Pyridazine-4,5-dicarboxylic Anhydride: Versatile Synthon for the Preparation of 1,3,7,8-Tetra-azaspiro[4.5]decane Derivatives with Nitrogen 1,3-Binucleophiles

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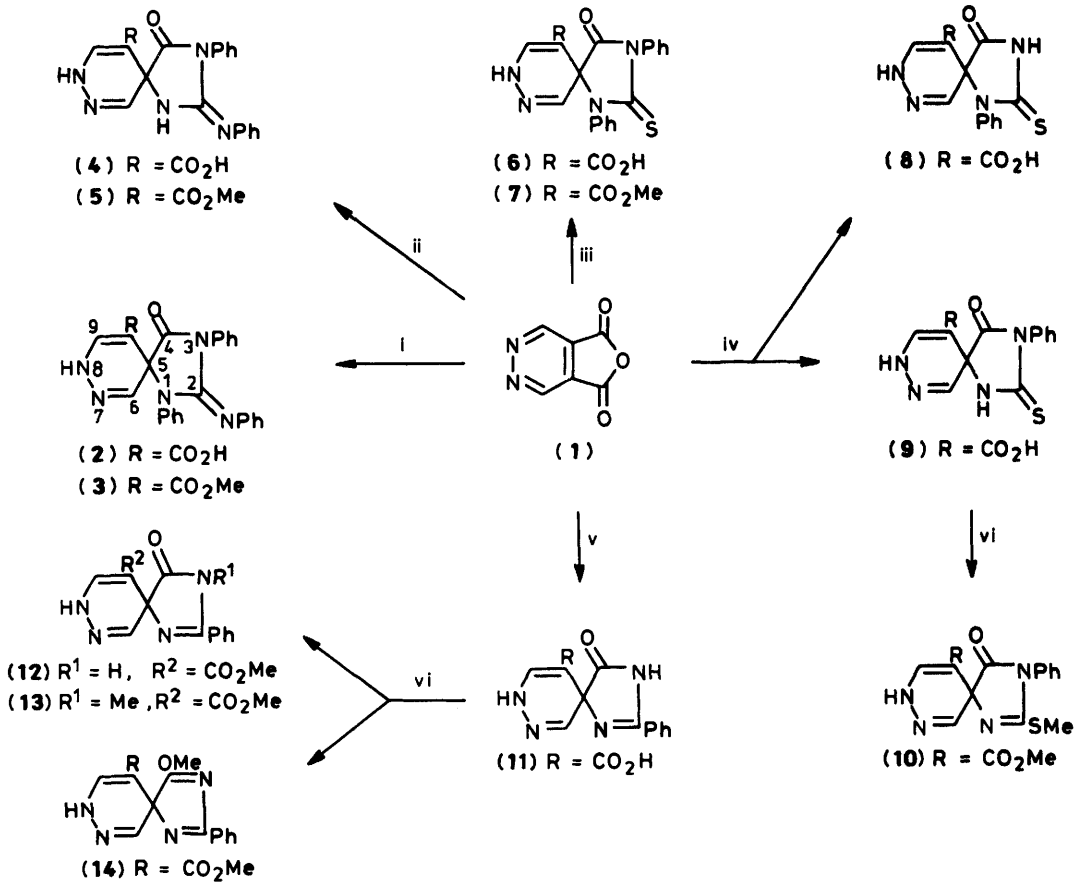
The title compound (**1**) reacted smoothly with 1,2,3-triphenyl- and 1,3-diphenyl-guanidine, with *N,N'*-diphenyl- and *N*-phenyl-thiourea, and with benzamidine to give in very good yields the 1,3,7,8-tetra-azaspiro[4.5]decane derivatives (**2**), (**4**), (**6**), (**9**), and (**11**), respectively, through a Smiles-type rearrangement. The reaction of compound (**1**) with 1,3-diphenylguanidine showed a different regiospecificity from that observed for the spiro-cyclization of dimethyl pyridazine-4,5-dicarboxylate (**15**) into methyl 4-oxo-1-phenyl-2-phenylimino-1,3,7,8-tetra-azaspiro[4.5]deca-6,9-diene-10-carboxylate (**19**), carried out with the same reagent in the presence of sodium hydride. The structures of the new heterospiro compounds were determined on the basis of chemical and spectroscopic evidence.

