A New Spiro Annelation Reaction in the Isoxazole Series: Applications and Limits

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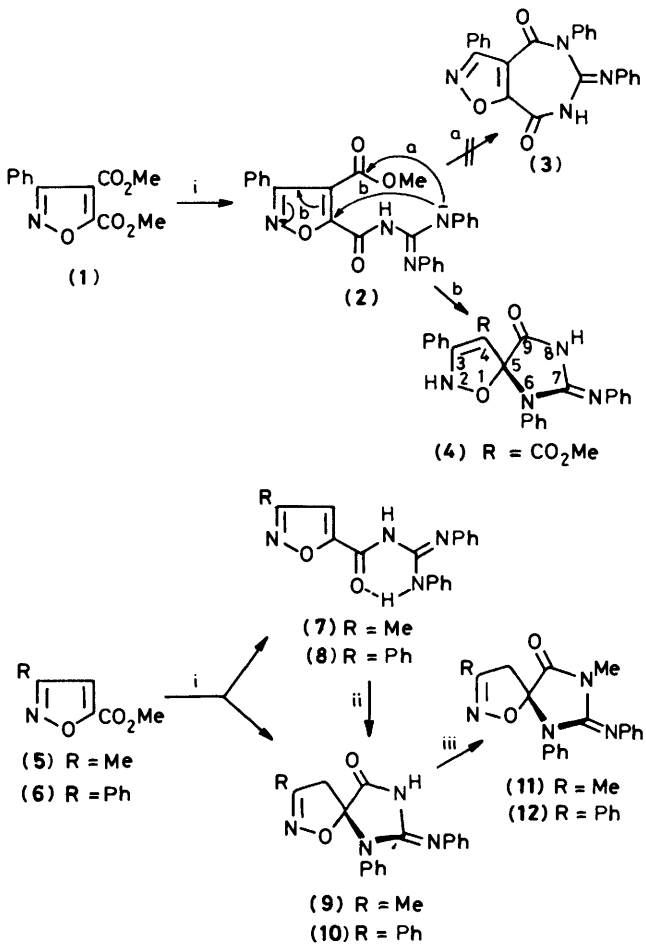
The isoxazole-5-carboxylates (**5**) and (**6**) reacted with 1,3-diphenylguanidine and NaH to give, besides the corresponding amides (**7**) and (**8**), the 1-oxa-2,6,8-triazaspiro[4.4]nonane derivatives (**9**) and (**10**), respectively; the latter compounds could also be obtained by partial conversion of (**7**) and (**8**) with a strong base. The limits of this spiro-cyclization reaction were shown through a detailed investigation of the behaviour of variously substituted isoxazoles towards the same reagents.

A number of 'mixed' spiro heterobicyclic systems containing the isoxazoline or isoxazolidine ring have been obtained in the past 15 years by various methods such as: (a) 1,3-dipolar cycloaddition of nitrile oxides or nitrones to exocyclic double bonds of five-membered heterocycles[1,2] and, conversely, of heterocyclic bifunctional nitrones with ethyl vinyl ether;[3] (b) electrophilic bromination of suitable 5-substituted isoxazoles having the 4-position free;[4] (c) rearrangements of 2,9-dioxa-1-azabicyclo[4.3.0]nonanes;[5] and, occasionally, (d) intramolecular condensation of isoxazolin-5-ones carrying a suitable chain at position 4.[6] However, attempts to synthesize 1-oxa-2,6,8-triazaspiro[4.4]nonanes both by methods (a)[1] and (b)[4b] were unsuccessful and, only more recently,[7] have we succeeded in obtaining this ring system through a new spiro-cyclization reaction which could be advantageously employed also with pyrimidine and pyridazine derivatives.[7,8]

