Synthesis and Spectroscopic Characterisation of 4,5-Dihydro-[1,2,3]triazolo[5,1-*f*][1,2,4]triazines. A Novel Condensed Heterocyclic Ring System

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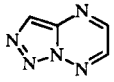
Received March 1, 1996

Dedicated to the memory of Professor Nicholas Alexandrou

The reaction of the 5-bromomethyl-1-dibenzoylamino-1,2,3-triazole (**5**) with aromatic amines gave the corresponding 5-arylaminomethyl-1-benzoylamino-1,2,3-triazoles **9**, which on treatment with phosphorus pentachloride gave the [1,2,3]triazolo[5,1-*f*][1,2,4]triazine derivatives **10**. Hydrolysis of the amide bond in **9** gave the 1-aminotriazoles **11**, which with ethyl orthoformate gave the [1,2,3]triazolo[5,1-*f*][1,2,4]triazines **12**, whereas with phosgene the triazolotriazinones **13** were obtained. The spectroscopic characteristics of all the new compounds are also given.

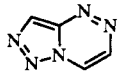
J. Heterocyclic Chem., **33**, 599 (1996).

Derivatives of 1,2,3-triazoles and 1,2,4-triazines and their condensed heterocyclic systems exhibit important biological activities and industrial applications [1,2], and many papers have been appeared concerning their synthesis and their chemical and physicochemical behaviour. However, although many studies have been published [3] on the fused [1,2,3]triazolopyrimidines, -pyridazines and -pyrazines, very few papers have appeared concerning the fused [1,2,3]triazolo[1,2,3]-, [1,2,4]- and [1,3,5]triazines [3] and not all the possible relevant ring systems are known. In particular, from the seven possible [1,2,3]triazolo[1,2,4]triazine ring systems only three are known, namely [1,5-*b*] [3], **1**, [5,1-*c*] [3], **2**, and [1,5-*d*] [4], **3**, while the others, to the best of our knowledge, have never been reported.



[1,5-*b*]

1



[5,1-*c*]

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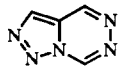

[1,5-*d*]

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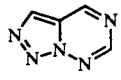

[5,1-*f*]

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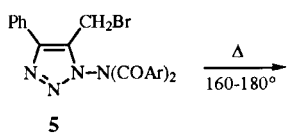
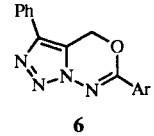
On the other hand, in the course of our work on the 1,2,3-triazoles [5,6], some [1,2,3]triazolo[1,3,4]oxadiazines **6** have been prepared [5] from the corresponding 1-(*N,N*-diaroyl)amino-5-bromomethyl-1,2,3-triazoles **5**, and recently we have reported [7] the synthesis of some pyrazolo[2,3]benzodiazepines **7** from compounds **5** *via* their triphenylphosphorylids that undergo sequential interesting and unexpected rearrangements.

Continuing the above work we now report the synthesis and spectroscopic characteristics of some derivatives of the missing [1,2,3]triazolo[5,1-*f*][1,2,4]triazine ring system **4** which have been prepared starting from compounds **5**.



5



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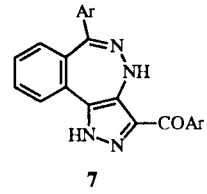

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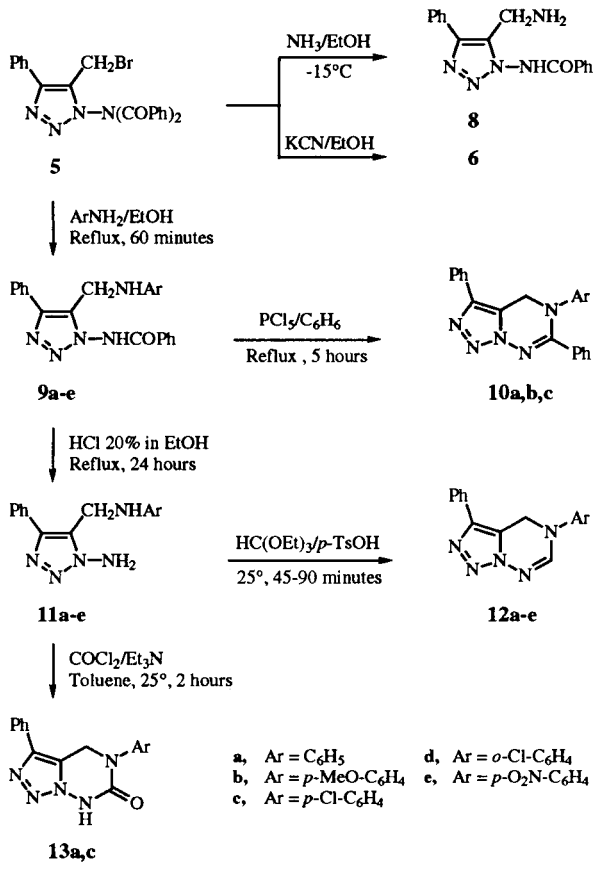
Results and Discussion.

