RING CLEAVAGE OF SOME BICYCLIC COMPOUNDS DERIVED FROM 1,2,4- TRIAZINE

*M. Heravi, Majid**
Bakavoli, Mehdi
Sadjadi Hashemi, Zohreh
Department of Chemistry, Faculty of Science, Ferdowsi University of Mashhad, P.O. Box 91735-654, Mashhad, Iran.

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ABSTRACT : *Ring cleavage occured when 1,2,4- triazino-1,2,4- triazines (3), (4) and (5) were treated with concentrated hydrochloric acid to yield N- substituted triazines (7) and (8). These confirm the given configuration assigned to the isomeric triazinotriazines. 6-Methyl-2-phenyl-7H-oxazolo [3,2-b][1,2,4]- triazin-7-one (9) underwent ring cleavage on treatment with sodium alkoxide to afford 3- alkoxy-1,2,4- triazines (10). Treatment of (9) with concentrated hydrochloric acid gave 6-methyl-2- phenacyl-1,2,4- triazin-3,5(4H)-dione (6). Under basic conditions, degradation of (9) occured followed by ring closure of an intermediate to give 1-amino-4-phenylimidazole-2(3H)-one (11).*

KEY WORDS : *Bicyclic compounds derived from 1,2,4- triazine, Ring cleavage.*

INTRODUCTION

Cleavage reactions are of interest because they often lead to compounds which are difficult to synthesize in other ways [1-4], or to interesting transformations into other heterocyclic systems [5-9].

Ring cleavage is very common in pyrimidine ring and bicyclic compounds derived from pyrimidines [10]. Replacement of heterooxygen and sulphur atoms in heterocyclic molecules by various hydrazines are known [11,12] which show that oxazolo [3,2-a] pyrimidine (1;X=O) can be opened and recyclized to give 4H-

* *To whom correspondence should be addressed*
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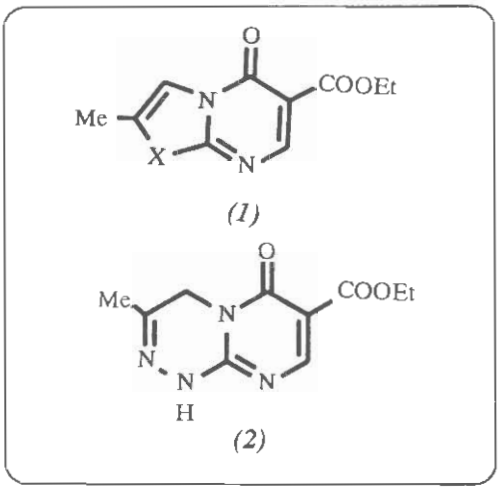
pyrimido [2,1-c][1,2,4] triazin-6(1H)-one *(2)* on reaction with hydrazine hydrate [13]. A few other ring cleavages in oxazolopyrimidine ring have also been reported [14-19].



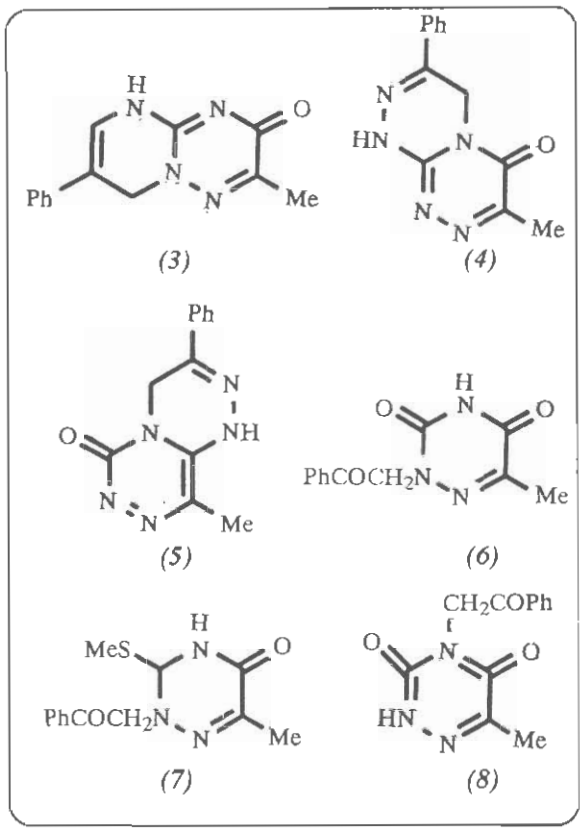
During the syntheses of some bicyclic compounds derived from 1,2,4- triazine, we became interested in ring cleavage of this system. Now we wish to report some of these cleavages and show the usefulness of these cleavages in verification of the given configuration as well as syntheses of some compounds which could not be synthesized by known and feasible procedures.

