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IMINOPHOSPHORANE-MEDIATED SYNTHESIS OF FUSED [1,2,4]TRIAZINES: PREPARATION OF THE NOVEL [1,2,4]TRIAZINO[4,3-b][1,2,4,5]TETRAZINE RING SYSTEM.

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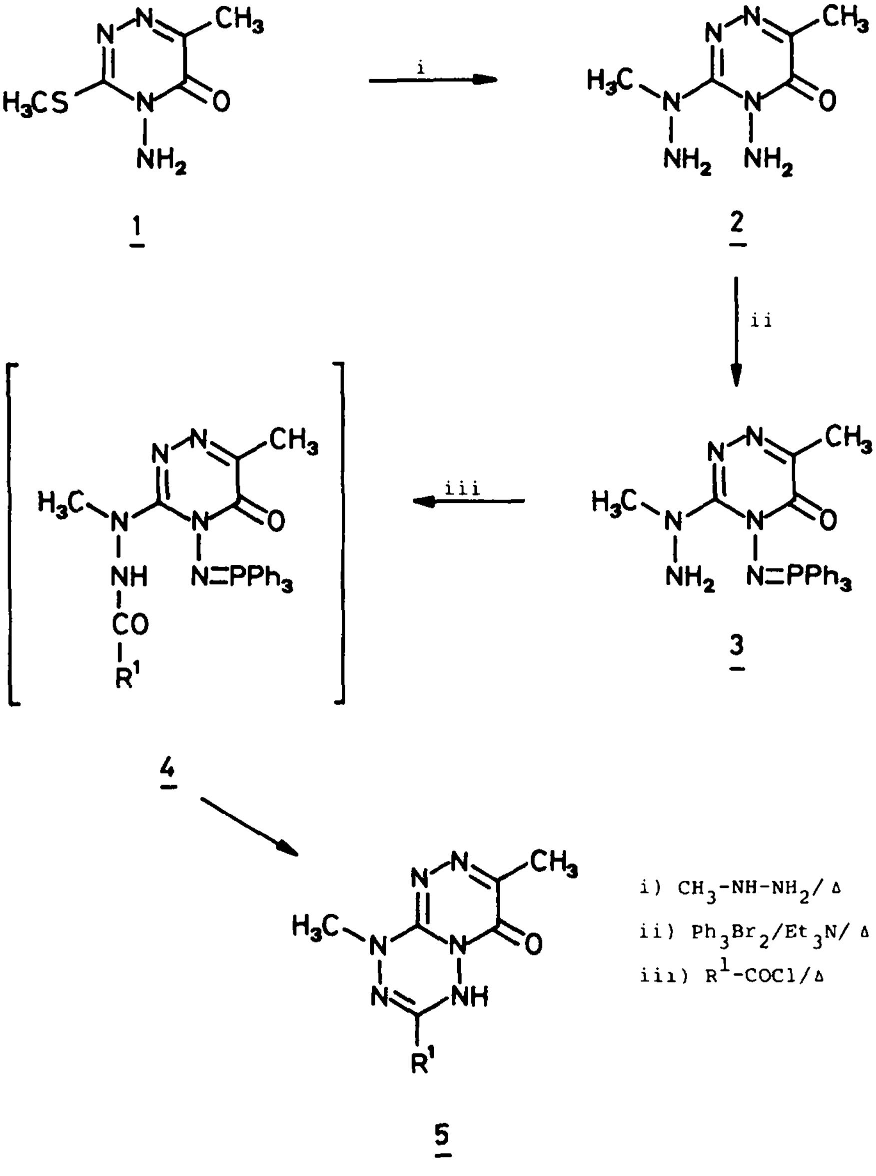
Abstract - 6-Methyl-3-(1-methylhydrazino)-5-oxo-4-triphenylphosphoranylideneamino-4,5-dihydro[1,2,4]triazine 3 reacts with acyl chlorides to give the corresponding 3-substituted-1,4-dihydro-1,7-dimethyl-6-oxo-4H-[1,2,4]triazino[4,3-b][1,2,4,5]tetrazines 5. On the other hand, the N-aminoheterocycle 4-amino-6-methyl-3-(1-methylhydrazino)-5-oxo-4,5-dihydro[1,2,4]triazine 2 reacts with carbonyl compounds to give 1,2,3,4-tetrahydro[1,2,4]triazino[4,3-b][1,2,4,5]tetrazines 6 which undergo dehydrogenation by the action of DDQ to give 5.

In the last few years we were involved in a program aiming to develop synthetic approaches to nitrogen-bridgehead heterocycles utilizing readily available 2-functionalized pyrylium cations or N-aminoheterocycles as starting materials. In this context, we have reported the preparation of several fused [1,2,4]triazines from the 2-ethoxycarbonyl-4,6-diphenylpyrylium cation e.g. pyrido[2,1-f][1,2,4]triazine[1-3], [1,3,4]oxadiazino[2,3-c]pyrido[2,1-f][1,2,4]triazine[4] and thiazolo-[2,3-c]pyrido[2,1-f][1,2,4]triazine[5] or from 4-amino[1,2,4]triazines e.g. thiadiazolo[2,3-c][1,2,4]triazine[6,7], and [1,2,4]triazolo[5,1-c][1,2,4]triazine[8,9]. We now describe two general methods for the preparation of some derivatives of the unknown [1,2,4]triazino[4,3-b][1,2,4,5]tetrazine ring system which contains the [1,2,4]triazine and [1,2,4,5]tetrazine moieties. The first method involves reaction of the iminophosphorane 3 derived from the N-aminoheterocycle 4-amino-6-methyl-3-(1-methylhydrazino)-5-oxo-4,5-dihydro[1,2,4]triazine 2 with acyl chlorides. The second one is based on the reaction of 2 with carbonyl compounds to give 1,2,3,4-tetrahydro[1,2,4]triazino[4,3-b][1,2,4,5]tetrazines which by dehydrogenation lead to [1,2,4]triazino[4,3-b][1,2,4,5]tetrazines. The synthesis of 1,2,3,4-tetrahydro[1,2,4,5]tetrazines has been achieved in only a limited number of ways, mostly involving the use of formazans as starting materials. The formazans are either converted directly to 1,2,3,4-tetrahydro[1,2,4,5]tetrazines or indirectly by processes involving verdazyls[10].