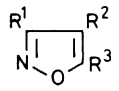
In fact, when the ester (**1**) was allowed to react with 1,3-diphenylguanidine (DPG) in the presence of sodium hydride, instead of the isoxazolodiazepine (**3**) [route (a)], we obtained in very good yield the heterospiran (**4**) [route (b)]. In order to establish the possibilities and the limits of this reaction, we then investigated the behaviour of various substituted isoxazoles towards the same binucleophile. The CO_2Me group at position 4 certainly favoured the spiro-cyclization process of the anionic intermediate (**2**), characterized by an intramolecular nucleophilic attack of the terminal NPh group on C-5; nevertheless, in contrast with our observation for pyrimidines[7] and pyridazines,[8] the reaction did not depend critically on the presence of a strongly electron-withdrawing group adjacent to the reactive centre. Treatment of the monocarboxylates (**5**) and (**6**) with DPG and NaH at room temperature in anhydrous tetrahydrofuran, afforded indeed a mixture of compounds (**7**) and (**9**), and (**8**) and (**10**), respectively, whose structures followed from chemical and spectroscopic evidence (see below). On the other hand, the amides (**7**) and (**8**) were partially converted, by heating with NaH, into the spirans (**9**) and (**10**) which reacted with diazomethane to yield the corresponding methyl derivatives (**11**) and (**12**), respectively. The greater tendency of the isoxazole to give spiro annelation reactions with respect to the above diazine ring systems, was probably due both to the lower aromaticity[9] of the starting materials and to the notable stability of the 2-isoxazoline moiety of the spiro structures. However, the reaction was hampered by the presence of a chlorine atom at position 4, and fully prevented when a strongly electron-releasing group was introduced at the same position, or the ester group was transferred from the 5- to the 3-position. In fact, when methyl 4-chloro-3-methylisoxazole-5-carboxylate (**13**) was treated with DPG and NaH, the derivative (**14**) was obtained as the major product, together with small amounts of the diastereoisomeric spirans (**19**) and (**20**); although these



Scheme 1. *Reagents:* i, PhNHC(=NPh)NHPh–NaH; ii, NaH, 80 °C; iii, CH_2N_2

minor components were not isolated owing to practical difficulties, they could be unambiguously detected in the reaction mixture by i.r., ^1H, and ^{13}C n.m.r. spectroscopy. In contrast, the esters (**15**) and (**17**) afforded only the corresponding amides (**16**) and (**18**), respectively, even by prolonged heating with the same reagents in refluxing tetrahydrofuran.

Although compounds (**7**) and (**8**) could be transformed into (**9**) and (**10**) by treatment with a strong base, attempts to extend this procedure to the isoxazole (**22**), for which the method (b) previously gave negative results,[4b] failed. When this compound was heated for a long time with NaH in boiling tetrahydrofuran,



(13) R^1 = Me, R^2 = Cl, R^3 = CO_2Me

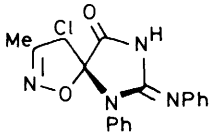
(14) R^1 = Me, R^2 = Cl, R^3 = CONHC(NPh)NHPh

(15) R^1 = Ph, R^2 = NH_2, R^3 = CO_2Et

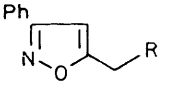
(16) R^1 = Ph, R^2 = NH_2, R^3 = CONHC(NPh)NHPh

(17) R^1 = CO_2Et, R^2 = H, R^3 = Me

(18) R^1 = CONHC(NPh)NHPh, R^2 = H, R^3 = Me



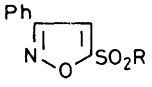
(19),(20)



(21) R = Br

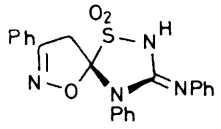
(22) R = NHCONHPh

(23) R = NPhC(NPh)NH_2

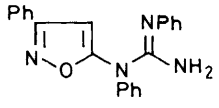


(24) R = Cl

(25) R = NHPh



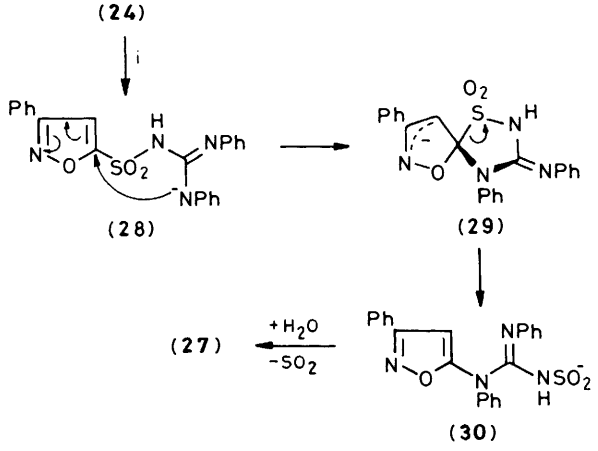
(26)