RESULTS AND DISCUSSION

The synthesis and structural elucidation of three isomeric 1,2,4- triazino-1,2,4- triazine *(3)*, *(4)* and *(5)* have already been reported [20].

Ring cleavage occured when 1,2,4- triazino [4,3-b][1,2,4] triazine *(3)* was refluxed in concentrated hydrochloric acid for a long period of time. The isolated product was identified as 6-methyl-2- phenacyl- 1,2,4- triazin-3,5(2H,4H) dione *(6)* which was synthesized unambiguously by hydrolysis of the methylmercapto group in 6-methyl-3-methylthio-2-phenacyl-1,2,4- triazin-5 (2H)-one*(7)* [21]. Hydrolytic ring cleavage followed by nucleophilic displacement of the hydrazino group can be suggested as the mechanism for the formation of *(6)* (Scheme 1).

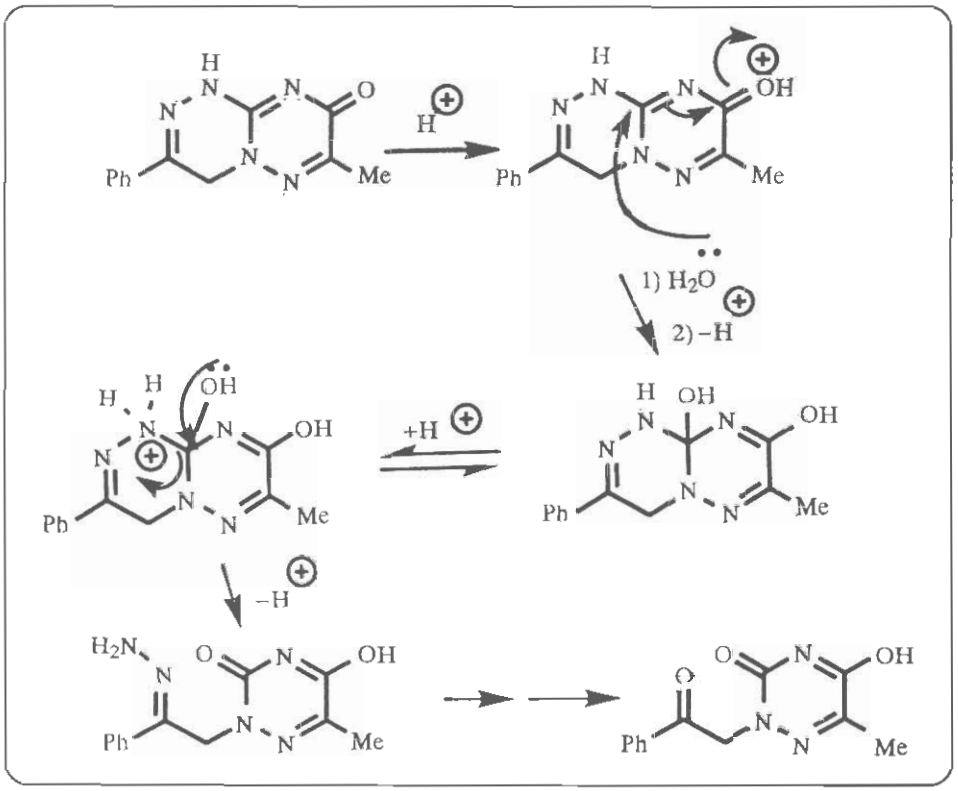
Treatment of 1,2,4- triazino[4,3-c][1,2,4] triazine *(4)* and 1,2,4- triazino [4,3-d][1,2,4] triazine *(5)* [20] with concentrated hydrochloric acid gave the same compound, 6- methyl-4-phenacyl-1,2,4- triazin- 3,5(2H) dione *(8)*. The same mechanism can be suggested for these cleavages.



These ring openings confirm the correct configuration assigned to the triazinotriazines *(3)*, *(4)* and *(5)* [20].

Treatment of *(9)* with concentrated hydrochloric acid gave a compound which was identified to be 6- methyl-2- phenacyl-1,2,4-triazin-3,5(4H)- dione *(6)*. This compound was obtained unambiguously by hydrolysis of 6-methyl-3- methylmercapto-2- phenacyl-1,2,4-triazin-5(4H)-one *(7)* [21].