The N-aminoheterocycle 2, readily available from 4-amino-6-methyl-3-methylthio-5-oxo-4,5-dihydro[1,2,4]triazine 1 and methylhydrazine, reacts with equimolecular amounts of triphenylphosphine dibromide in dry benzene in the presence of triethylamine to give the iminophosphorane 3 as a crystalline solid in 40 % yield. Support for the formulation 3 is clearly provided by its elemental analysis and spectral data. The I.R. spectrum shows two absorption bands in the region 3262-3183 cm^{-1} due to the amino group and a strong absorption band at 1642 cm^{-1} due to the carbonyl group in the [1,2,4]triazine ring; this wavenumber is similar to the one found for the iminophosphorane derived from 1. In the ^{1}H-N.M.R. spectrum the chemical shifts of the C-methyl and N-methyl groups are characteristic at δ 2.27 ppm and δ 3.33 ppm respectively, and the protons of the amino group appear at δ 4.60 as a broad singlet. The ^{31}P chemical shift occurs a δ 20.96 ppm, being this value almost identical to the one found in the iminophosphorane derived from 1. The mass spectrum shows the expected molecular ion, peaks are also found at [M - 16], m/z 277 and m/z 155.



i) CH_3-NH-NH_2/ Δ

ii) Ph_3Br_2/Et_3N/ Δ

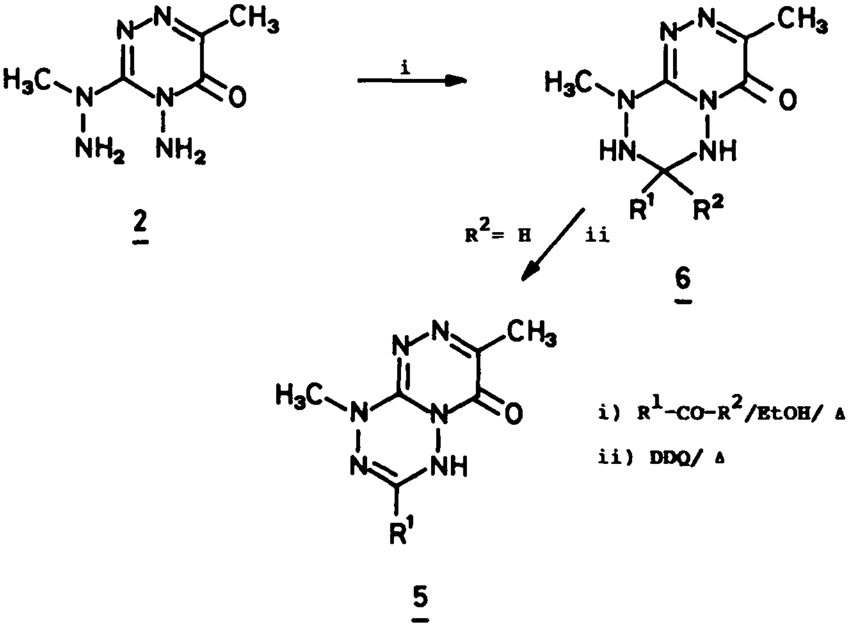
iii) R^1-COCl/Δ

Iminophosphorane 3 reacts with acyl chlorides in the presence of triethylamine in dry benzene for 6 h to give the corresponding 3-aryl-1,4-dihydro-1,7-dimethyl-6-oxo-4H-[1,2,4]triazino[4,3-b][1,2,4,5]tetrazines 5 in moderate to good yields (37-64 %). Structural elucidation of compounds 5 is based on microanalytical data and spectral evidence. Compounds 5 display in the I.R. absorption bands in the region 3296-3200 cm^{-1} due to the amino group; the ^1H-N.M.R. spectra show two singlets at δ 2.45 and δ 3.50 ppm due to the C-methyl and N-methyl groups respectively; the mass spectra show the expected molecular ion, peaks are also found at m/z $[M^+ - 28]$, [Ar-CNH], [Ar-CN] and [Ar].

Although it has been previously reported[11] that iminophosphoranes react with acyl chlorides to give imidoyl chlorides, we believe that the 3 → 5 conversion involves initial acylation on the amino group to give an acylamino derivative 4 as intermediate which undergoes intramolecular aza-Wittig reaction to give 5. This assumption is supported by the isolation in one case of the intermediate 4 which by heating leads to 5.

On the other hand, the N-aminoheterocycle 2 reacts with carbonyl compounds such as aldehydes, ketones and 1,2-dicarbonyl compounds in ethanol at reflux temperature to give the corresponding 1,2,3,4-tetrahydro[1,2,4]triazino[4,3-b][1,2,4,5] tetrazines 6 as crystalline solids. Yields are good (73-75 %) for aldehydes and moderate (20-50 %) for ketones. This transformation is conceptually similar to the reported preparation of hexahydro[1,2,4,5]tetrazines from aldehydes and 2,4-dimethylcarbonohydrazide[12] or 2,4-dimethylthiocarbonohydrazide[13].

