RING TRANSFORMATION OF OXAZOLO [3,2-b][1,2,4] TRIAZINES

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ABSTRACT : *6- Methyl-2- phenyl-7H- oxazolo [3,2-b] [1,2,4] triazine (1) underwent ring transformation on treatment with ammonia and primary amines to afford the corresponding imidazo [1,2-b] [1,2,4] triazine (2). Treatment of (1) with hydrazine hydrate gave the corresponding 3-aryl-4H-1,2,4- triazino [4,3-b] [1,2,4] triazin-8 (1H)-one (3).*

KEY WORDS : *Oxozolo triazine, Ring transformation, Ring cleavage, Triazino triazine, Imidazo triazine.*

INTRODUCTION :

Ring cleavage and ring transformation of bicyclic fused pyrimidines have been widely studied [1-6]. Ring transformation reactions generally are of interest because they may lead to the other fused heterocyclic systems [7-11] which are otherwise difficult to synthesize.

We have recently described the synthesis of some oxazolo [3,2-b] [1,2,4] triazines *(1)* [12] and became interested in the ring cleavage and ring transformation of this heterocyclic system. We now wish to report the ring transformation and ring expansion of *(1)* to the corresponding imidazo [1,2-b] [1,2,4] triazine (*2*; R_1= Ph; R_2=H, Me or Et) and triazino [4,3-b] [1,2,4]-triazines (*3*; R_1=Ph or -C_6H_4Br).

RESULTS AND DISCUSSION :

Treatment of (*1*; R_1= Ph) with large excess of ammonia in absolute ethanol for a long period of time gave a crystalline compound which was identified as 6- phenyl-2- methyl imidazo [1,2-b] [1,2,4] triazin-3 (4H)-one (*2*; R_1= Ph; R_2=H).

To establish the structure *(2)*, this compound was synthesized unambigously. Therefore, 3-amino-6- methyl- 1,2,4- triazin-5 (2H)-one *(4)* was synthesized via the reaction of amino-guanidine bicarbonate with pyruvic acid and

