Non Conventional Syntheses of Heterocyclic Compounds. 2. Synthesis of 1*H*-4,5-Dihydro-1,3,4-Benzotriazepine Derivatives

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Arylazoanils carrying aromatic methyl or ethyl groups in the position *ortho* to the imine function thermally cyclize to give 1*H*-4,5-dihydro-1,3,4-benzotriazepine derivatives in fairly good yields. A study of the effect of the substituents on both the aryl rings is reported. The reaction is interpreted as an internal oxo-reduction process.

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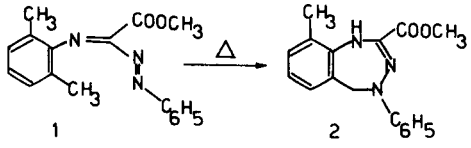
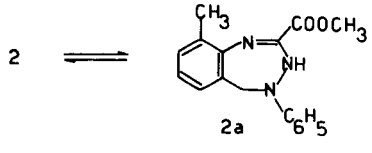
We recently gave in a short note [1] a preliminary account of an unexpected thermal cyclization of arylazoketimine **1** to benzotriazepine **2**, whose structure was demonstrated chemically:



In the present paper we report the results obtained on extending this new reaction to eleven other substrates.

A more correct definition of the dihydrobenzotriazepine structure concerns the possibility of the existence of the following tautomeric equilibrium:



In order to clarify this detail, the benzotriazepine derivative **2** labelled with ^{15}N in position 3 was synthetized [2]. Coupling of the proton with ^{15}N was never observed in the nmr spectra recorded in different solvents; this excluded the intervention of structure **2a**. The synthesis of the arylazoketimine substrates **5** was carried out according to the following general Scheme I (for the meaning of R, R', R'', R''' see Table I):

Scheme 1

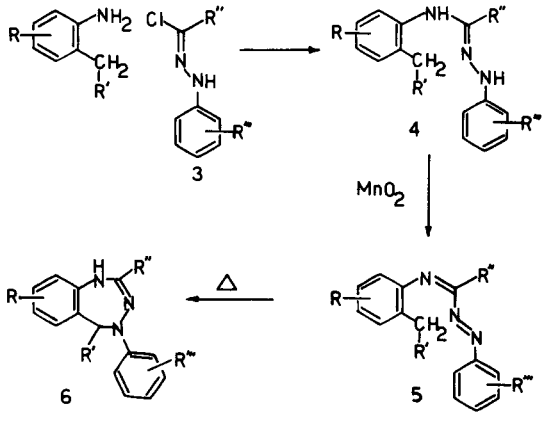


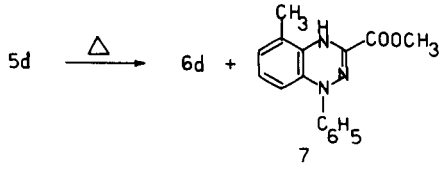
Table I

Substrate **5**	R	R'	R''	R'''	Yield % of **6**	Reaction time (hours)
a	6-Me	H	COOMe	H	82	2
b	4,6-diMe	H	COOMe	H	87	1.5
c	6-Et	Me	COOMe	H	65	1
d	H	H	COOMe	H	18	0.5
e	6-Me	H	COOMe	4-NO_2	73	0.5
f	6-Me	H	COOMe	2,4-diNO_2	50	0.3
g	6-Me	H	COOMe	2,4,6-triNO_2	46	0.15
h	6-Me	H	H	H	55	20
i	6-Me	H	CN	H	81	1.5

Halohydrazones **3** reacted with aromatic amines affording the arylaminohydrazones **4** which, in turn, were oxidized with manganese dioxide to give the corresponding arylazoanils **5**. These were then converted to dihydrobenzotriazepines **6** by heating in xylene solution in the presence of catalytic amounts of DABCO. Table I summarizes substrates, products, yields and the reaction time required for completing the transformation of **5**.