When benzene solutions of compounds 6a-f are heated in the presence of 2,3-dichloro-5,6-dicyanobenzoquinone the corresponding 1,4-dihydro[1,2,4]triazino [4,3-b][1,2,4,5]tetrazines 5 are isolated in excellent yields (76-96 %). Preparation of compound 5f is also achieved from the reaction of the N-aminoheterocycle 2 and N,N-dimethylformamide dimethylacetal in dry toluene at reflux temperature.



2

6

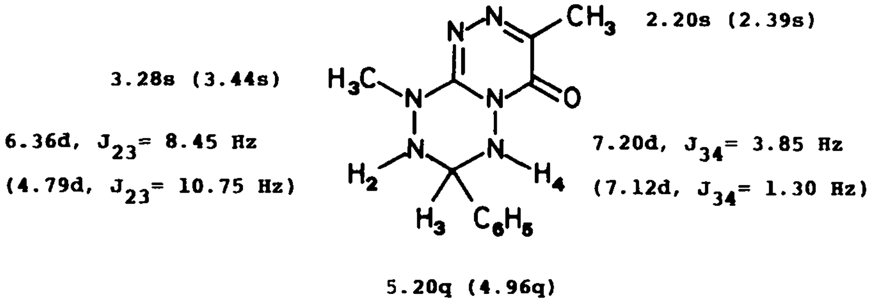
5

i) R^1-CO-R^2/EtOH/ Δ

ii) DDQ/ Δ

Support for the formulation 6 is clearly provided by their microanalytical and spectral data. The I.R. spectra show absorptions in the region 3245-3177 cm^{-1} due to the amino group and in the region 1693-1648 cm^{-1} due to the carbonyl group in the [1,2,4]triazine ring. The mass spectra show the expected molecular ion peaks; in addition, for compounds 6a-e peaks are also found at m/z $[M^+ - R^1]$, $[R^1\text{-CNH}]$ and $[M^+ - R^1\text{-CNH}]$. For compounds 6f-i the most characteristic fragments appear at m/z $[M^+ - R^1]$, $[M^+ - R^2]$, $[R^1\text{-CNH}]$, $[R^2\text{-CNH}]$, $[R^1\text{-CN}]$ and $[R^2\text{-CN}]$.

The ^1H-N.M.R. spectra of these derivatives are consistent with the 1,2,3,4-tetrahydro[1,2,3,4]tetrazine structure (see experimental part). In order to discuss the conformation of the tetrazine ring, the spectrum of compound 6a (R^1 =Ph, R^2 = H) was recorded at 300 MHz both in DMSO-d_6 (as all other derivatives) and in $CDCl_3$. Moreover, a NOE experiment (in DMSO-d_6 as solvent) shows an enhancement of the signal at δ 6.36 ppm by irradiation of the N-methyl group. With this experiment it is possible to assign the AMX systen formed by protons H_2, H_3 and H_4 (in parentheses, $CDCl_3$ values):



Several facts are remarkable in these data:

i) The N-H protons (H_2 and H_4) are well resolved and as narrow as the C-H proton (H_3): no ^{14}N nor prototropic broadenig is observed.

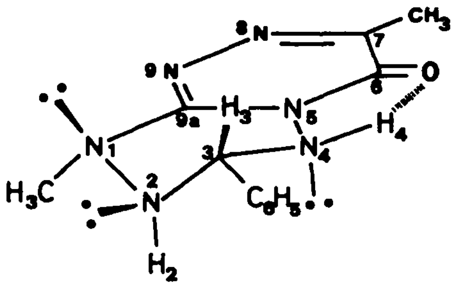
ii) The chemical shift of proton H_2 is very sensitive to the solvent nature, but not those of H_3 nor H_4.

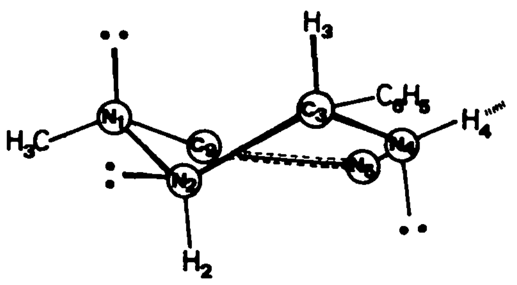
iii) The vicinal coupling constants are sensitive to solvent variation, indicating a modification of the tetrazine ring conformation. Using a Karplus equation of the form[14]

$$^3J_{HCNH} = 9.4\cos^2\Phi - 1.1\cos\Phi + 0.4$$

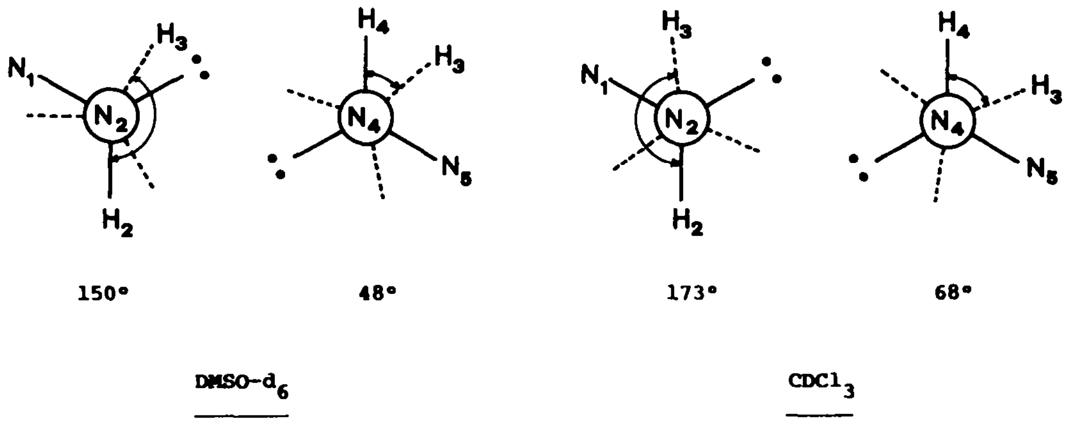
the following dihedral angles can be calculated: DMSO-d_6, Φ_{23}= 150°, Φ_{34}= 48°; $CDCl_3$, Φ_{23}= 173°, Φ_{34}= 68°.

