°C and then allowed to stand overnight at room temperature. The resultant mixture is poured into 40 ml of water, followed by filtration (for b) or extractive work up with ether (a, c). The crude material is refluxed in 40 ml of xylene under nitrogen (see time in table 1). Pure compounds 3 or 4 are isolated either by recrystallization or by column chromatography on silica gel.

References and Notes :

[1] S. Gelin and R. Gelin, Bull. Soc. Chim. Fr., 288 (1968).

[2] C. Deshayes and S. Gelin, Synthesis, 623 (1980).

[3] For a review in this area, see J. H. Boyer, Chem. Rev., 80, 495 (1980).

[4] O. Touster "The nitrosation of Aliphatic Carbon Atoms" in Organic Reactions, 7 a) 327, b) 353, edited by R. Adams, J. Wiley and Sons, Inc., N. Y. (1953).

[5] ^{1}H-NMR for the oximes (δ acetone-d_6) 2b : 2.00 (s, CH_3), 2.16 (s, CH_3), 6.86-7.01 (m, H-C=C), 11.63 (broad, OH) ; 2c : 2.00 (s, CH_3); 2.20 (s, CH_3), 6.70-6.85 (m, H-C=C), 11.83 (broad, OH).

[6] G. J. Karabatsos and R. A. Taller, Tetrahedron, 24, 3347 (1968).
R. Bucourt, R. Heymes, A. Lutz, L. Penasse and J. Perronet, Tetrahedron, 34, 2233 (1978).

[7] [a]D. St. C. Black and A. B. Boscacci, Aust. J. Chem., 30, 1353 (1977).
[b]D. St. C. Black, N. A. Blackmann and R. F. C. Brown, Tetrahedron Lett., 39, 3423 (1975) and Aust. J. Chem., 32, 1785 (1979)
[c]D. St. C. Black and A. B. Boscacci, Aust. J. Chem., 29, 2511 and 2561 (1976).

[8] N. S. Ooi and D. A. Wilson, J. Chem. Research (S), 366 (1980).

[9] J. E. Baldwin, J. Chem. Soc. Chem. Comm., 734 (1976).

[10] The 3-acetyl-6-methyl-4-oxo-5,6-dihydro-1,2,*4H*-oxazine was prepared in a 30% yield by nitrosation of the ethyl-3-oxo-4-hexenoate. ^{1}H-NMR (δ acetone-d_6) : 1.54 (d, 3H, J = 7 Hz), 2.38 (s, 3H), 2.71 (d, 2H, J = 8.5 Hz), 4.53-5.01 (m, 1H). The ^{13}C chemical shift of the C=N carbon atom appears at 153.0 ppm in DMSO-d_6.

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