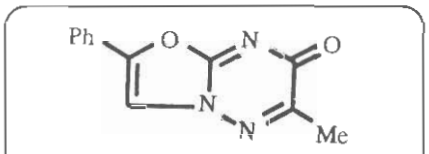
Reaction of 6- methyl-2- phenyl-7H- oxazolo [3,2-b][1,2,4] triazin-7-one *(9)* [21] with sodium alkoxides (RO^-Na^+; R=Me, Et, n- Propyl) afforded 6- methyl-2- phenacyl-3- alkoxy-1,2,4-triazin-5- ones (10; R=Me, Et, n-Propyl). This kind of ring cleavage involves the attack of



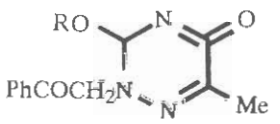
(Scheme 1)

nucleophile at position 8a of *(9)*. The reactivity of the oxazolo ring can be explained on the basis of the electronegativity of the oxygen atom causing electron deficiency at the carbon atom adjacent to it.

Treatment of *(9)* with 20% sodium hydroxide solution gave a crystalline product whose mass spectrum apparently shows M^+ at m/e 159. The ^{1}H-NMR spectrum showed two exchangable protons of an amino group at δ5.15, a singlet for one aromatic proton at δ7.01 and a multiplet for a phenyl group at δ7.4. The compound was soluble in acid and its PKa value was approximately *(11)*. For elucidation of its structure, it was reacted with benzaldehyde as we could assume it carries an amino group. The condensed product showed M^+ at m/e 263 showing that the molecular weight of starting material was 175 (microanalysis $C_9H_9N_3O$). The apparent molecular weight of 159 may have been due to ready loss of NH_2 in the mass spectrometer. Infrared spectrum of the resulting compound showed a sharp band in the carbonyl stretching region and its ^{13}C-NMR spectrum showed a signal which was characteristic for an

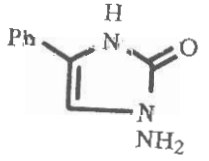


(9)