The calculated dihedral angles and the fact that the NOE effect (irradiation of the N-methyl at 3.28 ppm) is observed on H_2 (+ 12%) but not on H_3, strongly suggest the following conformation for 6a:





The tetrahydrotetrazine ring adopts a half-chair conformation, similar to that of ciclohexene[15] and other heterocyclic systems[16], with an equatorial position for the phenyl residue. This situation corresponds to the following Newman projections:



The ring is more flattened in DMSO-d_6 and, moreover, the N_2 nitrogen is less pyramidal than in $CDCl_3$. The H_4-N_4-C_3-H_3 dihedral angle is less sensitive to the solvent (60°-48° = 12° and 68°-60° = 8°) than the H_2-N_2-C_3-H_3 dihedral angle (180°-150° = 30° and 180°-173° = 7°). Perhaps, H_4 is intramolecularly bonded to the C_6=O carbonyl group, which could explain both its downfield appearance and the relative insensitivity of its chemical shift (∿ 7.15 ppm) to solvent effects. On the contrary, H_2 is shifted downfield by DMSO-d_6 (+ 1.57 ppm compared with $CDCl_3$), which also modifies its hybridization (it becomes more sp^2), indicating an intermolecular hydrogen-bond with the solvent.

Experimental

All melting points were determined using a Kofler hot-stage microscope and are uncorrected; I.R. spectra were recorded with a Nicolet FT 5DX spectrometer. ^{1}H-N.M.R. spectra were recorded at 80 MHz on a Varian FT-80 spectrometer or a Varian XL-300 working by the PFT technique with an Aspect 2000 Data System with 16K memory. ^{1}H chemical shifts and constants are accurated to 0.01 ppm and ± 0.2 Hz respectively. Mass spectra (70 eV) were obtained using a Hewlett-Packard 5993C instrument. Combustion analyses were performed with a Perkin-Elmer 240C instrument.

4-Amino-6-methyl-3-(1-methylhydrazino)-5-oxo-4,5-dihydro[1,2,4]triazine 2.

To a well stirred solution of 4-amino-6-methyl-3-methylthio-5-oxo-4,5-dihydro [1,2,4]triazine[17] 1 (2.20 g, 13 mmol) in isopropanol (30 ml), methylhydrazine (6.00 g, 130 mmol) was added. The reaction mixture was stirred at reflux temperature for 6 h. After cooling, the precipitated solid was separated by filtration and recrystallised from isopropanol to give 2 (61 %) as colourless needles, m.p. 152-153°C. (Found: C, 35.12; H, 5.80; N, 49.23. $C_5H_{10}N_6O$ requires: C, 35.29; H, 5.92; N, 49.38); i.r. (Nujol): 3330(s), 3296(s), 3199(s), 1676(vs), 1625(vs), 1557(vs), 1523(vs), 1381(vs), 1252(s), 1228(s), 1007(s) and 758(s) cm^{-1}; δ ($DMSO-d_6$): 2.35 (s, 3H), 3.20 (s, 3H), 5.5-6.8 (s broad, 4H); m/z (%): 170 (M^+, 16), 155 (10), 154 (100), 82 (15), 69 (21), 57 (32), 56 (23), 55 (13), 45 (47), 43 (28).

6-Methyl-3-(1-methylhydrazino)-5-oxo-4-triphenylphosphoranylideneamino-4,5-dihydro [1,2,4]triazine 3.

A solution of bromine (1.89 g, 11.8 mmol) in dry benzene (15 ml) was added dropwise to a stirred solution of triphenylphosphine (3.11 g, 11.8 mmol) in the same solvent (60 ml) at 0-5°C under nitrogen. The mixture was stirred for 1 h and then allowed to warm to room temperature. A solution of 4-amino-6-methyl-3-(1-methylhydrazino)-5-oxo-4,5-dihydro[1,2,4]triazine 2 (2.01 g, 11.8 mmol) and triethylamine (2.39 g, 23.6 mmol) in dry benzene was added; after the mixture had been heated for 24 h under reflux a precipitated solid was deposited. The salt was separated by filtration and the filtrate was concentrated to dryness to afford a crude product which was crystallised from benzene/n-hexane (1:1, v/v) to give the title phosphorane 3 (40 %) as yellow prisms, m.p. 191-193°C. (Found: C, 64.12; H, 5.27; N, 19.45. $C_{23}H_{23}N_6OP$ requires: C, 64.18; H, 5.38; N, 19.52); i.r. (Nujol): 3262 (m), 3183 (m), 1642 (vs), 1619 (m), 1494 (s), 1438 (vs), 1213 (m), 1112 (vs), 1013 (m), 750 (m), 721 (s) and 694 (s) cm^{-1}; δ ($CDCl_3$): 2.27 (s, 3H), 3.33 (s, 3H), 4.60 (s broad, 2H), 7.5-8.1 (m, 15H); m/z (%): 430 (M^+, 10), 414 (10), 278 (25), 277 (34), 276 (91), 262 (25), 185 (17), 184 (18), 183 (100), 152 (20), 122 (18), 108 (48), 107 (21), 77 (19), 57 (16), 51 (19), 43 (11).

