Chinese Chemical Letters Vol. 12, No. 9, pp 753– 756, 2001
http://www.imm.ac.cn/journal/ccl.html

Isomerization of 4-Amino-6-tert-butyl-3-methylthio-1, 2, 4-triazin-5 (4*H*)-one with Base

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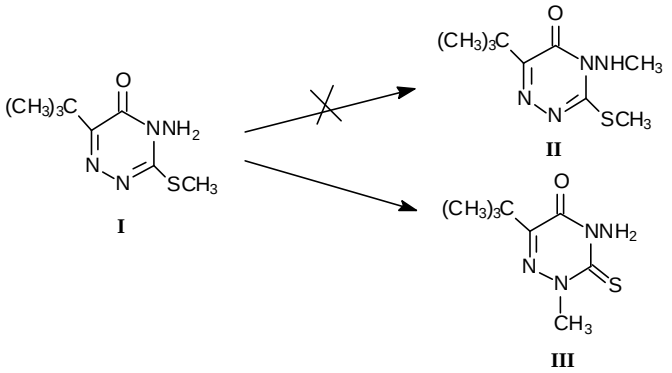
Abstract: Isomerizaton of 4-amino-6-tert-butyl-3-methylthio-1, 2, 4-triazin-5 (4*H*)-one in the presence of base is described. Mechanism of this rearrangement reaction involving four-member ring intermediate formation has been proposed.

Keywords: Isomerization, base, metribuzin.

4-Amino-6-tert-butyl-3-methylthio-1, 2, 4-triazin-5 (4*H*)-one I, named as Metribuzin[1], is an excellent selective herbicide. In the course of studying the reaction of I, we have found an unexpected reaction. We have attempted to prepare 6-tert-butyl-4-methylamino-3-methylthio-1, 2, 4-triazin-5 (4*H*)-one II from I with methyl iodide in the presence of sodium hydroxide in aqueous methanol, surprisingly, instead of II the product III 4-amino-6-tert-butyl-3, 4-dihydro-2-methyl-3-thioxo-1, 2, 4-triazin-5 (2*H*)-one was obtained (**Scheme 1**). III is the isomer of I. In the process of preparing I, Haglid and Wilmington have isolated III as a by-product, but they did not give a reasonable explanation[2,3]. All these prompted us to investigate this reaction further for understanding the mechanism of the isomerization of I.

Scheme 1



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Experimental

All organic solvents and reagents were of analytical grade. All reactions and purification were monitored by TLC (UV detection) (The solvent system: Petroleum ether:acetyl acetate=3:1 by v/v). The ^{1}H NMR spectrum was obtained on a Bruker DPX300 at 300K in $CDCl_3$. MS spectrum was recorded on AEI MS-50 instrument with 70eV electron impact ionization. GC-MS spectrum was gotten on HP6890.

The general procedure of the isomerization of 4-amino-6-tert-butyl-3-methylthio-1, 2, 4-triazin-5 (4*H*)-one I is as follows:

1 g (4.67mmol) of I, 12mL of methanol, and equal mole of sodium hydroxide (molar amount calculated on I) in 8mL distilled water were added into a flask equipped with reflux condenser. The reaction mixture was heated at 50-60°C with stirring for 2 hours, then the methanol was removed under reduced pressure, and the residue was filtered to give a white solid. Recrystallization from distilled water/methanol (4/1 by v/v) gave white crystals: mp 173-176°C; ^{1}H NMR ($CDCl_3$) δ (ppm) 1.42 (s, 9H, $3CH_3$), 4.21 (s, 3H, N-CH_3), 5.35 (s, 2H, NH_2); MS (*m/z*) 214 (M^+), 198 (6.0), 183 (23.3), 182 (100.0), 169 (5.6), 155 (21.2), 128 (20.1), 58 (27.7), 41 (27.2); IR (KBr, cm^{-1}) 3285, 3235, 2940, 1669, 1580, 1562, 1389, 1364, 1081, 1052, 972. The spectral data showed that the product was III 4-amino-6-tert-butyl-3, 4-dihydro-2-methyl-3-thioxo-1, 2, 4-triazin-5 (2*H*)-one.

Results and Discussion

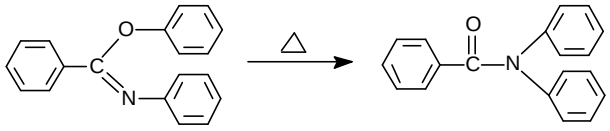
The different alkylating reagents such as methyl bromide, dimethyl sulfate, ethyl bromide, *n*-propyl bromide, *i*-propyl bromide, *n*-propyl iodide, *i*-propyl iodide, *n*-butyl iodide and *t*-butyl bromide, were used for alkylation of I. All reactions were conducted in the solution of 1 g of I and equal mole of sodium hydroxide in 8mL of water and 12mL of methanol at 50-60°C for 2 h. The major product of all these reactions is III. Thus sodium hydroxide may play an important role in the isomerization from I to III, and alkylation reagents are not involved in the reaction.

In order to confirm the role played by sodium hydroxide, I was treated with a variety of excess alkylating reagents (molar amount calculated on I) without sodium hydroxide heated at 50-60°C for 2 h in aqueous methanol, no reaction occurred. I was heated in the same conditions with different molar amount of sodium hydroxide without alkylating reagents, III was obtained in each case. Fartherly it was found when pH>12 (with sodium hydroxide or potassium hydroxide), I could isomerize to III at room temperature and even at -10°C. These results indicate that the action of hydroxide ion is directly involved in the mechanism of the isomerization.

The thermal rearrangement of imino ether is known (see **Scheme 2**)[4,5] and the compound I contains imino thio-ether unit, therefore the thermal changes of I were also tested. I was maintained at 150°C, 180°C, 200°C, 210°C, 220°C, 230°C, 240°C, 250°C

for some time under nitrogen atmosphere. But the isomer III was not detected by GC-MS spectroscopy.

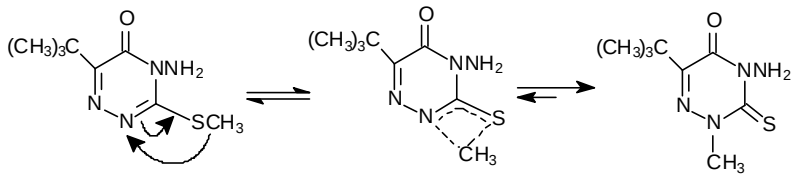
Scheme 2



Conclusions

On the basis of these observations, one can make the conclusion that the reaction does not involve the ionizing process. It is supposed that the reaction consists in the rupture of the bond between the methyl radical and the sulfur atom to form a methyl ion and an ionized residue. If the assumption is correct, when I was treated with various alkylating reagents and base, alkylated products should be gotten. But the result is not so. The fact can readily be explained in terms of a hypothesis of intramocular rearrangement. A detailed mechanism of isomerization can be proposed: the π electrons of N=C double bond and the isolated pairs of electron in the sulfur atom form a large π bond, and CH_3 in the sulfur atom is easy to occur 1, 3-σ migration[6]. When **I** with the action of hydroxide ion, a four-member ring intermediate is formed, and makes the S-CH_3 bond be cleaved and the methyl group has migrated to N atom of this four-member ring, but the function of base in the migration reaction is not clear (see **Scheme 3**).

Scheme 3



I intermediate **III**

Acknowledgments

The authors gratefully acknowledge associate professor Liang Xiaomei for obtain the ^{1}HNMR spectra.

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Received 20 February, 2001