Earlier results from our laboratory showed that pyridazine-4,5-dicarboxylic anhydride (**1**), readily available from the corresponding acid (**16**),[1] represents a useful intermediate for pyridazine and pyridazino[4,5-*d*]pyridazine derivatives;[1,2] moreover it has also been employed more recently for the synthesis of new heterospiro ring systems by reaction with *o*-phenylenediamine and 2-aminothiophenol, respectively.[3] We wish now to report some reactions of this compound with different nitrogen 1,3-binucleophiles, a convenient route to 1,3,7,8-tetra-azaspiro[4.5]decane derivatives with various substituents on the penta-atomic ring (Scheme 1).

Treatment of compound (**1**) with 1,2,3-triphenylguanidine (TPG) in anhydrous tetrahydrofuran at room temperature afforded 4-oxo-1,3-diphenyl-2-phenylimino-1,3,7,8-tetra-azaspiro[4.5]deca-6,9-diene-10-carboxylic acid (**2**) which was converted into the ester (**3**) by methylation with diazomethane.

When the anhydride (**1**) was allowed to react with 1,3-diphenylguanidine (DPG) under the same conditions, only one product was obtained, in quantitative yield, which was formulated as 4-oxo-3-phenyl-2-phenylimino-1,3,7,8-tetra-azaspiro[4.5]deca-6,9-diene-10-carboxylic acid (**4**) on the basis of chemical and spectroscopic evidence (see below).

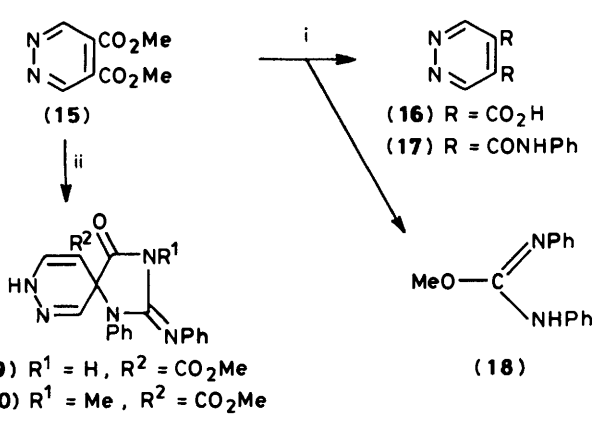


Scheme 1. *Reagents:* i, PhNHC(=NPh)NHPh; ii, PhNHC(=NH)NHPh; iii, PhNHCSNHPh, 80 °C; iv, $NH_2CSNHPh$; v, $PhC(=NH)NH_2$; vi, CH_2N_2

Table. Relevant spectroscopic properties of the new compounds (**2**)—(**7**), (**9**)—(**14**), (**19**) and (**20**)

