107. Synthesis of Polysubstituted Pyrrolizidines from Proline Derivatives and Conjugated Nitroolefins

by **Fulvia Felluga, Giuliana Pitacco, Cristina Visintin**, and **Ennio Valentin***

Dipartimento di Scienze Chimiche, Università, I-34127 Trieste

Dedicated with best wishes to Professor *Dieter Seebach* on the occasion of his 60th birthday

(12.II.97)

The stereochemistry of 1,3-dipolar cycloaddition of azomethine ylides derived from aromatic aldehydes and L-proline alkyl esters with several nitroolefins was investigated. Cyclic and acyclic nitroolefins add to the *anti* form of the ylide in a highly diastereoselective but poorly regioselective manner to give pyrrolizidine derivatives. In a few cases, the stereochemical results strongly support a stepwise mechanism.

Introduction. – The synthesis of the pyrrolizidine ring system (1-azabicyclo[3.3.0]-octane) is an important target for many research groups, owing to its presence in a great variety of plant species and to the various interesting biological properties of the compounds which contain it [1]. Several pathways have been proposed for the asymmetric synthesis of this molecular skeleton [2]. *Murray et al.* [3] recently reported on the enantioselective ring closure of an *N,N*-disubstituted *N*-acetylprolinamide *via* its *N*-acyl anion. A stereocontrolled synthesis has been proposed by *Pilli* and *Russowski* [4] by using the addition of a chiral boron enolate to cyclic *N*-acyliminium ions. An elegant synthesis of a pyrrolizidine alkaloid, (−)-hastanecine, was achieved by *Denmark* and *Thorarensen* [5] *via* a [3 + 2] cycloaddition of dimethyl maleate on a chiral cyclic nitronate followed by hydrogenolytic cleavage of the nitroso-acetal intermediate.

However, for racemic systems, the 1,3-dipolar cycloaddition reaction of five-membered ring azomethine ylides and suitable dipolarophiles is surely one of the most versatile methods, in particular because of its stereochemical and regiochemical aspects [6].

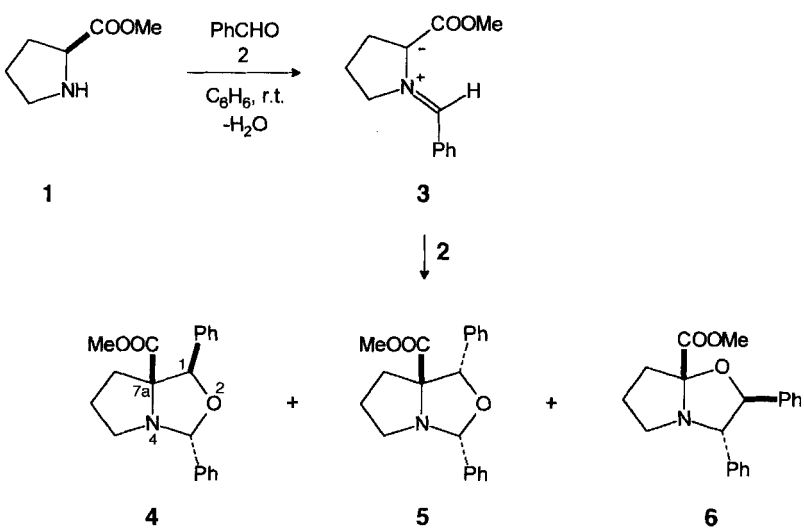
Imines of α-amino acids are known to react with dipolarophiles in both a decarboxylative [7] and non-decarboxylative 1,3-dipolar cycloaddition reaction [8] to give N-heterocycles. Similarly, azomethine ylides obtained from benzaldehydes and secondary α-amino esters have been found to react with dipolarophiles in a 1,3-dipolar cycloaddition to give indolizidine and pyrrolizidine derivatives [6b]. Owing to their great versatility in organic synthesis [9], conjugated nitroolefins have been also studied as dipolarophiles in several 1,3-dipolar cycloadditions, in particular with heteroaromatic N-ylides [10], with azomethine ylides prepared from dihydrotriazoles [11], and with α-cyanoaminosilanes ((silylmethyl)aminoacetonitriles) which act as azomethine-ylide equivalents [12].

Since our interest has been in the study of the reactivity of nitroolefins as 2π- and 4π-electron donors [13] as well as *Michael* acceptors [14], we envisaged that it could be interesting to investigate their behaviour as dipolarophiles, also in view of the fact that

nitroolefins had already been found to react as dipolarophiles with the enamine obtained from proline methyl ester and hydratropaldehyde (= α-methylbenzeneacetaldehyde) [13].

