A New Spiro Annellation Reaction in the Isoxazole Series: Applications and Limits. Part 2.[1] Reactivity of Ethyl 4-Nitro-3-phenylisoxazole-5-carboxylate with Nitrogen Binucleophiles

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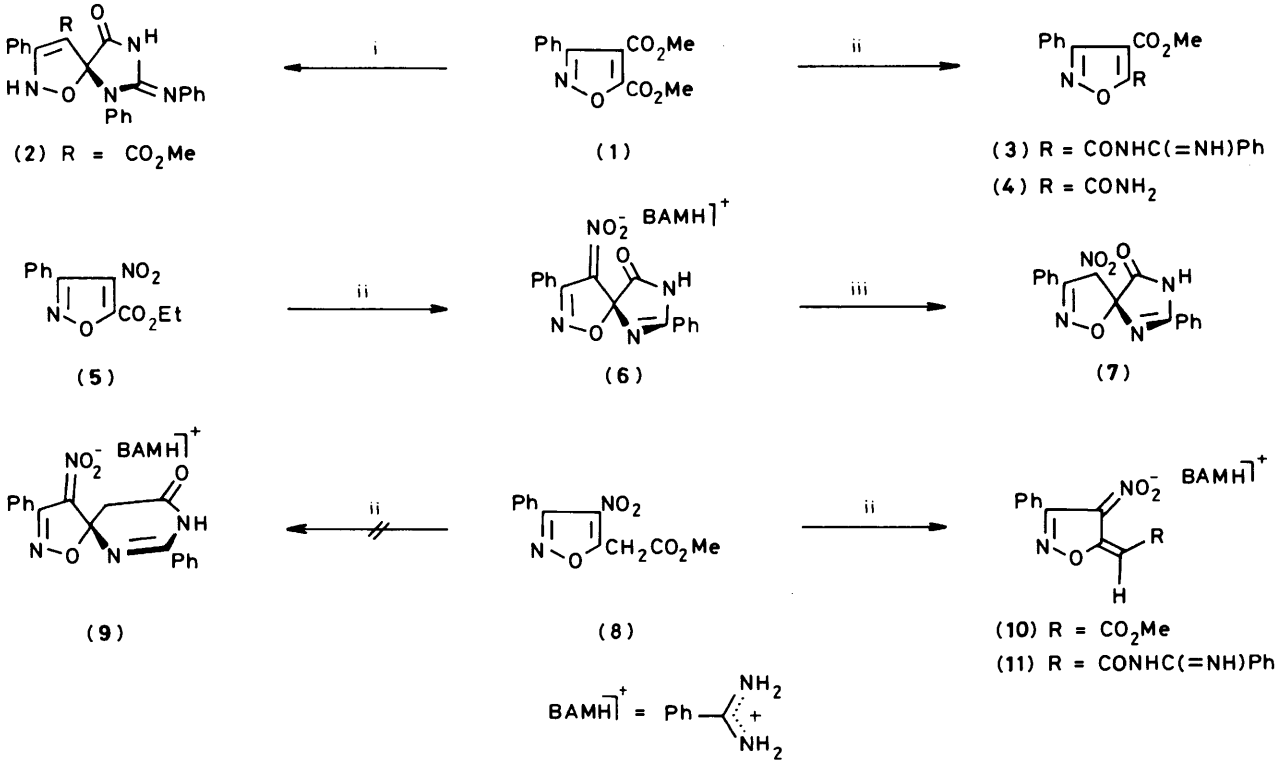
Treatment of the title compound (**5**) with benzamidine and 1,3-diphenylguanidine afforded in good yields the spiro nitronate (**6**) and a mixture of the regioisomeric salts (**12**) and (**13**), respectively; these products were easily converted into the corresponding nitro derivatives (**7**), (**14**), and (**15**), respectively, with hydrochloric acid. The same nitro ester (**5**) reacted smoothly with *o*-phenylenediamine and NaH to give, after acidification, the heterospiran (**16**). Some limits of this spiro annellation process are emphasized. The structures of the new compounds have been established on the basis of spectral data.

Pursuing our studies of new spiro-cyclization reactions of heterocyclic compounds,[2] we have shown that some isoxazole mono- and di-carboxylates react with 1,3-diphenylguanidine (DPG) in the presence of sodium hydride to give the previously unreported 1-oxa-2,6,8-triazaspiro[4.4]nonane ring system, through an 'incomplete' Smiles-type rearrangement.[1,2c] On the other hand, related work from this laboratory[3] strongly suggested that the spiro annellation could be highly favoured by the presence of a nitro group at the 4 position of the isoxazole ring.

