CONDENSATION OF N^1-TOSYLAMIDRAZONES WITH OXALYL DICHLORIDE AND DICHLOROPHOSPHORUS DERIVATIVES

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Abstract: A series of news 1,2,4-triazin-5,6-diones 2 and 1,2,4,3-triazaphospholines-3-oxides derivatives 3 have been synthesized. The products 2 and 3 were characterized by IR, ^1H, ^{13}C, and ^{31}P NMR and elemental analysis.

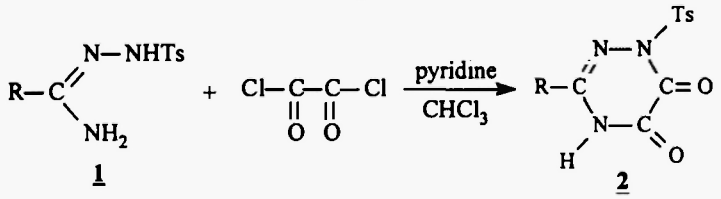
Introduction

Triazinones play a vital role in biological systems and industry. In fact, a large number of these compounds are known as pharmaceutical agents, herbicides and insecticides (1-6).
Owing to their pharmacoligical and biological properties heterocycles containing phosphorus are widely studied compounds. Some examples of their most important effects include herbicidal, insecticidal, antibacterial, antifungul and anticancer activities (7-14).
In continuation of our research directed towards the study on the reactivity of monosubstitued N^1-tosylamidrazones 1 and their use as versatile synthons in organic synthesis (15,16), we report here, the synthesis of 1,2,4-triazin-5,6-diones 2 and 1,2,4,3-triazaphospholines-3-oxides derivatives 3.

Results and Discussion

Action of oxalyl chloride on compounds 1

The required N^1-tosylamidrazones 1 was prepared as previously described (16). The latter compound underwent cyclisation when treated with oxalyl dichloride.
In fact, the addition, in cool conditions and within anhydrous chloroform of equimolar amounts of oxalyl dichloride to N^1-tosylamidrazones 1 in the presence of two equivalent molars of pyridine produces the corresponding 1,2,4-triazin-5,6-diones 2.
The reaction pathway proceed via a double nucleophilic attack of the hydrazinic nitrogen and the amino group on the two carbonyl centres (Schema 1).
The hydrazinic nitrogen of N^1-tosylamidrazones 1 has a very encumbered tosyl group, whereas the amino group is simple. It would seem reasonable that the first step in the reaction would involve the attack of the NH_2 group.



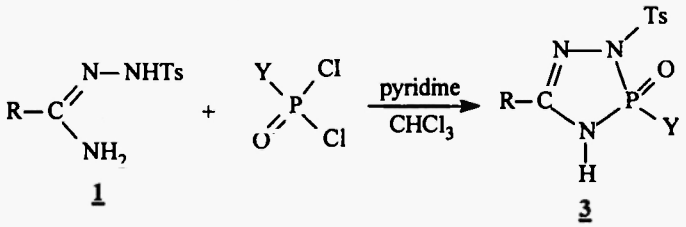
2a: R=Ph
2b: R=Ph-CH_2
2d: R=p-CH_3-C_6H_4
2e: R=p-Cl-C_6H_4-CH_2

Scheme-1

The structures compounds described herein were confirmed by IR, ^1H and ^{13}C NMR spectra. IR spectra show an intense bande at 1740cm^{-1} corresponding to the two C=O group, whereas C=N stretching appears in the region of 1650 cm^{-1}. We can also observe a bande towards 3300cm^{-1} due to the vibration of the NH group. ^1H NMR spectra of these compounds in DMSO show essentially the presence of a singlet characteristic of the NH group. ^{13}C NMR spectra exhibit three characteristic signals for the C=O and C=N moieties at about 146, 152 and 155 ppm.

Action of dichlorophosphorus derivatives on the compounds 1

The appropriate dichlorophosphorus derivatives, such as phenylphosphonic dichloride and phosphoryl trichloride have an electrophilic center which is attached to nucleofuge groupings. They react with N^1-tosylamidrazones **1**. The latter react with their two electrophilic sites 1,4 to yielding the corresponding 1,2,4,3-triazaphospholine-3-oxides 3 derivatives (Schema 2).