Compounds **5**, prepared [5] from the reaction of the corresponding 1-(*N,N*-diaroyl)amino-5-methyl-1,2,3-triazoles with *N*-bromosuccinimide (NBS), and bearing in adjacent positions the bromomethyl and the dibenzoylamino groups can be used in different ways for the preparation of a variety of fused 1,2,3-triazolo-heterocycles. They have been found however very sensitive to alkaline conditions, tending to cyclize to the triazolooxadiazines **6** rather than to give substitution products when reacted with certain nucleophiles. Thus, their interaction with potassium phthalimide [5] gave mainly compounds **6** and the same compounds **6** were obtained almost exclusively when **5** reacted with potassium cyanide, although tried under different experimental conditions. The reaction of **5** with hydrazine hydrate in ethanol at 25° gave also compound **6** among other unidentified products, whereas with ammonia in absolute ethanol, when carried out at -15°, the expected substitution product 5-aminomethyl-1,2,3-triazole **8** was obtained [8].

The reaction of **5** (Ar = Ph) however with aromatic amines in refluxing ethanol gave in good yields [9] the 5-arylamino-1-benzoylaminotriazoles **9**, which, on hydrolysis with 20% hydrochloric acid in ethanol, were converted to the 1-amino-5-arylaminotriazoles **11**. Treatment of the amides **9** with phosphorus pentachloride in refluxing benzene afforded the 4,5-dihydro-8*H*-[1,2,3]triazolo[5,1-*f*]-[1,2,4]triazines **10**, whereas the aminotriazoles **11** reacted with triethyl orthoformate and in the presence of *p*-toluenesulfonic acid at 25° to give in very good yields (>90%) the corresponding [1,2,3]triazolo[1,2,4]triazines **12** (Scheme 1).

The aminotriazoles **11** reacted also with phosgene in toluene at 25° and in the presence of triethylamine, giving in moderate yields the 4,5,6,7-tetrahydro-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]triazin-6-ones **13** (Scheme 1).

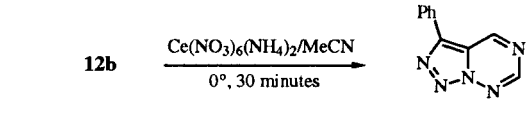
Scheme 1



It is noted that all the above reactions were carried out under argon, since the presence of air substantially diminishes the yields of the reaction products. Also, the purification of some of the compounds isolated, and especially of the amino derivatives **11**, was problematic, and column chromatography or repeated recrystallization did not improve their mps, which were changing when exposed to the air, making it difficult to obtain correct elemental analyses.

Acid hydrolysis of compound **12a** gave the starting aminotriazole **11a**, whereas oxidative hydrolysis of the 5-(4-methoxyphenyl) derivative **12b** with cerium ammonium nitrate [10] gave the fully aromatic parent compound **14** (Scheme 2).

Scheme 2



Analytical and spectral data of compounds **10-14** are in agreement with their structure.

Compounds **11** showed in their ir spectra bands at 3200-3300 cm^{-1} for the stretching vibration of the NH and NH_2 groups, whereas in their ^1H nmr spectra, taken in deuteriochloroform, the NH and NH_2 protons gave a broad singlet at δ 5.0-6.0 exchangeable with deuterium oxide. The CH_2 group gave a singlet peak at δ 4.1-4.5, except of the nitroderivative, **11e,** where these protons showed a doublet with a J = 4.8 Hz, as a result of their coupling with the N-H proton. The ^{13}C nmr spectra of **11** showed the expected peaks for the carbons of the two aromatic rings, while the C-4 and C-5 of the triazole ring appeared at δ = 143-145 and 128.5-132 ppm respectively, in agreement with the findings in other analogous 1,2,3-triazole derivatives [11], and the methylenic carbon appeared at δ = 35-40 ppm. In their mass spectra, besides the molecular ion $M^{+\cdot}$ which appeared with low abundance, the base peak corresponded either to the ion $PhC{\equiv}C\overset{+}{C}H_2$ at m/z 115, which is characteristic for the 4-phenyl-5-methyl-1,2,3-triazole derivatives, [9,12] or to the $Ar\overset{+}{N}H{=}CH_2$ ion. Other prominent peaks corresponded to the $[M-29]^+$ and $ArNH_2^{+\cdot}$ ions.

Triazolotriazines **10** and **12** showed in their ir spectra bands at 1580-1620 cm^{-1} attributed to the C=N bond stretching vibration, whereas the C=O bond of **13** gave a band at 1650-1670 cm^{-1}. In ^1H nmr of compounds **10, 12** and **13** the CH_2 protons gave a singlet at δ 5.1-5.5, suffering a downfield shift of ~1 ppm in respect to the methylenic protons of compounds **11**. The 6-H of the triazine ring appeared as singlet at δ 7.0-7.6 in compounds **12a-d** and at 8.25 in the nitro-derivative **12e**, the latter downfield shift being attributed rather to the solvent used (dimethyl sulfoxide-d_6) for recording the spectrum of **12e**. In the ^{13}C nmr spectra of compounds **10, 12** and **13** the methylenic carbon C-4 gave peaks at 42-47 ppm, which in compounds **12** showed a $^3J_{CNCH}$ with 6-H of 4.5-6.0 Hz and a $^1J_{CH}$ ~147 Hz. C-3 of the triazole ring appeared at δ = 140-142, whereas C-3a appeared at δ = 115-117, showing a high field shift of ~15 ppm in respect to the same carbon of the open form in compounds **11**. C-6 of the triazine ring in **12** appeared at 141-144 ppm with a $^1J_{CH}$ ~200 Hz. In the mass spectra of **10** and **12** a $[M+1]^+$ fragment appeared in most cases with moderate intensities, whereas the molecular ion $M^{+\cdot}$ appeared with low abundance. The $Ar\overset{+}{N}{\equiv}CPh$ and $Ar\overset{+}{N}{\equiv}CH$ ions constituted the base peaks in the spectra of **10** and **12** respectively. There was also the m/z 115 peak for the $PhC\overset{+}{C}{\equiv}CH_2$ fragment and a $[M-56]^{+\cdot}$ peak, corresponding to a four nitrogen atoms, $2N_2$, elimination of the molecular ion. It is noted that, contrary to what is known for the 1,2,3-triazoles [9,12,13], the $[M-28]^{+\cdot}$ peak was not observed in the mass spectra of compounds **10** and **12**.