For this reason, after compound (**5**) became recently available in high yield from α-nitroacetophenone oxime,[4] we decided to investigate its reactivity toward different nitrogen binucleophiles, in an effort to expand the scope of the above reaction. Our interest in this topic was also connected with the systematic research we have undertaken on the synthetic potentialities of difunctionalized 4-nitroisoxazoles.

Although the dicarboxylate (**1**) condensed smoothly with DPG and NaH to give the heterospiran (**2**)[2c] regioselectively, it was completely inert toward the same reagent in the absence of a strong base; on the other hand, attempts to obtain spiro compounds from (**1**) and benzamidine (BAM) were not successful. Whereas the ester (**1**) was converted very slowly into the isoxazole derivative (**3**) at room temperature, it afforded the amido ester (**4**) as the main product under more drastic conditions. Conversely, when ethyl 4-nitro-3-phenylisoxazole-5-carboxylate (**5**) was allowed to react with 2 equiv. of the latter binucleophile in anhydrous tetrahydrofuran at room temperature, the spiro nitronate (**6**) was isolated in 75% yield; this salt, whose structure followed from spectral evidence (see below),



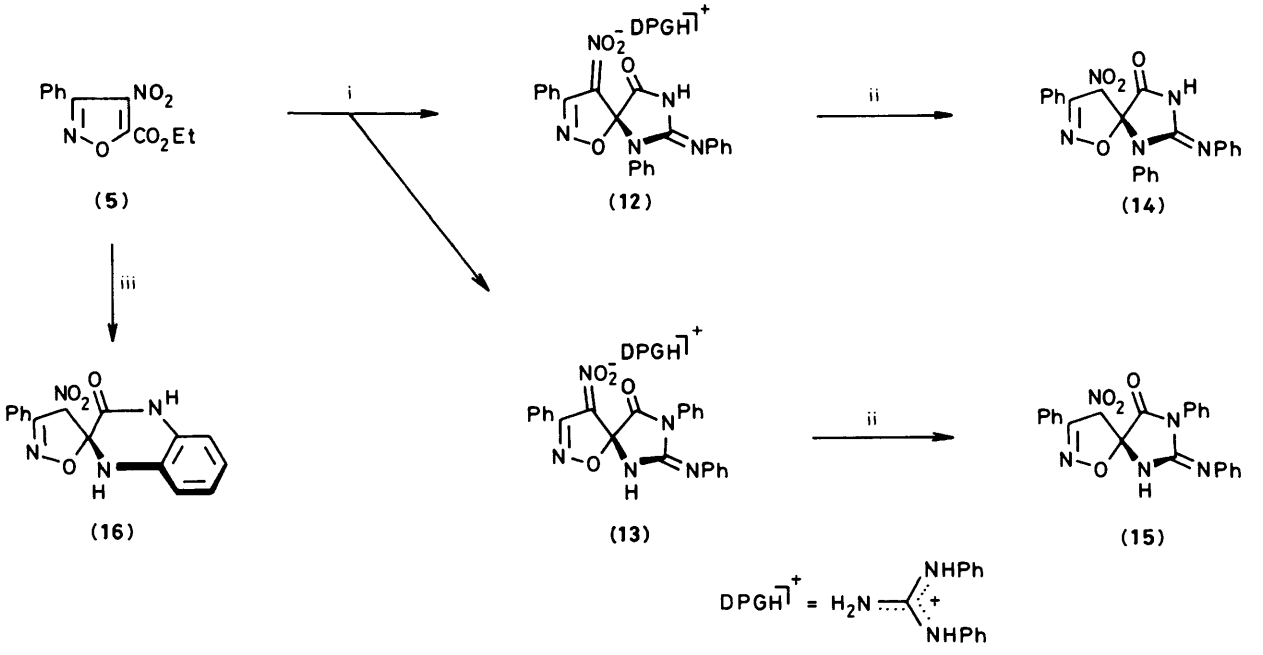
Scheme 1. *Reagents:* i, PhNHC(=NH)NHPh–NaH; ii, $PhC(=NH)NH_2$; iii, HCl

was easily transformed into the corresponding nitro derivative (**7**) with hydrochloric acid.

The course of the reaction changed completely on replacement of (**5**) with the homologous nitro ester (**8**)[4] containing a strongly acidic methylene group; no spiro cyclization into (**9**) was observed under the same conditions, but we obtained, through a preferential deprotonation, the nitronate (**10**) as the major product, together with a minor amount of the corresponding derivative (**11**).

The structures of all the new products were established on the basis of spectral evidence, the heterospirans (**2**), (**19**),[7] (**20**),[2e] and (**21**),[2e] and the salts (**22**),[3] (**23**), and (**24**), being used as model compounds; the last two nitronates were obtained by reaction of 3-methyl-4-nitroisoxazol-5(4*H*)-one with BAM and DPG, respectively.

