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NITROSATION OF KETONE DIANIONS

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Nitrosation of α,α′-dianions produced from ketones using a couple of bases was carried out with *tert*-butyl nitrite(*tert*-BuONO) in ether, and then two regioisomers of oximes(but not acetone)were obtained simultaneously. The ratio of these regioisomers was remarkably reversed by the addition of hexamethylphosphoric triamide(HMPA).

KEY WORDS regioisomer; nitrosation; α,α′-dianion; oxime

Since monoalkylation of α,α′-dianions produced from ketones was first reported by Trimitsis et al.,[1] the chemistry of dianions has been widely studied.[2] Recently, even dialkylation of the dianions was reported by Bates and Taylor.[3] In the papers presented until now, it is concluded that ketone dianions are very reactive and so useful nucleophilic intermediates.

When **only one kind of base**(e.g. sodium alkoxide) is used for nitrosation of ethyl methyl ketone (**1**) with alkyl nitrite, it is generally well known that only 2-hydroxyimino-3-oxo-butane (**3**) is obtained exclusively.[4] This result is explained by highly thermodynamic stability of monocarbanion,[5] which is prepared by deprotonation from ethyl group.

We investigated nitrosation of the dianions with *tert*-BuONO, in order to obtain regioisomers of oximes. As shown in Chart 1, when **1** was treated with *tert*-BuONO in the presence of **two kinds of bases**, i.e. potassium hydride(KH) and *n*-butyl lithium(*n*-BuLi), (in this case KH was first added, followed by the addition of *n*-BuLi), **3** and 1-hydroxyimino-2-oxo-butane(**4**) were obtained in 13% and 7% yield, respectively. This is the first report of the aldoxime **4** being prepared from the direct nitrosation of **1** with alkyl nitrite.

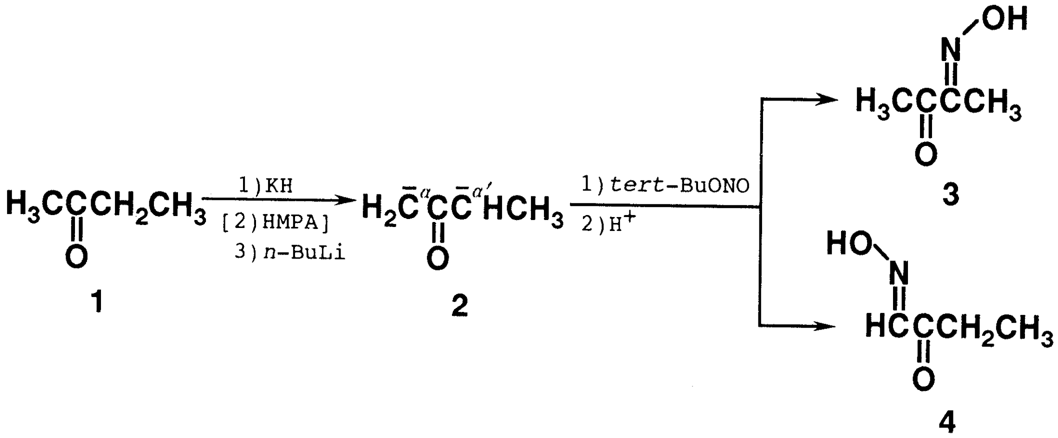

Chart 1

In the case of the reaction of methyl isopropyl ketone(**5**) under the same conditions as described above, acetoxime(**7**) and 1-hydroxyimino-2-oxo-3-methyl-butane(**8**) were obtained in 1.2 % and 0.9% yield, respectively(Chart 2). It is considered that **7** was formed by the cleavage of the bond between carbonyl carbon and α′-carbon(Cα′), after Cα′ was attacked by *tert*-BuONO.

Under these reaction conditions, ketoxime derivatives were always obtained predominantly, i.e., Cα′ was more readily attacked by *tert*-BuONO than α-carbon(Cα).

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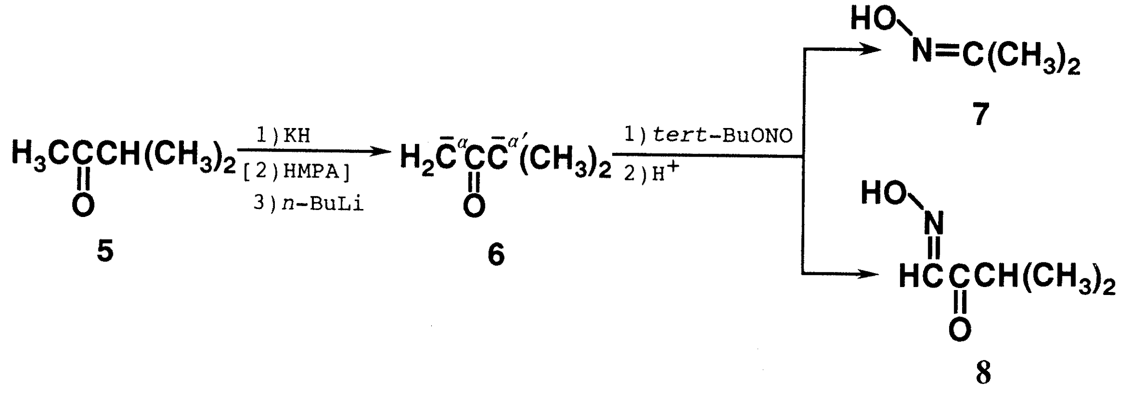