Reaction of Iminophosphorane 3 with Aroyl Chlorides: Preparation of 3-Aryl-1,4-dihydro-1,7-dimethyl-6-oxo-4H-[1,2,4]triazino[4,3-b][1,2,4,5]tetrazines 5.

To a solution of 6-methyl-3-(1-methylhydrazino)-5-oxo-4-triphenylphosphoranylideneamino-4,5-dihydro[1,2,4]triazine 3 (0.53 g, 1.2 mmol) in dry benzene (20 ml) the appropriate aroyl chloride (1.2 mmol) and triethylamine (1.2 mmol) were added. The reaction mixture was stirred at reflux temperature for 6 h. After cooling, triethylammonium chloride was deposited. The salt was separated by filtration and the filtrate was concentrated to dryness to afford a crude product, which was crystallised from ethanol to give 5. Elimination of the solvent from the filtrate leads to a crude product which recrystallised from diethyl ether gave triphenylphosphine oxide. The following derivatives 5 were obtained:

5a 3-Phenyl (37 %), m.p. 150-152°C (yellow prisms). (Found: C 56.16; H 4.59; N 32.66. $C_{12}H_{12}N_6O$ requires: C 56.24; H 4.72; N 32.79); i.r. (Nujol): 3296 (s), 3273 (s), 1670 (vs), 1625 (vs), 1551 (vs), 1528 (vs), 1245 (m), 1195 (m), 1092 (m), 990 (m), 939 (m), 775 (m), 752 (m) and 690 (s) cm^{-1}; δ ($CDCl_3$): 2.45 (s, 3H), 3.53 (s, 3H), 7.4-7.9 (m, 5H), 8.67 (s, 1H); m/z (%): 256 (M^+, 45), 228 (26), 161 (11), 144 (9), 110 (10), 104 (100), 103 (31), 77 (42), 69 (10), 56 (44), 54 (14), 51 (21), 43 (26).

5b 3-(p-Tolyl) (53 %), m.p. 190-191°C (yellow prisms). (Found: C 57.70; H 5.24; N 31.13. $C_{13}H_{14}N_6O$ requires: C 57.77; H 5.22; N 31.09); i.r. (Nujol): 3228 (s), 3199 (s), 1676 (vs), 1626 (s), 1523 (s), 1308 (m), 821 (m), 747 (m) and 719 (m) cm^{-1}; δ ($CDCl_3$): 2.46 (s, 6H), 3.50 (s, 3H), 7.4-7.8 (m, 4H), 8.65 (s, 1H); m/z (%): 270 (M^+, 47), 242 (20), 175 (10), 158 (10), 119 (10), 118 (100), 117 (70), 116 (21), 110 (13), 91 (28), 90 (14), 89 (14), 65 (16), 56 (28), 43 (23).

5c 3-(p-Metoxyphenyl) (64 %), m.p. 158-160°C (yellow prisms). (Found: C 54.42; H 4.79; N 29.26. $C_{13}H_{14}N_6O_2$ requires: C 54.54; H 4.93; N 29.35); i.r. (Nujol): 3233 (m), 3199 (m), 1676 (vs), 1625 (s), 1614 (s), 1517 (vs), 1262 (s), 1177 (m), 835 (m) and 747 (m) cm^{-1}; δ ($CDCl_3$): 2.45 (s, 3H), 3.50 (s, 3H), 3.90 (s, 3H), 6.8-8.0 (m, 4H), 8.50 (s, 1H); m/z (%): 286 (M^+, 30), 258 (10), 148 (10), 134 (9), 133 (100), 119 (10), 110 (11), 103 (10), 91 (11), 90 (10), 69 (8), 56 (10), 43 (16).

5d 3-(p-Chlorophenyl) (45 %), m.p. 177-178°C (yellow prisms). (Found: C 49.51; H 3.72; N 28.79. $C_{12}H_{11}ClN_6O$ requires: C 49.58; H 3.81; N 28.91); i.r. (Nujol): 3228 (m), 3200 (m), 1682 (vs), 1642 (m), 1625 (m), 1596 (m), 1523 (s), 1381 (vs), 1093 (m), 843 (m), 747 (m), 719 (m) and 679 (m) cm^{-1}; δ ($CDCl_3$): 2.48 (s, 3H), 3.52 (s, 3H), 7.4-7.9 (m, 4H), 8.65 (s, 1H); m/z (%): 292 (M^+ + 2, 14), 290 (M^+, 45), 264 (8), 262 (24), 195 (10), 140 (33), 139 (29), 138 (100), 137 (64), 113 (11), 111 (33), 110 (17), 102 (33), 96 (7), 81 (11), 76 (10), 75 (28), 69 (26), 56 (67), 43 (45).

6-Methyl-3-[1-methyl-2-(p-methoxybenzoyl)hydrazino]-5-oxo-4-triphenylphosphoranylideneamino-4,5-dihydro[1,2,4]triazine 4.

To a solution of 6-methyl-3-(1-methylhydrazino)-5-oxo-4-triphenylphosphoranylideneamino-4,5-dihydro[1,2,4]triazine 3 (0.53 g, 1.2 mmol) in dry benzene (20 ml), p-methoxybenzoyl chloride (0.20 g, 1.2 mmol) and triethylamine (0.12 g, 1.2 mmol) were added. The reaction mixture was stirred at room temperature for 2h. The solvent was removed under reduced pressure at 25°C and the residual material was slurried with cold ethanol (10 ml). The separated solid was collected by filtration, dried and recrystallised from ethanol to give title phosphorane 4 (65 %) as colourless prisms, m.p. 187°C. (Found: C 65.87; H 5.12; N 14.83. $C_{31}H_{29}N_6O_3P$ requires: C 65.95; H 5.18; N 14.88); i.r. (Nujol): 3216 (m), 1676 (s), 1636 (vs), 1602 (vs), 1494 (vs), 1438 (vs), 1257 (vs), 1234 (s), 1178 (m), 1109 (vs), 1053 (m), 1025 (m), 722 (m), 711 (m) and 693 (s) cm^{-1}; δ ($CDCl_3$): 2.26 (s, 3H), 3.73 (s, 3H), 3.92 (s, 3H), 6.95 (d, 2H, J= 9 Hz), 7.4-8.1 (m, 17H), 9.90 (s, 1H).