3a: R=Ph, Y=Ph
3b: R=Ph-CH_2, Y=Ph
3c: R=iPr, Y=Ph
3d: R=p-CH_3-C_6H_4, Y=Ph
3e: R=Ph, Y=Cl
3f: R=iPr, Y=Cl

SCHEME 2

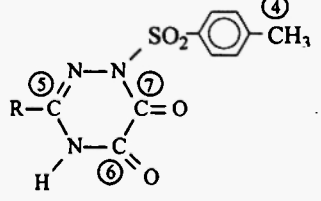
The structures assigned to compounds **3** were substantiated by their spectral data. Their IR spectra showed a band in the region 1100-1200 cm^{-1} characteristic of vP–O. The transformation of *N'*-tosylamidrazones **1** to 1,2,4,3-triazaphospholine-3-oxides **3** is confirmed with the ^{31}P NMR by the presence of signal in the range 13 ppm for compounds **3a-d** ,–o,4 ppm for compound **3e** and –0,7 ppm for compound **3f**. (Scheme-2)

Experimental Part

- 1 R: Spectra IR were determined for KBr on a JASCO FT-IR-420 spectrometer whose precision is of 2 cm^{-1} covering field 400 - 4000cm^{-1}.
- NMR: The spectra of NMR ^{1}H, NMR ^{13}C and ^{31}P NMR were recorded in solution in DMSO-d_6 on a spectrometer BRUKER (^{1}H at 300 MHz, ^{13}C at 75 MHz, ^{31}P at 121 MHz). All chemical shifts are given in δ units and refer to the center of the signal using tetramethylsilane (TMS) as internal standard for the ^{1}H and ^{13}C NMR and H_3PO_4 85% for ^{31}P NMR spectra as an external standard. The multiplicities of the signals are indicated by the following abbreviations: s:singulet, d:doublet , m: multiplet and the constants of coupling are expressed in Hz.
- Melting point: The melting points were determined in Electrothermal 9100 apparatus and are not corrected.
- The reactions were monitored by thin layer chromatography (TLC) using aluminium sheets with silica gel 60 F_{254} Merk.
- the N^1-tosylamidrazones have been prepared following the similar method to that presented in the literature (17).

Synthesis of 1,2,4-triazin-5,6-diones 2

For a solution of 0.01 mol of *N'*-tosylamidrazone **1** and 0.02 mol of pyridine within 40 ml of anhydrous chloroform, stirred magnetically in ice-cold water, we add drop by drop a solution of 0.01 mol of oxalyl dichloride within 20ml of anhydrous chloroform. Once the mixing is completed, we stir the mixture for 4 hours (TLC using chloroform as an eluant). Then we wash the mixture three times successively with 20 ml of distillated water, and we evaporate the solvent. The resulting compound **2** precipitates soon after the addition of diethyl ether. Finally, these compounds are purified by crystallization from methanol.



R= C_6H_5–; C_6H_5–CH_2–; p CH_3–C_6H_4–; p Cl–C_6H_4–CH_2–

2a : Yield : 85%, m.p = 260 °C. [methanol].
IR (cm $^{-1}$): $\nu_{C=N}$ = 1621, $\nu_{C=O}$ = 1715, ν_{N-H} = 3260.
^{1}H NMR (DMSO-d_6): δ (ppm): 2.40 (s, 3H), 7.46–7.52 (m, 10 H).
^{13}C NMR (DMSO-d_6): δ (ppm): C_4 21,7, C_{arom} 127.5–141.4, C_5 146.5, C_6 152.7, C_7 155.9.
Elemental Analysis for $C_{16}H_{13}N_3SO_4$: Calculated: %C 55.98, %H 3.79, %N 12.24, %S 9.33.
Found: %C 55.90, %H 3.69, %N 12.11, %S 9.31

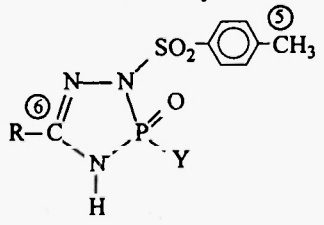
2b : Yield : 82%, m.p = 188 °C. [methanol].
IR (cm $^{-1}$): $\nu_{C=N}$ = 1651, $\nu_{C=O}$ = 1748, ν_{N-H} = 3277.
^{1}H NMR (DMSO-d_6): δ (ppm): 2.42 (s, 3H), 3.71 (s, 3H), 7.23–7.90 (m, 10 H).
^{13}C NMR (DMSO-d_6): δ (ppm): C_1 37,9, C_4 21,5, C_{arom} 125.8–143.6, C_5 146.2, C_6 152.6, C_7 155.3.
Elemental Analysis for $C_{17}H_{15}N_3SO_4$: Calculated: %C 57.15, %H 4.20, %N 11.76, %S 8.97.
Found: %C 57.16, %H 4.22, %N 11.69, %S 8.91