Except for the isoxazole derivatives (**10**) and (**11**), the ^{1}H n.m.r. spectra (see Experimental section) were of little use and the most convincing diagnostic data were obtained from the ^{13}C

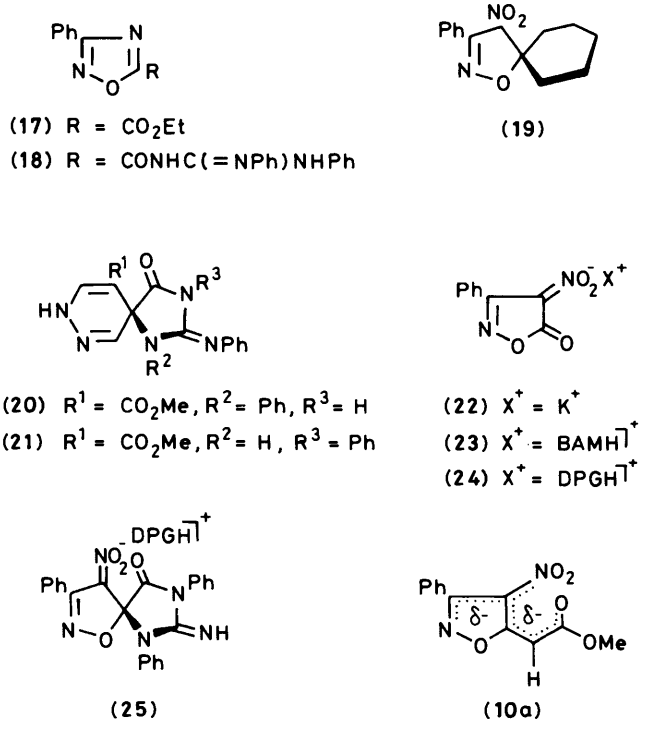


Scheme 2. *Reagents:* i, PhNHC(=NH)NHPh; ii, HCl; iii, *o*-$NH_2C_6H_4NH_2$–NaH, then HCl

The remarkable reactivity of (**5**) was exemplified by its reaction with DPG to give a mixture of the regioisomers (**12**) and (**13**) in very good yield; these were separated and converted into the spirans (**14**) and (**15**), respectively. The regioselective control observed in the cyclization of (**1**) with DPG and NaH was absent, probably due both to a different pattern of behaviour for the same binucleophile in the presence and in the absence of a strong base and because of the possibility of an alternative reaction path to that previously suggested for other isoxazole derivatives.[1] In fact, the behaviour of 4-nitroisoxazoles with simple nucleophiles,[5,6] suggests that the primary step of the spiro annellation process could involve attack of DPG at the 5-position of the heterocyclic ring.

Although compound (**5**) did not react with the less nucleophilic *o*-phenylenediamine (OPD) alone, when the reaction was carried out in the presence of NaH, we isolated, after acidification, the new ring-system (**16**) in 89% yield.

As reported for dimethyl 3-phenylisothiazole-4,5-dicarboxylate,[2c] attempts to extend the spiro cyclization to the 1,2,4-oxadiazole derivative (**17**) failed; when the latter compound was treated with DPG and NaH under different conditions, we obtained the corresponding amide (**18**). We have previously suggested[1] that the peculiar tendency of the isoxazole ring system to give rise to spiro annellation probably depends both on the low degree of aromaticity of the starting materials and to the stability of the 4,5-dihydroisoxazole structures of the final products. The above results agree well with this assumption and clearly show that a 4-nitro group can play a determining role in the process, making the nitro ester (**5**) a versatile synthon for such reactions.



Scheme 3.

Table. Relevant spectroscopic properties of the new products and reference compounds

