

FACILE DIRECT  $\alpha$ -OXIMATION OF KETONES USING *t*-BUTYL THIONITRATE

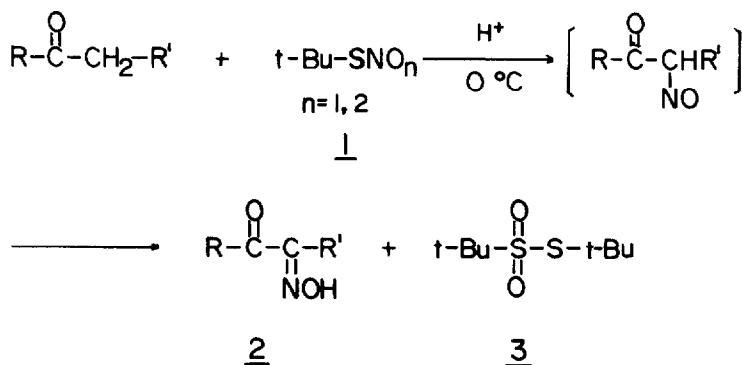
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**Summary :** Various ketones containing methylene groups at  $\alpha$ -position were found to react with *t*-butyl thionitrate at 0 °C in tetrahydrofuran to give the corresponding  $\alpha$ -oximinoketones in excellent yields.

Since quite stable *t*-butyl thionitrite or *t*-butyl thionitrate<sup>1</sup> can be prepared simply by treating *t*-butyl mercaptan with dinitrogen tetroxide, intensive studies on *t*-butyl thionitrate chemistry for organic synthesis such as deamination,<sup>2</sup> unsymmetrical disulfides,<sup>3</sup> thioimines,<sup>4</sup> and desulfurizations<sup>5</sup> have been reported. All these reactions apparently involve initial nitrosation on heteroatoms such as nitrogen and sulfur. We have recently reported that  $\alpha$ -oximino- $\alpha$ -haloketones were obtained by treating  $\alpha$ -haloketones with alkyl thionitrites via nitrosation on carbon atom.<sup>6</sup>

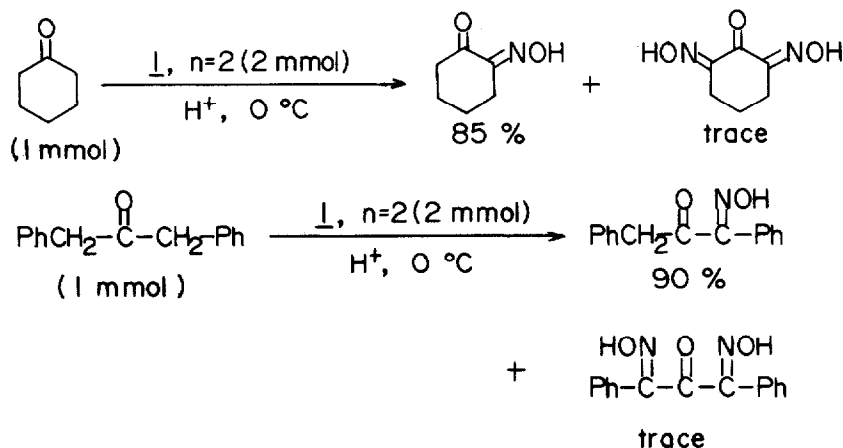
We now have found that various ketones containing  $\alpha$ -methylene group reacted readily with *t*-butyl thionitrate (1,  $n=2$ ) at 0 °C to afford the corresponding  $\alpha$ -oximinoketones (2) in excellent yields as shown below.



The  $\alpha$ -oximinoketones have been known to be an important intermediate for the synthesis of aminoacids.<sup>7</sup> Although alkyl nitrite, nitrous acid, or sodium nitrite in acetic acid are used for the synthesis of  $\alpha$ -oximinoketones,<sup>8</sup> the yields are varied and selectivity for mono oximation on the methylene carbon is low when the ketones have two methylene group at both  $\alpha$ -positions.