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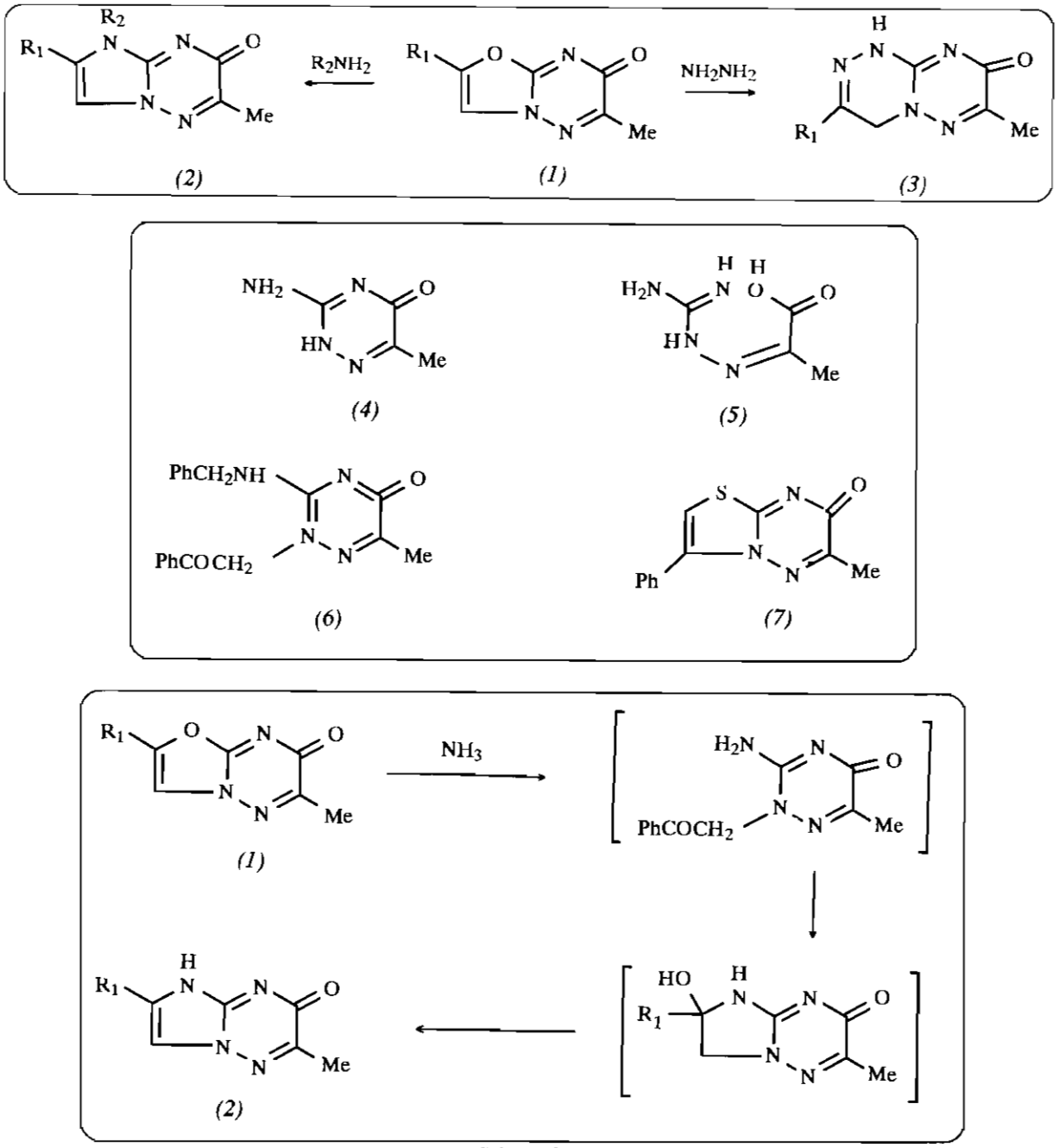
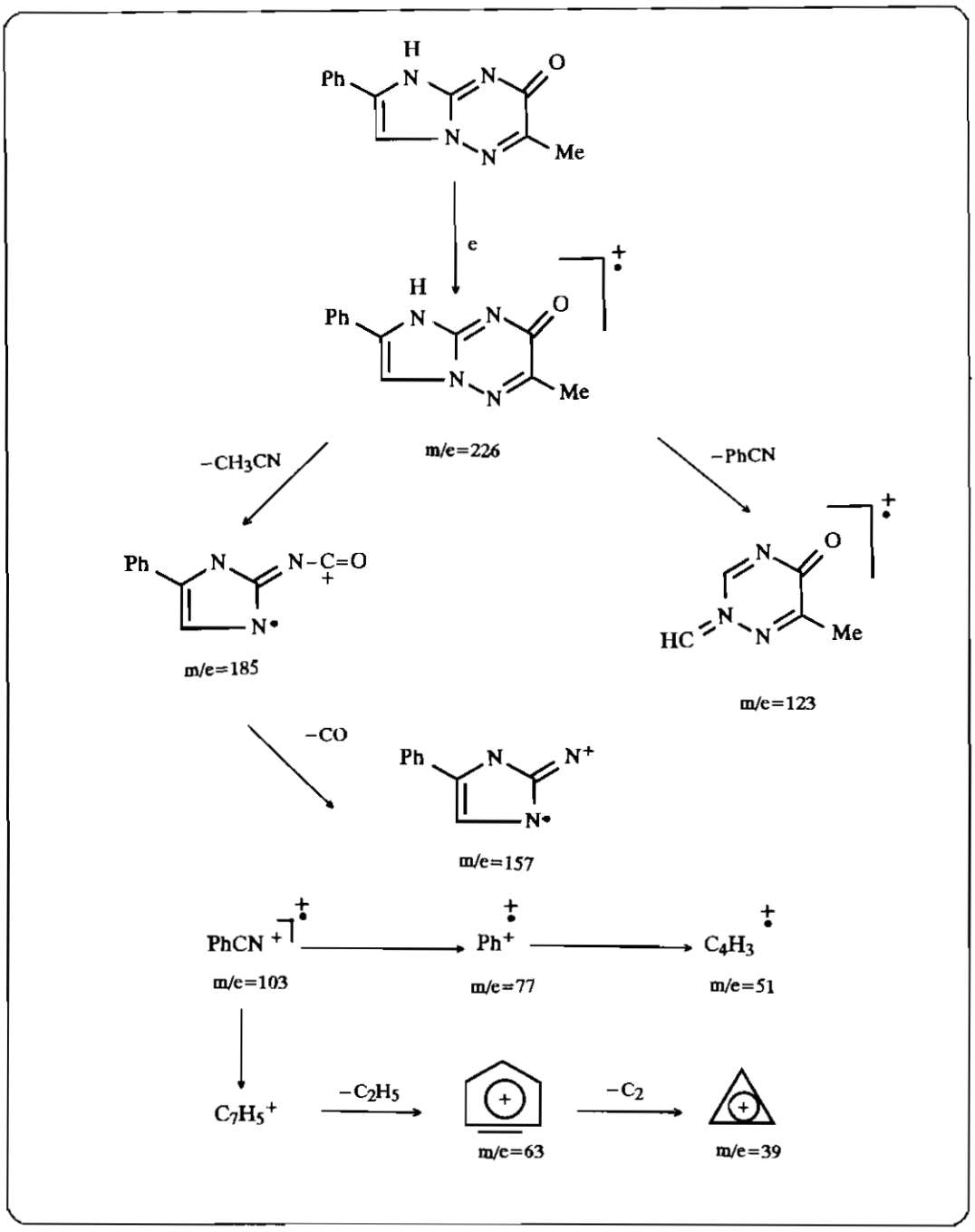