Results. – The reaction between L-proline methyl ester (**1**) with benzaldehyde **2** in 1:2 molar ratio, carried out at room temperature, furnished a solid mixture of oxapyrrolizidines **4**–**6** in the ratio of 86:12:2, as determined by integration of their respective benzylic protons (*Scheme 1*). This type of reaction, already known for the homologue methyl pipecolate (= methyl piperidinecarboxylate) which furnished the corresponding oxaindolizidines [6b], is a 1,3-cycloaddition of the carbonyl compound to the azomethine ylide **3**. The mixture of oxapyrrolizidines **4**–**6** was a mixture of kinetic control. In fact, on standing at room temperature in the crystalline state for a long period (40 days) or in $CHCl_3$ solution (10 days), the initial composition gradually changed to the final one which resulted to be 16:78:6.

Scheme 1



The existence of isomer **6**, albeit in small percentage, was indicated by the presence of two *d* at 5.24 and 4.65 ppm (J = 9.8 Hz) for the benzylic protons in the ^{1}H-NMR spectrum of the crude reaction mixture. The configuration of the oxapyrrolizidines **4** and **5** was determined by means of NOE difference measurements (*Table 1*), while that of **6** was assigned as shown in *Scheme 1*, with the two vicinal Ph groups in *trans* configuration.

The interconversion among the stereo- and regioisomers of the oxapyrrolizidines is due to a 1,3-dipolar cycloreversion reaction [15]. It was, therefore, of interest to investigate whether the aldehyde could be replaced by some other dipolarophile, such as a conjugated nitroolefin. Thus, several cyclic and acyclic nitroolefins **7** were added to the mixture **4**–**6**, as shown in *Scheme 2*. The reactions with the more reactive nitroolefins were carried out in Et_2O at -30–$0°$, while those with the less reactive nitroolefins were performed neat, at room temperature. As expected, the mixture of oxapyrrolizidines **4**–**6** formed under kinetic control, in which **4** largely predominated, was more reactive in the

Table 1. *The Most Significant NOE Difference Measurement Data*

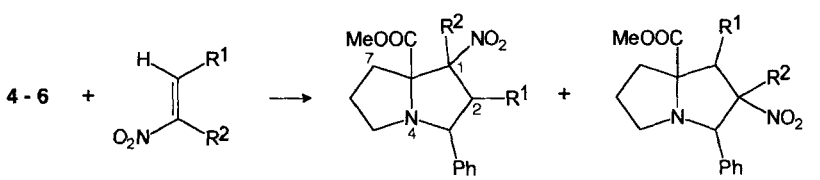
	Irradiated proton	Enhanced proton (η %)
4	H–C(3)	MeO (1%), H_o of Ph–C(3) (95), arom. H of Ph–C(1) (7%)
	H–C(1)	arom. H of Ph–C(1) (15%)
5	MeO	H–C(1) (2%), H–C(3) (1%)
	H–C(3)	H–C(1) (15%)
8a	H–C(1)	H–C(3) (8%), Me (13%)
	H–C(2)	H_o (15%), Me (5%)
	H–C(3)	Me (4%), MeO (2%)
	MeO	H–C(1) (1%)
	Me	H–C(1) (13%), H–C(2) (15%), H–C(3) (8%)
9a	H–C(1)	H–C(2) (9%), Me (5%)
	H–C(2)	H–C(1) (9%)
	H–C(3)	Me (3%), H_o (8%)
	MeO	H–C(3) (1%)
9'a	H–C(1)	H_o (11%), Me (7%)
	H–C(2)	H–C(3) (9%), Me (7%)
	H–C(3)	H–C(2) (10%)
	Me	H–C(2) (7%), H–C(1) (12%)
	MeO	Me (1%)
8b	H–C(3)	H–C(2) *cis* to NO_2 (6%), H_o (9%)
	Me	H–C(2) *trans* to NO_2 (5%)
	MeO	H–C(3) (1%)
9b	H–C(3)	H–C(1) *cis* to NO_2 (3%), H_o (16%)
	Me	H–C(1) *trans* to NO_2 (3%), H_o (9%)
	MeO	H–C(3) (1%)
8c	H–C(1)	H–C(3) (6%)
	H–C(3)	H–C(1) (9%), H_o of Ph–C(3) (18%)
	MeO	H–C(1) (2%)
9c	H–C(1)	H_o of Ph–C(1) (16%), H_o of Ph–C(3) (14%)
	H–C(2)	H–C(3) (15%), H_o of Ph–C(1) (24%)
	H–C(3)	H–C(2) (17%), H_o of Ph–C(3) (19%)
	MeO	H–C(2) (1%), H–C(3) (1%), H_o of Ph–C(1) (3%)
8d	H–C(2)	H_o of Ph–C(2) (21%), H_o of Ph–C(3) (13%)
	H–C(3)	H_o of Ph–C(2) (11%), H_o of Ph–C(3) (21%)
	Me	H–C(3) (11%), H_o of Ph–C(2) (12%), MeO (5%)
	MeO	Me (1%)
9d	H–C(1)	H_o of Ph–C(1) (14%)
	H–C(3)	Me (6%), H_o of Ph–C(3) (15%)
	Me	H–C(3) (6%), H_o of Ph–C(1) (18%)
	MeO	H_o of Ph–C(1) (2%)
9e	H–C(1)	H–C(7) (9%), H_o of Ph–C(1) (27%), H_o of Ph–C(3) (14%)
	H–C(3)	H_o of Ph–C(3) (15%), H_o of Ph–C(2) (33%)
	MeO	H_o of Ph–C(1) (4%)
8f	H–C(5)	H–C(6) (6%), H_β–C(8) (8%), H_o (9%)
	H–C(5a)	H–C(5) (13%)
	MeO	H_β–C(8) (1%)
	H_o	H–C(5) (8%), H–C(5a) (13%)

Table 1 (cont.)

