Ring Opening Reaction of 3,6-Dihydro-2-(1*H*)pyrimidinones with Hydroxylamine Hydrochloride

Choji Kashima, Akira Katoh, Yuko Yokota and Yoshimori Omote*

Department of Chemistry, University of Tsukuba, Sakura-mura,
Niihari-gun, Ibaraki 305, Japan

Received February 25, 1981

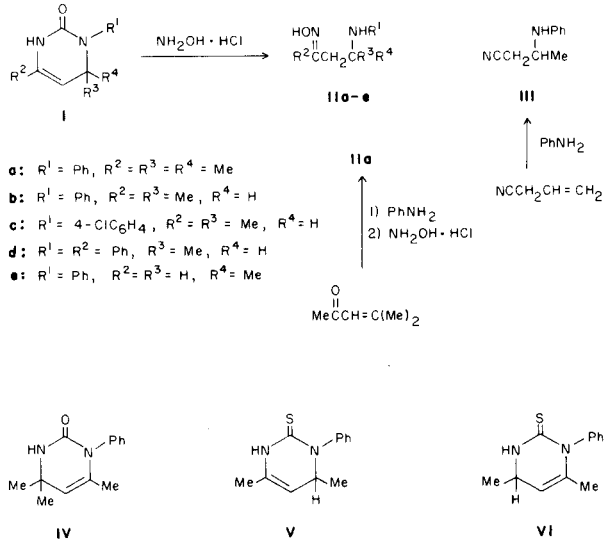
1,4,6-Trisubstituted 3,6-dihydro-2-(1*H*)pyrimidinones (Ia-d) easily underwent the ring opening reaction with hydroxylamine hydrochloride to afford the oximes (IIa-d) in good yields. In the case of 3,6-dihydro-6-methyl-1-phenyl-2-(1*H*)pyrimidinone (Ie), 2-anilinobutyronitrile (III) was obtained in addition to the oxime (IIe). Dihydro-2-(1*H*)pyrimidinone (IV) and -thiones (V and VI) did not undergo the ring opening reaction.

J. Heterocyclic Chem., 18, 1469 (1981).

In the previous paper (1), we reported on the regioselective preparation of 3,4- and 3,6-dihydro-2-(1*H*)pyrimidinones and -thiones by the treatment of 2-(1*H*)pyrimidinones and -thiones with Grignard reagents, organolithium reagents, lithium aluminum hydride or sodium borohydride. As the study of the extensive usage (2) of these 3,4- and 3,6-dihydro-2-(1*H*)pyrimidinones and -thiones, we wish to describe the ring opening reaction of dihydro-2-(1*H*)-pyrimidinones and -thiones with hydroxylamine hydrochloride.

Table 1

Compound No.	Bp °C/10^{-4} mm Hg	Yield %	Formula	Analysis % Calcd. (Found) C	H	N
IIa	100	68	$C_{12}H_{18}N_2O$	68.86 (68.96)	8.79 (8.75)	13.57 (13.66)
IIb	90	72	$C_{11}H_{16}N_2O$	68.71 (68.55)	8.38 (8.29)	14.57 (14.67)
IIc	123	78	$C_{11}H_{15}N_2OCl$	58.27 (57.96)	6.66 (6.64)	12.35 (12.22)
IId	140	63	$C_{16}H_{18}N_2O$	75.56 (75.23)	7.13 (7.08)	11.01 (10.97)
IIe	120	10	$C_{10}H_{14}N_2O$	67.36 (66.98)	7.91 (7.98)	15.72 (15.42)



Results and Discussion.

When 3,6-dihydro-4,6,6-trimethyl-1-phenyl-2-(1*H*)-pyrimidinone (Ia) reacted with hydroxylamine hydrochloride in the presence of sodium hydroxide in absolute ethanol, the product, bp 100°/10^{-4} mm Hg, the formula $C_{12}H_{17}N_2O$, and a broad band at 2800-3500 cm^{-1} due to the O-H stretching in the ir spectrum, was obtained. The nmr spectrum showed at δ 1.33 (s, 6H), 1.90 (s, 3H), and 2.54 (s, 2H) attributable to geminal dimethyl, methyl and methylene protons, respectively, in addition to the characteristic peaks of the aniline protons at δ 6.6-7.0 (m, 3H) and 7.0-7.4 (m, 2H). The product was found to be 2-anilino-2-methylpentan-4-one oxime (IIa) by these spectral data and comparison with a sample independently obtained from mesityl oxide, aniline, and hydroxylamine hydrochloride. The reaction of other 1,4,6-trisubstituted 3,6-dihydro-2-(1*H*)pyrimidinones (Ib-d) with hydroxylamine hydrochloride was examined and the results were summarized in Table 1 and 2.

3,4-Dihydro-4,4,6-trimethyl-1-phenyl-2-(1*H*)pyrimidinone (IV) and dihydro-2-(1*H*)pyrimidinethiones (V and VI) did not react with hydroxylamine hydrochloride under the same conditions.