Structural assignments to different products are based both on analytical data and the unequivocal interpretation of ^{1}H nmr spectra in accordance with that of **2**.

The modest yields obtained for compounds **6f** and **6g** can be ascribed to a concurrent reduction process of **5f** and **5g** affording **4f** and **4g** respectively, possibly involving the solvent. In the case of substrate **5d** where one of the "ortho" positions of the arylketimine moiety is unsubstituted, we observed both cyclization to benzotriazepine **6d** and an electrocyclic reaction (already known in literature [3]) to 1,4-dihydro-1,2,4-benzotriazine **7**, which is the main reaction product.



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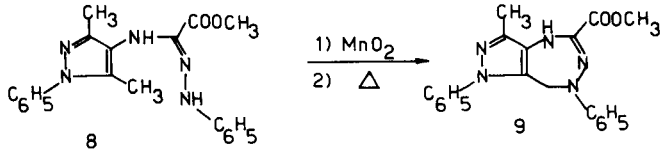
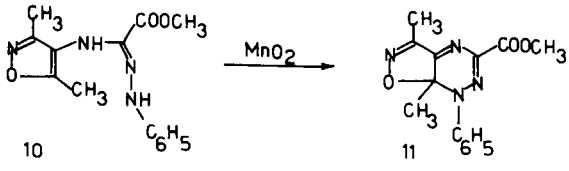
In addition to those reported in Table I, two etherocyclic substrates **8** and **10** were investigated. The arylazomine derivative prepared from 4-amino-3,5-dimethyl-1-phenylpyrazole, gave **9**, the first term of the 1*H*,4*H*-pyrazolo[5,4-*e*][1,2,4]triazepine class in very good



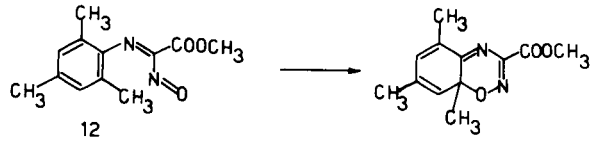
8 9

overall yields. A different evolution of the reaction was observed in the case of the isoxazole substrate **10**, which was rapidly converted by oxidation, even at room temperature, into the 4*H*-isoxazolo[5,4-*e*][1,2,4]triazine derivative **11**, analytical and spectral data confirming the assigned



10 11

structure. The electrocyclic reaction converting **10** to **11** shows some analogy with that of the nitrosoketimine **12** studied by Gilchrist and coworkers [4]. In the case in hand



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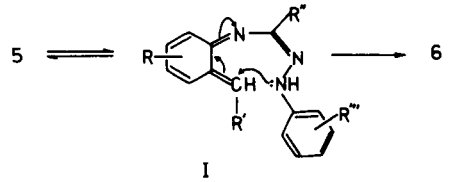
this reaction path can be ascribed to the lower aromaticity of the isoxazole ring, in which the connection between positions 4 and 5 possesses a marked double bond character [5]. In our view, the most satisfactory mechanistic hypothesis for the formation of dihydrobenzotriazepines **6**, whose critical step is the carbon-nitrogen bond formation, involves the possibility that, at the reaction temperature, the following equilibrium could be active for the substrates:



I

Final products **6** could be formed by the addition of the NH of the hydrazonic function of I to the unsaturated conjugated system. Alternatively, the conversion of **5** into I can even be regarded as an internal oxo-reduction process, the arylimine moiety of **5** being transformed into an *ortho*-quinoid system and the arylazo group into an arylhydrazone function. The said transformation ought to be favoured by the electronic availability of the arylimine moiety of the substrate and by an electronic deficiency of the rest of the molecule. In this case the transformation rates of the arylazoimines **5** into **6** could give a rough evaluation of this tendency; experimental data are in agreement with this interpretation. In fact the strong accelerating effect of the electron withdrawing groups R'' and R''' is evident from Table I. An analogous accelerating effect further supporting this view was observed when ethyl groups or three methyl groups were present in the arylamine system.