Scheme 1

subsequent cyclization of the corresponding pyruvic acid guanylhydrazone *(5)*. Treatment of *(6)* with phenacyl bromide in the mixture of propan- 2-ol and triethylamine gave a compound identical to (*2*; R_1= Ph; R_2=H).

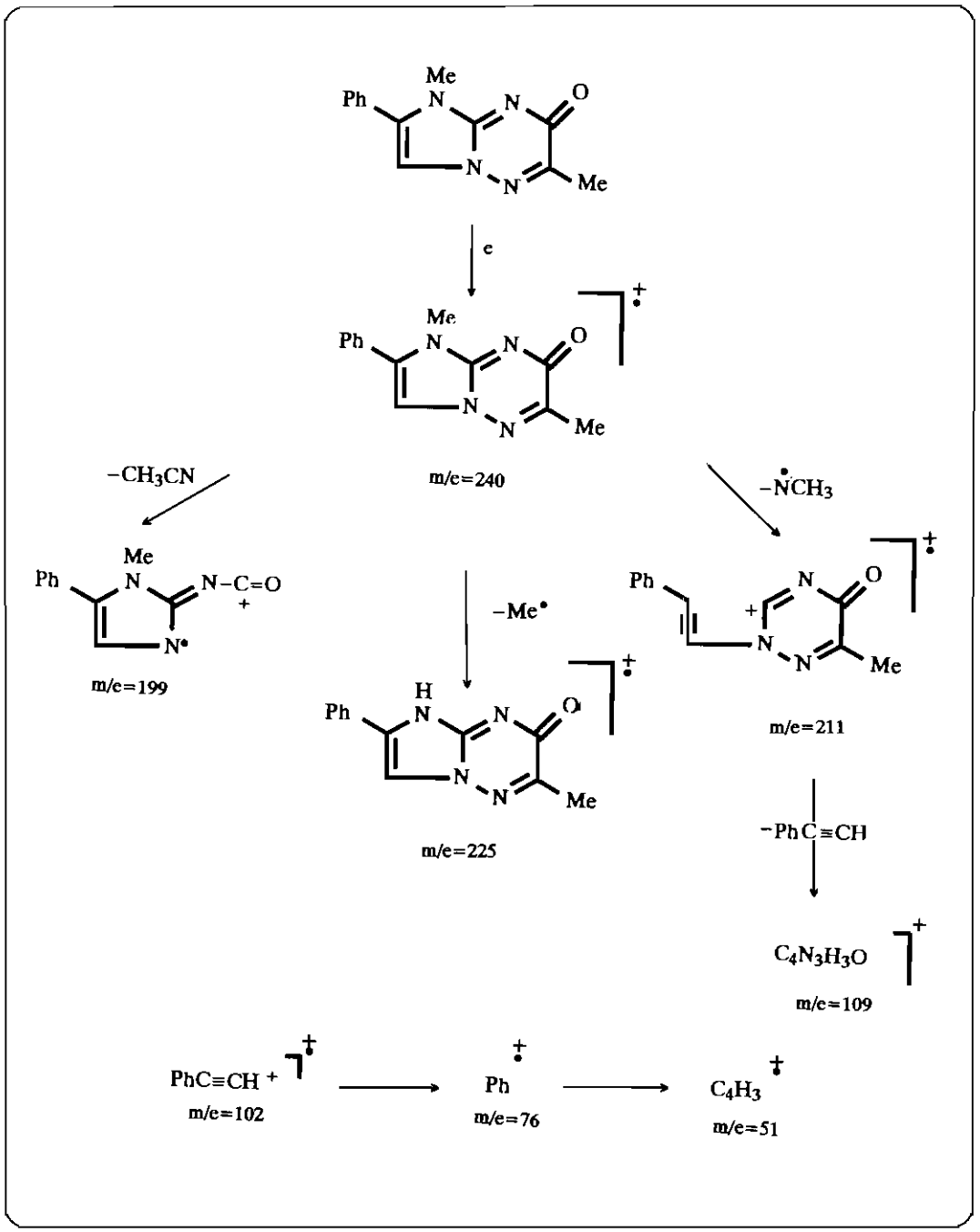
It was concluded that this kind of ring transformation involves the attack of ammonia as a nucleophile at either position 2 or more likely position (8a) of the oxazolo [3,2-b] [1,2,4] triazine (1; R_1=Ph). The attack leads to the opening of the oxazolo ring followed by cyclization and loss of water (Scheme 1).

When methylamine and ethylamine were used instead of ammonia, N- substituted imidazo [1,2-b] [1,2,4] triazines (*2*; R_1=Ph; R_2=Me or Et) were obtained, but with aniline, the starting material was recovered, showing that aniline is not nucleophilic enough to attack. However,