Compd.	δ_c[$(CD_3)_2SO$]/p.p.m.[a]	$\nu_{max.}$(KBr)/cm^{-1}
(2)	50.3 (OMe), 91.6 (C-4/C-5), 93.2 (C-5/C-4), 121.8 and 123.4 (*p*-and *o*-C of C=NPh), 163.8 (C-3/CO_2Me), 168.9 (CO_2Me/C-3), 178.9 (CONH)	1 775 (CONH), 1 700 (CO_2Me)[2c]
(3)	52.9 (OMe), 113.7 (C-4)	1 730 (CO_2Me), 1 620 (CONH)
(4)[b]	52.8 (OMe), 112.1 (C-4)	1 748 (CO_2Me), 1 715 ($CONH_2$)
(6)	99.0 (s, C-5), 114.65 (s, C-4), 153.2 (s, C-3), 184.0 (s, CONH)	1 730 (CONH)
(7)	91.3 (d, C-4), 94.7 (d, C-4), 99.9 (s, C-5), 112.9 (s, C-4), 152.1 (s, C-3), 153.0 (s, C-3), 177.6 (s, CONH)	1 758 (CONH)
(10)	49.45 (q, OMe), 74.6 (d, CH), 115.1 (s, C-4), 156.5 (s, C-3)	1 670 (CO_2Me)
(11)	103.0 (d, CH), 113.6 (s, C-4), 155.1 (s, C-3)	1 680 (CONH)
(12)	99.7 (s, C-5), 112.3 (s, C-4), 153.5 (s, C-3), 178.9 (s, CONH)	1 770 and 1 710 (CONH)
(13)	95.1 (s, C-5), 113.0 (s, C-4), 152.7 (s, C-3), 168.35 (s, CONPh)	1 770 (CONPh)
(14)	93.0 (d, C-4), 97.1 (s, C-5), 100.2 (s, C-5), 110.0 (s, C-4), 123.7 and 123.9 (d, *o*- and *p*-C of C=NPh), 175.6 (s, CONH)	1 790 (CONH)
(15)	90.1 (d, C-4), 94.15 (d, C-4), 95.4 (s, C-5), 99.9 (s, C-5), 108.4 (s, C-4), 122.0 and 123.9 (d, *o*- and *p*-C of C=NPh), 167.2 (s, CONPh)	1 798 (CONPh)
(16)	83.2 (d, C-4), 89.1 (d, C-4), 95.6 (s, C-5), 110.8 (s, C-4), 115.3 (s, C-4)	1 683 (CONH)
(16)[c]	95.15 (s, C-5), 115.2 (s, C-4)	
(18)	156.9 (C-3/C=N), 160.1 (C=N/C-3), 168.1 (C-5/CONH), 172.7 (CONH/C-5)	1 620 (CONH)
(19)	89.7 (s, C-5), 95.3 (d, C-4), 152.2 (s, C-3)	1 560 and 1 360 (NO_2)[7]
(19)[c]	86.3 (s, C-5), 121.3 (s, C-4), 154.2 (s, C-3)	
(20)	50.9 (OMe), 66.5 (C-5), 92.6 (C-10), 122.4 (*p*- and *o*-C of C=NPh), 180.65 (CONH)	1 770 and 1 740 (CONH)[2e]
(21)	51.1 (OMe), 56.8 (C-5), 93.45 (C-10), 121.8 and 122.3 (*p*-and *o*-C of C=NPh), 172.6 (CONPh)	1 760 (CONPh)[2e]
(22)	14.3 (q, 3-Me), 107.75 (s, C-4), 156.7 (s, C-3), 167. 95 (s, CO)	1 718 and 1 690 (CO)
(23)	14.3 (q, 3-Me), 107.1 (s, C-4), 155.9 (s, C-3), 167.0 (s, CO)	1 710 (CO)
(24)	14.5 (q, 3-Me), 107.3 (s, C-4), 156.1 (s, C-3), 167.3 (s, CO)	1 685 (CO)

[a] The multiplicities of the signals were obtained from the off-resonance spectra. [b] The ^{13}C n.m.r. spectrum was recorded in $CDCl_3$. [c] The ^{13}C n.m.r. spectra were obtained by addition of aqueous sodium hydroxide to the [$(CD_3)_2SO$] solutions.

n.m.r. spectra (Table). In particular, whereas the C-4 and C-5 quaternary carbons of (**5**) resonated at δ 133.5 and between δ 154.7 and 157.05, respectively,[4] the corresponding atoms of the spiro nitronates (**6**), (**12**), and (**13**) gave rise to two signals at δ 112.3—114.65 and 95.1—99.7, respectively. The latter, shows a small downfield shift with respect to the C-5 resonance of compound (**19**), and was more strictly comparable with that of the 1-oxa-2,6,8-triazaspiro[4.4]nonane derivative (**2**); as for the assignment of the former, it was unambiguously achieved by comparison with the spectra of the salts (**22**)—(**24**) in the same solvent and with those of the model compound (**19**) both in neutral and alkaline medium. Whereas the former were characterized by a resonance at δ 107.1—107.75 for the C-4 carbon, the off-resonance pattern of (**19**) in $(CD_3)_2SO$ showed for the same atom, a doublet at δ 95.3 which changed into a singlet at δ 121.3 on addition of aqueous sodium hydroxide.

