

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

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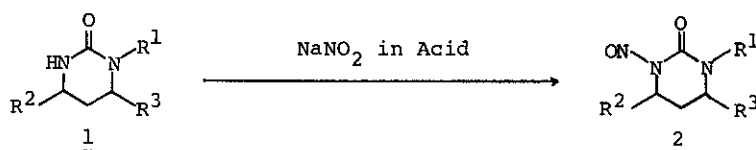
Abstract—— 1,4,6-Trisubstituted tetrahydro-2(1H)-pyrimidinones (1) were treated with sodium nitrite in acidic conditions to afford the corresponding 3-nitroso-2(1H)-pyrimidinones (2) in high yields. The decomposition of 2a with potassium hydroxide was also discussed.

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 ν_{max} (KBr) 1690, 1490, and 740 cm^{-1} ; ¹H-nmr(δ , CDCl₃) 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); ¹³C-nmr(δ , CDCl₃) 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.

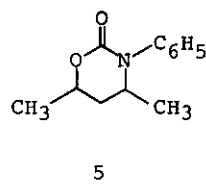
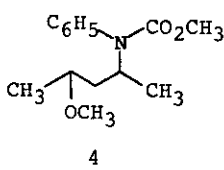
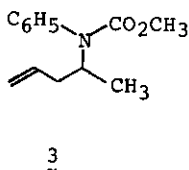
Table 1



Compound	R ¹	R ²	R ³	Acid *	Product ³	Mp (°C)	Yield (%)	Recovered (%, %)
1a	C ₆ H ₅	CH ₃	CH ₃	A	2a	114-115	93	0
1b	p-CH ₃ C ₆ H ₄	CH ₃	CH ₃	A	2b	198-200 (decomp.)	70	24
1c	p-CH ₃ OC ₆ H ₄	CH ₃	CH ₃	A	2c	87-88	87	0
1d	p-ClC ₆ H ₄	CH ₃	CH ₃	B	2d	108-110	68	27
1e	p-BrC ₆ H ₄	CH ₃	CH ₃	B	2e	116-117	48	39
1f	CH ₃	C ₆ H ₅	C ₆ H ₅	A	2f	175-176 (decomp.)	42	39
1g	p-CH ₃ C ₆ H ₄	H	H	A	2g	160-161 (decomp.)	92	0
1h	C ₆ H 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 products³, 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.



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.

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