(27)

no spiran was isolated or detected, and all the starting material was recovered unchanged after neutralization with hydrochloric acid; similar results were also obtained with (**23**), prepared from the bromo derivative (**21**) and DPG. These findings clearly demonstrated that the spiro-cyclization, strongly dependent on the nature of the 4 substituents was also drastically influenced by the nature of the isoxazole C-5 substituent.

Finally, in the light of the above results, we investigated the possibility of obtaining the new heterospiro ring (**26**), starting from 5-chlorosulphonyl-3-phenylisoxazole (**24**); unfortunately, its reaction with DPG and NaH did not afford the desired product, but gave a mixture of the isoxazole derivatives (**25**) and (**27**) which was separated by flash chromatography. Whereas the formation of the guanidine (**27**) could be accounted for by a true Smiles-type rearrangement* of the intermediate (**28**) into



Scheme 2. *Reagents:* i, PhNHC(=NPh)NHPh–NaH

* The formation of the spirocyclic products reported above could be explained on the basis of a similar process which, however, was 'incomplete' and stopped at the first step.

the aminosulphinic acid (**30**), followed by loss of SO_2 (Scheme 2), compound (**25**) probably came from a competitive intramolecular attack of the terminal NPh group on the sulphur atom of (**28**).

The spectral data of the new compounds (Table) agreed well with the assigned structures. In particular, the i.r. spectra of the isoxazoles (**7**), (**8**), (**14**), and (**16**) showed absorption at 1 605—1 620 cm^{-1} attributable to an amidic CO group strongly bound by an intramolecular hydrogen bond; conversely, those of the spiroisoxazolines (**9**)—(**12**) and (**19**), (**20**) were characterized by absorption at higher frequency (1 730—1 765 cm^{-1}) due to the pseudoimidic CO of the iminohydantoin ring. Finally, the spectra of compounds (**23**) and (**27**) exhibited, besides absorption at 3 480 and 3 380 cm^{-1} (terminal NH_2), absorption at 1 640 and 1 668 cm^{-1}, respectively, which could be assigned to the guanidine moiety. However, the clearest evidence for the different structures came from the ^1H and ^{13}C n.m.r. patterns; the ^1H n.m.r. spectra of the derivatives containing the isoxazole ring with the 4 position free, displayed a singlet at δ 6.34—7.08 for 4-H [only for (**18**), a small coupling with the 5-methyl group was observed], whereas the off-resonance ^{13}C n.m.r. spectra of the same compounds exhibited a doublet at δ 88.3—107.55 (C-4) which appeared as a singlet at lower field for (**14**) and (**16**), respectively.

In contrast, the ^1H n.m.r. spectra of the spirans (**9**)—(**12**) were characterized by an AB system (J 18 Hz) for the non-equivalent methylene protons and the corresponding off-resonance ^{13}C n.m.r. spectra showed, in addition to a triplet at δ 39.3—43.3 (4-H_2), a singlet at δ 96.4—97.6 attributable to the quaternary C-5 spiro carbon. Moreover, when a methyl group was present at position 3, its ^1H n.m.r. resonance exhibited a measurable upfield shift on going from compound (**7**) to the corresponding spirans (**9**) and (**11**). A comparable shift was also observed between the 3-Me signal of the predominant open-chain product (**14**) and those of the isomers (**19**) and (**20**), whose structures were strongly supported by the presence in the ^1H and ^{13}C n.m.r. spectra (Table) of other diagnostic resonances for the CHCl group and the spiro carbon, respectively.