Compound	$\delta_H[(CD_3)_2SO]$/p.p.m.	$\delta_C[(CD_3)_2SO]$/p.p.m.	$\nu_{max.}$(KBr)/cm^{-1}
(**2**)	6.30—7.60 (16 H, m, 3 × Ph and CO_2H), 7.25 (1 H, s, 6-H), 7.62 (1 H, d,[a] *J* 4 Hz, 9-H), 10.95 (1 H, br d,[b] *J* 4 Hz, NH)	64.7 (C-5), 93.7 (C-10), 120.8 and 121.5 (*p*- and *o*-C of >C=NPh)	1 755 (CONPh), 1 660 (conj. CO_2H)
(**3**)	3.70 (3 H, s, CO_2Me), 6.35—7.65 (15 H, m, 3 × Ph), 7.32 (1 H, s, 6-H), 7.60 (1 H, s,[c] 9-H), 11.70 (1 H, br s,[b] NH)	51.3 (OMe), 64.5 (C-5), 92.5 (C-10), 120.8 and 121.5 (*p*-and *o* C of >C=NPh)	1 760 (CONPh), 1 695 (conj. CO_2Me)
(**4**)	6.70—8.40 (2 H, br s,[b] 1-NH and CO_2H), 6.82 (1 H, s, 6-H), 6.85—7.55 (10 H, m, 2 × Ph), 7.60 (1 H, d,[a] *J* 4.2 Hz, 9-H), 10.83 (1 H, br d,[b] *J* 4.2 Hz, 8-NH)	57.2 (C-5), 94.6 (C-10), 121.8 and 122.2 (*p*- and *o*-C of >C=NPh)	1 770 and 1 735 (CONPh), 1 660 (conj. CO_2H)
(**5**)	3.67 (3 H, s, CO_2Me), 6.70—7.60 (10 H, m, 2 × Ph), 6.90 (1 H, s, 6-H), 7.67 (1 H, d,[a] *J* 4 Hz, 9-H), 8.20 (1 H, s,[b] 1-NH), 10.96 (1 H, br d,[b] *J* 4 Hz, 8-NH)	51.1 (OMe), 56.8 (C-5), 93.45 (C-10), 121.8 and 122.3 (*p*- and *o*-C of >C=NPh)	1 760 (CONPh), 1 690 (conj. CO_2Me)
(**6**)	7.00—7.60 (11 H, m, 2 × Ph and CO_2H), 7.18 (1 H, s, 6-H), 7.66 (1 H, d,[a] *J* 4 Hz, 9-H), 11.01 (1 H, br d,[b] *J* 4 Hz, 8-NH)	66.45 (C-5), 92.65 (C-10), 180.8 (C=S)	1 750 (CONPh), 1 660 (conj. CO_2H)
(**7**)	3.71 (3 H, s, CO_2Me), 7.00—7.60 (10 H, m, 2 × Ph), 7.14 (1 H, s, 6-H), 7.72 (1 H, d,[a] *J* 4 Hz, 9-H), 11.16 (1 H, br d,[b] *J* 4 Hz, 8-NH)	51.7 (OMe), 66.05 (C-5), 91.3 (C-10), 180.7 (C=S)	1 760 (CONPh), 1 690 (conj. CO_2Me)
(**9**)	7.04 (1 H, s, 6-H), 7.20—7.60 (6 H, m, Ph and CO_2H), 7.78 (1 H, d,[a] *J* 4 Hz, 9-H), 10.85 (1 H, br s,[b] 1-NH), 11.18 (1 H, br d,[b] *J* 4 Hz, 8-NH)	59.4 (C-5), 93.8 (C-10), 180.6 (C=S)	1 773 (CONPh), 1 665 (conj. CO_2H)
(**10**)	2.46 (3 H, s, SMe), 3.73 (3 H, s, CO_2Me), 6.52 (1 H, s, 6-H), 7.45 (5 H, s, Ph), 7.65 (1 H, d.[a] *J* 4 Hz, 9-H), 9.27 (1 H, br d[b] *J* 4 Hz, 8-NH)	12.4 (SMe), 51.1 (OMe), 66.9 (C-5), 94.6 (C-10), 180.6 (C=S)	1 745 (CONPh), 1 685 (conj. CO_2Me)
(**11**)	6.48 (1 H, s, 6-H), 7.45—7.65 (5 H, m, ArH_3, CO_2H, and NH), 7.70 (1 H, d,[a] *J* 4 Hz, 9-H), 7.95—8.20 (2 H, m, ArH_2), 10.81 (1 H, br d,[b] *J* 4 Hz, 8-NH)	65.9 (C-5), 95.4 (C-10)	1 740 (CONH), 1 680 (conj. CO_2H)
(**12**)	3.55 (3 H, s, CO_2Me), 6.53 (1 H, s, 6-H), 7.45—7.69 (3 H, m, ArH_3), 7.73 (1 H, d,[a] *J* 4 Hz, 9-H), 7.95—8.15 (2 H, m, ArH_2), 10.90 (1 H, br d,[b] *J* 4 Hz, 8-NH), 11.57 (1 H, br s,[b] NH)	51.3 (OMe), 67.6 (C-5), 94.65 (C-10)	1 740 (CONH), 1 685 (conj. CO_2Me)
(**13**)[d]	3.18 (3 H, s, NMe), 3.65 (3 H, s, CO_2Me), 6.37 (1 H, s, 6-H), 7.40—7.75 (6 H, m, Ph and 9-H), 9.43 (1 H, br s,[b] 8-NH)	29.3 (NMe), 51.4 (OMe), 66.8 (C-5), 95.6 (C-10)	1 745 (CONMe), 1 700 (conj. CO_2Me)
(**14**)[d]	3.58 (3 H, s, CO_2Me), 4.13 (3 H, s, OMe), 6.24 (1 H, s, 6-H), 7.30—7.60 (3 H, m, ArH_3), 7.73 (1 H, s,[c] 9-H), 8.20—8.40 (2 H, m, ArH_2), 9.95 (1 H, br s,[b] 8-NH)		1 705 (conj. CO_2Me)
(**19**)	3.57 (3 H, s, CO_2Me), 6.97 (1 H, s, 6-H), 7.00—7.50 (10 H, m, 2 × Ph), 7.55 (1 H, d,[a] *J* 4 Hz, 9-H), 9.10—9.50 (1 H, br s,[b] 3-NH), 10.78 (1 H, br d,[b] *J* 4 Hz, 8-NH)	50.9 (OMe), 66.5 (C-5), 92.6 (C-10), 122.4 (*p*- and *o*-C of >C=NPh)	1 700 (CONH and conj. CO_2Me); 1 770 and 1 740 (CONH), 1 690 (conj. CO_2Me)[e]
(**20**)	3.11 (3 H, s, NMe), 3.56 (3 H, s, CO_2Me), 6.40—7.00 (10 H, m, 2 × Ph), 7.10 (1 H, s, 6-H), 7.61 (1 H, d,[a] *J* 3.6 Hz, 9-H), 10.97 (1 H, br d,[b] *J* 3.6 Hz, 8-NH)	26.1 (NMe), 51.1 (OMe), 64.4 (C-5) 92.2 (C-10), 120.85 and 121.6 (*p*- and *o*-C of >C=NPh)	1 740 (CONMe), 1 690 (conj. CO_2Me)