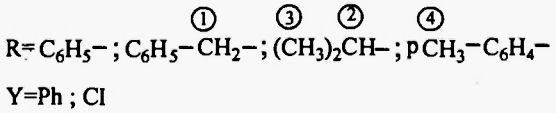
2d :Yield : 80%, m.p = 226 °C. [methanol].
IR (cm $^{-1}$): $\nu_{C=N}$ = 1613, $\nu_{C=O}$ = 1724 , ν_{N-H} = 3290.
^{1}H NMR (DMSO-d_6): δ (ppm): 2.36 (s, 3H), 2.41 (s, 3H), 7.31–7.96 (m, 9H).
^{13}C NMR (DMSO-d_6): δ (ppm): C_2 21.1, C_4 21.5, C_{arom} 125.8–142.7, C_5 146.3, C_6 152.5, C_7 155.7.
Elemental Analysis for $C_{17}H_{15}N_3SO_4$: Calculated: %C 57.15, %H 4.20, %N 11.76, %S 8.97.
Found: %C 57.20, %H 4.23, %N 11.71, %S 8.93

2e : Yield : 74%, m.p = 166 °C. [methanol].
IR (cm $^{-1}$): $\nu_{C=N}$ = 1655, $\nu_{C=O}$ = 1749, ν_{N-H} = 3283.
^{1}H NMR (DMSO-d_6): δ (ppm): 2.51 (s, 3H), 3.62 (s, 2H), 7.35–7.95 (m, 9H).
^{13}C NMR (DMSO-d_6): δ (ppm): C_3 37.7, C_4 22.1, C_{arom} 129.0–143.5, C_5 146.8, C_6 153.2, C_7 155.9.
Elemental Analysis for $C_{17}H_{14}N_3SO_4Cl$: Calculated: %C 52.11, %H 3.58, %N 10.72, %S 8.18, %Cl 9.06.
Found: %C 52.23, %H 3.51, %N 10.71, %S 8.21, %Cl 8.96.

Synthesis OF 1,2,4,3-triazaphospholine-3-oxide derivatives 3

To a stirred solution of *N'*-tosylamidrazone (0.01 mol) and pyridine (0.02 mol) in anhydrous chloroform (20 mL) was added dropwise phenylphosphonic dichloride (0.01 mol) or phosphoryl chloride (0.012 mol) in chloroform. Once the addition was complete, the solution was heated in case of phenylphosphonic dichloride. With phosphoryl chloride, we stir the mixture for 4 hours at room temperature. Then we wash the mixture three times successively with 20 ml of distillated water, and we evaporate the solvent. The resulting compound 3 precipitates soon after the addition of diethyl ether. Finally, these compounds are purified by crystallization from ethanol.





3a : Yield : 90%, m.p = 140 °C. [ethanol].
IR (cm $^{-1}$): $\nu_{P=O}$ = 1169, $\nu_{C=N}$ = 1602, ν_{N-H} : 3117.
^{31}P NMR (DMSO-d_6): δ (ppm): 13.7.
^{1}H NMR (DMSO-d_6): δ (ppm): 2.36 (s, 3H), 7.15–7.80 (m, 15H).
^{13}C NMR (DMSO-d_6): δ (ppm): C_5 21.7, C_{arom} 127.8–131.5, C_6 144.1.
Elemental Analysis for $C_{20}H_{18}N_3SO_3P$: Calculated: %C 58.40, %H 4.38, %N 10.21, %S 7.79, %P 7.53.
Found: %C 58.33, %H 4.31, %N 10.23, %S 7.66, %P 7.60.