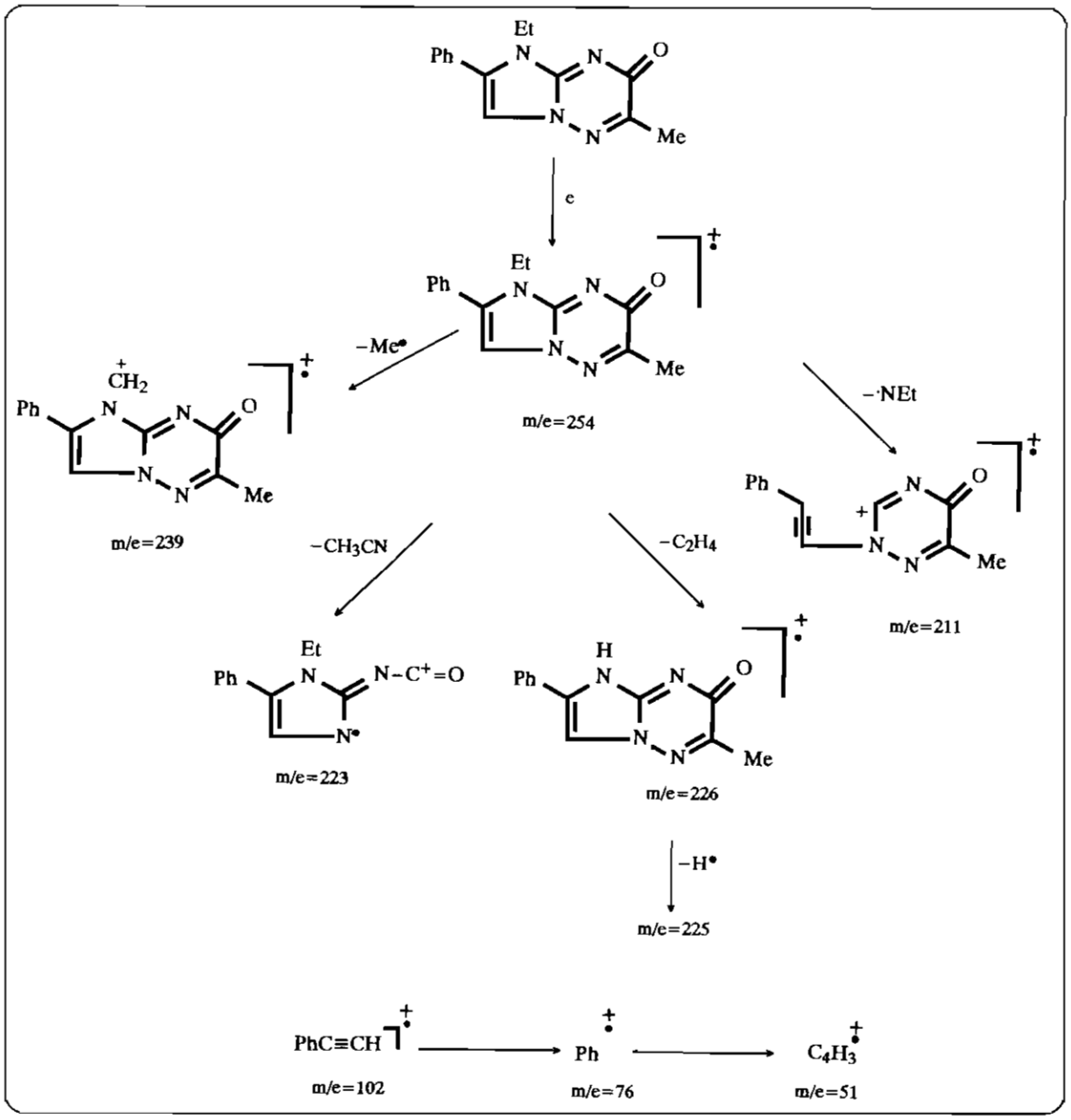
Scheme 2

benzylamine reacted with *(1)* but the product was identified to be 3- benzylamino-2- phenacyl-6- methyl-1,2,4- triazin-5- one *(6)*. Compound *(6)* was insoluble in ordinary solvents for NMR work. However mass spectral fragmentation pattern of this compound might confirm the structure. The suggested mass spectral pattern of (*2*; R_1=Ph, R_2=H, Me, Et) and *(6)* are shown in schemes 2,3,4 and 5 respectively. Probably benzylamine is nucleophilic enough to start attacking and bringing about the cleavage process but too bulky to carry on and afford the cyclized product. However, this result can confirm the suggested mechanism (Scheme 1).



