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# THERMAL CYCLIZATION OF cis-DIENONE-OXIMES

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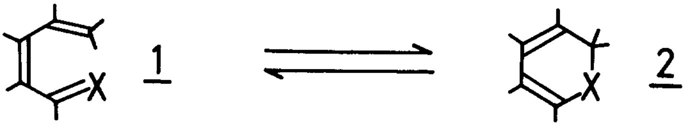
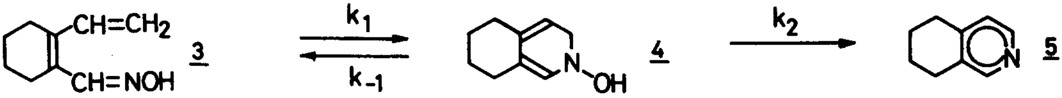
It is well known 1) that cis-dienones 1 (X = O) are in thermal equilibrium below 100° with 2H-pyrans 2 (X = O). In this communication we wish to describe thermal reactions of oximes and oxime derivatives of several cis-dienones 1 (X = NOR) which are valence isomers of 1,2-dihydropyridines 2 (X = NOR) 2).



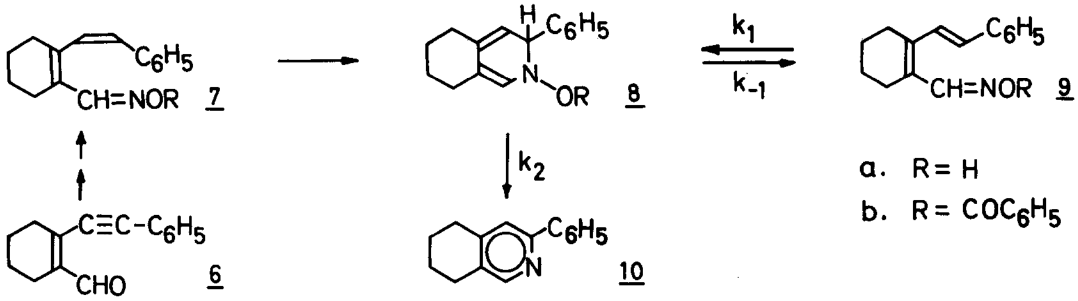
Aldoxime 3 3) is converted to 5,6,7,8-tetrahydroisoquinoline 5 at 70°. Similar rates are observed for this conversion in alcohol and in benzene solution indicating that it is the cyclization to intermediate 4 rather than the elimination of water from 4 which is occurring in the rate determining step. No cis,trans-isomerization of the vinyl double bond is observed in oxime 3 recovered after 70 % conversion to 5 as shown by a deuterium labeling experiment. This proves that ring closure to 4 is irreversible ($k_2 \gg k_{-1}$ in scheme 1).

Scheme 1



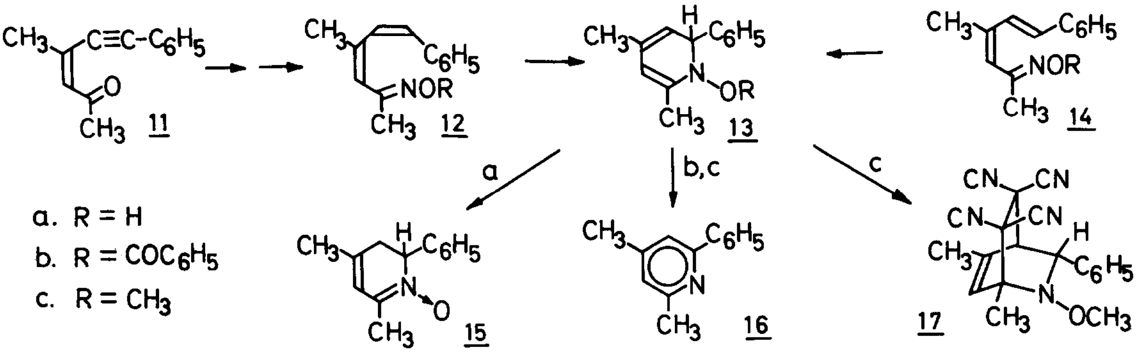
Oxime 7a 4) obtained from 6 1) through oximation followed by partial catalytic reduction is transformed quantitatively into its trans-isomer 9a at 100° in iso-octane. As in the cis,trans-isomerization of the parent aldehydes 1) a bicyclic valence isomer can be assumed as an intermediate. 9a is stable in iso-octane at 100°. In iso-butanol however it is rapidly converted to 10 at the same temperature, presumably through 8a. Apparently 8a shows two different modes of reaction: Ring opening to 9a ($k_{-1}$ in scheme 2) and elimination of water to 10 ($k_2$), the latter process competing with the former only in the polar solvent.

