HETEROCYCLES, Vol 16, No 11, 1981

PREPARATION AND DECOMPOSITION OF 1,4,6-TRISUBSTITUTED 3-NITROSO-TETRAHYDRO-2(1H)-PYRIMIDINONES

Choji Kashima*, Akira Katoh, and Yoshimori Omote
Department of Chemistry, University of Tsukuba, Sakura-mura,
Niihari-gun, Ibaraki 305, Japan

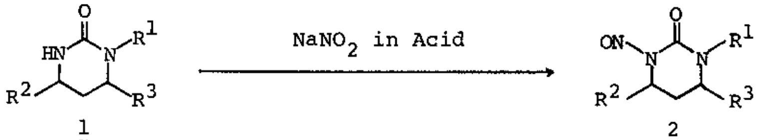
Abstract—— 1,4,6-Trisubstituted tetrahydro-2(1H)-pyrimidinones (**1**) were treated with sodium nitrite in acidic conditions to afford the corresponding 3-nitroso-2(1H)-pyrimidinones (**2**) in high yields. The decomposition of **2a** with potassium hydroxide was also discussed.

Many papers on the preparation of various N-nitrosamines have been reported in relation to their powerful chemical carcinogens. Previously we reported that 1,4,6-trisubstituted tetrahydro-2(1H)-pyrimidinones (**1**) were easily obtained by the reduction of 2(1H)-pyrimidinones with sodium borohydride in various conditions.[1] Whereas, it is well known that N-methylurea reacts with sodium nitrite to give N-nitrosomethylurea.[2] Since 1,4,6-trisubstituted tetrahydro-2(1H)-pyrimidinones (**1**) are regarded as cyclic ureas, it is possible to undergo the nitrosation on nitrogen atom at N-3 position in the pyrimidine ring.

In this paper, we wish to report on nitrosation of 1,4,6-trisubstituted tetrahydro-2(1H)-pyrimidinones with sodium nitrite. A typical nitrosation is as follows. To the solution of 4,6-dimethyl-1-phenyl-tetrahydro-2(1H)-pyrimidinone (**1a**, 1 mmol) in 6N hydrochloric acid (1 ml) was added slowly sodium nitrite (6 mmol) at room temperature. After 1 hr stirring, the mixture was neutralized with 10% sodium hydroxide, and extracted with dichloromethane. By column chromatography with chloroform/ethyl acetate (20:1) mixture on silica gel and recrystallization from benzene/hexane mixture, 4,6-dimethyl-3-nitroso-1-phenyl-tetrahydro-2(1H)-pyrimidinone (**2a**)[3] was obtained in 93% yield; mp 114-115 °C; ir $\nu_{max.}$(KBr) 1690, 1490, and 740 cm^{-1}; ^{1}H-nmr(δ,CDCl$_3$) 1.08 (d, 3H, J=7.0 Hz), 1.25 (d, 3H, J=7.0 Hz), 1.8-2.5 (m, 2H), 3.7-4.2 (m, 1H), 4.3-4.8 (m, 1H), and 7.1-7.4 ppm (m, 5H); ^{13}C-nmr(δ,CDCl$_3$) 19.3 (q), 21.1 (q), 36.0 (t), 47.2 (d), 52.2 (d), 128.0 (d), 128.5 (d), 129.3 (d), 139.3

(s), and 152.1 ppm (s). Similarly, the nitrosation of other 1,4,6-trisubstituted tetrahydro-2(1H)-pyrimidinones (1b-h) were examined and the results were listed in Table 1.

Table 1

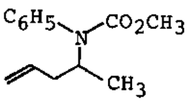


1 2

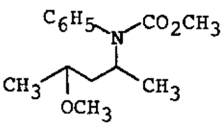
Compound	R^1	R^2	R^3	Acid*	Product[3]	Mp (°C)	Yield (%)	Recovered (1,%)
1a	C_6H_5	CH_3	CH_3	A	2a	114-115	93	0
1b	p-$CH_3C_6H_4$	CH_3	CH_3	A	2b	198-200(decomp.)	70	24
1c	p-$CH_3OC_6H_4$	CH_3	CH_3	A	2c	87-88	87	0
1d	p-ClC_6H_4	CH_3	CH_3	B	2d	108-110	68	27
1e	p-BrC_6H_4	CH_3	CH_3	B	2e	116-117	48	39
1f	CH_3	C_6H_5	C_6H_5	A	2f	175-176(decomp.)	42	39
1g	p-$CH_3C_6H_4$	H	H	A	2g	160-161(decomp.)	92	0
1h	C_6H_5	H	CH_3	A	2h	93-94	96	0

* A = 6N hydrochloric acid. B = concentrated hydrochloric acid.

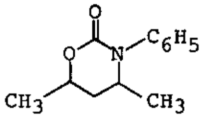
When compound 2a (2 mmol) was treated with potassium hydroxide (20 mmol) in methanol (15 ml) with stirring overnight at room temperature, three products[3], methyl N-sunstituted N-phenylcarbamates 3 (bp 48 °C/10^{-4} Torr., 40%), 4 (bp 59 °C/10^{-4} Torr., 29%) and tetrahydro 4,6-dimethyl-3-phenyl-1,3-oxazin-2-one 5 (mp 89-90 °C, 17%), were obtained.



3



4



5

References

(1) C. Kashima, A. Katoh, Y. Yokota, and Y. Omote, J. Chem. Soc., Perkin Trans. 1, 1981, 1622.

(2) F. Arndt, Org. Synth., Coll. Vol., II, 461(1943).

(3) Satisfactory elemental analyses were obtained for all new compounds.

Received, 24th July, 1981