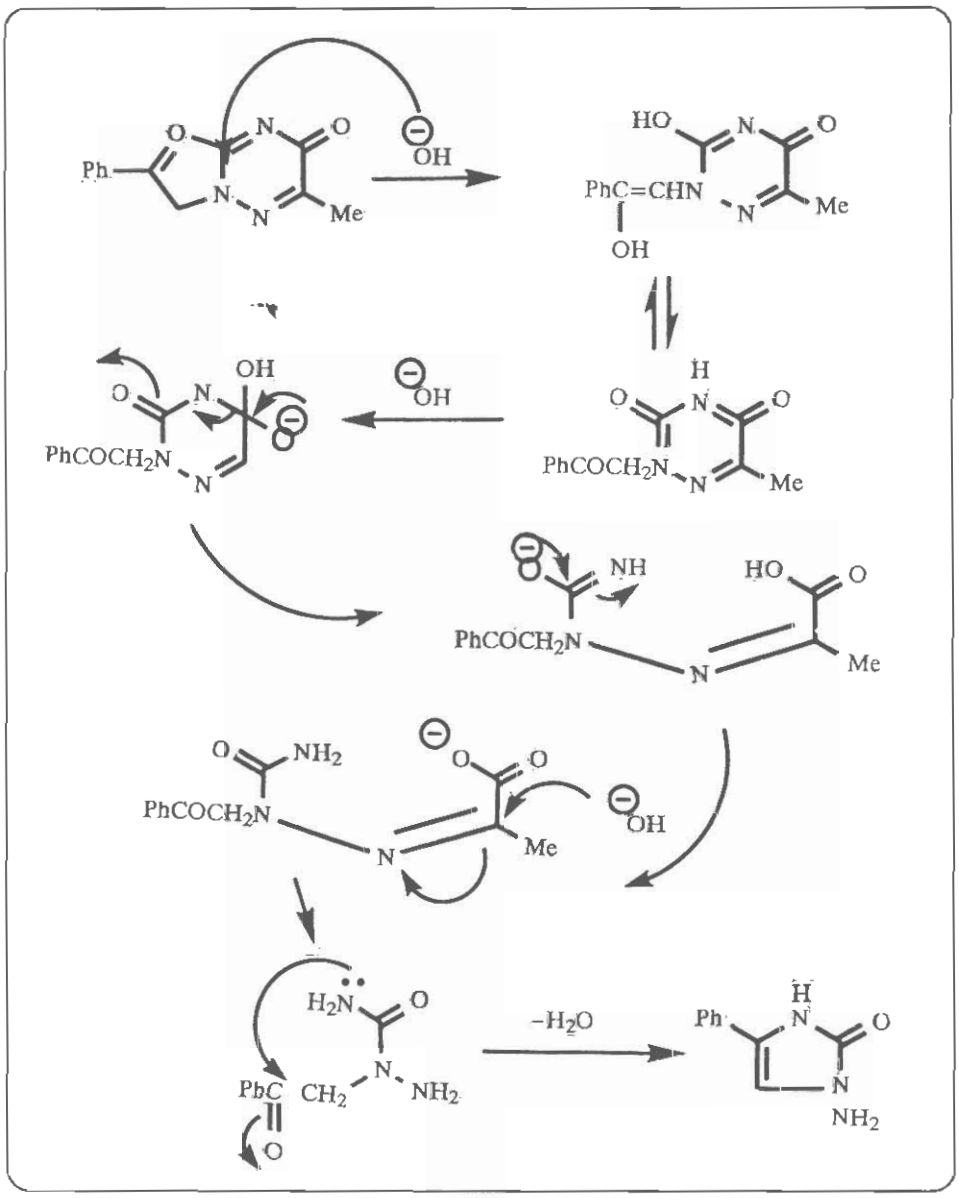


(10)

R=Me, Et, n-Propyl



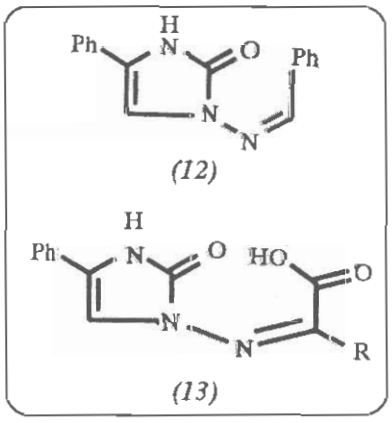
(11)



(Scheme 2)

amide carbonyl group. The above evidence suggest the formation of 1-amino-4- phenyl imidazol- 2(3H)-one *(11)*. The suggested mechanism is depicted in scheme 2.

Compound *(11)* was reacted with benzaldehyde, glyoxalic acid and pyruvic acid to yield the corresponding condensed product *(12)* and (13; R=H or Me). Treatment with polyphosphoric acid and thionyl chloride for cyclization was not successful.



(12)

(13)

EXPERIMENTAL

Melting points were taken on a *Kofler Heizbank Richert* type 7841 (Germany) and are uncorrected.

^{1}H-NMR spectra were measured on a *Perkin Elmer* R32/90 MHz model (England) at normal temperature using tetramethylsilane as a standard. d_6-DMSO was used as solvent for all compounds. Infrared spectra were recorded using the Nujol mull and KBr disk technique on a *Perkin Elmer* 297 double beam spectrometer *Pye Unicam*, SP-1100 (England) and *Schimadzu* 4300 (Japan). Mass spectra were recorded on an AEIMS 9025 and *Finnigan-mat* 8430 GC/mass spectrometer. Microanalysis were performed by Butterworth Laboratories LTD, Teddington, Middlesex England and Research Institute of Petroleum Industry, Ray, Iran.

Treatment of 6-methyl-phenyl- 4H-1,2,4-triazino [4,3-b] [1,2,4] triazin-8 (1H)-one(3) with concentrated hydrochloric acid

The above compound (1g) was refluxed in concentrated hydrochloric acid (20mL) for 48 hrs. The solution was cooled to room temperature and water was added. The solution was left in an ice bath for one more hr. The precipitated solid was filtered off, washed thoroughly with water and dried to yield a single compound which was identified as 6- methyl-2-phenacyl-1,2,4- triazin-3,5 (4H)- dione (0.6g; 59%) m.p. 205-207°C (from ethanol).

^{1}H-NMR [d_6-DMSO] δ2.1 (s, H, Me); 5.41(s, 2H, CH_2); 7.6-8.05(m, 5H, Ph); 12.79(s, 1H*, NH).

MS: m/z 245(M^+). Anal. Calcd. for $C_{12}H_{11}N_3O$, C, 58.77; H, 4.52; N, 17.13; Found, C, 58.24; H, 4.58; N, 17.11.