3b:Yield : 90%, m.p=126 °C. [ethanol].
IR (cm $^{-1}$): $\nu_{P=O}$ = 1169 , $\nu_{C=N}$ = 1620, ν_{N-H} = 3125.
^{31}P NMR (DMSO-d_6): δ (ppm): 13.9.
^{1}H NMR (DMSO-d_6): δ (ppm): 2.39 (s, 3H), 3.68 (s, 2H), 7.10–7.57 (m, 15H).
^{13}C NMR (DMSO-d_6): δ (ppm): C_1 36.0, C_5 21.6, C_{arom} 126.0–145.3, C_6 144.8.
Elemental Analysis for $C_{21}H_{20}N_3SO_3P$: Calculated: %C 59.30, %H 4.71, %N 9.88, %S 7.53.

Found: %C 59.31, %H 4.76, %N 9.80, %S 7.62.

3c : Yield : 90%,.m.p= 136°C. [ethanol].
IR (cm^{-1}): $\nu_{P=O}$ = 1160 , $\nu_{C=N}$ = 1633, ν_{N-H} = 3120.
^{31}P NMR (DMSO-d_6): δ (ppm): 13.5.
^{1}H NMR (DMSO-d_6): δ (ppm): 1.07 (d, 6H, $^{3}J_{HH}$=6.9), 2.37 (s, 3H), 2.85 (m, 1H), 7.4–7.72 (m, 9H), 9.20 (s, 1H).
^{13}C NMR (DMSO-d_6): δ (ppm): C_2 30.1, C_3 19.5, C_5 21.6,C_{arom} 126.0–134.9, C_6 144.8.
Elemental Analysis for $C_{17}H_{20}N_3SO_3P$: Calculated: %C 54.11, %H 5.31, %N 11.13, %S 8.49.
Found: %C 54.21, %H 5.36, %N 11.20, %S 8.53.

3d : Yield : 90%, m.p = 144 °C. [ethanol].
IR (cm^{-1}): $\nu_{P=O}$ = 1171, $\nu_{C=N}$ = 1605, ν_{N-H} = 3111.
^{31}P NMR (DMSO-d_6): δ (ppm): 13.8.
^{1}H NMR (DMSO-d_6): δ (ppm): 2.27 (s, 3H), 2.33 (s, 3H), 7.11–7.80 (m, 14H).
^{13}C NMR (DMSO-d_6): δ (ppm): C_4 21.6, C_5 21.6, C_{arom} 126.0–135.6, C_6 144.3.
Elemental Analysis for $C_{21}H_{20}N_3SO_3P$: Calculated: %C 59.30, %H 4.71, %N 9.88, %S 7.53.
Found: %C 59.32, %H 4.70, %N 9.81, %S 7.61.

3e : Yield : 90%, m.p = 202°C. [ethanol].
IR (cm^{-1}): $\nu_{P=O}$ = 1157, $\nu_{C=N}$ = 1601, ν_{N-H} = 3115.
^{31}P NMR (DMSO-d_6): δ (ppm): -0,4.
^{1}H NMR (DMSO-d_6): δ (ppm): 2.36 (s, 3H), 6.8 (s, 1H), 7.34–7.78 (m, 9H),
^{13}C NMR (DMSO-d_6): δ (ppm): C_5 21.3, C_{arom} 126.8–136.6, C_6 143.3.
Elemental Analysis for $C_{14}H_{13}N_3SO_3PCl$: Calculated: %C 45.47, %H 3.52, %N 11.36, %S 8.67, %Cl 9.60.
Found: %C 45.54, %H 3.61, %N 11.42, %S 8.71, %Cl 9.70.

3f : Yield : 90%, m.p = 158°C. [ethanol].
IR (cm^{-1}): $\nu_{P=O}$ = 1171, $\nu_{C=N}$ = 1602 , ν_{N-H} = 3100.
^{31}P NMR (DMSO-d_6): δ (ppm): -0,7.
^{1}H NMR (DMSO-d_6): δ (ppm): 1.12 (d, 6H, $^{3}J_{HH}$=6.9), 2.39 (s, 3H), 2.72 (m, 1H), 7.45-7.94(d, 5H).
^{13}C NMR (DMSO-d_6): δ (ppm): C_2 30.6, C_3 19.4, C_5 21.6, C_{arom} 127.1–144.9, C_6 145.1.
Elemental Analysis for $C_{11}H_{15}N_3SO_3PCl$: Calculated: %C 58.30, %H 6.63, %N 18.54, %S 14.14, %Cl 15.66.
Found: %C 58.43, %H 6.71, %N 18.62, %S 14.21, %Cl 15.71.

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