	Irradiated proton	Enhanced proton (η %)
9f	H–C(5)	H_β–C(6) (8%)
	H–C(8a)	H_α–C(8) (7%)
	MeO	H–C(5) (1%), H_β–C(8) (2%)
8g	H–C(5)	H_{ax}–C(7) (5%), H_{ax}–C(9) (9%), H_o (10%)
	H–C(5a)	H_o (21%)
	MeO	H–C(5) (1%), H_{eq}–C(9) (3%)
9g	H–C(5)	H_{ax}–C(6) (7%), H_{ax}–C(9) (12%), H_o (14%)
	H–C(9a)	H_{ax}–C(9) (12%), H_o (11%)
	MeO	H_{ax}–C(8) (5%)
11	H–C(2)	H_β–C(5) (5%), H_β–C(7) (4%)
	H_β–C(5)	H–C(2) (4%), H_α–C(5) (26%), H–C(6) (7%)
	H–C(6)	H_β–C(5) (5%), H_β–C(7) (6%)
	H_β–C(7)	H–C(2) (3%), H–C(6) (7%)
	Me	H–C(3) (12%), Me (5%)
17	Me	H–C(3) (15%), MeO (7%), arom. H of Ph–C(2) (14%)
	H–C(2)	H_o of Ph–C(2) (21%), H_o of Ph–C(3) (15%)
	H–C(3)	Me (5%), H_o of Ph–C(2) (12%), H_o of Ph–C(3) (22%)

presence of a nitroolefin than that obtained under thermodynamic control, in which **5** prevailed. This latter compound in fact did not react at room temperature. Therefore, the kinetic mixture of oxapyrrolizidines **4–6** was used in the subsequent reactions, without prior purification to avoid any equilibration. For this reason, the kinetic mixture **4–6** was not completely free of benzaldehyde. However, since benzaldehyde is a by-product of the reactions with the nitroolefins, it was eliminated at the stage of purification of the products.

Scheme 2



7a R^1 = Me, R^2 = H
b R^1 = H, R^2 = Me
c R^1 = Ph, R^2 = H
d R^1 = Ph, R^2 = Me
e $R^1 = R^2$ = Ph
f $R^1 - R^2 = (CH_2)_3$
g $R^1 - R^2 = (CH_2)_4$

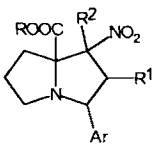
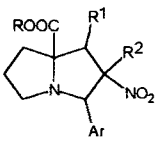
8a R^1 = Me, R^2 = H
b R^1 = H, R^2 = Me
c R^1 = Ph, R^2 = H
d R^1 = Ph, R^2 = Me
e $R^1 = R^2$ = Ph
f $R^1 - R^2 = (CH_2)_3$
g $R^1 - R^2 = (CH_2)_4$

9a R^1 = Me, R^2 = H
b R^1 = H, R^2 = Me
c R^1 = Ph, R^2 = H
d R^1 = Ph, R^2 = Me
e $R^1 = R^2$ = Ph
f $R^1 - R^2 = (CH_2)_3$
g $R^1 - R^2 = (CH_2)_4$

Thus, the reactions of the kinetic mixture **4–6** with the nitroolefins **7** afforded the regioisomers **8** and **9** with predominance of the latter compound, except in the case of (*E*)-2-nitro-1-phenylpropene (**7d**), which gave the regioisomer **8d** as the main product

(for relative regioisomer ratios, see *Table 2*). Almost all the products were isolated by chromatography, and their configurational assignments were made by means of NOE difference spectroscopy (*Table 1*).

Table 2. *Ratio of Regioisomers*[a])

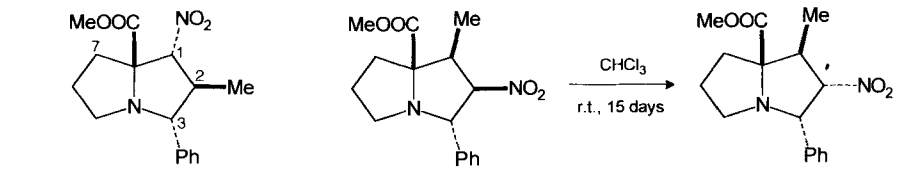
Entry	Substrates	Nitroolefin		
1	**4–6**	**7a**	35	65
2	**4–6**	**7b**	15	85
3	**4–6**	**7c**	40	60
4	**4–6**	**7d**	90	10
5	**4–6**	**7e**	5	95
6	**4–6**	**7f**	45	55
7	**4–6**	**7g**	36	64
8	**12/13**	**7d**	50	50
9	**16**	**7d**	80	20
10	**19/20**	**7c**	100	0
11	**19/20**	**7d**	100	0

[a]) Determined by integration of the appropriate ^{1}H-NMR signals in the crude reaction mixtures.