When a solution of compound 4 (1.2 mmol) in dry benzene (20 ml) is heated under reflux for 6h, triphenylphosphine oxide and compound 5c were isolated as before in almost quantitative yield.

General Procedure for the Preparation of 3-Substituted-1,2,3,4-tetrahydro-1,7-dimethyl-6-oxo-2*H*,4*H*-[1,2,4]triazino[4,3-b][1,2,4,5]tetrazines 6.

To a hot solution of 4-amino-6-methyl-3-(1-methylhydrazino)-5-oxo-4,5-dihydro [1,2,4]triazine 2 (0.85 g, 5 mmol) in ethanol (25 ml), the appropriate carbonyl compound (5 mmol) and 1N hydrochloric acid (1 ml) were added. The reaction mixture was heated under reflux temperature for 6 h. After cooling, the solvent was removed under reduced pressure and the residual material recrystallised from ethanol to give 6. The following derivatives 6 were obtained:

6a 3-Phenyl (75 %), m.p. 179-180°C (colourless needles). (Found: C 55.70; H 5.43; N 32.42. $C_{12}H_{14}N_6O$ requires: C 55.80; H 5.46; N 32.54); i.r. (Nujol): 3216 (s), 3165 (s), 1681 (vs), 1659 (vs), 1562 (vs), 1534 (vs), 1398 (s), 1109 (s), 1030 (m), 962 (m), 747 (s), 718 (m), 701 (s) and 656 (m) cm^{-1}; δ (DMSO-d_6): 2.20 (s, 3H), 3.28 (s, 3H), 5.20 (dd, 1H, J= 3.85, 8.45 Hz), 6.36 (d, 1H, J= 8.45 Hz), 7.20 (d, 1H, J= 3.85 Hz), 7.4-7.8 (m, 5H); m/z (%): 258 (M$^+$, 18), 257 (28), 182 (10), 181 (100), 154 (22), 139 (23), 112 (25), 104 (30), 90 (11), 77 (20), 57 (7), 48 (8), 43 (7).

6b 3-(p-Tolyl) (75 %), m.p. 185-186°C (white prisms). (Found: C 57.26; H 5.91; N 30.81. $C_{13}H_{16}N_6O$ requires: C 57.34; H 5.92; N 30.86); i.r. (Nujol): 3216 (s), 1653 (vs), 1562 (vs), 1115 (m), 1053 (m), 815 (m), 752 (m) and 679 (m) cm^{-1}; δ (DMSO-d_6): 2.23 (s, 3H), 2.34 (s, 3H), 3.32 (s, 3H), 5.22 (dd, 1H, J= 3.7, 8.5 Hz), 6.38 (d, 1H, J= 8.5 Hz), 7.22 (d, 1H, J= 3.7 Hz), 7.2-7.5 (m, 4H); m/z (%): 272 (M$^+$, 29), 271 (22), 181 (100), 154 (18), 139 (33), 118 (41), 112 (22), 104 (10), 96 (7), 91 (40), 69 (18), 65 (19), 57 (22), 55 (15), 43 (27).

6c 3-(p-Metoxyphenyl) (75 %), m.p. 165-167°C (white prisms). (Found: C 54.12; H 5.53; N 29.11. $C_{13}H_{16}N_6O_2$ requires: C 54.16; H 5.59; N 29.15); i.r. (Nujol): 3228 (vs), 1648 (vs), 1552 (vs), 1528 (vs), 1399 (s), 1246 (s), 1110 (m), 1036 (m), 1025 (m) and 759 (w) cm^{-1}; δ (DMSO-d_6): 2.20 (s, 3H), 3.30 (s, 3H), 3.80 (s, 3H), 5.16 (dd, 1H, J= 3.9, 9.0 Hz), 6.35 (d, 1H, J= 9.0 Hz), 7.30 (d, 1H, J= 3.9 Hz), 6.9-7.5 (m, 4H); m/z (%): 288 (M$^+$, 43), 287 (31), 181 (74), 155 (35), 154 (27), 140 (16), 139 (79), 135 (19), 134 (73), 133 (17), 120 (14), 119 (15), 112 (25), 107 (15), 96 (14), 91 (29), 77 (38), 69 (34), 65 (18), 64 (15), 57 (41), 55 (27), 45 (29), 43 (40).

6d 3-(p-Chlorophenyl) (73 %), m.p. 183-184°C (white prisms). (Found: C 49 18; H 4.39; N 28.65. $C_{12}H_{13}ClN_6O$ requires: C 49.24; H 4.48; N 28.71); i.r.(Nujol): 3205 (vs), 1648 (vs), 1568 (vs), 1251 (m), 1092 (s), 1053 (m), 905 (w), 826 (m) and 752 (m) cm^{-1}; δ (DMSO-d_6): 2.25 (s, 3H), 3.32 (s, 3H), 5.32 (dd, 1H, J= 3.9, 8.0 Hz), 6.45 (d, 1H, J= 8.0 Hz), 7.36 (d, 1H, J= 3.9 Hz); 7.6 (s, 4H); m/z (%): 294 (M$^+$ + 2, 5), 293 (7), 292 (M$^+$, 16), 291 (14), 182 (9), 181 (100), 155 (6), 154 (22), 140 (15), 139 (32), 138 (28), 126 (9), 125 (7), 124 (11), 113 (10), 112 (26), 111 (24), 77 (10), 75 (15), 69 (15), 57 (22), 45 (25), 43 (26).