In the ir spectrum of **14** the C=N bond showed a stretching vibration band at 1620 cm^{-1}, whereas in the ^1H nmr spectrum the 4-H and 6-H of the triazine ring gave two singlets at δ = 8.9 and 9.7 respectively. All the

carbons of compound **14** appeared in the aromatic region in its ^{13}C nmr spectrum while C-6 and C-4 gave peaks at δ = 155.1 and 150.1 respectively. In the mass spectrum, the molecular ion appeared with low abundance and the base peak appeared at m/z 114, corresponding to a $[M-2N_2-HCN]^{+\cdot}$ fragment. There was also a peak at m/z 141, corresponding to the $[M-56]^{+\cdot}$ ion, while an $[M-28]^{+\cdot}$ peak, typical for the 1,2,3-triazole derivatives [12,13], was not observed.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. The ir spectra were recorded as nujol mulls on a Perkin-Elmer 297 spectrophotometer. The ^1H nmr and ^{13}C nmr spectra, reported in δ units, were obtained with a Brucker AM 300 (at 300 and 75 MHz respectively) instrument. All nmr spectra were obtained by using tetramethylsilane (TMS) as internal standard in deuteriochloroform or dimethyl sulfoxide-d_6 solutions. The mass spectra were obtained at 70 eV with a VG TS-250 spectrometer. Accurate masses were measured with the same as above instrument and with a resolution of 6000. Elemental analyses of C, H and N were performed with a Perkin-Elmer 240B CHN Analyser. Column chromatography was carried out on silica gel (Merck 60; 0.063-0.2 mm), using *n*-hexane/ethyl acetate or methylene chloride/ethyl acetate mixtures of increasing polarity as eluent.

1-(*N,N*-Dibenzoyl)amino-5-bromomethyl-4-phenyl-1,2,3-triazole (**5**) was prepared by reacting the 1-(*N,N*-dibenzoyl)amino-5-methyl-4-phenyl-1,2,3-triazole with *N*-bromosuccinimide, according to the literature [6].

5-Arylaminomethyl-1-benzoylamino-4-phenyl-1,2,3-triazoles **9a-e**.

Compounds **9** were prepared from **5** and the corresponding anilines as described previously [9]. Mps and spectroscopic data of compounds **9a-e** were identical to those given previously [9].

Preparation of 5-Aryl-3,6-diphenyl-4,5-dihydro-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]triazines **10**. General Procedure.

A mixture of the amide **9** (1 mmole) and phosphorus pentachloride (0.250 g, 1.2 mmoles) in dry benzene (10 ml) was refluxed under argon for 5 hours. The mixture was cooled and then triethylamine was added and kept under stirring for 12 hours, then washed with 5% hydrochloric acid (10 ml) and water. After drying (sodium sulfate) the solvent was removed and the residue was chromatographed in a silica gel column with methylene chloride/ethyl acetate (1:1) as eluent.

3,5,6-Triphenyl-4,5-dihydro-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]triazine (**10a**).

This compound was prepared from **9a** (0.369 g, 1 mmole) as white crystals, (0.105 g, 30%), mp 195-197° (from methylene chloride-diethyl ether); ir: ν 1585, 1550 cm^{-1}; ^1H nmr (deuteriochloroform): δ 5.39 (s, 2H, CH_2), 6.95-7.53 (m, 13H), 7.66-7.69 (m, 2H); ^{13}C nmr (deuteriochloroform): δ 47.2 (CH_2), 116.7 (C-3a), 140.5 (C-3), 153.2 (C-6); 3-phenyl: 126.1 (C-2,C-6), 128.1 (C-4), 129.0 (C-3,C-5), 130.1 (C-1); 6-phenyl: 128.3 (C-2,C-6), 129.7 (C-3,C-5), 130.5 (C-4), 132.0 (C-1); *N*-phenyl: 125.1 (C-2,C-6), 126.5 (C-4), 129.4 (C-3,C-5), 144.1 (C-1); ms: m/z 352 (1) [M+1], 351 (0.5) [M^+], 295 (16) [M-56], 294 (27), 181 (15), 180 (100) [Ph-C≡N-Ph], 115 (20), 104 (9), 77 (52).

Anal. Calcd. for $C_{22}H_{17}N_5$: C, 75.19; H, 4.88; N, 19.93. Found: C, 75.20; H, 4.82; N, 20.11.

3,6-Diphenyl-5-*p*-methoxyphenyl-4,5-dihydro-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]triazine (**10b**).