EXPERIMENTAL

Melting points are uncorrected. The ^{15}N nmr spectra were recorded on a XL-200 Varian spectrometer and the ^{1}H nmr spectra on a A90 Varian spectrometer, using deuteriochloroform as solvent unless otherwise stated and tetramethylsilane as internal standard; chemical shifts are given in δ units and refer to the center of the signal (s, singlet, m, multiplet, d, doublet, dd, double doublet, t, triplet).

Chlorohydrazones **3**.

Methyl chloro(phenylhydrazono)acetate [6], ethyl chloro[(4-nitrophenyl)hydrazono]acetate [7], methyl chloro[(2,4-dinitrophenyl)hydrazono]acetate [8] and chloro(phenylhydrazono)acetonitrile [9] were known in the literature.

Methyl Chloro-[(2,4-dinitrophenyl)hydrazono]acetate (**3f**) and Methyl Chloro-[(2,4,6-trinitrophenyl)hydrazono]acetate (**3g**).

A mixture of nitric acid (d 1.47, 86%, 8.2 ml) and concentrated sulfuric acid (8.2 ml) was dropped into a solution of methyl

chloro[(4-nitrophenyl)hydrazono]acetate [7] (30 g) in concentrated sulfuric acid (150 ml) under stirring and cooling (15°). The solution was left to stand at 25° for 30 minutes then poured into ice; the product was extracted with chloroform and the organic layer washed with water, with 5% sodium bicarbonate solution, dried over sodium sulfate, then evaporated to dryness. The residue (28 g) was chromatographed on a silica gel column (eluant, chloroform); the first product eluted was **3f**, yellow crystals with mp 127° (benzene) (10.5 g). The following fractions gave **3g**, dark yellow crystals with mp 146° (benzene) (7.0 g).

Anal. Calcd. for $C_9H_6ClN_5O_6$: C, 31.09; H, 1.74; N, 20.15. Found: C, 30.91; H, 1.56; N, 19.76.

Arylaminoarylhydrazones **4**.

These intermediates (except **4h**) were prepared by treating the suitable arylamine with equimolar amounts of the corresponding chloro(arylhydrazono)derivative **3** and triethylamine in refluxing alcoholic solution for about two hours. Solvent was removed under reduced pressure and the residue treated with water and ethyl ether. The organic layer was washed with water, dried over sodium sulfate, then evaporated to dryness to give the title compounds which were purified by crystallization. In a few cases the products directly crystallized from the reaction mixture.

Methyl [(2,6-Dimethylphenyl)amino](phenylhydrazono)acetate (**4a**).

This compound had mp 86° (*n*-hexane), yield 75%; ^{1}H nmr: 2.30 (6H, s, $2CH_3$), 3.97 (3H, s, $COOCH_3$), 6.50 and 6.92 (2 x 1H, 2s exchanging with deuterium oxide, 2 NH), 7.0 (8H, m, aromatic).

Anal. Calcd. for $C_{17}H_{19}N_3O_2$: C, 68.66; H, 6.44; N, 14.13. Found: C, 68.53; H, 6.36; N, 14.11.

Methyl [(2,4,6-Trimethylphenyl)amino](phenylhydrazono)acetate (**4b**).

This compound had mp 103° (*n*-hexane), yield 76%; ^{1}H nmr: 2.28 and 2.35 (6H and 3H, 2s, $3CH_3$), 3.95 (1H, s, $COOCH_3$), 6.41 (1H, broad s exchanging with deuterium oxide, NH), 6.7 (3H, m, aromatic in position 2,4 and 6 of C_6H_5 group), 6.9 (2H, s, aromatic of C_6H_2group), 7.1 (2H + 1H exchanging with deuterium oxide, m, aromatic in position 3 and 5 of C_6H_5 group and NH).

Anal. Calcd. for $C_{18}H_{21}N_3O_2$: C, 69.43; H, 6.80; N, 13.50. Found: C, 69.05; H, 6.61; N, 13.21.