When 3,6-dihydro-6-methyl-1-phenyl-2-(1*H*)-pyrimidinone (Ie) was also treated with hydroxylamine hydrochloride, two products, bp 120°/10^{-4} mm Hg (compound A) and mp 55-57° (compound B), were formed. Compound A was assigned to be 2-anilinobutan-4-one oxime (IIe) by means of the spectral data and elemental analysis (see Table 1 and Table 2). Compound B showed two strong ir bands at 3360 and 2250 cm^{-1} due to N-H and C≡N stretching, respectively. The nmr spectrum showed at δ 1.32 (d, 3H, J = 6.0 Hz) and 2.48 (t, 2H, J = 4.0 Hz) assignable to methyl and methylene protons as well as the characteristic peaks of the aniline protons at δ 6.5-6.9 (m, 3H) and 7.0-7.4 (m, 2H). From these data, compound B was deduced to be 2-anilinobutyronitrile (III), which was identical with an authentic sample (mp 57-58°) obtained from crotononitrile and aniline (3).

0022-152X/81/071469-02$02.25

Table 2

The IR and NMR Spectra of the Oximes (IIa-e)

Compound No.	IR Spectra (a) (cm^{-1})	Nmr Chemical Shift (b) (δ, ppm) $-CH_3$	C-H and N-H	$-CH_2-$	Aromatic
IIa	2800-3500, 1605, 1495, 740, 690	1.33 (s, 6H) 1.88 (s, 3H)		2.52 (s, 2H)	6.6-7.0 (m, 3H) 7.0-7.4 (m, 2H)
IIb	2800-3500, 1600, 740	1.22 (d, 3H, J = 6.0 Hz) 1.90 (s, 3H)	3.5-4.1 (m, 2H)	2.3-2.6 (d, d, 2H, J = 6.0 and 4.0 Hz)	6.5-6.9 (m, 3H) 7.0-7.4 (m, 2H)
IIc	2800-3500, 1600, 810	1.24 (d, 3H, J = 6.0 Hz) 1.83 (s, 3H)	3.5-4.0 (m, 2H)	2.2-2.5 (d, d, 2H, J = 6.0 and 4.0 Hz)	6.4-6.7 (m, 2H) 7.0-7.4 (m, 2H)
IId	2800-3500, 1600, 1510, 760, 695	1.20 (d, 3H, J = 6.0 Hz)	3.6-4.1 (m, 2H)	2.6-3.0 (d, d, 2H, J = 13.0 and 7.0 Hz) 3.1-3.5 (d, d, 2H, J = 13.0 and 6.5 Hz)	6.4-6.8 (m, 3H) 7.0-7.8 (m, 7H)
IIe	2800-3500, 1600, 1500, 745, 690	1.22 (d, 3H, J = 6.0 Hz)	3.4-3.9 (m, 2H) 7.48 (t, 1H, J = 6.0 Hz)	2.38 (t, 2H, J = 6.0 Hz)	6.5-6.9 (m, 3H) 7.0-7.3 (m, 2H)

(a) Measured at neat. (b) Measured in deuteriochloroform.

It is concluded that 1,4,6-trisubstituted 3,6-dihydro-2-(1*H*)pyrimidinones undergo the ring opening reaction with hydroxylamine hydrochloride to afford oximes and nitrile in good yields.

EXPERIMENTAL

Ir spectra were recorded on a Jasco ITA-1 infrared spectrophotometer. Nmr spectra were taken on a Hitachi R-20 spectrometer. Florisil (100-200 mesh, Iwaki Kagaku Co., Ltd.) was used for column chromotography.

Reaction of 3,6-Dihydro-2-(1*H*)pyrimidinones with Hydroxylamine Hydrochloride.

To the solution of 3,6-dihydro-2-(1*H*)pyrimidinone (3 mmoles) in the presence of sodium hydroxide (6.6 mmoles) in absolute ethanol (40 ml) was added hydroxylamine hydrochloride (3.3 mmoles) and the mixture was refluxed for 34 hours. The reaction mixture was diluted with water, extracted with dichloromethane, and dried over anhydrous magnesium sulfate. The crude product was chromatographed with benzene/ethyl acetate (2:1) or (4:1) on Florisil, followed by vacuum distillation. The analytical data were summarized on Tables 1 and 2.

Alternative Preparation of Compound IIa.

The mixture of mesityl oxide (10 mmoles) and aniline (40 mmoles) was heated at 200° for 5 hours in a sealed tube. To the mixture in absolute ethanol (80 ml) was added hydroxylamine hydrochloride (10 mmoles) and anhydrous potassium carbonate (5 mmoles). The reaction mixture was refluxed for 12 hours and was treated according to the procedure described above, yield 8%.

REFERENCES AND NOTES

(1) C. Kashima, A. Katoh, Y. Yokota and Y. Omote, *J. Chem. Soc., Perkin Trans. I,* in press.

(2) C. Kashima, A. Katoh, Y. Yokota and Y. Omote, *Heterocycles,* **14**, 285 (1980).

(3) A. Mevis *Bull. Soc. Chim. Belg.*, **40**, 726 (1931); *Chem. Abstr.*, **26**, 2701 (1932).