This compound was prepared from **9b** (0.399 g, 1 mmole) as white crystals, (0.141 g, 37%), mp 175-177° (from chloroform-*n*-hexane); ir: ν 1595, 1580, 1550 cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.72 (s, 3H, OCH_3), 5.31 (s, 2H, CH_2), 6.74 (d, J = 8.9 Hz, 2H), 6.98 (d, J = 8.9 Hz, 2H), 7.18-7.32 (m, 4H), 7.36-7.46 (m, 4H), 7.65-7.67 (m, 2H); ^{13}C nmr (deuteriochloroform): δ 47.7 (t, J = 146.5 Hz, CH_2), 55.5 (q, J = 144.1 Hz, OCH_3), 116.5 (t, J = 5.4 Hz, C-3a), 140.4 (C-3), 153.3 (C-6); 3-phenyl: 126.0 (C-2,C-6), 128.0 (C-4), 128.9 (C-3,C-5), 130.6 (C-1); 6-phenyl: 132.0 (C-1), 128.2 (C-2,C-6), 129.7 (C-3,C-5), 130.3 C-4); *N*-phenyl: 114.6 (C-3,C-5), 126.7 (C-2,C-6), 136.9 (C-1) 158.0 (C-4); ms: m/z 382 (1) [M+1], 325 (21) [M-56], 324 (38), 221 (18), 210 (100) [Ph-C≡N-C_6H_4-OMe(*p*)], 195 (4), 134 (4), 115 (6), 92 (5), 77 (10).

Anal. Calcd. for $C_{23}H_{19}N_5O$: C, 72.42; H, 5.02; N, 18.36. Found: C, 72.33; H, 4.90; N, 18.11.

5-*p*-Chlorophenyl-3,6-diphenyl-4,5-dihydro-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]triazine (**10c**).

This compound was prepared from **9c** (0.403 g, 1 mmole) as white crystals, (0.162 g, 42%), mp 204-206° (from methylene chloride-diethyl ether); ir: ν 1585, 1555 cm^{-1}; ^1H nmr (deuteriochloroform): δ 5.32 (s, 2H, CH_2), 6.70 (d, J = 8.7 Hz, 2H), 7.19 (d, J = 8.7 Hz, 2H), 7.20-7.48 (m, 8H), 7.61-7.65 (m, 2H); ^{13}C nmr (deuteriochloroform): δ 47.1 (CH_2), 116.6 (C-3a), 140.4 (C-3), 152.8 (C-6); 3-phenyl: 126.0 (C-2,C-6), 128.1 (C-4), 128.9 (C-3,C-5), 130.3 (C-1); 6-phenyl: 128.3 (C-2,C-6), 129.6 (C-3,C-5), 130.6 (C-4), 132.0 (C-1); *N*-phenyl: 126.2 (C-2,C-6), 129.4 (C-3,C-5), 131.5 (C-4), 142.5 (C-1); ms: m/z 388/386 (1) [M+1], 331/329 (16) [M-56], 328 (31), 216 (36), 215(17), 214 (100) [Ph-C≡N-C_6H_4-Cl(*p*)], 190 (7), 151 (3), 138 (4), 115 (27), 113/111 (42), 103 (6), 91 (35), 77 (20).

Anal. Calcd. for $C_{22}H_{16}N_5Cl$: C, 68.48; H, 4.18; N, 18.15. Found: C, 68.60; H, 4.45; N, 18.14.

Preparation of 1-Amino-5-arylaminomethyl-4-phenyl-1,2,3-triazoles **11**. General Procedure.

Compound **9** (1 mmole) was refluxed under argon atmosphere for 24 hours in a mixture of ethanol (25 ml) and concentrated hydrochloric acid (7 ml). After evaporation of the solvent to dryness, a 10% sodium bicarbonate solution (10 ml) was added and the precipitated solid was filtered and washed with ethyl ether. When the amine was not solidified, the sodium bicarbonate solution was extracted with methylene chloride, dried (sodium sulfate) and after evaporation of the solvent the solidified amine was recrystallized from the appropriate solvent.

1-Amino-5-phenylaminomethyl-4-phenyl-1,2,3-triazole (**11a**).

This compound was prepared from **9a** as white crystals, 0.21 g (80%), mp 119-121° (from *n*-hexane-diethyl ether); ir: ν 3300, 3200 (NH_2, NH), 1595 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 4.39 (s, 2H, CH_2), 6.61 (m as t, 1H), 6.67 (m as t, 2H), 7.09 (m as t, 2H), 7.35 (m as t, 1H), 7.44 (m as t, 2H), 7.55 (m, 2H); ^{13}C nmr

(dimethyl sulfoxide-d_6): δ 40.3 (CH_2), 129.7 (C-5tr), 143.1 (C-4tr); 4-phenyl: 126.5 (C-2,C-6), 127.6 (C-4), 128.7 (C-3,C-5), 131.4 (C-1): *N*-phenyl: 112.6 (C-2,C-6), 116.7 (C-4), 128.8 (C-3,C-5), 148.0 (C-1); ms: m/z 266 (97) [M+1], 265 (3) [M^+], 250 (2), 237 (7), 236 (14) [M-29], 221 (5), 208 (55), 207 (3), 206 (6), 180 (6), 115 (95), 106 (100), 104 (5), 93 (24), 77 (35).

Anal. Calcd. for $C_{15}H_{15}N_5$: C, 67.90; H, 5.70; N, 26.40. Found: C, 67.69; H, 5.65; N, 26.40.

1-Amino-5-(*p*-methoxyphenyl)aminomethyl-4-phenyl-1,2,3-triazole (**11b**).