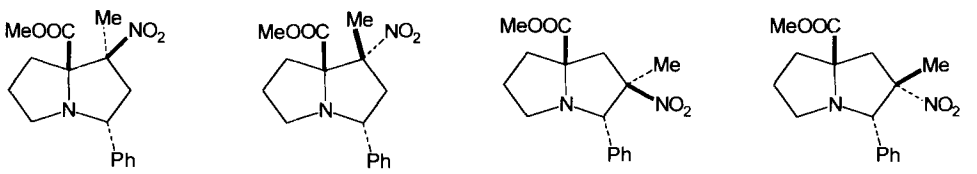
The reactions with the aliphatic linear nitroolefins **7a** and **7b** revealed a more complicated feature than those performed with the other nitroolefins. In the reaction of **4–6** with (*E*)-1-nitropropene (**7a**), three isomers, **8a**, **9a**, and **9′a**, were separated (*Scheme 3*), the two latter compounds being diastereoisomers of the same regioisomer. The only difference in the structures of **9a** and **9′a** was the configuration at C(2), as shown by DIFNOE measurements (*Table 1*) and confirmed by a comparison of their respective benzylic proton resonances (5.33 ppm for **9a** and 5.08 for **9′a**). The higher chemical-shift value clearly indicates the *cis* relationship between H–C(3) and the NO_2 group in **9a** [11]. The cycloadduct **9a** was a product of kinetic control as it completely converted into its diastereoisomer **9′a**, in $CHCl_3$ solution within two weeks. Since, in the other reactions, it was difficult to identify the products of kinetic formation, the reaction with **7a** was useful in clarifying the reaction mechanism. In the presence of 2-nitropropene (**7b**), the kinetic mixture **4–6** yielded the four isomeric pyrrolizidines **8b**, **8′b**, **9b**, and **9′b** (*Scheme 3*). The ratio **8b**/**8′b** was 4:1, while that of **9b**/**9′b** was 9:1. The pyrrolizidine **8′b** could not be isolated by chromatography, and therefore, its structure was tentatively assigned (see *Scheme 3*). The pair of diastereoisomeric regioisomers **9b** and **9′b** differed in the configuration of the C-atom bearing the NO_2 group. Their respective benzylic protons resonated at 5.11 and 4.58 ppm, suggesting for the former a *cis* relationship with the NO_2 group and for the latter a *trans* one [11].

The reactions with the aromatic nitroolefins **7c–e** were simpler than the previous ones as only two regioisomers **8c–e** and **9c–e** were formed in each case (see *Tables 1* and *2*). They were isolated by chromatography, with the exception of isomer **8e** which was only identified in the crude reaction mixture. In spite of its relative abundance (5%), compound **8e** was not recovered from the chromatographic separation.

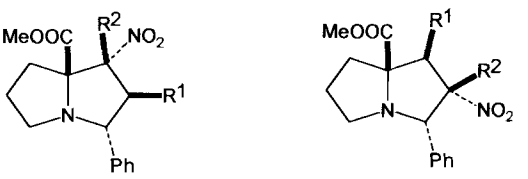
Scheme 3



8a **9a** **9'a**



8b [8'b] **9b** [9'b]

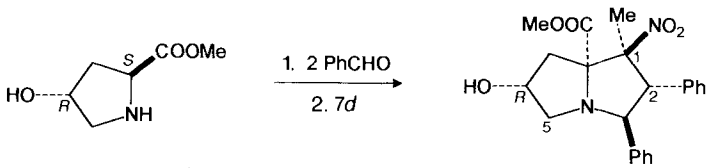


8c R^1 = Ph, R^2 = H
d R^1 = Ph, R^2 = Me
e R^1 = R^2 = Ph

9c R^1 = Ph, R^2 = H
d R^1 = Ph, R^2 = Me
e R^1 = R^2 = Ph

With the aim of studying also an asymmetric 1,3-dipolar cycloaddition [12], we prepared the optically active (2*S*,4*R*)-4-hydroxyproline methyl ester **10** [16], which was reacted with benzaldehyde and then with (*E*)-2-nitro-1-phenylpropene (**7d**; *Scheme 4*). The pyrrolizidine **11** was obtained as a single, optically pure stereoisomer in spite of the presence of five asymmetric centres. Its configuration was determined by DIFNOE experiments after a complete analysis of the ^{1}H- and ^{13}C-NMR spectra.