The presence of a conjugated nitronate moiety in the spirans (**6**), (**12**), and (**13**) was confirmed by their u.v. spectra which displayed a strong absorption at *ca.* 345 nm; this band, attributable to a $-N{=}C{-}C{=}NO_2^-$ system, was almost identical with that exhibited by the salts (**22**)—(**24**) in methanol (see Experimental section) and by the spiran (**19**) in alkaline solution [$\lambda_{max.}$ (MeOH + 1M NaOH 1:1, v/v) 250sh and 335 nm (log ε 3.66 and 3.95)].

The relative assignment of the regioisomers (**12**) and (**13**) was accomplished by careful comparison of their ^{13}C n.m.r. spectra with those of the well established model compounds (**2**), (**20**), and (**21**). Likewise for the latter two derivatives, an upfield shift (δ 4.6 p.p.m.) was observed for C-5 on going from (**12**) to (**13**), owing to the replacement of the adjacent 6-NPh group by NH; moreover, the CO resonance of compound (**12**), identical with that of the spiran (**2**), showed a diagnostic difference (δ 10.55 p.p.m.) with respect to the corresponding one of (**13**), which was comparable with that observed for the isomeric reference products (**20**) and (**21**) (δ 8.05 p.p.m.).

The alternative 7-imino structure (**25**) was discarded since the ^{13}C n.m.r. spectra of the spirans (**14**) and (**15**), as well as those of compounds (**2**), (**20**), and (**21**), characteristically displayed signals in the region δ 121.8—123.9 for the *o*- and *p*-phenyl carbons of a C=NPh system.[8]

On going from the salts (**6**), (**12**), and (**13**) to the corresponding nitro derivatives (**7**), (**14**), and (**15**), characterized by a complex tautomerism, the ^{13}C n.m.r. patterns gave rise to a considerable increase of the signals; among these, some doublets were easily identified at δ 90.1—94.7 (Table) due to diastereoisomeric CH–NO_2 structures. Similar doublets were also observed at slightly higher field in the spectrum of (**16**), together with other singlets at δ 95.6—115.3; on addition of aqueous sodium hydroxide, all these signals were replaced by two singlets at δ 95.15 and 115.2, attributable to the C-5 and C-4 carbons, respectively, of the corresponding nitronate.

Whereas the i.r. spectrum of the latter compound exhibited a band at 1 683 cm^{-1} (amidic CO), those of the heterospirans (**6**) and (**7**), and (**12**)—(**15**) were characterized by absorptions at higher frequency (1 700—1 800 cm^{-1}) for the imidazolone and pseudoimidic CO groups, respectively. All the spectral data of the salt (**10**) (Table and Experimental section) fully agreed with a structure of the type (**10a**) showing a very strong delocalization which probably also involved the ester CO group; such an electronic drift was notably reduced in the corresponding amide (**11**), as shown by its spectroscopic properties.

Experimental

I.r. spectra were obtained for dispersions in KBr with a Perkin-Elmer 283 spectrometer. Unless otherwise stated, u.v. spectra were taken for solutions in methanol with a Cary 14 spectrophotometer, whilst the ^1H and ^{13}C n.m.r. spectra were measured in $(CD_3)_2SO$ solutions with Perkin-Elmer R32 and Varian FT-80A instruments respectively; chemical shifts are reported in p.p.m. downfield from internal tetramethylsilane. M.p.s. are uncorrected. Silica-gel plates (Merck F_{254}) and silica-gel 60 (Merck 230—400 mesh) were employed for analytical and

column chromatography, respectively. Sodium hydride refers to an 80% dispersion in oil (Merck-Schuchardt) and ether to diethyl ether. Tetrahydrofuran (THF) was dried by distillation over sodium wire and $LiAlH_4$.

Reactions of Compounds (**1**), (**5**), *and* (**8**) *with Benzamidine* (*BAM*).—Except where further details are given, the reaction conditions were as indicated in the following general procedure. A solution of the ester (2 mmol) in anhydrous THF (5 ml) was added dropwise to freshly sublimed (40—50 °C/0.02 mmHg) BAM (2—4 mmol) in THF (15—20 ml) and the mixture was stirred at room temperature for the times reported below.

(i) Compound (**1**) (0.522 g) was treated with BAM (0.24 g) for 90 h. Removal of the solvent left a residue which was stirred with water (10 ml) to give a product containing nearly equimolecular amounts of the unchanged (**1**) and *methyl* 5-(N-*benzimidoylcarbamoyl*)-3-*phenylisoxazole*-4-*carboxylate* (**3**) (^{1}H n.m.r.); treatment of this mixture with carbon tetrachloride (5—10 ml) afforded compound (**3**) as a white solid (0.36 g, 52%), m.p. 153—154 °C (from ethyl acetate) (Found: C, 65.2; H, 4.3; N, 11.9. $C_{19}H_{15}N_3O_4$ requires C, 65.3; H, 4.3; N, 12.0%); δ_H 3.84 (3 H, s, CO_2Me), 7.40—7.85 (8 H, m, Ph and ArH_3), 8.10—8.30 (2 H, m, ArH_2), 9.98 (1 H, br s, NH), and 10.40 (1 H, br s, NH).