This compound was prepared from **9b** as white crystals, 0.118 g (40%), mp 109-111° (from *n*-hexane-methylene chloride); ir: ν 3300, 3260 (NH_2, NH), 1590 cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.70 (s, 3H, OCH_3), 4.39 (s, 2H, CH_2), 5.83 (bs, NH), 6.55 (d, J = 8.9 Hz, 2H), 7.11 (d, J = 8.9 Hz, 2H), 7.32-7.43 (m, 3H), 7.60-7.62 (m, 2H); ^{13}C nmr (deuteriochloroform): δ 37.7 (t, J = 139.0 Hz, CH_2), 55.7 (q, J = 143.2 Hz, OCH_3), 130.1 (t, J = 5.3 Hz, C-5tr), 144.5 (C-4tr); 4-phenyl: 127.1 (C-2,C-6), 128.2 (C-4), 128.9 (C-3,C-5), 131.8 (C-1): *N*-phenyl: 114.2 (dd, J = 159.3 and 5.2 Hz, C-2,C-6), 115.1 (dd, J = 157.8 and 6.6 Hz, C-3,C-5), 141.4 (C-1) 152.9 (C-4); ms: m/z 295 (24) [M^+], 266 (1) [M-29], 249 (0.5), 238 (33) [M-57], 210 (1), 136 (100), 123 (56), 115 (46), 108 (7), 92 (20), 77 (4); hrms: Calcd. for $C_{16}H_{17}N_5O$: 295.1433/296.1467. Found: 295.1462/296.1433.

1-Amino-5-(*p*-chlorophenyl)aminomethyl-4-phenyl-1,2,3-triazole (**11c**).

This compound was prepared from **9c** as white crystals, 0.209 g (70%), mp 124-126° (from *n*-hexane-ethyl acetate); ir: ν 3230, 3110 (NH_2, NH), 1600 cm^{-1}; ^1H nmr (deuteriochloroform-dimethyl sulfoxide-d_6 4:1): δ 4.44 (s, 2H, CH_2), 6.15 (bs, NH), 6.74 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 8.3 Hz, 2H), 7.32 (m as t, 1H), 7.49 (m as t, 2H), 7.65 (m, 2H); ^{13}C nmr (deuteriochloroform-dimethyl sulfoxide-d_6 5:1): δ 36.7 (CH_2), 128.6 (C-5tr), 143.4 (C-4tr); 4-phenyl: 126.6 (C-2,C-6), 127.6 (C-4), 128.5 (C-3,C-5), 131.2 (C-1): *N*-phenyl: 115.4 (C-2,C-6), 122.0 (C-4), 128.5 (C-3,C-5), 145.1 (C-1); ms: m/z 299/301 (7) [M^+], 270/272 (7) [M-29], 255 (3), 242/244 (14), 240 (3), 214/216 (3) 140/142 (63), 138/140 (3), 132 (15), 127/129 (19), 115 (100), 111/113 (12), 104 (6), 103 (8), 77 (16).

Anal. Calcd. for $C_{15}H_{14}N_5Cl$: C, 60.10; H, 4.71; N, 23.36. Found: C, 60.00; H, 5.00; N, 23.10.

1-Amino-5-(*o*-chlorophenyl)aminomethyl-4-phenyl-1,2,3-triazole (**11d**).

This compound was prepared from **9d** as white crystals, 0.189 g (63%), mp 134-136° (from *n*-hexane-chloroform); ir: ν 3260, 3230, 3200 (NH_2, NH), 1620 cm^{-1}; ^1H nmr (deuteriochloroform): δ 4.59 (s, 2H, CH_2), 5.50 (bs, NH), 6.57 (dd, J = 8.1 and 1.3 Hz, 1H), 6.67 (ddd, J = 7.9, 7.4 and 1.3 Hz, 1H), 7.03 (ddd, J = 8.1, 7.4 and 1.3 Hz, 1H), 7.23 (dd, J = 7.9 and 1.4 Hz, 1H), 7.39-7.78 (m, 3H), 7.64-7.68 (m, 2H); ^{13}C nmr (deuteriochloroform): δ 36.4 (t, J = 139.8 Hz, CH_2), 129.7 (C-5tr), 145.0 (C-4tr); 4-phenyl: 127.4 (C-2,C-6), 128.5 (C-4), 129.0 (C-3,C-5), 130.8 (C-1): *N*-phenyl: 112.0, 120.0 (C-2,C-6), 118.7 (C-4), 127.8, 129.3 (C-3,C-5), 142.7 (C-1); ms: m/z 299/301 (5) [M^+], 270/272 (6) [M-29], 255 (3), 253 (4), 242/244 (18), 240 (3), 214/216 (3), 140/142 (61), 138 (5), 137 (7), 131 (8), 127/129 (32), 115 (100), 111/113 (5), 104 (8), 103 (10), 77 (32); hrms: Calcd. for $C_{15}H_{14}N_5Cl$: 299.0938/301.0908. Found: 299.0836/301.0873; Calcd. for [M+H]: 300.1016. Found: 300.1024.

1-Amino-5-(*p*-nitrophenyl)aminomethyl-4-phenyl-1,2,3-triazole (**11e**).