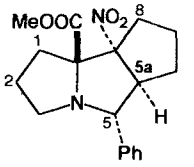
Scheme 4



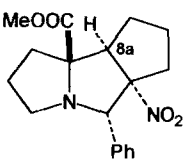
10 **11**

The reactions of the mixture **4**–**6** with the cyclic nitroolefins **7f** and **7g** furnished two pairs of regioisomers **8f**/**9f** and **8g**/**9g**, respectively (see *Tables 1* and *2*). The fusion between the rings is *cis* in both the decahydrocyclopenta[*a*]pyrrolizine derivatives **8f** and

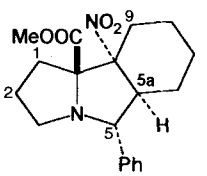
9f and in the decahydro-1*H*-cyclopent[*a*]isoindoles **8g** and **9g**, as determined by DIFNOE measurements. In particular for these latter compounds, the *cis* fusion can be also confirmed by the ^{1}H-NMR signals (C_6D_6) of the H-atoms at the bridgehead C-atoms that are equatorial with respect to the six-membered ring in both regioisomers **8g** and **9g**. Their respective $w_{1/2}$ (width at half-height; ^4J(H,H)) in fact was 10.4 Hz for **8g** and 12.0 Hz for **9g**. As a consequence, the NO_2 group linked to the other bridgehead C-atom is axial.



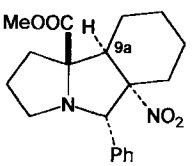
8f



9f



8g



9g

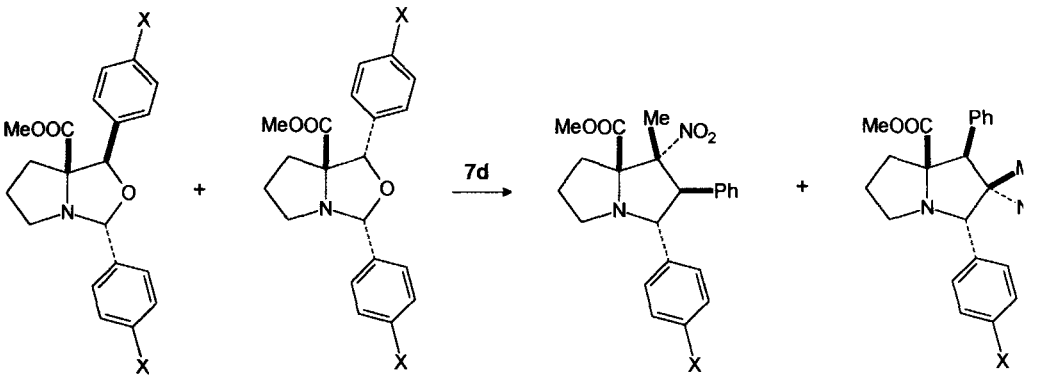
As shown above, all cycloadditions proceeded with high diastereoselectivity, as the geometry of the nitroolefin was retained in all the cycloadducts **8** and **9**, with the exception of compound **9a**, derived from 1-nitropropene (*Scheme 3*).

To study the diastereoselectivity of these reactions also with a nitroolfin in (*Z*)-configuration, we prepared (*Z*)-2-nitro-1-phenylpropene [17] for the reason that its (*E*)-isomer reacted with the same substrates in a highly regioselective manner (the ratio **8d**/**9d** was 9:1). The reaction of (*Z*)-2-nitro-1-phenylpropene with the mixture of substrates **4**–**6** was neither regio- nor diastereoselective, since the same regioisomers **8d** and **9d** (see above) as before were obtained in the ratio of 1:1. Therefore, the geometry of the (*Z*)-nitroolefin was not retained in either product. The higher percentage of the isomer **9d**, when compared with that obtained for the same isomer in the reaction of **4**–**6** with the (*E*)-nitroolefin, is just due to the reactivity of the (*Z*)-nitroolefin.

The influence of the electronic effects on the reactivity of these azomethine ylides with conjugated nitroolefins was studied with the oxapyrrolizidines **12** and **13** derived from L-proline methyl ester with 4-methoxybenzaldehyde and on the oxapyrrolizidine **16** derived from 4-nitrobenzaldehyde (*Scheme 5*). From the reaction with 4-nitrobenzaldehyde, a mixture of three oxapyrrolizidines was actually obtained, from which the single stereoisomer **16**, which is the main product (65%) of the kinetic mixture, could be isolated. The mixture **12**/**13** 65:35 and the oxapyrrolizidine **16** were reacted with (*E*)-2-nitro-1-phenylpropene (**7d**). From **12**/**13**, two regioisomers **14** and **15** were obtained in a 1:1 ratio. Their NMR data were almost identical with those of **8d** and **9d** and hence, they were assigned the same configuration. This result that has to be compared with the ratio of 9:1 previously obtained for **8d** and **9d** from **4**–**6** could be due to the influence of

electronic factors on the regiochemistry of the reaction. The electron-donating properties of the MeO group in **12**/**13** might speed up the reaction of the azomethine ylide with the electron-poor olefin, therefore, strongly decreasing the regioselectivity [18].