When the reaction was carried out at reflux for 60 h, the ester (**1**) was completely consumed; evaporation to dryness afforded a semisolid residue which was dried under reduced pressure and treated with benzene (5—10 ml) to give a pale yellow solid (0.47 g) containing *methyl* 5-*carbamoyl*-3-*phenylisoxazole*-4-*carboxylate* (**4**) as the major product together with a small amount of compound (**3**) (t.l.c., ^{1}H and ^{13}C n.m.r. spectra). An analytical sample of (**4**), obtained by repeated crystallizations from benzene, melted at 131 °C (Found: C, 58.3; H, 4.0; N, 11.35. $C_{12}H_{10}N_2O_4$ requires C, 58.5; H, 4.1; N, 11.4%); δ_H ($CDCl_3$) 3.79 (3 H, s, CO_2Me), 6.78 (1 H, br s, NH of the NH_2 group), 7.40—7.68 (5 H, m, Ph), and 8.41 (1 H, br s, NH of the NH_2 group).

(ii) The nitro ester (**5**) (0.524 g) was treated with BAM (0.48 g) for 24 h. The yellow solid which separated was filtered off, washed with ether and dried overnight at 100 °C under reduced pressure to yield *benzamidinium* 9-*oxo*-3,7-*diphenyl*-1-*oxa*-2,6,8,-*triazaspiro*[4.4]*nona*-2,6-*diene*-4-*nitronate* (**6**) (0.685 g, 75%), which gradually sintered above 130 °C and melted at 143—144 °C (decomp.) (Found: C, 63.3; H, 4.6; N, 18.15. $C_{24}H_{20}N_6O_4$ requires C, 63.15; H, 4.4; N 18.4%); δ_H 7.0 (5 H, br s, 2 × NH_2 and NH), 7.30—7.85 (13 H, m, 2 × Ph and ArH_3), and 8.05—8.15 (2 H, m, ArH_2); $\lambda_{max.}$ 236, 255sh, and 344 nm (log ε 4.49, 4.29, and 4.01).

(iii) The isoxazole derivative (**8**) (0.524 g) was allowed to react with BAM (0.48 g) for 9 days. The yellow solid was filtered off, washed with ether (10 ml), dried, and extracted exhaustively with the same solvent (Soxhlet; 5 × 20 ml); the ethereal extracts were combined and evaporated to dryness to give *benzamidinium* 5-(*methoxycarbonylmethylene*)-3-*phenyl*-4,5-*dihydroisoxazole*-4-*nitronate* (**10**) (0.126 g), which gradually sintered above 90 °C and melted at 102—103 °C, after crystallization from ethyl acetate (Found: C, 59.45; H, 4.5; N, 14.6. $C_{19}H_{18}N_4O_5$ requires C, 59.7; H, 4.7; N, 14.65%); δ_H 3.52 (3 H, s, CO_2Me), 5.67 (1 H, s, CH), 7.35—7.95 (10 H, m, 2 × Ph), and 9.10 (4 H, vbr s, 2 × NH_2); $\lambda_{max.}$ 228, 260sh, 300sh, and 438 nm (log ε 4.41, 3.84, 3.06, and 3.24). The pale yellow solid recovered from the extractions consisted nearly exclusively (t.l.c., ^{1}H and ^{13}C n.m.r. spectra) of *benzamidinium* 5-(N-*benzimidoylcarbamoylmethylene*)-3-*phenyl*-4,5-*dihydroisoxazole*-4-*nitronate* (**11**) (0.2 g, 21%); an analytical sample, obtained by washing with acetone (10 ml) and ether, followed by prolonged drying at 50—60 °C under reduced pressure, melted at 142 °C (decomp.) (Found: C, 64.0 H, 5.0; N, 18.2, $C_{25}H_{22}N_6O_4$ requires C, 63.8; H, 4.7; N, 17.9%); δ_H 6.98 (1 H, s, CH), 7.20—8.0 (15 H, m, 3 × Ph), and 9.10 (6 H, br s, 2 × NH_2 and 2 × NH); $\lambda_{max.}$ 231 and 354 nm (log ε 4.59 and 4.14).

The original tetrahydrofuran filtrate was evaporated to dryness to yield a semisolid residue which was stirred with water (15—20 ml) and filtered to give a second crop of compound (**10**) (0.43 g; overall yield 73%).