[a] Signal collapses to a singlet on deuteriation. [b] Signal disappears on deuteriation. [c] The lack of coupling for 9-H is probably due to rapid exchange of the adjacent 8-NH proton. [d] Spectra recorded in $CDCl_3$. [e] Spectrum recorded in CCl_4.

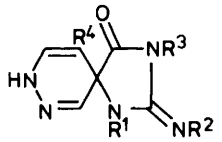


Scheme 2. *Reagents:* i, PhNHCSNHPh–NaH; ii, PhNHC(=NH)NHPh–NaH

Compound (**1**) was completely inert towards *N*,*N*′-diphenylurea, but it reacted with *N*,*N*′-diphenylthiourea (DPTU) in refluxing tetrahydrofuran to yield quantitatively the heterospiro compound (**6**), which was transformed into (**7**) with diazomethane. Compound (**1**) also underwent a strongly regioselective spiro-cyclization with *N*-phenylthiourea, affording the derivative (**9**) as the predominant product with a small amount of the isomer (**8**) which was shown to be present by diagnostic ^{13}C n.m.r. resonances (Experimental section); treatment of compound (**9**) with diazomethane yielded almost exclusively the methylthio derivative (**10**).

Finally, pyridazine-4,5-dicarboxylic anhydride (**1**) reacted with benzamidine to give in good yield 4-oxo-2-phenyl-1,3,7,8-tetra-azaspiro[4.5]deca-1,6,9-triene-10-carboxylic acid (**11**) which was converted by an excess of diazomethane into a mixture containing mainly the ester (**12**) together with small amounts of the dimethyl derivatives (**13**) and (**14**).

The synthetic value of compound (**1**) is demonstrated by the fact that the corresponding ester (**15**) does not react with DPTU, and afforded only traces of compound (**7**) on treatment



(21) $R^1 = R^2 = Ph$, $R^3 = H$, $R^4 = CO_2H$
(22) $R^1 = R^3 = Ph$, $R^2 = H$, $R^4 = CO_2H$
(23) $R^1 = R^2 = Ph$, $R^3 = H$, $R^4 = CO_2Et$

with the same reagent in the presence of sodium hydride; under these conditions a complex mixture was obtained from which the pyridazine derivatives (**16**) and (**17**), and *O*-methyl-*N*,*N*'-diphenylisourea (**18**), were isolated as the main products (Scheme 2).

The structures of the new heterospiro compounds were determined on the basis of chemical and spectroscopic evidence. In particular, the ^1H n.m.r. spectra in $(CD_3)_2SO$ (Table) exhibited a singlet at δ 6.48—7.32 p.p.m. and two doublets at δ 7.55—7.78 and 9.27—11.18 (6-, 9-H, and NH, respectively, of the dihydropyridazine moiety), whereas the proton-coupled ^{13}C n.m.r. spectra in the same solvent characteristically showed two singlets at δ 56.8—67.6 and 91.3—95.4 p.p.m. (C-5 and -10 quaternary carbons).

Compound (**4**), obtained from the reaction of the anhydride (**1**) with DPG (see above), was shown to be the 3-phenyl compound rather than the alternative 1-phenyl regioisomer (**21**) as it consumed only 1 mol equiv. of diazomethane to give exclusively the derivative (**5**) rather than the isomeric methyl ester (**19**). Compound (**19**) was obtained as the sole product from the reaction of the diester (**15**) and DPG in the presence of sodium hydride [by the method previously reported for the corresponding ethyl ester (**23**)]; its structure has been unambiguously determined by an *X*-ray analysis of its 3-methyl derivative.[4,5] The presence of a CONH group in compound (**19**) was confirmed by its conversion into (**20**) with diazomethane.