*t*-Butyl thionitrate appears to be better reagent for the C-nitrosation of ketones due both to the more facile cleavage of sulfur-nitrogen bond than that of oxygen-nitrogen bond of nitrites and also to the better leaving group of the sulfinyl group<sup>8</sup> than alkoxy group (RO<sup>-</sup>) in the nitrosating step. Indeed, *t*-butyl thionitrate reacted with propiophenone to give the higher yield of the oxime than those obtained using nitrites.<sup>9</sup>

Moreover, *t*-butyl thionitrate resulted in a selectivity towards the mono oximation on the  $\alpha$ -carbon of the ketones which have two methylene groups at its both  $\alpha$ -positions as shown below.



The selectivity is probably due to a steric effect by the bulky *t*-butyl group and the mild reaction conditions.

In contrast to the above high selectivity, when methyl nitrite (2 mmole) was used with cyclohexanone (1 mmole) or dibenzyl ketone (1 mmol), 2,6-dioximinocyclohexanone (61%) or 1,3-dioximinodibenzyl ketone (68%) was obtained respectively.

In a typical run, *t*-butyl thionitrate (167 mg, 1.2 mmol) was added onto a phenylacetone solution (134 mg, 1 mmol, anhydrous THF solution containing HCl gas: 4 ml) at 0 °C. After being stirred for ca. 40 min. at 0 °C the reaction mixture was three times extracted with ether. The combined ethereal solution was concentrated and then, purified by the preparative TLC (Merck Silica gel, 60 F<sub>254</sub>, 1 mm x 20 cm x 20 cm, ether/*n*-hexane=1/1, v/v) to afford the product of  $\alpha$ -oximinoketone (93%) together with *t*-butylthiosulfonic S-ester (**3**, 95%, <sup>1</sup>H NMR (CDCl<sub>3</sub>-DMSO-d<sub>6</sub>),  $\delta$  1.41 (s, 9 H), 1.5 (s, 9 H)).<sup>8</sup>

Other products were purified by preparative TLC or column chromatography (Silical gel, Merck Kieselgel 60, 70-230 mesh CH<sub>2</sub>Cl<sub>2</sub>/*n*-hexane=1/1, v/v). The products obtained were identified by comparing their mp, IR, and <sup>1</sup>H NMR with those of authentic samples. The results obtained are summarized in Table 1.

Table 1. Synthesis of  $\alpha$ -oximinoketones with  $t$ -BuSNO<sub>2</sub> in THF

Run	Substrate	<u>1</u>	$\frac{\text{1}}{\text{Substrate}}$	Reaction time (h)	Product (% Yield) <sup>a</sup>
1		n=2	1.2	0.3	
2	"	n=1	1.2	3	" (30)
3		n=2	1.2	0.6	
4	"	n=1	1.5	4	" (50)
5		n=2	1.4	0.4	
6		n=2	1.2	1	
7		n=2	1.5	1	
8		n=2	1.4	4.5	
9	"	n=1	1.5	6.3	" (0) <sup>b</sup>

a. Isolated Yields.

b. Most of Starting Material was Recovered.

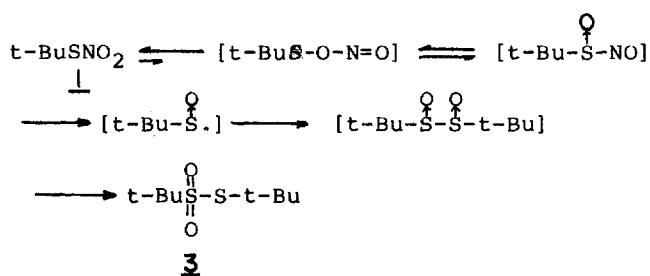
When  $t$ -butyl thionitrite (1, n=1) which is less stable than  $t$ -butyl thionitrate (1, n=2) was used as the nitrosating reagent, the yields of oxime are low (Run 2,4 and 9) due to its instability, where the thionitrite decomposed readily to the corresponding di- $t$ -butyl disulfide.<sup>10</sup> The reaction appears to be initiated by forming nitroso compound intermediate, which converts quickly to the oxime by a proton migration.

**Acknowledgement** : This research was supported by grants from Korea Science and Engineering Foundation and Korea Advanced Institute of Science & Technology

**References and Notes**

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t-Butyl thionitrate is known to be in equilibrium with sulfinyl nitrite and convert to the stable thiosulfonic S-ester.



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(Received in Japan, 20 February 1989)