Reaction of Compound (**5**) *with* 1,3-*Diphenylguanidine* (*DPG*).—DPG (1.668 g, 8 mmol) was added to a solution of (**5**) (1.048 g, 4 mmol) in anhydrous THF (8 ml) and the mixture was stirred at room temperature for 48 h. The white solid which separated was filtered off and washed with the minimum amount of the same solvent; after washing several times with ether, it was dried at 60—70 °C under reduced pressure to give 1,3-*diphenylguanidinium* 9-*oxo*-3,8-*diphenyl*-7-*phenylimino*-1-*oxa*-2,6,8-*triazaspiro*[4.4]*non*-2-*ene*-4-*nitronate* (**13**) (0.35 g) which sintered at *ca.* 155 °C and melted at 159 °C (Found: C, 68.0; H, 4.5; N, 17.2. $C_{36}H_{30}N_8O_4$ requires C, 67.7; H, 4.7; N, 17.55%); δ_H 6.80—7.80 (25 H, m, 5 × Ph) and 9.0 (5 H, vbr s, NH and NH/NH_2 of $DPGH^+$); $\lambda_{max.}$ 230sh and 344 nm (log ε 4.53 and 4.05). Evaporation to dryness of the tetrahydrofuran mother liquors left a residue which was washed with ether to give a pale yellow solid (1.92 g) containing almost exclusively compounds (**13**) and (**14**) (t.l.c. and ^{13}C n.m.r. spectrum); the two regioisomers were separated by column chromatography with ethyl acetate as eluant. After the first band, consisting of a very small amount of sticky products was discarded, the second one gave a further crop of the nitronate (**13**) (0.67 g, overall yield 40%), whereas the slowest running band afforded 1,3-*diphenylguanidinium* 9-*oxo*-3,6-*diphenyl*-7-*phenylimino*-1-*oxa*-2,6,8-*triazaspiro*[4.4]*non*-2-*ene*-4-*nitronate* (**12**) (0.86 g, 34%) which was washed repeatedly with ether and dried under reduced pressure; this salt gradually darkened above 120 °C and melted at 145—150 °C (decomp.) (Found C, 67.5; H, 5.0; N, 17.5. $C_{36}H_{30}N_8O_4$ requires C, 67.7; H, 4.7; N, 17.55%); δ_H 5.90 (5 H, vbr s, NH and NH/NH_2 of $DPGH^+$) and 6.90—7.60 (25 H, m, 5 × Ph); $\lambda_{max.}$ 248 and 345 nm (log ε 4.55 and 3.96).

Treatment of the Nitronates (**6**), (**12**), *and* (**13**) *with Hydrochloric Acid.*—A suspension of the salt (0.5—1 mmol) in aqueous hydrochloric acid (0.5 M; 25—50 ml) was stirred overnight at room temperature; the corresponding nitro derivative was filtered, washed with water, and dried over KOH and P_2O_5.

(i) Compound (**6**) afforded 4-*nitro*-9-*oxo*-3,7-*diphenyl*-1-*oxa*-2,6,8-*triazaspiro*[4.4]*nona*-2,6-*diene* (**7**) (81%), as an ivory coloured solid which gradually sintered with darkening above 150 °C and melted at 171—172 °C (decomp.) (Found: C, 60.9; H, 3.5; N, 16.5. $C_{17}H_{12}N_4O_4$ requires C, 60.7; H, 3.6; N, 16.7%); δ_H [$(CD_3)_2SO$ + D_2O] 7.45—8.25 (10 H, m, 2 × Ph).

(ii) The salt (**12**) gave 4-*nitro*-9-*oxo*-3,6-*diphenyl*-7-*phenylimino*-1-*oxa*-2,6,8-*triazaspiro*[4.4]*non*-2-*ene* (**14**) (90%) as a white product, m.p. 161—162 °C (decomp.) (Found: C, 64.5; H, 4.1; N, 16.2. $C_{23}H_{17}N_5O_4$ requires C, 64.6; H, 4.0; N, 16.4%); δ_H [$(CD_3)_2SO$ + D_2O] 7.20—7.80 (15 H, m, 3 × Ph).

(iii) Compound (**13**) yielded 4-*nitro*-9-*oxo*-3,8-*diphenyl*-7-*phenylimino*-1-*oxa*-2,6,8-*triazaspiro*[4.4]*non*-2-*ene* (**15**) as a white solid (quantitative yield), m.p. 159—160 °C (Found: C, 64.4; H, 3.9; N, 16.2. $C_{23}H_{17}N_5O_4$ requires C, 64.6; H, 4.0; N, 16.4%); δ_H [$(CD_3)_2SO$ + D_2O] 7.10—7.80 (15 H, m, 3 × Ph).