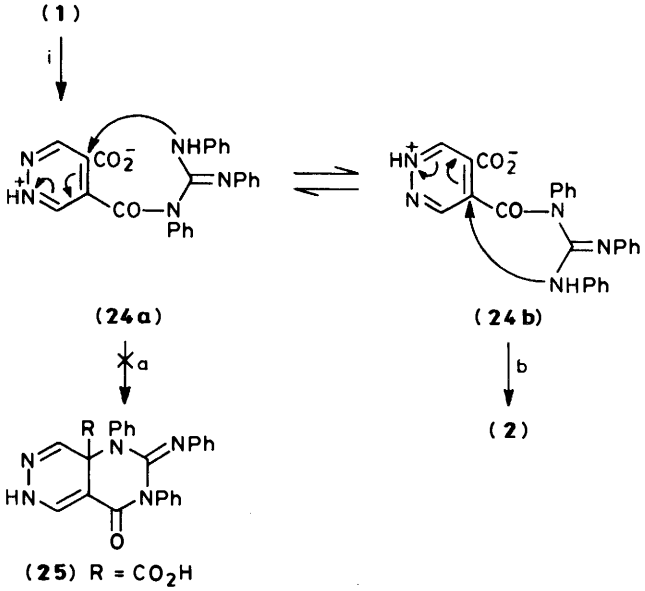
The 2-imino structure (**22**) was ruled out since the ^{13}C n.m.r. spectrum of compound (**4**) characteristically showed two resonances at δ 121.8 and 122.2 p.p.m. which, according to the findings of Jackman and Jen for some cyclic amidines and guanidines,[6] are diagnostic for the *p*- and *o*-phenyl carbons of a Ph–N=C< system. The replacement of the 1-NH group by NPh caused a reasonable downfield shift (Δδ 9.7 p.p.m.) for the ^{13}C n.m.r. resonance of the vicinal spiro carbon on going from the ester (**5**) to the isomer (**19**)

The differing regiospecificities observed in the reactions of compounds (**1**) and (**15**) with DPG is very interesting synthetically; it results primarily from the difference in behaviour of the nucleophile in the presence of a strong base compared with that in the absence of base.

The most important evidence for the structure of compound (**9**) [from the reaction of (**1**) with *N*-phenylthiourea, see above], came from the ^{13}C n.m.r. signal at δ 59.4 p.p.m.; on the basis of the C-5 resonances of the spirans (**4**) and (**6**) (δ 57.2 and 66.45 p.p.m., respectively), this was assigned to a spiro-carbon bonded to an NH group.

For compounds (**11**)—(**13**), the CO amidic stretching vibrations (Table) were comparable with those reported for 'unconjugated' imidazolone ring systems.[7,8]

The formation of compound (**2**) could be accounted for by an intramolecular attack at position 5 of the pyridazine ring by the terminal NHPh group of the intermediate (**24**) (Scheme 3, route b). This Smiles-type rearrangement partially resembled those reported for pyridine, pyrimidine, and benzothiazole derivatives under acid catalysis,[9,10] and its driving-force was certainly due, on the basis of the behaviour of other pyridazine amido-acids,[11]



Scheme 3. *Reagents:* i, TPG

to the presence of a strongly electron-withdrawing ^+NH group in the zwitterionic structure (**24b**). Similar considerations could be applied also to the heterospiro compounds (**4**), (**6**), (**9**), and (**11**), respectively. Condensed dihydropyridazine structures of the type (**25**), coming from an alternative ring-closure (route a), were ruled out on the basis of i.r. evidence. In fact, the spectra of the above compounds (Table) showed, besides bands between 1 735 and 1 773 cm^{-1} for the amidic CO, a strong absorption at 1 660—1 680 cm^{-1} which clearly indicated the presence of a conjugated enamino-carboxy group; on the other hand, the CO ester stretching vibrations of the corresponding methylation products were comparable with that (1 695 cm^{-1}) of the well established spiro structure (**23**).[4,5]

Experimental

Unless otherwise stated, i.r. spectra were measured for dispersions in KBr with a Perkin-Elmer 283 spectrometer, and u.v. spectra for solutions in methanol with a Cary 14 recording spectrophotometer. ^1H N.m.r. spectra were recorded on a Perkin-Elmer R32 instrument and ^{13}C n.m.r. spectra were obtained by the Fourier-transform technique with a Varian FT-80A spectrometer; chemical shifts are reported in p.p.m. downfield from internal tetramethylsilane, and coupling constants in Hz. M.p.s are uncorrected. Silica-gel plates (Merck F_{254}) and silica gel 60 (Merck 230—400 mesh) were used for analytical and preparative t.l.c., and for column chromatography, respectively. Sodium hydride refers to an 80% dispersion in oil (Merck–Schuchardt); tetrahydrofuran was dried by distillation over sodium wire and $LiAlH_4$. Extracts were dried over sodium sulphate and solvents were removed under reduced pressure. Ether refers to diethyl ether.