Methyl [(2,6-Diethylphenyl)amino](phenylhydrazono)acetate (**4c**).

This product was obtained as a viscous oil purified by column chromatography (silica gel-chloroform), yield 73%. The ^{1}H nmr spectrum showed the presence of two stereoisomers [10]: 1.2 (6H, 2 superimposed t, 2 CH_2-C*H*$_3$), 2.7 (4H, 2 superimposed q, 2 C*H*$_2$$CH_3$), 3.5 (1H, broad s, NH), 3.97 (3H, s, $COOCH_3$), 6.6-7.3 (8H + 1H exchanging with deuterium oxide, aromatic and C_6H_5-N*H*).

Anal. Calcd. for $C_{19}H_{23}N_3O_2$: C, 70.13; H, 7.12; N, 12.91. Found: C, 69.71; H, 7.45; N, 12.70.

Methyl [(2-Methylphenyl)amino](phenylhydrazono)acetate (**4d**).

This product showed mp 106° (2-propanol), yield 68%; ^{1}H nmr: 2.37 (3H, s, CH_3), 3.93 (3H, s, $COOCH_3$), 6.17 (1H, broad s exchanging with deuterium oxide, NH), 6.34 (1H, d, aromatic in position 6 of C_6H_4 group), 6.7 (9H + 1H exchanging with deuterium oxide, m, aromatic and NH).

Anal. Calcd. for $C_{16}H_{17}N_3O_2$: C, 67.82; H, 6.05; N, 14.83. Found: C, 67.74; H, 6.00; N, 14.68.

Ethyl [(2,6-Dimethylphenyl)amino][(4-nitrophenyl)hydrazono]acetate (**4e**).

This product was obtained as an orange colored solid with mp 140°, yield 67%. ^{1}H nmr spectrum showed the presence of two stereoisomers [10] in solution: 1.5 (3H, m, CH_2-C*H*$_3$), 2.33 (6H, s, $2CH_3$), 4.4 (2H, 2 superimposed q, C*H*$_2$-CH_3), 5.98, 6.78, 7.41 and 10.95 (2H in total, s exchanging with deuterium oxide, 2NH), 6.66 (2H, m, aromatic in position 2,6 of C_6H_4 group), 7.2 (3H, m, aromatic of C_6H_3 group), 8.02 (2H, aromatic in position 3,5 of C_6H_4 group).

Anal. Calcd. for $C_{18}H_{20}N_4O_4$: C, 60.66; H, 5.66; N, 15.72. Found: C, 60.86; H, 5.63; N, 15.49.

Methyl [(2,6-Dimethylphenyl)amino][(2,4-dinitrophenyl)hydrazono]acetate (**4f**).

This product showed mp 155° (ethanol), yield 85%; the ^{1}H nmr spectrum showed the presence of two stereoisomers [10] in solution in an about 1:1 ratio; 2.30 (6H, s, $2CH_3$), 4.13 (3H, 2s, $COOCH_3$), 6.47 (1H, broad s exchanging with deuterium oxide, NH), 7.20 (3H, m, aromatic), 8.10 (2H, m, aromatic in position 5 and 6 of 2,4-dinitrophenyl group), 9.03 (1H, dd, aromatic in position 3 of 2,4-dinitrophenyl group), 10.28 (1H, broad s exchanging with deuterium oxide, NH).

Anal. Calcd. for $C_{17}H_{17}N_5O_6$: C, 52.71; H, 4.42; N, 18.08. Found: C, 52.76; H, 4.41; N, 18.04.

Methyl [(2,6-Dimethylphenyl)amino][(2,4,6-trinitrophenyl)hydrazono]acetate (**4g**).

This compound had mp 211° (acetic acid), yield 77%; the ^{1}H nmr spectrum (DMSO) showed the presence of two stereoisomers [10] in solution: 2.18 and 2.28 (6H, 2s, CH_3 of the two stereoisomers), 3.80 and 4.08 (3H, 2s, $COOCH_3$ of the two stereoisomers), 7.08 and 7.15 (3H, 2s, aromatic of the xylidine group of the two stereoisomers), 8.70 and 8.84 (2H, 2s, aromatic of trinitrophenyl group of the two stereoisomers), 9.15, 10.35 and 13.23 (2H, 3s exchanging with deuterium oxide, 2NH).