4-*Nitro*-3-*phenyl*-3′,4′-*dihydro*-3′-*oxospiro*[*isoxazole*-5(4H),2′(1′H)-*quinoxaline*] (**16**).—Sodium hydride (0.12 g, 4 mmol) was added to a solution of (**5**) (0.524 g, 2 mmol) and OPD (0.216 g, 2 mmol) in anhydrous THF (15 ml) and the mixture was stirred at room temperature until the starting material (**5**) was completely consumed (4—5 days). The orange residue left by removal of the solvent was dissolved in water (15

ml) and extracted with ether (2 × 10 ml); acidification of the aqueous solution with concentrated hydrochloric acid (pH 1) precipitated the *spiro compound* (**16**) as a yellow solid which was filtered off, washed with water, and dried over KOH and P_2O_5 (0.575 g, 89%). An analytical sample, obtained by crystallization from acetone and prolonged drying at 100 °C under reduced pressure, melted at 178 °C (decomp.) (Found: C, 59.6; H, 3.6; N, 17.15. $C_{16}H_{12}N_4O_4$ requires C, 59.3; H, 3.7; N, 17.3%); δ_H [$(CD_3)_2SO$ + D_2O] 7.15—7.95 (9 H, m, Ph and ArH_4).

5-[(N^1,N^2-*Diphenylamidino*)*carbamoyl*]-3-*phenyl*-1,2,4-*oxadiazole* (**18**).—DPG (0.422 g, 2 mmol) and NaH (0.12 g, 4 mmol) were stirred in anhydrous THF (15 ml) until evolution of gas ceased; ethyl 3-phenyl-1,2,4-oxadiazole-5-carboxylate (**17**)[9] (0.436 g, 2 mmol) in THF (5 ml) was added and the mixture was stirred at room temperature for 24 h. After removal of the solvent, the residue was treated with ice-cold water (30 ml) and made weakly acidic (pH 5—6) with concentrated hydrochloric acid; the yellow solid was filtered off, dried, and washed with ether to give a product (0.68 g) containing the *amide* (**18**) as the major component (t.l.c., ^1H, and ^{13}C n.m.r. spectra), which was purified by column chromatography with chloroform as eluant, m.p. 207—208 °C (from ethyl acetate) (Found: C, 68.7; H, 4.2; N, 18.4. $C_{22}H_{17}N_5O_2$ requires C, 68.9; H, 4.5; N, 18.3%); δ_H 7.20—7.65 (13 H, m, 2 × Ph and ArH_3), 7.95—8.10 (2 H, m, ArH_2), and 9.20 (2 H, vbr s, 2 × NH).

Benzamidinium 5-*Oxo*-3-*phenyl*-4,5-*dihydrosoxazole*-4-*nitronate* (**23**).—Freshly sublimed BAM (0.24 g, 2 mmol) was added to 3-methyl-4-nitroisoxazol-5(4 *H*)-one[3] (0.288 g, 2 mmol) in water (15 ml) and the mixture was stirred for 1 h and set aside overnight. The ivory coloured solid was filtered off, washed with water (5 ml), and dried over KOH and P_2O_5 to give the *salt* (**23**) (0.432 g, 82%), m.p. 168—169 °C (Found: C, 49.7; H, 4.5; N, 21.5. $C_{11}H_{12}N_4O_4$ requires C, 50.0; H, 4.6; N, 21.2%); δ_H 2.21 (3 H, s, 3-Me), 7.60—8.0 (5 H, m, Ph), and 9.10 (4 H, br s, 2 × NH_2); $\lambda_{max.}$ 222 and 336 nm (log ε 4.31 and 4.0).

1,3-*Diphenylguanidinium* 5-*Oxo*-3-*phenyl*-4,5-*dihydroisoxazole*-4-*nitronate* (24).—Operating as above, reaction of 3-methyl-4-nitroisoxazol-5(4 *H*)-one (0.288 g, 2 mmol) with DPG (0.422 g, 2 mmol) in water (15 ml), afforded *compound* (**24**) (0.66 g, 93%) as a white solid, which gradually melted at 145—150 °C, resolidified at higher temperature, and then re-melted at 215—220 °C (decomp.) (Found: C, 57.5; H, 4.8; N, 19.7. $C_{17}H_{17}N_5O_4$ requires C, 57.5; H, 4.8; N, 19.7%); δ_H 2.22 (3 H, s, 3-Me), 7.20—7.60 (10 H, m, 2 × Ph), and 8.85 (4 H, vbr s, NH/NH_2 of $DPGH^+$); $\lambda_{max.}$ 220sh, 235sh, 245sh, and 334 nm (log ε 4.35, 4.25, 4.16, and 4.05).

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