Experimental

I.r. spectra were measured for dispersions in KBr with a Perkin-Elmer 283 spectrometer. ^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, coupling constants in Hz. M.p.s are uncorrected. Silica-gel plates (Merck F_{254}) and silica-gel 60 (Merck 230—400 mesh) were employed for analytical and flash 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 Compounds (**5**), (**6**), (**13**), (**15**), (**17**), *and* (**24**) *with* 1,3-*Diphenylguanidine* (DPG) *and* NaH.—Except where further details are reported, the reactions were carried out at room temperature in anhydrous tetrahydrofuran for 18—24 h according to the general method previously reported;[7,8] after evaporation to dryness of the reaction mixture, the residue was treated with ice-cold dilute hydrochloric acid (20—50 ml; pH 5—6).

(*i*) Methyl 3-methylisoxazole-5-carboxylate (**5**)[10] (1 g) gave an ivory coloured solid which was filtered off and dried (1.96 g). The aqueous mother liquors were extracted with dichloromethane (3 × 20 ml) to yield a second crop (0.22 g) of the same

material. The raw product, which largely consisted of the isomers (**7**) and (**9**) (*ca.* 3:2; ^{1}H n.m.r. spectrum), was stirred with methanol (60 ml) and filtered to give a white solid (0.8 g) containing almost exclusively (t.l.c. and ^{1}H n.m.r. spectrum) 5-[(N^1,N^2-*diphenylamidino*)*carbamoyl*]-3-*methylisoxazole* (**7**), m.p. 163—165 °C after two crystallizations from the same solvent (Found: C, 67.3; H, 5.0; N, 17.3. $C_{18}H_{16}N_4O_2$ requires C, 67.5; H, 5.0; N, 17.5%).

Evaporation to dryness of the methanol solution left a yellow residue which was resolved into two components by flash chromatography with ethyl acetate–n-hexane (2:1 v/v) as eluant. The first band gave a second crop (0.35 g) of compound (**7**), whereas the slower running band afforded 9-*oxo*-3-*methyl*-6-*phenyl*-7-*phenylimino*-1-*oxa*-2,6,8-*triazaspiro*[4.4]*non*-2-*ene* (**9**) (0.6 g); an analytical sample, obtained by crystallization from ethyl acetate, gradually wrinkled above 210 °C and melted at 217—218 °C (Found: C, 67.4; H, 5.0; N, 17.5. $C_{18}H_{16}N_4O_2$ requires C, 67.5; H, 5.0; N, 17.5%).

(*ii*) Methyl 3-phenylisoxazole-5-carboxylate (**6**)[11] (1.2 g) afforded a solid which was filtered off and dried; the crude product (2.2 g) was then stirred with ether (2 × 50 ml) to give a white solid (0.95 g) consisting nearly exclusively (t.l.c. and ^{1}H n.m.r. spectrum) of 9-*oxo*-3,6-*diphenyl*-7-*phenylimino*-1-*oxa*-2,6,8-*triazaspiro*[4.4]*non*-2-*ene* (**10**), m.p. 231—232 °C after crystallization from methanol and drying under reduced pressure at 150 °C for 1—2 h (Found: C, 72.5; H, 4.6; N, 14.9. $C_{23}H_{18}N_4O_2$ requires C, 72.2; H, 4.7; N, 14.65%).

The ethereal filtrate was evaporated to dryness to leave a solid (1.18 g) containing 5-[(N^1,N^2-*diphenylamidino*)*carbamoyl*]-3-*phenylisoxazole* (**8**) as the predominant product (t.l.c. and ^{1}H n.m.r. spectrum); an analytical sample, obtained by two crystallizations from ether, partially melted at *ca.* 75—80 °C, resolidified at higher temperature, and then re-melted at 120 °C (Found: C, 72.35; H, 4.9; N, 14.3. $C_{23}H_{18}N_4O_2$ requires C, 72.2; H, 4.7; N, 14.65%).