Anal. Calcd. for $C_{17}H_{16}N_6O_8$: C, 47.22; H, 3.73; N, 19.44. Found: C, 46.98; H, 3.71; N, 19.27.

[(2,6-Dimethylphenyl)amino]formaldehyde Phenylhydrazone (**4h**).

Treatment of a **4a** with a 10% alcoholic potassium hydroxide solution at 50° under nitrogen, gave **4h** after removal of the solvent, dilution of the red residue with water and neutralization with acetic acid. The title compound was purified by column chromatography (silica gel-chloroform) and was obtained as a light pink solid with mp 115° dec (benzene), yield 28%; ^{1}H nmr: 7.1 (9H, m, aromatic and CH), 5.5 (2H, broad s exchanging with deuterium oxide, 2NH), 2.35 (6H, s, $2CH_3$).

Anal. Calcd. for $C_{15}H_{17}N_3$: C, 75.28; H, 7.16; N, 17.56. Found: C, 75.61; H, 7.13; N, 17.25.

[(2,6-Dimethylphenyl)amino](phenylhydrazono)acetonitrile (**4i**).

This compound showed mp 155°, yield 55%; ^{1}H nmr: 7.68 (1H, broad s exchanging with deuterium oxide, N-NH), 7.2 (8H, m, aromatic), 5.04 (1H, broad s exchanging with deuterium oxide, NH), 2.33 (6H, s, $2CH_3$).

Anal. Calcd. for $C_{16}H_{16}N_4$: C, 72.66; H, 6.10; N, 21.19. Found: C, 72.44; H, 6.05; N, 21.10.

Methyl{[(4-(3,5-Dimethyl-1-phenyl)pyrazolyl]amino}(phenylhydrazono)acetate (**8**).

The 4-amino-3,5-dimethyl-1-phenylpyrazole was prepared according to the method reported in the literature [11]. The title compound was purified by column chromatography (silica gel - benzene:ethyl acetate - 80:20) and was a yellow foamy solid which could not be crystallized, mp 49-51°, yield 88%. The product is easily oxidised by exposure on air; ^{1}H nmr: 2.23 (3H, s, CH_3), 2.30 (3H, s, CH_3), 3.97 (3H, s, $COOCH_3$), 6.30 (1H, broad s exchanging with deuterium oxide, NH), 6.80-7.50 (10H + 1H exchanging with deuterium oxide, m, aromatic and NH).

Methyl [4-(3,5-Dimethyl)isoxazolyl]amino(phenylhydrazono)acetate (**10**).

The amino-3,5-dimethylisoxazole was known in literature [12]. The title product was purified by column chromatography (silica gel - chloroform:-ethyl acetate - 95:5) and, owing its low stability, directly submitted to the manganese dioxide oxidation; yield 35%.

Arylazoarylimines (**5**).

These substrates were prepared by treating solutions of the arylaminoarylhydrazones **4** described above in methylene chloride with two fold in weight of active manganese dioxide. The reaction was generally fast and its end was checked by thin layer chromatography (eluant:chloroform); no by-products were detectable. The oxidizing

reagent was removed by suction filtration on a cell cake, then the clear solution was evaporated to dryness at 30°. The residue, generally a deeply colored oil, was directly submitted to thermal cyclization; only in two cases the products were fully characterized. Despite being used in a crude state, satisfactory resutls were generally obtained.

Methyl [(2,6-Dimethylphenyl)imino] (phenylazo)acetate (**5a**).

This compound was a red solid with mp 73°, yield 91%; the ^{1}H nmr showed the presence of two stereoisomers: 2.20 (6H, 2 close s, $2CH_3$), 3.64 and 4.04 (3H, 2s, OCH_3), 7.1-8.1 (8H, m, aromatic).