6e 3-Methyl (82 %), m.p. 178°C (white needles). (Found: C 41.68; H 6.23; N 43.00. $C_7H_{12}N_6O$ requires: C 42.85; H 6.16; N 42.83); i.r. (Nujol): 3234 (vs), 1648 (vs), 1568 (vs), 1529 (s), 1387 (s), 1353 (m), 1262 (m), 1206 (m), 1149 (s), 1115 (m), 1075 (m), 979 (s), 883 (m), 753 (s), 724 (m), 679 (m) and 639 (m) cm^{-1}; δ (DMSO-d_6): 1.25 (d. 3H, J= 6.0 Hz), 2.27 (s,3H), 3.32 (s, 3H), 3.75-4.50 (m, 1H), 6.0 (d, 1H, J= 11 Hz), 7.23 (d, 1H, J= 4.0 Hz); m/z (%): 196 (M$^+$, 53), 195

(6), 181 (100), 154 (22), 139 (12), 126 (6), 124 (6), 112 (27), 98 (6), 97 (6), 84 (15), 83 (10), 82 (25), 69 (23), 57 (33), 55 (24), 45 (46).

6f 1,7-Dimethyl-6-oxo-1,2,3,4-tetrahydro-2*H*,3*H*,4*H*-[1,2,4]triazino[4,3-b][1,2,4,5] tetrazine (52 %), m.p. 263-265°C (white prisms). (Found: C 39.43; H 5.64; N 46.18. $C_6H_{10}N_6O$ requires: C 39.56; H 5.53; N 46.13); i.r. (Nujol):3222 (vs), 3143 (vs), 1676 (vs), 1557 (vs), 1540 (vs), 1517 (s), 1438 (s), 1347 (m), 1325 (m), 1308 (m), 1160 (s), 1113 (s), 1104 (s) and 967 (s) cm^{-1}; δ (DMSO-d_6): 2.27 (s, 3H), 3.36 (s, 3H), 4.20 (dd, 2H, J=7.0 Hz, J= 4.0 Hz), 6.24 (t, 1H, J=7.0 Hz), 7.25 (t, 1H, J= 4.0 Hz); m/z (%): 182 (M$^+$, 100), 181 (20), 155 (9), 154 (39), 126 (8), 112 (91), 111 (8), 98 (9), 84 (31), 82 (23), 70 (35), 69 (62), 57 (45), 56 (24), 55 (38), 53 (15).

6g 1,3,3,7-Tetramethyl-6-oxo-1,2,3,4-tetrahydro-2*H*,4*H*-[1,2,4]triazino[4,3-b][1,2,4, 5]tetrazine (25 %), m.p. 132°C (colourless prisms). (Found: C 45.59; H 6.59; N 39.99. $C_8H_{14}N_6O$ requires: C 45.70; H 6.71; N 39.97); i.r. (Nujol): 3211 (vs), 1653 (vs), 1562 (vs), 1483 (s), 1030 (m), 968 (w), 888 (w), 871 (m) and 752 (m) cm^{-1}; δ (DMSO-d_6): 1.29 (s, 6H), 2.26 (s, 3H), 3.35 (s, 3H), 5.95 (s, 1H), 7.05 (s, 1H); m/z (%): 210 (M$^+$, 24), 195 (85), 154 (12), 138 (15), 112 (27), 82 (12), 69 (15), 57 (24), 56 (65), 45 (41), 43 (36), 42 (100).

6h 3,3-Diethyl-1,7-dimethyl-6-oxo-1,2,3,4-tetrahydro-2*H*,4*H*-[1,2,4]triazino[4,3-b] [1,2,4,5]tetrazine (20 %), m.p. 123-125°C (colourless prisms). (Found: C 50.31; H 7.48; N 35.16. $C_{10}H_{18}N_6O$ requires: C 50.40; H 7.60; N 35.27); i.r. (Nujol): 3245 (vs), 3188 (vs), 1665 (vs), 1568 (vs), 1432 (vs), 1398 (s), 1296 (s), 1211 (s), 1143 (m), 1019 (m), 861 (s) and 679 (m) cm^{-1}; δ (DMSO-d_6): 1.00 (m, 6H), 1.62 (m, 4H), 2.30 (s, 3H), 3.37 (s, 3H), 5.82 (s, 1H), 6.71 (s, 1H); m/z (%): 238 (M$^+$, 10) 210 (6), 209 (62), 154 (11), 139 (5), 112 (16), 84 (17), 57 (12), 56 (100), 55 (12), 45 (13), 43 (14), 42 (22).

6i 3-Phenyl-1,3,7-trimethyl-6-oxo-1,2,3,4-tetrahydro-2*H*,4*H*-[1,2,4]triazino[4,3-b] [1,2,4,5]tetrazine (30 %), m.p. 257°C (white prisms). (Found: C 57.27; H 5.88; N 30.81. $C_{13}H_{16}N_6O$ requires: C 57.34; H 5.92; N 30.80); i.r. (Nujol): 3233 (vs), 3211 (vs), 1659 (vs), 1568 (vs), 1523 (m), 1398 (m), 1274 (m), 1211 (m), 1115 (m), 1030 (m), 939 (m), 888 (w), 838 (w), 754 (m), 712 (m), 702 (m) and 678 (m) cm^{-1}; δ (DMSO-d_6): 1.53 (s, 3H), 2.24 (s, 3H), 3.30 (s, 3H), 6.52 (s, 1H), 7.4-7.6 (m, 5H), 7.75 (s, 1H); m/z (%): 272 (M$^+$, 11), 257 (48), 195 (23), 119 (12), 118 (100), 112 (12), 104 (36), 103 (10), 77 (61), 69 (10), 57 (10), 51 (17), 45 (15), 43 (18).