(*iii*) Methyl 4-chloro-3-methylisoxazole-5-carboxylate (**13**) (1.75 g) gave a yellow solid (3.3 g) mainly consisting (t.l.c., ^{1}H, and ^{13}C n.m.r. spectra) of 4-*chloro*-5-[(N^1,N^2-*diphenylamidino*)-*carbamoyl*]-3-*methylisoxazole* (**14**) with a small amount (overall 10—15%) of the *spirans* (**19**) and (**20**). Compound (**14**), after purification by treatment with methanol (25 ml), filtration, and crystallization from the same solvent, melted at 138—139 °C (Found: C, 61.2; H, 4.4; N, 15.7. $C_{18}H_{15}N_4O_2Cl$ requires C, 60.9; H, 4.2; N, 15.8%).

(*iv*) Ethyl 4-amino-3-phenylisoxazole-5-carboxylate (**15**)[12] (1.35 g) afforded a semi-solid product which was extracted with dichloromethane (2 × 50 ml); removal of the solvent from the combined extracts left a gummy residue which was dried under reduced pressure to give a solid (2.1 g) containing nearly exclusively (t.l.c. and ^{1}H n.m.r. spectrum) 4-*amino*-5-[(N^1,N^2-*diphenylamidino*)*carbamoyl*]-3-*phenylisoxazole* (**16**), m.p. 165—166 °C after purification by flash chromatography with ethyl acetate as eluant and crystallization from ethanol (Found: C, 69.35; H, 4.9; N, 17.4. $C_{23}H_{19}N_5O_2$ requires C, 69.5; H, 4.8; N, 17.6%). When the reaction was carried out at reflux for 18 h, similar results were obtained.

(*v*) Ethyl 5-methylisoxazole-3-carboxylate (**17**)[13] (1 g) yielded 3-[(N^1,N^2-*diphenylamidino*)*carbamoyl*]-5-*methylisoxazole* (**18**) as an ivory coloured product (1.82 g, 88%). m.p. 145—146 °C from ethyl acetate (Found: C, 67.6; H, 5.1; N, 17.2. $C_{18}H_{16}N_4O_2$ requires C, 67.5; H, 5.0; N, 17.5%). When the reaction was carried out at reflux for 15 h, only compound (**18**) was isolated in comparable yields.

(*vi*) 5-Chlorosulphonyl-3-phenylisoxazole (**24**)[14] (1.3 g) gave an orange semi-solid product which was extracted with ether (3 × 50 ml); removal of the solvent from the combined extracts left a residue which solidified after prolonged drying under reduced pressure. The crude product (1.76 g) was resolved into two components by flash chromatography with n-hexane–ethyl acetate (3:1 v/v) as eluant. The faster running band afforded 5-*phenylaminosulphonyl*-3-*phenylisoxazole* (**25**) (0.75 g), m.p. 120.5—121 °C (from carbon tetrachloride) (Found: C, 59.7; H, 4.0; N, 9.0. $C_{15}H_{12}N_2O_3S$ requires C, 60.0; H, 4.0; N, 9.3%). The second band yielded 5-[N-*phenyl*-N-(N^2-*phenylamidino*)*amino*]-3-*phenylisoxazole* (**27**) as a pale yellow solid (0.6 g), m.p. 137—138 °C (from carbon tetrachloride) (Found: C, 74.35; H, 5.1; N, 15.8. $C_{22}H_{18}N_4O$ requires C, 74.6; H, 5.1; N, 15.8%).

Methyl 4-*Chloro*-3-*methylisoxazole*-5-*carboxylate* (**13**).—4-Chloro-3-methylisoxazole-5-carboxylic acid[15] (2 g) in ether (100 ml) was treated with an excess of etheral diazomethane and set aside overnight. Removal of the solvent gave the *ester* (**13**) (2.1 g, 97%), m.p. 58—59 °C (from n-hexane) (Found: C, 41.2; H, 3.5; N, 8.1. $C_6H_6ClNO_3$ requires C, 41.0; H, 3.4; N, 8.0%); $\nu_{max.}$(KBr) 1 735 cm^{-1}; δ(CDCl$_3$) 2.34 (3 H, s, 3-Me) and 3.98 (3 H, s, OMe).

Methylation of Compounds (**9**) *and* (**10**) *with Diazomethane.*—A suspension of the heterospiran (1 mmol) in ether–methanol (2.5:1 v/v; 35 ml) was treated with an excess of ethereal diazomethane (2.5 mmol) and set aside overnight; the reaction mixture was then evaporated to dryness.