Anal. Calcd. for $C_{17}H_{17}N_3O_2$: C, 69.15; H, 5.76; N, 14.24. Found: C, 68.80; H, 5.60; N, 14.10.

[(2,6-Dimethylphenyl)imino] (phenylazo)acetonitrile (**5i**).

The product was a red-brown solid with mp 71°, yield 94%; ^{1}H nmr: 2.25 (6H, 2 close s, $2CH_3$), 7.17 (3H, m, C_6H_3), 7.68 (3H, m, aromatic in position 3, 4 and 5 of xylyl group), 8.14 (2H, m, aromatic in position 2 and 6).

Anal. Calcd. for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38; N, 21.36. Found: C, 72.88; H, 5.49; N, 20.92.

Benzotriazepines (**6**).

Convesion of arylazoarylimines **5** into 1,2,4-benzotriazepines **6** was carried out by refluxing a xylene solution of **5** in the presence of catalytic amount of DABCO. Fading of the colour was indicative of the progress of the reaction. Removal of the solvent gave a solid residue which was directly crystallized from a suitable solvent. In a few cases the final product **6** separated by cooling the reaction solution.

2-Methoxycarbonyl-4,5-dihydro-4-phenyl-9-methyl-1*H*-1,3,4-benzotriazepine (**6a**).

This compound had mp 110° (*n*-hexane), yield 82%; ^{1}H nmr: 2.30 (3H, s, CH_3), 3.99 (3H, s, $COOCH_3$), 4.75 (2H, s, CH_2), 6.7-7.7 (8H + 1H exchanging with deuterium oxide, m, aromatic and NH).

Anal. Calcd. for $C_{17}H_{17}N_3O_2$: C, 69.15; H, 5.76; N, 14.24. Found: C, 69.34; H, 5.79; N, 14.18.

2-Methoxycarbonyl-4,5-dihydro-4-phenyl-7,9-dimethyl-1*H*-1,3,4-benzotriazepine (**6b**).

This compound showed mp 157° (benzene-*n*-hexane), yield 87%; ^{1}H nmr: 2.27 (6H, s, $2CH_3$), 3.95 (3H, s, $COOCH_3$), 4.69 (2H, s, CH_2), 6.8-7.4 (7H, m, aromatic), 7.55 (1H, broad s exchanging with deuterium oxide, NH).

Anal. Calcd. for $C_{18}H_{19}N_3O_2$: C, 69.88; H, 6.19; N, 13.58. Found: C, 69.77; H, 6.06; N, 13.33.

2-Methoxycarbonyl-9-ethyl-4,5-dihydro-5-methyl-4-phenyl-1*H*-1,3,4-benzotriazepine (**6c**).

This compound had mp 148° (methanol), yield 65%; ^{1}H nmr: 1.30 (3H, t, CH_3-CH_2), 1.49 (3H, d, CH_3-CH), 2.69 (2H, q, CH_2-CH_3), 3.95 (3H, s, $COOCH_3$), 5.10 (1H, q, CH-CH_3), 6.7-7.4 (8H, m, aromatic), 7.90 (1H, broad s exchanging with deuterium oxide, NH).

Anal. Calcd. for $C_{19}H_{21}N_3O_2$: C, 70.59; H, 6.50; N, 13.00. Found: C, 70.49; H, 6.30; N, 13.21.

2-Methoxycarbonyl-4,5-dihydro-4-phenyl-1*H*-1,3,4-benzotriazepine (**6d**).

This compound was separated from **7** by precipitating its hydrochloride from an ethereal solution of the crude reaction mixture, mp 146° (*n*-hexane), yield 18%; ^{1}H nmr: 3.96 (3H, s, $COOCH_3$), 4.73 (2H, s, CH_2), 6.8-7.4 (9H, m, aromatic), 7.70 (1H, broad s exchanging with deuterium oxide, NH).