This compound was prepared from **9e** as pale yellow crystals, 0.279 g (90%), mp 233-236° (from ethanol-diethyl ether); ir: ν 3340, 3290, 3200 (NH_2, NH), 1590 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 4.57 (d, J = 4.7 Hz, 2H, CH_2), 6.73 (d, J = 9.2 Hz, 2H), 7.37 (m as t, 1H), 7.46 (m as t, 2H), 7.57 (t, J = 4.7 Hz, NH), 7.71 (m, 2H), 8.04 (d, J = 9.2 Hz, 2H); ^{13}C nmr (dimethyl sulfoxide-d_6): δ 35.3 (CH_2), 128.6 (C-5tr), 143.2 (C-4tr); 4-phenyl: 126.5 (C-2,C-6), 127.8 (C-4), 128.7 (C-3,C-5), 131.1 (C-1): *N*-phenyl: 111.5 (C-2,C-6), 125.9 (C-3,C-5), 136.4 (C-4), 153.6 (C-1); ms: m/z 282 (2), 281 (10) [M-29], 265 (7), 264 (2), 253 (1), 251 (1), 217 (4), 151 (30), 138 (4), 132 (37), 131 (8), 116 (19), 115 (100), 106 (7), 105 (45), 104 (11), 103 (6), 77 (14).

Anal. Calcd. for $C_{15}H_{14}N_6O_2$: C, 58.06; H, 4.55; N, 27.08. Found: C, 57.81; H, 4.62; N, 27.16.

Preparation of 5-Aryl-3-phenyl-4,5-dihydro-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]triazines **12**. General Procedure.

A mixture of the amine **11** (1 mmole), *p*-toluenesulfonic acid (0.172 g, 1 mmole) and ethyl orthoformate (2 ml) was stirred at 20-25° for 45-90 minutes. The precipitated solid was filtered and washed with ethyl ether to give **12** in yields above 90% for all derivatives **12a-e**. Compound **12d** was separated by column chromatography (silica gel with *n*-hexane/ethyl acetate 1:1 as eluent).

3,5-Diphenyl-4,5-dihydro-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]triazine (**12a**).

This compound was prepared from **11a** as white crystals, 0.25 g (90%), mp 177-180° (from ethyl acetate-*n*-hexane); ir: ν 1600, 1580 cm^{-1}; ^1H nmr (deuteriochloroform-dimethyl sulfoxide-d_6 5:1): δ 5.32 (s, 2H, CH_2), 7.30-7.53 (m, 8H), 7.45 (s, 1H, 6-H), 7.67-7.70 (m, 2H); ^{13}C nmr (deuteriochloroform-dimethyl sulfoxide-d_6 5:1): δ 43.2 (CH_2), 115.2 (C-3a), 141.0 (C-3), 142.0 (C-6); 3-phenyl: 125.7 (C-2,C-6), 127.9 (C-4), 128.9 (C-3,C-5), 130.0 (C-4); *N*-phenyl: 119.4 (C-2,C-6), 126.3 (C-4), 129.8 (C-3,C-5), 141.4 (C-1); ms: m/z 276 (10) [M+1], 275 (0.5) [M^+], 219 (49) [M-56], 116 (16), 115 (30), 104 (100), 89 (3), 77 (82); hrms: Calcd. for $C_{16}H_{13}N_5$: 275.1171/276.1205. Found: 275.1203/276.1170.

5-*p*-Methoxyphenyl-3-phenyl-4,5-dihydro-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]triazine (**12b**).

This compound was prepared from **11b** as white crystals, 0.275 g (90%), mp 165-174° (from ethyl acetate-*n*-hexane); ir: ν 1620, 1590 cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.84 (s, 3H, OCH_3), 5.25 (s, 2H, CH_2), 7.00 (d, J = 8.9 Hz, 2H), 7.23 (s, 1H, 6-H), 7.24 (d, J = 8.9 Hz, 2H), 7.32 (m as t, 1H), 7.41 (m as t, 2H), 7.63-7.67 (m, 2H); ^{13}C nmr (deuteriochloroform): δ 44.5 (CH_2), 55.4 (OCH_3), 115.3 (C-3a), 141.2 (C-3), 143.0 (d, J = 199.8 Hz, C-6); 3-phenyl: 126.0 (C-2,C-6), 128.2 (C-4), 129.0 (C-3,C-5), 130.4 (C-1); *N*-phenyl: 115.3 (C-3,C-5), 122.6 (C-2,C-6), 135.2 (C-1), 158.6 (C-4); ms: m/z 306 (21) [M+1], 305 (2) [M^+], 249 (25) [M-56], 172 (1), 134 (100), 121 (6), 115 (21), 107 (29), 92 (22), 89 (18), 77 (9); hrms: Calcd. for $C_{17}H_{15}N_5O$: 305.1277. Found: 305.1214.

5-*p*-Chlorophenyl-3-phenyl-4,5-dihydro-8*H*-[1,2,3]triazolo-[5,1-*f*][1,2,4]triazine (**12c**).

This compound was prepared from **11c** as white crystals, 0.278 g (90%), mp 184-186° (from ethanol); ir: ν 1605, 1590 cm^{-1}; ^1H

nmr (deuteriochloroform-dimethyl sulfoxide-d_6 5:1): δ 5.36 (s, 2H, CH_2), 7.34-7.47 (m, 7H), 7.62 (s, 1H, 6-H), 7.70-7.74 (m, 2H); ^{13}C nmr (deuteriochloroform-dimethyl sulfoxide-d_6 5:1): δ 42.1 (td, J = 147.4 and 4.5 Hz, CH_2), 114.7 (t, J = 5.4 Hz, C-3a), 140.0 (C-3), 141.1 (d, J = 201.4 Hz, C-6); 3-phenyl: 124.9 (C-2,C-6), 127.0 (C-4), 128.7 (C-3,C-5), 130.1 (C-1); *N*-phenyl: 119.8 (dd, J = 163.2 and 7.6 Hz, C-2,C-6), 128.7 (dd, J = 167.2 and 5.0 Hz, C-3,C-5), 129.2 (C-4), 139.3 (t, J = 7.6 Hz, C-1); ms: m/z 312/310 (16) [M+1], 311/309 (2) [M+], 255/253 (46) [M-56], 218 (17), 217 (17), 140/138 (100), 127/125 (7), 116 (31), 115 (61), 113/111 (82), 103 (6), 89 (18), 77 (9) 75 (40).