(*i*) Compound (**9**) gave 9-*oxo*-3,8-*dimethyl*-6-*phenyl*-7-*phenylimino*-1-*oxa*-2,6,8-*triazaspiro*[4.4]*non*-2-*ene* (**11**) (0.31 g, 92.7%), m.p. 154 °C from ether (Found: C, 68.4; H, 5.5; N, 16.5. $C_{19}H_{18}N_4O_2$ requires C, 68.25; H, 5.4; N, 16.8%).

(*ii*) The spiran (**10**) afforded 9-*oxo*-8-*methyl*-3,6-*diphenyl*-7-*phenylimino*-1-*oxa*-2,6,8-*triazaspiro*[4.4]*non*-2-*ene* (**12**) (0.39 g, quantitative yield), m.p. 150.5—151.5 °C after purification by flash chromatography with ether–light petroleum (b.p. 30—50 °C) (1:1 v/v) as eluant and crystallization from ether (Found: C, 72.7; H, 5.0; N, 14.05. $C_{24}H_{20}N_4O_2$ requires C, 72.7; H, 5.1; N, 14.1%).

5-[N-*Phenyl*-N-(N^2-*phenylamidino*)*aminomethyl*]-3-*phenylisoxazole* (**23**).—A mixture of 5-bromomethyl-3-phenylisoxazole (**21**)[16] (0.5 g) and DPG (0.89 g) in anhydrous tetrahydrofuran (30 ml) was refluxed with stirring for 72 h; the pale yellow solid obtained by removal of the solvent was stirred with ether (60 ml) for 15—30 min and filtered. Evaporation to dryness of the ethereal filtrate gave *compound* (**23**) (0.77 g, quantitative yield), m.p. 126—127 °C from methanol (Found: C, 74.9; H, 5.6; N, 15.1. $C_{23}H_{20}N_4O$ requires C, 75.0; H, 5.5; N, 15.2%).

Reactions of Compounds (**7**), (**8**), (**22**), *and* (**23**) *with* NaH.—The isoxazole derivative (2 mmol) and NaH (2 mmol) were gently refluxed in anhydrous tetrahydrofuran (30—50 ml) for 20—24 h; the solvent was removed under reduced pressure and the residue was treated with ice-cold dilute hydrochloric acid (15—20 ml; pH 6—7).

(*i*) Compound (**7**) gave a gummy product which was extracted with chloroform (2 × 30 ml); evaporation of the solvent left a solid (0.62 g) containing the starting material and the *spiran* (**9**) (*ca.* 4:1; ^{1}H n.m.r. spectrum) which were separated by the method described above.

(*ii*) The amide (**8**) afforded, after similar work-up, a mixture (0.75 g) of the unchanged starting compound and the *spiran* (**10**) (*ca.* 3:1; ^{1}H n.m.r. spectrum) which was resolved into the two components by the method reported above.

(*iii*) 5-Phenylcarbamoylaminomethyl-3-phenylisoxazole (**22**)[4b] was quantitatively recovered unchanged from the reaction.