Reactions of the Anhydride (**1**) *with* 1,3-*Binucleophiles.—General procedure.* Except where further details are reported, the reaction conditions and the proportions of reagents were as follows: the 1,3-binucleophile (3—8 mmol) was added to a solution of freshly prepared compound (**1**) (3—8 mmol) in anhydrous tetrahydrofuran (40—70 ml) and the mixture was stirred at room temperature for 16—48 h. The solid obtained by filtration or evaporation to dryness of the reaction mixture was washed with ether and dried under reduced pressure.

(i) Compound (**1**) (0.9 g) was allowed to react with TPG (1.73 g) to yield the *heterospiro compound* (**2**) (1.88 g) as a white solid, m.p. 204—205 °C (Found: C, 68.7; H, 4.3; N, 16.1. $C_{25}H_{19}N_5O_3$ requires C, 68.6; H, 4.4; N, 16.0%); $\lambda_{max.}$ 269 and 297sh nm (log ε 4.01 and 3.91). Evaporation to dryness of the mother-liquors gave a second crop of the same product (0.67 g, overall yield 97%).

(ii) Reaction of compound (**1**) (0.75 g) with DPG (1.06 g), afforded *compound* (**4**) (1.09 g), m.p. 161—162 °C (decomp.) (from tetrahydrofuran) (Found: C, 63.5; H, 4.45; N, 19.2. $C_{19}H_{15}N_5O_3$ requires C, 63.2; H, 4.2; N, 19.4%); $\lambda_{max.}$ 265sh and 304 nm (log ε 3.84 and 3.75). Evaporation to dryness of the filtrate afforded a second crop of (**4**) (0.71 g, quantitative yield).

(iii) The anhydride (**1**) (1.05 g) and *N,N'*-diphenylthiourea (1.6 g) in anhydrous tetrahydrofuran were refluxed with stirring for 24 h. Removal of the solvent left a solid which was washed with chloroform (10 ml) to give 4-*oxo*-1,3-*diphenyl*-2-*thioxo*-1,3,7,8-*tetra-azaspiro*[4.5]*deca*-6,9-*diene*-10-*carboxylic acid* (**6**) (2.64 g, quantitative yield). An analytical sample obtained by dissolution in aqueous ammonium hydroxide, re-precipitation with hydrochloric acid (pH 3), and crystallisation from ether melted at 221—222 °C (decomp.) (Found: C, 60.2; H, 4.0; N, 14.5; S, 8.7. $C_{19}H_{14}N_4O_3S$ requires C, 60.3; H, 3.7; N, 14.8; S, 8.5%); $\lambda_{max.}$ 235, 280, and 308 nm (log ε 4.22, 4.17, and 3.76). When the reaction was carried out at room temperature for 50—60 h, compound (**6**) was obtained in lower yield together with variable amounts of the anhydride (**1**) and the corresponding acid (**16**).

(iv) Treatment of compound (**1**) (0.45 g) with *N*-phenylthiourea (0.46 g) yielded a yellow solution which was evaporated to dryness to give a pale yellow solid (0.9 g) mainly containing 4-*oxo*-3-*phenyl*-2-*thioxo*-1,3,7,8-*tetra-azaspiro*[4.5]-*deca*-6,9-*diene*-10- *carboxylic acid* (**9**), together with a small amount of the isomer (**8**); $\delta_C[(CD_3)_2SO]$ 67.6 (C-5), 92.3 (C-10), and 181.2 p.p.m. (C=S). Compound (**9**) was purified by dissolution in aqueous sodium hydroxide and re-precipitation with concentrated hydrochloric acid (pH 3), m.p. 209—210 °C (Found: C, 51.5; H, 3.3; N, 18.4; S, 10.7. $C_{13}H_{10}N_4O_3S$ requires C, 51.7; H, 3.3; N, 18.5; S, 10.6%); $\lambda_{max.}$ 275, 302, and 325sh nm (log ε 4.25, 3.80, and 3.52).