Scheme 2



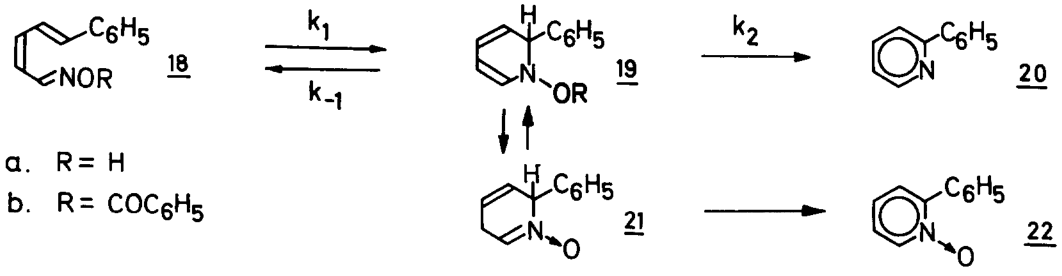
The stereoisomeric dienone-oximes 12a (prepared from ketone 11 [5]) and 14a [6] are both converted to 15 [6] at 60°. In dilute solution (alcohol, $10^{-3}$ m) a precursor of 15 is formed from 12a and from 14a showing weak UV-absorption (300 nm, ε 2000) typical for 1,2-dihydropyridines [7]. Attempts to isolate this precursor of presumed structure 13a at -20° however lead only to 15.

Scheme 3



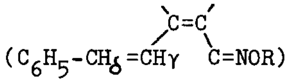
5-Phenyl-pentadienaldoxime 18a [6] contrasts with the other oximes investigated in showing thermal stability up to 160°. Reflux in cyclohexanol for 18 hours leads to 2-phenylpyridine 20 and its N-oxide 22 each in about 25 % yield. The low reactivity of 18a indicates a low concentration of 19a in equilibrium with 18a ($k_{-1} \gg k_1$ in scheme 4). A further equilibrium between 19a and its tautomer 21 is assumed since 22 has been shown [6] to be formed from 21 at 50° [8].

Scheme 4



The benzoates 7b, 9b, 12b, 14b and 18b (see table), prepared from the oximes with benzoylchloride in pyridine, are converted to the respective 2-phenylpyridines when warmed at 50° in dilute solution. As dienone-oximes are readily obtained from pyridine-N-oxides 6) 9), this reaction constitutes an efficient path to 2-arylpyridine derivatives. The first order rate constants for the disappearance of the oxime benzoates as measured by UV-spectroscopy show little dependence on solvent polarity (see last column in table). This points to the formation of a 1-benzoyloxy-1,2-dihydropyridine in the rate determining step of the aromatization reaction. Such a two step process is further supported by the absence of isosbestic points during the thermolysis of compounds 7b, 9b, 12b and 14b in iso-octane.