(*iv*) Compound (**23**) gave a sticky product which was

Table. Relevant spectroscopic properties of the new compounds

Compound	$\delta_H(CDCl_3)$/p.p.m.	$\delta_C(CDCl_3)$/p.p.m.	$\nu_{max.}$(KBr)/cm^{-1}
(7)	2.30 (3 H, s, 3-Me), 6.60 (1 H, s, 4-H), 7.15—7.50 (10 H, m, 2 × Ph), 8.90 (2 H, br s, 2 × NH)	11.4 (3-Me), 107.55 (C-4)	1 620 (CONH)
(8)	7.08 (1 H, s, 4-H), 7.25—7.95 (15 H, m, 3 × Ph), 9.25 (2 H, br s, 2 × NH)	104.9 (C-4)	1 615 (CONH)
(9)[a]	1.68 (3 H, s, 3-Me), 3.01 and 3.31 (2 H, AB system, *J* 18 Hz, 4-H_2), 7.10—7.60 (10 H, m, 2 × Ph), 9.8 (1 H, br s, NH)	12.0 (3-Me), 43.3 (C-4), 96.4 (C-5)	1 725 and 1 735 (CONH)
(10)[a]	3.54 and 3.74 (2 H, AB system, *J* 18 Hz, 4-H_2), 7.10—7.70 (15 H, m, 3 × Ph), 9.75 (1 H, br s, NH)	39.7 (C-4), 97.5 (C-5)	1 730 (CONH)
(11)	1.72 (3 H, s, 3-Me), 2.69 and 3.39 (2 H, AB system, *J* 18 Hz, 4-H_2), 3.27 (3 H, s, NMe), 6.50—7.35 (10 H, m, 2 × Ph)	12.3 (3-Me), 26.4 (NMe), 42.7 (C-4), 96.9 (C-5)	1 765 (CONMe)
(12)	3.15 and 3.76 (2 H, AB system, *J* 18 Hz, 4-H_2), 3.27 (3 H, s, NMe), 6.50—7.55 (15 H, m, 3 × Ph)	26.5 (NMe), 39.3 (C-4), 97.6 (C-5)	1 752 (CONMe)
(14)[a]	2.22 (3 H, s, 3-Me), 7.10—7.60 (10 H, m, 2 × Ph), 10.30 (2 H, br s, 2 × NH)	9.3 (3-Me), 111.0 (C-4)	1 610 (CONH)
(16)	4.24 (2 H, br s, NH_2), 6.90—7.80 (15 H, m, 3 × Ph), 9.4 (2 H, br s, 2 × NH)	128.6 (C-4),[b] 147.2 (C-5)	1 638 (NH_2), 1 605 (CONH)
(18)	2.4 (3 H, d, *J* 0.7 Hz, 5-Me), 6.34 (1 H, q, *J* 0.7 Hz, 4-H), 6.80—7.60 (10 H, m, 2 × Ph), 9.40 (2 H, br s, 2 × NH)	12.1 (5-Me), 101.9 (C-4)	1 695 and 1 665 (CONH)
(19), (20)[a,c]	1.80 (3 H, s, 3-Me), 1.88 (3 H, s, 3-Me), 5.58 (1 H, s, CHCl), 5.82 (1 H, s, CHCl)	10.3 (3-Me), 10.4 (3-Me), 63.5 (CHCl), 63.6 (CHCl), 96.5 (C-5)	1 730 (CONH)
(23)	3.90 (2 H, br s, NH_2), 5.18 (2 H, s, CH_2), 6.63 (1 H, s, 4-H), 6.85—7.10 (3 H, m, ArH), 7.15—7.60 (10 H, m, 2 × Ph), 7.65—7.95 (2 H, m, ArH)	45.8 (CH_2), 100.8 (C-4)	3 480 and 3 380 (NH_2), 1 640 (guanidine system)
(25)	7.08 (1 H, s, 4-H), 7.20—7.40 (6 H, m, Ph and NH), 7.45—7.60 (3 H, m, ArH), 7.65—7.90 (2 H, m, ArH)	106.8 (C-4), 162.5 (C-3/C-5), 165.3 (C-5/C-3)	3 225 (NH), 1 350 and 1 165 (SO_2)
(27)	3.75 (2 H, br s, NH_2), 6.58 (1 H, s, 4-H), 6.95—7.60 (13 H, m, 2 × Ph and ArH), 7.70—7.90 (2 H, m, ArH)	88.3 (C-4), 163.3 (C-3/C-5), 164.8 (C-5/C-3)	3 480 and 3 380 (NH_2), 1 668 (guanidine system)

[a] Spectra recorded in [$(CD_3)_2SO$]. [b] This signal is partially overlapped by the resonances of the aromatic carbons. [c] These values refer to the mixture of the two isomers and were obtained from the spectra of the crude reaction product of (**13**) with DPG and NaH.

extracted with dichloromethane (2 × 50 ml); removal of the solvent left a semi-solid brown residue (0.6 g) mainly containing the starting material (t.l.c. and ^{1}H n.m.r. spectrum).

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