Anal. Calcd. for $C_{16}H_{12}N_5Cl$: C, 62.04; H, 3.90; N, 22.61. Found: C, 62.00; H, 3.68; N, 22.41.

5-*o*-Chlorophenyl-3-phenyl-4,5-dihydro-8*H*-[1,2,3]triazolo-[5,1-*f*][1,2,4]triazine (**12d**).

This compound was prepared from **11d** as white crystals, 0.276 g (90%), mp 164-166° (from ethyl acetate-*n*-hexane); ir: ν 1620, 1600 cm^{-1}; ^1H nmr (deuteriochloroform): δ 5.20 (s, 2H, CH_2), 7.02 (s, 1H, 6-H), 7.30-7.59 (m, 7H), 7.61-7.64 (m, 2H); ^{13}C nmr (deuteriochloroform): δ 45.2 (td, J = 147.6 and 4.7 Hz, CH_2), 115.2 (t, J = 5.9 Hz, C-3a), 141.3 (C-3), 144.1 (d, J = 201.2 Hz, C-6); 3-phenyl: 126.0 (C-2,C-6), 128.2 (C-4), 129.0 (C-3,C-5), 130.4 (C-1); *N*-phenyl: 128.8, 128.9, 131.3, 131.9, 139.2; ms: m/z 312/310 (17) [M+1], 311/309 (5) [M+], 255/253 (40) [M-56], 218 (24), 217 (26), 140/138 (100), 127/125 (2), 116 (19), 115 (63), 113/111 (62), 103 (2), 89 (17), 77 (8), 75 (35); hrms: Calcd. for $C_{16}H_{12}N_5Cl$: 309.0781. Found: 309.0721.

5-*p*-Nitrophenyl-3-phenyl-4,5-dihydro-8*H*-[1,2,3]triazolo[5,1-*f*]-[1,2,4]triazine (**12e**).

This compound was prepared from **11e** as light yellow crystals, 0.290 g (90%), mp 290-293° (almost insoluble in all common solvents, therefore not recrystallized but washed with boiling butanol, methanol and diethyl ether); ir: ν 1620, 1600, 1580 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 5.33 (s, 2H, CH_2), 7.40 (m as t, 1H), 7.51 (m as t, 2H), 7.79 (d, J = 9.2 Hz, 2H), 7.80 (m, 2H), 8.27 (s, 1H, 6-H), 8.33 (d, J = 9.2 Hz, 2H); ^{13}C nmr (dimethyl sulfoxide-d_6): δ 42.3 (CH_2), 116.8 (C-3a), 140.4 (C-3), 141.4 (C-6); 3-phenyl: 125.8 (C-2,C-6), 128.0 (C-4), 128.9 (C-3,C-5), 130.1 (C-1); *N*-phenyl: 118.1 (C-2,C-6), 124.9 (C-3,C-5), 143.5 (C-4), 146.5 (C-1); ms: m/z 292 (1) [M-28], 264 (33) [M-56], 218 (19), 217 (13), 170 (0.5), 149 (100), 122 (10), 115 (51), 114 (23), 92 (5), 89 (6), 77 (8), 76 (29), 75 (14); [14].

Preparation of 5-Aryl-3-phenyl-4,5,6,7-tetrahydro-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]triazin-6-ones **13**. General Procedure.

To a solution of aminotriazole **11** (1 mmole) in dry toluene (6 ml), under an argon atmosphere, a 20% solution of phosgene in toluene (0.89 ml, 1.8 mmoles) and triethylamine (0.48 ml, 3.5 mmoles) were added. The mixture was stirred at 25° for 2 hours and then diluted with methylene chloride (20 ml) and washed with 5% aqueous hydrochloric acid (10 ml) and water (10 ml). After drying (sodium sulfate) the solvent was removed and from the residue on treatment with ethyl ether compounds **13** were precipitated and recrystallized from the appropriate solvent.

3,5-Diphenyl-4,5,6,7-tetrahydro-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]-triazin-6-one (**13a**).

This compound was prepared from **11a** (0.265 g, 1 mmole) as white crystals 0.14 g (48%), mp 246-248° dec (from *n*-hexane-chloroform); ir: ν 3200 (vw), 1645, 1580 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 5.26 (s, 2H, CH_2), 7.14-7.39 (m, 3H), 7.42-7.49 (m, 5H), 7.70-7.73 (m, 2H); ^{13}C nmr (dimethyl sulfoxide-d_6); δ 44.5 (CH_2), 117.2 (C-3a), 141.2 (C-3), 150.4 (C-6); 3-phenyl: 126.1 (C-2,C-6), 127.9 (C-4), 128.8 (C-3,C-5), 130.0 (C-1); *N*-phenyl: 125.2 (C-2,C-6), 126.7 (C-4), 128.9 (C-3,C-5), 139.5 (C-1); ms: m/z 292 (8) [M+1], 264 (4), 263 (25), 262 (20), 219 (7), 186 (6), 134 (6), 116 (11), 115 (100), 106 (22), 105 (9), 104 (12), 89 (9), 77 (20).