Anal. Calcd. for $C_{16}H_{15}N_3O_2$: C, 68.31; H, 5.37; N, 14.94. Found: C, 68.53; H, 5.30; N, 14.60.

The 3-carbomethoxy-1,4-dihydro-5-methyl-1-phenyl-1,2,4-benzotriazine (**7**) was purified by column chromatography (silica gel-chloroform), mp 115° (2-propanol), yield 62%; ^{1}H nmr: 2.07 (3H, s, CH_3), 3.86 (3H, s, $COOCH_3$), 6.0-7.4 (9H, m, aromatic and NH); ms: 192.

2-Methoxycarbonyl-4,5-dihydro-9-methyl-4-(4-nitrophenyl)-1*H*-1,3,4-benzotriazepine (**6e**).

This compound had mp 214° (toluene), yield 73%; ^{1}H nmr: 1.50 (3H, t, CH_3-CH_2), 2.35 (3H, s, CH_3), 4.50 (2H, q, CH_2CH_3), 4.87 (2H, s, CH_2), 7.15 (3H, m, aromatic), 7.27 and 8.20 (each 2H of AA'-BB' system, aromatic of $C_6H_4NO_2$), 7.90 (1H, broad s exchanging with deuterium oxide, NH).

Anal. Calcd. for $C_{17}H_{16}N_4O_4$: C, 60.00; H, 4.71; N, 16.47. Found: C, 60.20; H, 4.90; N, 16.10.

2-Methoxycarbonyl-4,5-dihydro-4-(2,4-dinitrophenyl)-9-methyl-1*H*-1,3,4-benzotriazepine (**6f**).

This product showed mp 183° (toluene), yield 50%; ^{1}H nmr: 2.36 (3H, s, CH_3), 4.00 (3H, s, $COOCH_3$), 4.74 (2H, s, CH_2), 7.10 (3H, m, aromatic of benzotriazepine ring), 7.65 (1H, d, aromatic in position 6 of dinitrophenyl group), 7.97 (1H, broad s exchanging with deuterium oxide, NH), 8.28 (1H, dd, aromatic in position 5 of dinitrophenyl group), 8.57 (1H, d, aromatic in position 3 of dinitrophenyl group).

Anal. Calcd. for $C_{17}H_{15}N_5O_6$: C, 52.99; H, 3.92; N, 18.18. Found: C, 52.93; H, 3.98; N, 18.04.

2-Methoxycarbonyl-4,5-dihydro-9-methyl-4-(2,4,6-trinitrophenyl)-1*H*-1,3,-4-benzotriazepine (**6g**).

This compound had mp 227° (acetic acid), yield 46%; the product was separated by column chromatography (silica gel-chloroform) from **4g**, which was concurrently formed in a 23% yield. ^{1}H nmr (DMSO): 2.38 (3H, s, CH_3), 3.88 (3H, s, $COOCH_3$), 4.83 (2H, s, CH_2), 7.1 (3H, m, aromatic of benzotriazepine ring), 8.07 (1H, s, exchanging with deuterium oxide, NH), 9.08 (2H, s, aromatic of trinitrophenyl group).

Anal. Calcd. for $C_{17}H_{14}N_6O_8$: C, 47.44; H, 3.28; N, 19.53. Found: C, 47.66; H, 3.22; N, 19.83.

4-Phenyl-4,5-dihydro-9-methyl-1*H*-1,3,4-benzotriazepine (**6h**).

This compound had mp 127° (diisopropyl ether-*n*-hexane), yield 55%. The product was purified by column chromatography; it was identical to the product obtained by hydrolysis and decarboxylation of **6a** [1]; ^{1}H nmr: 2.22 (3H, s, CH_3), 4.63 (2H, s, CH_2), 6.10 (1H, broad s exchanging with deuterium oxide, NH), 6.7-7.3 (9H, m, aromatic).

Anal. Calcd. for $C_{15}H_{15}N_3$: C, 75.95; H, 6.33; N, 17.72. Found: C, 75.92; H, 6.52; N, 17.58.