(v) Reaction of the anhydride (**1**) (0.6 g) with freshly sublimed (40—50 °C/0.02 mmHg) benzamidine (0.48 g) gave compound (**11**) (0.63 g) as a white solid. Concentration of the mother-liquors afforded a second crop of the same material (0.15 g, 72%), m.p. 165—166 °C (from ethyl acetate) (Found: C, 57.8; H, 3.7; N, 20.7. $C_{13}H_{10}N_4O_3$ requires C, 58.1; H, 3.85; N, 21.0%); $\lambda_{max.}$ 233, 258, and 270 nm (log ε 4.20, 3.91, and 3.91).

Dimethyl Pyridazine-4,5-*dicarboxylate* (**15**).—This compound was prepared in 70% yield by the method previously reported for the corresponding diethyl ester,[12] m.p. 52 °C (from ether) (lit.,[13] yellow liquid which solidifies if evacuated for 2 h*) (Found: C, 49.2; H, 4.1; N, 14.1. $C_8H_8N_2O_4$ requires C, 49.0; H, 4.1; N, 14.3%); $\nu_{max.}$ 3 080, 3 060, 1 740, 1 435, 1 320, 1 300, and 1 260 cm^{-1}; $\delta_H(CDCl_3)$ 3.99 (6 H, s, 2 × CO_2Me) and 9.50 (2 H, s, 3- and 6-H); $\delta_C(CDCl_3)$ 53.3 (q, 2 × OMe), 127.4 (s, C-4 and -5), 148.8 (d, C-3 and -6), and 163.9 p.p.m. (s, 2 × C=O).

Reactions of Compound (**15**) *with* 1,3-*Diphenylguanidine* (DPG) *and* N,N'-*Diphenylthiourea* (DPTU).—(i) Treatment of compound (**15**) (1.96 g) with DPG (2.11 g) and sodium hydride (0.6 g), according to the general method described in a preceding paper,[4] gave *methyl* 4-*oxo*-1-*phenyl*-2-*phenylimino*-1,3,7,8-*tetra-azaspiro*[4.5]*deca*-6,9-*diene*-10-*carboxylate* (**19**) (3.08 g, 82%), m.p. 223—224 °C (from methanol) (Found: C, 63.7; H, 4.6; N, 18.6. $C_{20}H_{17}N_5O_3$ requires C, 64.0; H, 4.6; N, 18.7%); $\lambda_{max.}$ 245 and 315 nm (log ε 4.38 and 3.76).

(ii) The ester (**15**) (0.98 g) reacted under the same conditions with DPTU (1.14 g) and sodium hydride (0.3 g) to yield a suspension which was extracted with ether (4 × 25 ml); acidification of the aqueous phase with concentrated hydrochloric acid (pH 1) precipiated the acid (**16**) (0.29 g). The gummy residue (1.62 g) obtained from the ethereal extracts was resolved into three components by column chromatography with n-hexane–ethyl acetate (2:1 v/v) as eluant.

The fastest running band gave *O*-methyl-*N,N'*-diphenylisourea (**18**) (0.69 g) as a yellow oil; $\nu_{max.}$ (cap. film) 3 400 (NH) and 1 665 cm^{-1} (C=N); $\delta_H(CDCl_3)$ 3.87 (3 H, s, OMe), 5.75 (1 H, s, NH), and 6.85—7.35 (10 H, m, 2 × Ph).

The second band yielded a small amount of DPTU (0.14 g), and the slowest running band afforded pyridazine-4,5-dicarboxanilide (**17**) (0.25 g), identical (m.p., i.r., and ^1H n.m.r. spectra) with an authentic sample.[4] Nearly identical results were obtained when the reaction was carried out at reflux for 24 h.

Methylation of Compounds (**2**), (**4**), (**6**), (**9**), (**11**), *and* (**19**) *with Diazomethane*.—A suspension or a solution of the heterospirane (2 mmol) in ether–methanol 1:1 v/v (50 ml) [only methanol was employed for compound (**11**)] was treated with an excess of ethereal diazomethane (5 mmol) and set aside overnight; the reaction mixture was then evaporated to dryness.

(i) Compound (**2**) gave *methyl* 4-*oxo*-1,3-*diphenyl*-2-*phenylimino*-1,3,7,8-*tetra-azaspiro*[4.5]*deca*-6,9-*diene*-10-*carboxylate* (**3**) (0.86 g, 95%) as a white solid, m.p. 242 °C (from ethanol) (Found: C, 69.2; H, 4.7; N, 15.5. $C_{26}H_{21}N_5O_3$ requires C, 68.9; H, 4.65; N, 15.4%); $\lambda_{max.}$ 295 nm (log ε 3.93).