Chart 2

The results of this nitrosation of the dianion from ethyl methyl ketone using two kinds of bases(KH and *n*-BuLi) with *tert*-BuONO was studied using a semiempirical molecular orbital method(AM1 method).[6,7] The experimental result(entry 1) could be reasonably explained in terms of the electron densities of the highest occupied molecular orbital(HOMO) at the α- and α'- position of the dianion, as shown in Fig.1.

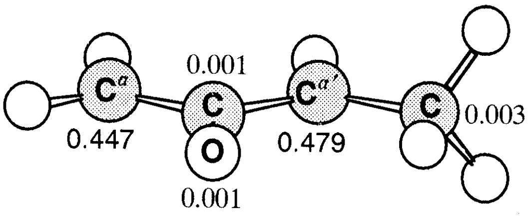

Fig.1. Electron Densities of HOMO of **2**

The ratio of these regioisomers, on the contrary, was remarkably reversed by the addition of HMPA to the reaction mixture, i.e., C^{α} became more reactive than $C^{\alpha'}$ to this nitrosation, as shown in Table I(entries 2, 4).

First, compound **1** or **5** was added to a dry ether solution of 1.3eq of KH at 0°C, followed by the addition of 1.5eq of HMPA. Subsequently, the reaction mixture was treated with 1.5eq of *n*-BuLi at the same temperature. To the resultant ether solution, 2.0eq of *tert*-BuONO was added dropwise with stirring at -78°C. After stirring for 1h at the same temperature, the reaction mixture was poured over ice-water, acidified with H_3PO_4, and the desired hydroxyimino derivatives were obtained.

When HMPA was added to the reaction mixture, it could be considered that the lithium cation was easily solvated by HMPA, and then the electron density on the α-carbon atom increased.[8] This may be the reason why the reactivity of the methyl group is higher than that of the methylene group of the dianions of the ketones in the nitrosation of alkyl methyl ketones in the presence of two kinds of bases by the addition of HMPA . A further study of the influence of HMPA on the nitrosation reaction of ketone derivatives is now in progress.

In addition to the reaction of the dianions of **1** and **5**, the differences in the behavior of some of lithium bases in the nitrosation of the dianions of acetone were also studied(Chart 3). As shown in Table I(entries 5, 6, 7, 8), the yield of 1-hydroxyimino-2-oxo-propane increased as the following order of bases:

PhLi< *n*-BuLi < *sec*-BuLi < *tert*-BuLi

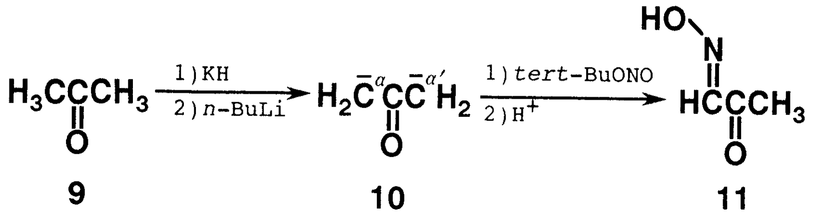

Chart 3

TABLE I. Nitrosation of Alkyl Methyl Ketones with *tert*-BuONO in the Presence of Two Kinds of Bases(KH and R-Li)

Entry	Reactant	R-Li	Additive	Product No.(%) Ketoxime type	Product No.(%) Aldoxime type
1	**1**	*n*-BuLi	—	**3** (13)	**4** (7)
2	**1**	*n*-BuLi	HMPA	**3** (3)	**4** (14)
3	**5**	*n*-BuLi	—	**7** (1.2)	**8** (0.9)
4	**5**	*n*-BuLi	HMPA	**7** (0.4)	**8** (1.2)
5	**9**	*tert*-BuLi	—	—	**11** (24)
6	**9**	*sec*-BuLi	—	—	**11** (22)
7	**9**	*n*-BuLi	—	—	**11** (18)
8	**9**	PhLi	—	—	**11** (12)

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5) Unpublished data: this stability was calculated by the *ab initio* MO method with MP2/6-31G* basis set in our laboratory.

6) The molecular orbital calculations by the AM1 method were performed with the MOPAC93.[7] Geometry optimization of dianion **2** was performed by Eigenvector Following routine(EF) method. In this calculation, coordination of a counter cation to **2** was not considered.

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