Scheme 5



12 X = MeO
16 X = NO_2

13 X = MeO

14 X = MeO
17 X = NO_2

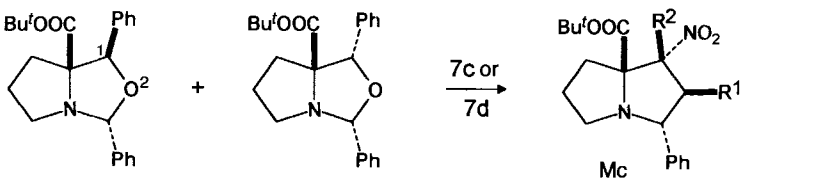
15 X = MeO
18 X = NO_2

As expected from the presence of an electron-withdrawing group at the aromatic ring of the azomethine ylide [18], the oxapyrrolizidine **16**, although of kinetic formation, was stable at room temperature for several months. The reaction with **7d** was, therefore, carried out at the temperature of fusion of the components for 2 h under Ar. Only under these forcing conditions, the nitroolefin **7d** was able to replace the aldehyde incorporated in the oxapyrrolizidine and to form the corresponding pyrrolizidines **17** and **18** in the ratio of 4:1. In spite of the different reaction conditions used, the composition of the product mixture was similar to that obtained from the oxapyrrolizidines **4**–**6**. The configuration of the products was the same as for **8d** and **9d** (*Table 1*).

Finally, the influence of steric factors on the regio- and stereoselectivity of the reactions was studied with the oxapyrrolizidines **19** and **20** derived from benzaldehyde and L-proline *tert*-butyl ester. They were reacted with (*E*)-β-nitrostyrene (**7c**) and (*E*)-2-nitro-1-phenylpropene (**7d**). Both reactions were regiospecific as only one regioisomer was isolated in each case, **21c** and **21d**, respectively (*Scheme 6*). Their formation derived from the approach of the nitroolefin from the less hindered side. The configuration of the cycloadducts **21c** and **21d** was the same as for the products **8c** and **8d**, isolated from the previous reactions. Both the ^{1}H- and ^{13}C-chemical shifts and the coupling constants were very similar.

Whereas the regioisomeric oxapyrrolizidines were found to interconvert, in no case an interconversion between the regioisomeric pyrrolizidines was observed. Even after prolonged heating the stereoisomer **8d** in benzene, no traces of its regioisomer **9d** were detected in its ^{1}H-NMR spectrum. Attempts were also made to verify the reversibility of the cycloadduct formation by capturing the ylide with other dipolarophiles such as dimethyl maleate and diethyl azodicarboxylate in excess in refluxing toluene, but unsuccessfully.

Scheme 6



19 **20** **21c** R^1 = Ph, R^2 = H
d R^1 = Ph, R^2 = Me

Conclusions. – As already found for similar reactions with different azomethine ylides [10] [11] [13], most of the products derive from the *endo* approach of the nitroolefin to the azomethine ylide in the '*anti*' form, with the exception of 2-nitropropene which prefers the *exo* approach, as demonstrated by the orientation of the NO_2 group in both **8b** and **9b**. Therefore, it seems that the approach of the nitroolefin is determined mainly by the steric encumbrance of the substituent at the olefin C(*β*)-atom.

Differently from other cases reported in the literature concerning the reactivity of conjugated nitroolefins with azomethine ylides [10] [11] [13], the reactions are not regiospecific, save the reactions of the azomethine ylide derived from L-proline *tert*-butyl ester (*Table 2, Entries 10* and *11*). In the other cases (*Table 2, Entries 1–3* and *5–7*), that regioisomer is favoured in which the NO_2 group is further away from the methoxycarbonyl group, with the exception of the reaction with (*E*)-2-nitro-1-phenylpropene (**7d**) (*Table 2, Entry 4*), suggesting a repulsion between the two groups in the transition state. Furthermore, the stereochemical course of the reaction depends upon the electronic nature and steric size of the substituents on the azomethine ylide, at least as far as regiochemistry is concerned. Finally, the finding that in two cases the geometry of the nitroolefin was not retained in the products – the pyrrolizidine **9a** derived from (*E*)-1-nitropropene (**7a**) and **9d** derived from (*Z*)-2-nitro-1-phenylpropene – is in favour of the intermediacy of a betaine-type intermediate. Therefore, at least for these two cases, a stepwise process can be envisaged. Probably in the other cases the mechanism follows a non-synchronous concerted pathway.