Scheme 3

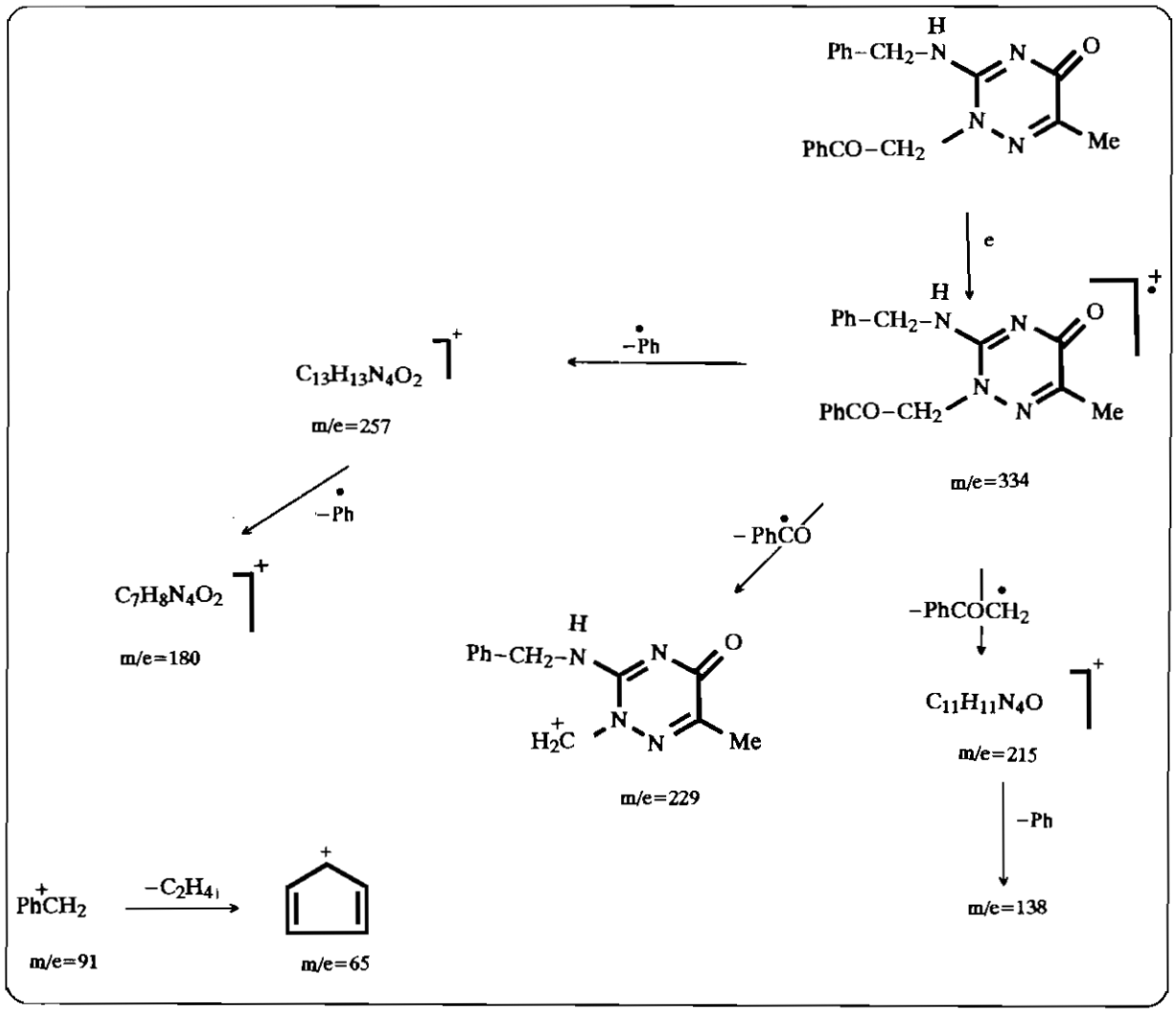
Treatment of (*1*; R_1=Ph or -C_6H_4Br) with a large excess of hydrazine hydrate in DMF gave derivatives which were identified as 1,2,4-triazino [4,3-b] [1,2,4] triazines (*3*; R_1=Ph or -C_6H_4Br), one of which had already been prepared by a different route [13]. It was also observed that the ring transformation could not be brought about by treating the thiazolo [3,2-b] [1,2,4] triazine *(7)* [14] with ammonia, primary amines and hydrazine hydrate. The greater reactivity of the oxazolo analogue can be explained on the basis of the greater electronegativity of the oxygen atom causing a greater electron deficiency at the carbon adjacent to it.



Scheme 4

EXPERIMENTAL :

Melting points were taken on a *Kofler Hazbank Richert* type 7841 and are uncorrected. ^{1}H-NMR spectra were measured on a *Perkin-Elmer* R 32/90 MHz model and a *Varian* T-60A/60 MHz spectrometer at normal temperature, using tetramethylsilane as internal standard. DMSO d_6 was used as solvent for all compounds. Infrared spectra were recorded on a *Pye Unicam*, SP-1100 and *Schimadzu* 4300 using the nujol mull and KBr disc techniques. Mass spectra were recorded on an AEI MS 902S and Finigan-mate 8430 GC mass spectrometer. Microanalysis were performed by Butterworth Laboratories, Ltd., Teddington, Middelsex, England and Research Institute of Petroleum industry, Ray, Iran.