Treatment of 7- methyl-3- phenyl-4H-1,2,4-triazino [3,4-c][1,2,4] triazin-6 (1H)- one (4) and 9- methyl-3-phenyl-4H- 1,2,4-triazino [4,3-d][1,2,4] triazin-6 (1H) one (5) with concentrated hydrochloric acid

Compounds *(4)* and *(5)* (1g) were refluxed in concentrated hydrochloric acid (20mL) for 72 hrs. The solution was cooled in an ice bath and water (20mL) was added. The precipitated solid was filtered off, washed with water and dried to give the product. This compound was identified as 6- methyl-4- phenacyl-1,2,4- triazin-3,5 (2H)-dione (0.6g; 63%) m.p. 140-141°C (from ethanol).

^{1}H-NMR[d_6-DMSO]δ2.15(s,3H,Me);5.35(s, 2H, CH_2); 7.75 and 8.1(m,5H,Ph); 12.55(s,1H*, NH).

MS: m/z 245(M^+). Anal. Calcd. for $C_{12}H_{11}N_3O_3$, C, 58.77; H, 4.52; N, 17.13; Found, C, 58.65; H, 4.52; N, 17.03.

Treatment of 6- methyl-2- phenyl- 7H-oxazolo [3,2-b][1,2,4] triazin-7-one (9) with concentrated hydrochloric acid

6- Methyl-2- phenyl-7H-oxazolo [3,2-b][1,2,4] triazin-7-one *(9)* (0.5g) was refluxed in concentrated hydrochloric acid for 2 hrs and subsequently chilled in an ice bath for one more hr. The precipitated solid was filtered off, washed with water and dried to yield the product which was identical to 6- methyl-2- phenacyl-1,2,4- triazin- 3,5(2H,4H)-dione (0.25g; 78%).

6-Methyl-2- phenacyl-3- alkoxy-1,2,4-triazin-5- one (2)

General procedure:

To the appropriate amount of alcohol (20mL), sodium (0.23g, 0.01 mole) was added. To this solution 6- methyl-2- phenyl-7H- oxazolo [3,2-b][1,2,4] triazin-5- one *(9)* (2.77g; 0.01mole) was added. The reaction mixture was refluxed for 5 hrs. The solvent was evaporated under reduced pressure. To the crude, water (10mL) was added. The solution was acidified by dilute HCl. The precipitated solid was filtered off, washed with water to get the title compounds. Crystallisation solvents, melting points, yields, alcohols used, ^{1}H-NMR and Mass spectral data are reported in Table 1.

Treatment of 6- methyl-2- phenyl- 7H-oxazolo [3,2-b][1,2,4] triazin-7- one (9) with sodium hydroxide solution

Compound *(1)* (2g) was dissolved in 20%

Table 1: Reaction conditions, products and yields.

Alcohol used	Cryst. solvent	m.p.	Yield	Mass spectrum	^{1}H-NMR
MeOH	$CHCl_3$	228-229	69%	259	2.2(s,3H,Me) 3.4(s,3H,OMe) 5.4(s,2H,CH_2) 7.4-8.0(m,5H,Ph)
EtOH	$CHCl_3$	224-236	44%	273	1.3(t,3H,Me) 2.5(s,3H,Me) 4.4(q,2H,CH_2) 5.5(s,2H,CH_2) 7.5-8.2(m,5H,Ph)
n-PrOH	$CHCl_3$	240-241	49%		0.9-1.2(t,3H,Me) 1.72(m,2H,CH_2) 2.2(s,3H,Me) 3.3-3.7(t,2H,CH_2) 5.6(s,2H,CH_2) 7.4-8.0(m,5H,Ph)

sodium hydroxide solution (20mL). The reaction mixture was refluxed for 1 hr and subsequently chilled in an ice bath. The precipitated solid was filtered off, washed with water and dried to give the product which was identified as 1-amin-4-phenylimidazol-2 (3H)-one (0.7g, 45%), m.p. 235-236°C (from isopropanol).

^{1}H-NMR [d_6-DMSO] δ5.16(s, 2H, NH_2), 7.01(s, 1H*, CH), 7.4(m, 5H, Ph), 14.31(s, 1H, NH).

MS: m/e 158(M^+). Anal. Calcd. for $C_9H_9N_3O$, C, 61.70; H, 5.17; N, 23.98. Found: C, 61.92; H, 5.00; N, 24.04.

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