Anal. Calcd. for $C_{16}H_{13}N_5O$: C, 65.97; H, 4.50; N, 24.04. Found: C, 65.68; H, 4.80; N, 23.87.

5-*p*-Chlorophenyl-3-phenyl-4,5,6,7-tetrahydro-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]triazin-6-one (**13c**).

This compound was prepared from **11c** (0.299 g, 1 mmole) as white crystals 0.145 g (45%), mp 198-201° (from *n*-hexane-ethyl acetate); ir: ν 3200, 1670, 1590 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 5.08 (s, 2H, CH_2), 7.27-7.33 (m, 1H), 7.35-7.46 (m, 6H), 7.68-7.71 (m, 2H); ^{13}C nmr (dimethyl sulfoxide-d_6); δ 43.5 (CH_2), 116.8 (C-3a), 142.4 (C-3), 154.4 (C-6); 3-phenyl: 126.0 (C-2,C-6), 127.9 (C-4), 128.7 (C-3,C-5), 131.3 (C-1); *N*-phenyl: 125.3 (C-2,C-6), 127.1 (C-4), 127.8 (C-3,C-5), 138.3 (C-1); ms: m/z 299 (9), 298 (4), 297 (14) [M-28], 296 (3), 262 (2), 155/153 (9), 142/140 (16), 139 (8), 138 (12), 116 (14), 115 (100), 113/111 (11), 103 (12), 89 (11), 75 (11).

Anal. Calcd. for $C_{16}H_{12}N_5OCl$: C, 58.99; H, 3.71; N, 21.50. Found: C, 58.92; H, 3.97; N, 21.34.

3-Phenyl-8*H*-[1,2,3]triazolo[5,1-*f*][1,2,4]triazine (**14**).

To a stirred solution of compound **12b** (0.152 g, 0.5 mmole) in acetonitrile (5 ml), cooled in ice-bath, a solution of cerium ammonium nitrate (0.822 g, 1.5 mmoles) in water (6 ml) was added dropwise. Stirring was continued for 30 minutes at 0° and then the reaction mixture was poured into water (20 ml) and the mixture was extracted with methylene chloride (3 x 20 ml) and dried (sodium sulfate). After evaporation of the solvent, the residue was chromatographed on a silica gel column (*n*-hexane/ethyl acetate mixture as eluent) to give 0.02 g (20%) of compound **14**, mp 177-180° (from *n*-hexane/ethyl acetate); ir: ν 1620, 1580 cm^{-1}; ^1H nmr (deuteriochloroform): δ 7.42-7.63 (m, 3H), 8.02-8.07 (m, 2H), 8.94 (s, 1H, 4-H), 9.83 (s, 1H, 6-H); ^{13}C nmr (deuteriochloroform): δ 126.5 (C-3a), 130.0 (C-3), 150.1 (C-4), 155.1 (C-6); phenyl: 127.2 (C-2,C-6), 128.7 (C-4), 129.1 (C-1), 129.5 (C-3,C-5); ms: m/z 197 (5) [M+], 141 (11) [M-56], 114 (100), 113 (10), 88 (15), 75 (4); hrms: Calcd. for $C_{10}H_7N_5$: 197.0701/198.0739. Found: 197.0675/198.0730.

Hydrolysis of Compound **12a**.

A slurry of compound **12a** (0.0275 g, 0.1 mmole) in a 20% ethanolic hydrochloric acid solution (2.5 ml) was refluxed for 24 hours. The solvent was evaporated to dryness, and to the residue 10% solution of sodium carbonate (7 ml) was added and this was extracted with methylene chloride (3 x 10 ml). The organic layer after drying (sodium sulfate) and evaporation of the solvent gave a mixture of products which was chromatographed on a silica gel preparative tlc plate (using ethyl acetate-methylene chloride 1:1 as eluent) to give 0.014 g (50%) of **11a**, mp 118-121°, with spectroscopic characteristics identical to that described above.

Reaction of **5** with Potassium Cyanide.

To a solution of 5 (Ar = Ph) (0.115 g, 0.25 mmole) in ethanol (2 ml) a solution of potassium cyanide (0.027 g, 0.41 mmole) in

water (1 ml) was added and the mixture was refluxed for 1 hour. From the reaction mixture after cooling a solid was precipitated, which was separated by filtration and washed with ethyl ether to give 0.035 g (50%) of 3,6-diphenyl-4*H*-[1,2,3]triazolo[5,1-*d*]-[1,3,4]oxadiazine (**6**), mp 232-234° (lit [6] 237°). Spectroscopic data of this compound (ir, ^{1}H nmr, ms) were in agreement to those given in the literature [6] and identical with those of an authentic sample of compound **6**.

Compound **6** was also formed exclusively (tlc monitoring) when a solution of **5** (0.115 g, 0.25 mmole) and triethylbenzylammonium chloride (0.015 g) in methylene chloride (3 ml) was allowed to react with a solution of potassium cyanide (0.065 g, 1 mmole) in water (2 ml) under stirring for 5 hours at 25° (two phase system conditions).

Acknowledgment.

One of us, E. L., wishes to thank the State Scholarship Foundation of Greece for a financial support.

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[14] It was not possible to have elemental analysis of **12e** since it was not possible to be recrystallized from all common solvents.