The formation of a single stereoisomer from the chiral azomethine ylide obtained from the proline derivative **10** deserves a comment. The diastereofacial selectivity in the approach of the dipolarophile can be rationalized by assuming a significant polar and steric influence of the OH group of the ylide. The only attack of the nitroolefin in fact occurs from the face opposite to that containing the OH group. As a consequence, in the product **11**, the OH group at C(6) and the methoxycarbonyl group at C(7a) are *cis* to each other. In the parent (2*S*,4*R*)-4-hydroxyproline derivative **10**, they were *trans*. Therefore, this approach produced an inversion of configuration at the original C(α) atom, although, owing to a different group priority, it is still (*S*).

Financial support by the *M.U.R.S.T.* and *C.N.R.* (Rome) and the University of Trieste is gratefully acknowledged.

Experimental Part

General. M.p.s: *Büchi-SHP-20* apparatus; uncorrected. Thin-layer chromatography (TLC): *Merck-60F-254* glass-backed silica-gel plates, AcOEt/light petroleum ether 1:4 as eluent; visualisation by UV light (254 nm)

or I_2. Flash chromatography (FC): silica gel *Merck 60*, 230–400 mesh. IR Spectra: *Jasco-200* FTIR. NMR ($CDCl_3$). Spectra: *Jeol-EX400* instrument. MS: *VG-7070* spectrometer at 70 eV.

1. *Synthesis of* **4**–**6**. To a suspension of *L*-proline methyl ester hydrochloride (1.0 g, 6.0 mmol) in benzene, an equimolar amount of $NaHCO_3$ in 1 ml of H_2O was added under stirring until CO_2 had completely evolved. Then, benzaldehyde (**2**; 12.0 mmol) was added at r.t. The mixture was stirred for 2 h and the H_2O formed removed by azeotropic distillation. Evaporation left an oil which, on standing in the refrigerator at −20° gave white crystalline **4**/**5**/**6** 86:12:2. For the sake of clarity, the spectroscopic data of **4** and **5** are given separately.

*(1*R*,3*R*,7a*R*)-Methyl Tetrahydro-1,3-diphenyl-1*H,3H-*pyrrolo[1,2-*c*]oxazole-7a-carboxylate* (**4**): ^{1}H-NMR ($CDCl_3$): 7.54 (*m*, 10 arom. H); 6.33 (*s*, H–C(3)); 5.05 (*s*, H–C(1)); 3.09 (*s*, MeO); 2.78 (*m*, 1 H–C(5)); 2.66 (*m*, 1 H–C(5), 1 H–C(7)); 2.34 (*dt*, *J* = 7.8, 7.8, 13.7, 1 H–C(7)); 1.84 (*m*, 2 H–C(6)). ^{13}C-NMR ($CDCl_3$): 175.8 (*s*, C=O); 138.2 (*s*); 135.5 (*s*); 128.9 (2*d*); 128.3 (2*d*); 128.0 (*d*); 126.7 (2*d*); 126.2 (*d*); 125.5 (2*d*); 96.9 (*d*, C(3)); 86.7 (*d*, C(1)); 79.2 (*s*, C(7a)); 51.4 (*q*, MeO); 49.2 (*t*, C(5)); 34.4 (*t*, C(7)); 24.3 (*t*, C(6)).

*(1*R*,3*S*,7a*S*)-Methyl Tetrahydro-1,3-diphenyl-1*H,3H-*pyrrolo[1,2-*c*]oxazole-7a-carboxylate* (**5**): ^{1}H-NMR ($CDCl_3$): 7.54 (*m*, 10 arom. H); 5.76 (*s*, H–C(3)); 5.36 (*s*, H–C(1)); 3.87 (*s*, MeO); 2.55 (*m*, 2 H–C(5)); 1.90 (*ddd*, *J* = 2.4, 7.6, 13.2, 1 H–C(7)); 1.64 (*m*, 1 H–C(6)); 1.50 (*m*, 1 H–C(6)); 1.36 (*ddd*, *J* = 6.8, 10.7, 13.2, 1 H–C(7)). ^{13}C-NMR ($CDCl_3$): 175.7 (*s*, C=O); 138.0 (*s*), 135.7 (*s*); 128.1 (2*d*); 128.0 (2*d*); 127.4 (2*d*); 126.8 (2*d*); 126.0 (2*d*); 93.2 (*d*, C(3)); 82.8 (*d*, C(1)); 77.1 (*s*, C(7a)); 52.6 (*q*, MeO); 49.9 (*t*, C(5)); 32.6 (*t*, C(7)); 25.6 (*t*, C(6)).

*(2*R*,3*R*,7a*S*)-Methyl Hexahydro-2,3-diphenylpyrrolo[2,1-*b*]oxazole-7a-carboxylate* (**6**) identified from the **4**–**6** mixture: ^{1}H-NMR ($CDCl_3$): 5.30 (*d*, *J* = 9.8, H–C(2)); 4.68 (*d*, *J* = 9.8, H–C(3)); 3.63 (*s*, MeO); 2.75 (*m*); 2.08 (*m*, H–C(7)). ^{13}C-NMR ($CDCl_3$): 175.3 (*s*); 103.5 (*s*, C(7a)); 79.2 (*d*, C(2)); 72.0 (*d*, C(3)); 59.4 (*q*, MeO); 49.6 (*t*, C(5)); 36.6 (*t*, C(7)); 25.2 (*t*, C(5)).