6j 3-(p-Bromophenyl)-1,3,7-trimethyl-6-oxo-1,2,3,4-tetrahydro-2*H*,4*H*-[1,2,4]triazino [4,3-b][1,2,4,5]tetrazine (50 %), m.p. 222°C (white prisms). (Found: C 44.40; H 4.29; N 23.99. $C_{13}H_{15}BrN_6O$ requires: C 44.46; H 4.31; N 23.93); i.r. (Nujol): 3177 (s), 3160 (s), 1693 (vs), 1670 (vs), 1557 (vs), 1398 (s), 1274 (m), 1200 (m), 1115 (m), 1075 (m), 1030 (m), 1007 (s), 843 (m), 826 (s), 775 (m), 752 (m) and 724 (s) cm^{-1}; δ (DMSO-d_6): 1.55 (s, 3H), 2.25 (s, 3H), 3.28 (s, 3H), 6.50 (s, 1H), 7.64 (s, 4H), 7.68 (s, 1H); m/z (%): 352 (M$^+$ + 2, 8), 350 (M$^+$, 8), 337 (31), 335 (32), 199 (11), 198 (88), 196 (100), 195 (47), 184 (25), 182 (26), 157 (35), 155 (37), 154 (17), 117 (14), 112 (29), 103 (29), 102 (17), 76 (26), 69 (32), 57 (23), 45 (36), 43 (43).

6k 3-Acetyl-1,3,7-trimethyl-6-oxo-1,2,3,4-tetrahydro-2*H*,4*H*-[1,2,4]triazino[4,3-b][1,2,4,5]tetrazine (35 %), m.p. 202-204°C (colourless prisms). (Found: C 45.22; H 5.79; N 35.10. $C_9H_{14}N_6O_2$ requires: C 45.37; H 5.92; N 35.27); i.r. (Nujol): 3205 (s), 3182 (s), 1721 (vs), 1659 (vs), 1562 (vs), 1523 (m), 1404 (m), 1364 (m), 1262 (m), 1115 (m), 1030 (m), 888 (w), 747 (w) and 701 (w) cm^{-1}; δ (DMSO-d_6): 1.50 (s, 3H), 2.33 (s, 6H), 3.24 (s, 3H), 6.80 (s, 1H), 7.84 (s, 1H); m/z (%): 238 (M^+, 5), 196 (5), 195 (49), 154 (14), 126 (5), 113 (5), 112 (20), 98 (10), 57 (15), 45 (10), 43 (53), 42 (100).

General Procedure for the Preparation of 5 from 6.

To a solution of the appropriate 1,7-dimethyl-6-oxo-1,2,3,4-tetrahydro-2*H*,4*H*-[1,2,4]triazino[4,3-b][1,2,4,5]tetrazine 6 (1.5 mmol) in dry benzene (50 ml), 2,3-dichloro-5,6-dicyanobenzoquinone (1.5 mmol) was added. The resultant green solution was stirred at reflux temperature for 4 h. The precipitated solid was separated by filtration, and identified as 2,3-dichloro-5,6-dicyanohydroquinone. The filtrate was concentrated to dryness and the residual material was recrystallised from ethanol to give 5. The following compounds 5 were obtained:

5a (87 %); 5b (93 %); 5c (86 %); 5d (76 %).

5e 1,4-Dihydro-1,3,7-trimethyl-6-oxo-4*H*-[1,2,4]triazino[4,3-b][1,2,4,5]tetrazine (59 %), m.p. 192-194°C (yellow prisms). (Found: C 43.35; H 5.27; N 43.12. $C_7H_{10}N_6O$ requires: C 43.29; H 5.19; N 43.27); i.r. (Nujol): 3222 (vs), 1687 (vs), 1648 (vs), 1534 (vs), 1421 (s), 1398 (vs), 1330 (m), 1245 (m), 1195 (m), 1025 (m), 957 (m), 781 (m) and 752 (m) cm^{-1}; δ ($CDCl_3$): 2.20 (s, 3H). 2.48 (s, 3H), 3.45 (s, 3H), 8.53 (s, 1H); m/z (%): 194 (M^+, 61), 166 (32), 154 (5), 153 (5), 139 (5), 110 (7), 109 (5), 99 (36), 83 (7), 82 (20), 71 (11), 69 (13), 56 (100), 55 (32), 54 (11), 53 (15)m 42 (56), 41 (49).

5f 1,4-Dihydro-1,7-dimethyl-6-oxo-4*H*-[1,2,4]triazino[4,3-b][1,2,4,5]tetrazine (80 %), m.p. 189-192°C (yellow prisms). (Found: C 39.92; H 4.41; N 46.66. $C_6H_8N_6O$ requires: C 40.00; H 4.48; N 46.64); i.r. (Nujol): 3118 (m), 3092 (m), 1683 (vs), 1647 (s), 1551 (s), 1534 (s), 1398 (s), 1092 (m), 928 (m), 747 (m), 718 (m) and 679 (m) cm^{-1}; δ (DMSO-d_6): 2.28 (s, 3H), 3.21 (s, 3H), 7.26 (s, 1H), 10.26 (s, 1H); m/z (%): 180 (M^+, 77), 152 (45), 85 (43), 83 (14), 69 (11), 68 (18), 57 (17), 56 (97), 55 (26), 54 (10), 53 (15), 43 (53), 28 (100).

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