Table cis-Dienone-oximes and oxime derivatives


$(C_6H_5\text{-}CH_\delta{=}CH_\gamma\text{-}C{=}C\text{-}C{=}NOR)$

| | mp. | UV-maximum nm/ε (EtOH) | NMR-signal for γ- & δ-H δ-value/coupling const. | cyclization in i-BuOH: t½ | solvent effect (a) |
|---|---|---|---|---|---|
| 7a | 121-124° | 242/21000 | 6.20 & 6.44 d/12 cps | | |
| b | 90-91° | 236/26500 | 6.28 & 6.60 d/12 cps | 102'/73.0° | 0.27 |
| 9a | 143-145° | 320/34000 | 6.78 d/16 cps (b) | | |
| b | 101-103° | 324/34500 | 6.82 d/16.5 cps (b) | 19'/73.0° | 0.61 |
| 12a | 76-78° | 264/13400 | 6.42 s (2H) | 360'/51.5° (c) | |
| b | 74-76° | 271sh/13500 | 6.52 s (2H) | 38'/51.5° | |
| 14a 6) | 92-94° | 310/25000 | 6.75 & 7.60 d/16 cps | 119'/51.5° | |
| b | 85-87° | 319/18000 | 6.98 d/17 cps | 12.4'/51.5° | 0.75 |
| c | oil | 315/22000 | 6.72 & 7.85 d/17 cps | | |
| 18b 6) | 85-87° | 324/42000 | 6.80 d/15 cps (b) | 300'/51.5° | 0.33 |

(a) $k_{i\text{-BuOH}}/k_{i\text{-Octane}}$ (b) signal for γ-H and aromatic H not separated

(c) approximate value

The oxime benzoates undergo cyclization at a higher rate than the respective oximes (see table). This indicates a stabilization of the cyclic structure 2 (X = NOR) relative to its valence isomer 1 (X = NOR) through benzoylation. Further evidence of such an effect is given by a shift of the equilibrium 8 ⇌ 9 upon benzoylation: Oxime 9a is more stable than its bicyclic valence isomer 8a; the relative stability of 8b and 9b is reversed, 8b being formed irriversibly from 9b during its conversion to 10 in iso-octane.

There is only indirect evidence for the formation of 1,2-dihydropyridines 2 (X = NOR) in the reactions of cis-dienone derivatives 1 (X = NOR) described so far. Starting with oxime methyl ether 14c (obtained as an oil from 14a with dimethylsulfate and sodium in methanol) we have been able to trap a cyclic valence isomer 13c through cycloaddition: At 60° in ethanol 14c is converted to 16; under reflux in acetonitrile with tetracyanoethylene the 1 : 1 adduct 17 (mp. 158 - 160°; UV: 265, 261, 255 nm, 330) is obtained in 20 % yield. The isolation of this cycloadduct derived from 13c further supports the assumption that in the other reactions of cis-dienone derivatives described in this communication 1,2-dihydropyridines 2 (X = NOR) are formed as labile intermediates.

## Acknowledgement

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## Footnotes and References

1) E.N. Marvell, G. Caple, T.A. Gosink and G. Zimmer, J. Amer. chem. Soc. 88, 619 (1966); P. Schiess and H.L. Chia, Helv. chim. Acta 53, 485 (1970); P. Schiess, R. Seeger and Chr. Suter, Helv. chim. Acta 53, 1713 (1970).

2) This work was presented in part at the meeting of the Swiss chemical Society, St. Gallen, October 4, 1969 (rf. Chimia 24, 24 (1970) and at the IUPAC Conference on Cycloaddition Reactions, Munich, September 7-10, 1970.

3) P. Schiess and H.L. Chia, Helv. chim. Acta 53, 485 (1970).

4) All new compounds were characterized by their IR-, UV-(ethanol) and NMR-($CDCl_3$) spectra and gave satisfactory elemental analyses.

5) P. Schiess, publication forthcoming.

6) see preceding communication.

7) E.M. Fry, J. org. Chem. 28, 1869 (1963); E. Fraenkel, J.W. Cooper and J.M. Fink, Angew. Chem. 82, 518 (1970).

8) 1-Hydroxi-2-phenyl-1,2,4,5-tetrahydropyridine, formed together with 22 from 21 at 50° (6) is converted to 20 in low yield at 160° in cyclohexanol.

9) T.J. VanBergen and R.M. Kellogg, J. org. Chem. 36, 1715 (1971).