Scheme 5

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

The compound *(1)* (2.27g, 0.01mol) was suspended in ethanol (50mL). To this slurry, concentrated ammonia (20mL) was added and the reaction mixture was refluxed for 22hrs. During the reflux, ammonia (1mL) was added to the flask during an interaval of 1 hr. The solution was evaporated off to dryness. The solid was crystallized from dioxane to give the (*2*; R_1= Ph; R_2= H) (0.85g, 38%), m.p. above 260°C; ^{1}H-NMR [DMSO d_6], δ(ppm) 2.5 (s, 3H, Me), 3.4(s, 1H, NH), 7.3-7.7 (m, 5H, Ph), 8.0 (s, 1H, CH). M^+(MS) m/z 226. 226M^+(5), 185(6), 183(42), 169(10), 157(20), 142(30), 123(42), 103(100), 95(58), 89(70), 77(86), 63(64), 51(44).

3- Amino-6- methyl-1,2,4- triazin-5 (2H)-one (4)

To the solution prepared from amino-guanidine bicarbonate (13.5g), concentrated hydrochloric acid (30mL), water (70mL) and pyruvic acid (8.8g, 0.1mol) were added. The reaction mixture was boiled for few minutes. To this solution 30% sodium hydroxide was added and then cooled to room temperature. The solid

was filtered off and crystallised from ethanol (4.8g, 38%), m.p. 223°C, ^{1}H-NMR [DMSO d_6] δ(ppm) 1.9 (s, 3H, Me), 3.7(s, 2H, NH_2), 13.3 (s, 1H, NH).

2- Methyl-6- phenyl- 5H- imidazo [1,2-b] [1,2,4] triazin-3-one (2; R_1=Ph; R_2=H)

The compound *(4)* (1.25g, 0.01mol) was dissolved in a mixture of ethanol (25mL) and triethylamine (5mL). To this solution phenacyl bromide (2g; 0.01mol) was added and the reaction mixture was refluxed for 8 hrs. The solvent was evaporated off. To the residue, water (10mL) was added. The solid was filtered off and crystallised from dioxane (1.43g, 63%) m.p. above 260°C. This compound was identical to the product of ring transformation.

2,5- Dimethyl-6- phenylimidazo [1,2-b] [1,2,4] triazin-3-one (2; R_1=Ph; R_2= Me)

The compound *(1)* (2.27g, 0.01mol) was suspended in ethanol (50mL). To this solution 33% methylamine (20mL) was added. The reaction mixture was refluxed for 30 hrs. Methylamine (0.5mL) was added to the reaction mixture every 1/2 hr. The solvent was evaporated off. The solid was crystallised from dioxane (0.97g, 40%), m.p. above 260°C, ^{1}H-NMR [DMSO d_6] δ(ppm) 2.21 (s, 3H, Me), 3.2 (s, 3H, Me), 7.3-7.6 (m, 5H, Ph), 7.9 (s, 1H, CH). M^+ (mass spectrum) m/z 240. 240 M^+(100), 225(24), 211(34), 199(42), 171(18), 157(24), 109(56), 162(56), 81(30), 7(53), 51(18).

2- Methyl-5- ethyl-6- phenylimidazo [1,2-b] [1,2,4] triazin-3- one (2; R_1=Ph; R_2=Et)

This compound was synthesized according to the above procedure except that ethylamine was used instead of methyl amine (1.21g, 40%), m.p. above 260°C from dioxane. ^{1}H-NMR [DMSO d_6] δ(ppm) 1.1 (t, 3H, Me), 2.21(s, 3H, Me), 3.4 (q, 2H, CH_2), 7.1-7.5(m, 5H, Ph), 7.9 (s, 1H, CH). M^+(MS) m/z 254. 254 M^+(38), 244(32), 226(12), 218(32), 182(24), 154(10), 123(32), 105(100), 77(44), 51(66).