(ii) The spiran (**4**) afforded *methyl* 4-*oxo*-3-*phenyl*-2-*phenylimino*-1,3,7,8-*tetra-azaspiro*[4.5]*deca*-6,9-*diene*-10-*carboxylate* (**5**) (0.68 g, 91%) as a yellow solid, m.p. 237—238 °C (decomp.) (from ethanol) (Found: C, 63.8; H, 4.6; N, 18.4. $C_{20}H_{17}N_5O_3$ requires C, 64.0; H, 4.6; N, 18.7%); $\lambda_{max.}$ 310 nm (log ε 3.84).

(iii) The acid (**6**) gave *methyl* 4-*oxo*-1,3-*diphenyl*-2-*thioxo*-1,3,7,8-*tetra-azaspiro*[4.5]*deca*-6,9-*diene*-10-*carboxylate* (**7**) (0.71 g, 90%) as a pale yellow solid, m.p. 235—236 °C (decomp.) (from methanol) (Found: C, 61.15; H, 4.1; N, 14.4; S, 8.3. $C_{20}H_{16}N_4O_3S$ requires C, 61.2; H, 4.1; N, 14.3; S, 8.2%); $\lambda_{max.}$ 235, 280, and 308 nm (log ε 4.24, 4.18, and 3.85).

(iv) Compound (**9**) afforded quantitatively a yellow solid containing almost exclusively (^1H and ^{13}C n.m.r. spectra) the *methylthio derivative* (**10**) which was purified by column chromatography with ethyl acetate–n-hexane (2:1 v/v) as eluant, m.p. 199—200 °C (from ethyl acetate) (Found: C, 54.3; H, 4.3; N, 16.9; S, 9.8. $C_{15}H_{14}N_4O_3S$ requires C, 54.55; H, 4.3; N, 17.0; S, 9.7%).

(v) The derivative (**11**) yielded a product (0.55 g) which was resolved into three components by preparative layer chromatography with ether–light petroleum (b.p. 30—50 °C) (5:1 v/v) as eluant. The fastest running band gave a small amount (0.05 g) of *methyl* 4-*methoxy*-2-*phenyl*-1,3,7,8-*tetra-azaspiro*[4.5]*deca*-1,3,6,9-*tetraene*-10-*carboxylate* (**14**) which gradually decomposed above 80 °C and melted at *ca.* 105 °C, after crystallisation from cyclohexane (Found: C, 60.3; H, 4.9; N, 18.7. $C_{15}H_{14}N_4O_3$ requires C, 60.4; H, 4.7; N, 18.8%); $\lambda_{max.}$ 235, 274, and 327 nm (log ε 4.26, 4.04, and 3.68).

The second band afforded *methyl* 3-*methyl*-4-*oxo*-2-*phenyl*-1,3,7,8-*tetra-azaspiro*[4.5]*deca*-1,6,9-*triene*-10-*carboxylate* (**13**) (0.165 g) which gradually decomposed above 70 °C and melted at *ca.* 99 °C, after crystallisation from n-hexane (Found: C, 60.15; H, 4.9; N, 18.55. $C_{15}H_{14}N_4O_3$ requires C, 60.4; H, 4.7; N, 18.8%); $\lambda_{max.}$ 230, 268, and 330 nm (log ε 4.28, 3.75, and 3.71).

The slowest running band yielded *methyl* 4-*oxo*-2-*phenyl*-1,3,7,8-*tetra-azaspiro*[4.5]*deca*-1,6,9-*triene*-10-*carboxylate* (**12**) (0.31 g), m.p. 234—235 °C (from ethyl acetate) (Found: C, 58.9;

* The i.r. and ^1H n.m.r. data are inconsistent with the assigned structure.

H, 4.3; N, 19.8. $C_{14}H_{12}N_4O_3$ requires C, 59.15; H, 4.25; N, 19.7%); $\lambda_{max.}$ 234, 261, and 325 nm (log ε 4.32, 4.08, and 3.69).

(vi) The ester (**19**) yielded *methyl 3-methyl-4-oxo-1-phenyl-2-phenylimino-1,3,7,8-tetra-azaspiro*[4.5]*deca-6,9-diene-10-carboxylate* (**20**) (0.74 g, 95%), m.p. 254—255 °C (from ethyl acetate) (Found: C, 64.6; H, 4.9; N, 18.0. $C_{21}H_{19}N_5O_3$ requires C, 64.8; H, 4.9; N, 18.0%); $\lambda_{max.}$ 235sh, 265, and 295 nm (log ε 4.25, 4.01, and 3.92).

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Received 26*th January* 1984; *Paper* 4/146