2-Cyano-4,5-dihydro-9-methyl-4-phenyl-1*H*-1,3,4-benzotriazepine (**6i**).

This compound showed mp 162° (benzene), yield 81%; ^{1}H nmr: 2.31 (3H, s, CH_3), 4.76 (2H, s, CH_2), 6.21 (1H, broad s, NH) 6.8-7.5 (8H, m, aromatic).

Anal. Calcd. for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38; N, 21.36. Found: C, 73.16; H, 5.55; N, 21.17.

5-Methoxycarbonyl-7,8-dihydro-3-methyl-1,7-diphenyl-1*H*,4*H*-pyrazolo-[5,4-*e*] [1,2,4]triazepine (**9**).

The reaction was completed in 15 minutes; the title product was purified by column chromatography (silica gel-ethyl ether) and obtained as a colourless solid with mp 142° (ethyl ether), yield 87%; the ^{1}H nmr spectra in different solvents show that **9** is present in solution as a 3:2 mixture of two tautomers whose interconversion is fast in the presence of trifluoroacetic acid as a catalyst as shown by cohalescence of a few signals; (deuteriochloroform): 2.35 (3H, s, CH_3), 3.99 (3H, s, OCH_3), 4.78 and 4.94 (2s collapsing into a s at 4.85 after addition of trifluoroacetic acid, 2H, CH_2), 6.60-7.50 (10H, m, aromatic), 8.30 (broad s NH); (carbon disulphide):2.12 and 2.23 (2s collapsing into a s at 2.19 after addition of trifluoroacetic acid, 3H, CH_3), 3.84 (3H, s, OCH_3), 4.67 and 4.83 (2s collapsing into a s at 4.78 after addition of trifluoroacetic acid, 2H, CH_2), 6.4-7.4 (10H, m, aromatic), 0.07 (broad s, NH); (hexadeuteriobenzene): 1.98 and 2.40 (2s collapsing into a s at 2.02 after addition of trifluoroacetic acid, 3H, CH_3), 3.43 and 3.50 (2s collapsing into a s at 3.66 after addition of trifluoroacetic acid, 3H, OCH_3), 4.58 (2H, s, CH_2), 6.5-7.5 (10H, m, aromatic), 8.10 (broad s exchanging with deuterium oxide, NH).

Anal. Calcd. for $C_{20}H_{19}N_5O_2$: C, 66.47; H, 5.30; N, 19.38. Found: C, 66.16; H, 5.60; N, 19.16.

5-Methoxycarbonyl-7,9-dihydro-3,9-dimethyl-7-phenylisoxazolo[5,4-*e*][1,-2,4]triazine (**11**).

Oxidation of **10** (10.9 g) with active manganese dioxide (22 g) in refluxing methylene chloride (110 ml) solution for 20 minutes gave, after removal of the solid by filtration on a cell cake and evaporation of the solvent, a residue which was first crystallized from cyclohexane then from 2-propanol. The product was a dark-yellow solid with mp 146°, yield 49%; ^{1}H nmr: 1.40 (3H, s, CH_3 on saturated carbon), 2.44 (3H, s, CH_3 in position 5), 4.07 (3H, s, OCH_3), 7.2-7.8 (10H, m, aromatic); ms: 286.

Anal. Calcd. for $C_{14}H_{14}N_4O_3$: C, 58.73; H, 4.93; N, 19.57. Found: C, 58.62; H, 4.75; N, 19.52.

REFERENCES AND NOTES

[1] R. Fusco and F. Sannicolò, *Tetrahedron Letters*, **23**, 1829 (1982).

[2] Labelled **6a** was synthesized following the reaction sequence reported in Scheme I, starting from a labelled methyl chloro(phenylhydrazono)acetate. This was obtained by coupling the phenyldiazonium chloride, prepared from aniline, hydrochloric acid and labelled sodium nitrite (95% isotopic purity), with methyl 2-chloro-3-oxobutyrate.

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