Treatment of (1; R_1=Ph) with benzylamine

The compound (*1*; R_1=Ph) (2.27g, 0.01mol) was suspended in benzene (50mL). To this mixture, benzylamine (1.07g; 0.1mol) was added. The reaction mixture was refluxed for 12 hrs. and then cooled to room temperature. The white needles were filtered off to afford *(9)* (1.8g, 53.9%), m.p. 241-242°C. The compound was not soluble in ordinary deutrated solvent for NMR work. M^+(MS) m/z 334. 334M^+ (18), 293(22), 257(22), 243(26), 215(18), 187(32), 150(44), 91(100), 55(50).

Treatment of (1; R_1=Ph or -C_6H_4Br) with hydrazine hydrate

The compound (*1*; R_1=Ph or -C_6H_4Br) (0.5g) was dissolved in DMF (15mL) and hydrazine hydrate (6mL) was added. The reaction mixture was refluxed for 12 hrs, then cooled to room temperature. The solution was poured into water (10mL) and the yellow crystalline product was filtered off, and recrystallised from DMF to give the products (*3*; R_1=Ph) (0.3g, 56%), m.p. 284-285°C (decomp). ^{1}H-NMR [DMSO d_6] δ(ppm) 2.14 (s, 3H, Me), 5.06 (s, 2H, CH_2), 7.6 (m, 5H, Ph), 13.62 (s, 1H, NH); Anal. Calcd. for $C_{12}H_{11}N_3O$: C, 59.74; H, 4.95; N, 29.03. Found: C, 59.7; H, 4.73; N, 29.14.

(*3*; R_1=C_6H_4Br) (0.4g, 76%), m.p. 296-297°C; ^{1}H-NMR [DMSO d_6] δ(ppm) 2.12 (s, 3H, Me), 5.05 (s, 2H, CH_2), 7.69 (s, 4H, C_6H_4), 13.57 (s, 1H, NH). Anal. Calcd. for $C_{12}H_{10}N_5OBr$: C, 45.02; H, 3.5; N, 21.87. Found: C, 45.08; H, 3.41; N, 21.62.

REFERENCES :

[1] Clark, J., Gelling, I., Southon, I.W., and Morton, M.S., *J. Chem. Soc.,* (c) 494 (1970).

[2] Clark, J., and Morton, M.S., *J. Chem. Soc., Perkin Trans I,* 1812 (1974).

[3] Clark, J., *Lect. Heterocyclic Chem.,* **3,** 7992 (1976).

[4] Helzheim, A., and Pusch, H., *Chemica (Switz.),* **1969,** 303 (1969).

[5] Brown, J., and Humn, E., *J. Chem. Soc.,* (c),

1515 (1970).

[6] Plas, H.C., and Jongesan, H.C., *Rec. Traw. Chim.*, **87**, 1065 (1968).

[7] Van Meeteren, H.W., and Vander Plas, H.C., *Tetraherdon lett.*, 4517 (1966).

[8] Vander Plas, H.C., Hasse, B., Zuurdeeg, B., and Vollering, M.C., *Rec. Traw. Chim.*, **85**, 1011 (1966).

[9] Vander Plas, H.C., Jongesen, H., Guretsen, G., and Vollering, M.C., *Rec. Traw. Chim.*, **90**, 1246 (1971).

[10] Taoufic, J., Couqueletm, J.D., Couquelet, J.M., and Carpy, *J. Heterocyclic Chem.*, **21**, 305 (1984).

[11] Heravi, M.M., and Bakavoli, M., *J. Sci. I. R. Iran*, **2**, 361 (1990).

[12] Heravi, M.M., and Bakavoli, M., *J. Sci. I. R. Iran*, **(3,4)**, 107 (1992).

[13] Heravi, M.M., and Bakavoli, M., *J. Research in Sci. and Tech.*, **28** (1992).