On standing in $CHCl_3$ soln. for 4 days at r.t., the ratio **4**/**5**/**6** changed into 16:78:6.

2. *Nitroolefins*. (*E*)-β-Nitrostyrene (= (*E*)-(2-nitroethenyl)benzene; **7c**) was purchased from *Aldrich Chemicals*; (*E*)-1-nitropropene (**7a**) [19], 2-nitropropene (**7b**) [19] (*E*)-2-nitro-1-phenylpropene (= (*E*)-(2-nitroprop-1-enyl)benzene; **7d**) [20], α-nitrostilbene (= (*E*)-1,1′-(1-nitroethen-1,2-diyl)bis[benzene]; **7e**) [21], 1-nitrocyclopentene (**7f**) [22], and 1-nitrocyclohexene (**7g**) [22] were prepared by literature procedures.

3. *Reactions with the Nitroolefins*. 3.1. *General Procedure*. To a soln. of the kinetic mixture **4**/**5**/**6** in Et_2O was added dropwise an equimolar amount of the nitroolefin **7** in Et_2O, either at −30° (**7a**,**b**,**f**) or at r.t., under Ar. The reaction was monitored to determine the degree of conversion. If after 48 h this was poor, the solvent was eliminated, and the mixture was allowed to react neat. The product ratio was determined by ^{1}H-NMR analysis, by integration of the appropriate proton peaks. The products were then separated by FC.

3.2. *Reaction of* **4**–**6** *with (E)-1-Nitropropene* (**7a**). With **7a** (0.5 g, 5.7 mmol) and **4**–**6** (1.85 g, 5.7 mmol) at −30° in Et_2O. After the addition, the soln. was warmed up to r.t. and the solvent evaporated: **8a**/**9a**/**9′a** 35:7:58 which was separated by FC (AcOEt/light petroleum ether 2:98 → 20:80): *(1*R*,2S*,3*R*,7a*R*)-Methyl Hexahydro-2-methyl-1-nitro-3-phenyl-1*H-*pyrrolizine-7a-carboxylate* (**8a**): 0.39g (26%). Oil. R_f 0.35. IR (film): 1735 (CO_2Me), 1530, 1370 (NO_2), 1595, 780, 710, 695 (Ph). ^{1}H-NMR ($CDCl_3$): 7.38 (*m*, 5 arom. H); 5.48 (*d*, *J* = 10.4, H–C(1)); 4.13 (*d*, *J* = 12.2, H–C(3)); 3.86 (*s*, MeO); 3.27 (*ddq*, *J* = 6.4, 10.4, 12.2, H–C(2)); 2.53 (*ddd*, *J* = 5.5, 9.2, 11.6, 1 H–C(5)); 2.38 (*m*, 1 H–C(5), 1 H–C(7)); 1.85 (*m*, 1 H–C(6)); 1.77 (*m*, 1 H–C(6)); 1.47 (*ddd*, *J* = 7.0, 12.2, 13.1, 1 H–C(7)); 1.14 (*d*, *J* = 6.4, Me). ^{13}C-NMR ($CDCl_3$): 173.6 (*s*, C=O); 134.7 (*s*); 129.3 (2*d*); 128.5 (2*d*); 128.2 (*d*); 95.7 (*d*, C(1)); 75.7 (*s*, C(7a)); 68.3 (*d*, C(3)); 53.2 (*q*, MeO); 50.8 (*t*, C(5)); 36.8 (*d*, C(2)); 31.9 (*t*, C(7)); 25.4 (*t*, C(6)); 13.8 (*q*, Me). MS: 304 (0.01, M^+), 258 (9, $[M - NO_2]^+$), 246 (53, $[MH - CO_2Me]^+$), 199 (100, $[M - NO_2 - CO_2Me]^+$), 184 (72, $[M - NO_2 - CO_2Me - Me]^+$), 156 (10), 128 (8), 115 (9), 91 (20), 86 (53), 84 (85), 77 (15). HR-MS: 258.14951 ($C_{16}H_{20}NO_2^+$, $[M - NO_2]^+$; calc. 258.14940).

*(1*R*,2S*,3*R*,7a*S*)-Methyl Hexahydro-1-methyl-2-nitro-3-phenyl-1*H-*pyrrolizine-7a-carboxylate* (**9a**): 0.07g (5%). Oil. R_f 0.25. IR (film): 1720 (CO_2Me), 1550, 1355 (NO_2), 1600, 1500, 750, 715 (Ph). ^{1}H-NMR ($CDCl_3$): 7.37 (*m*, 5 arom. H); 5.45 (*dd*, *J* = 9.3, 11.0, H–C(2)); 5.33 (*d*, *J* = 9.3, H–C(3)); 3.81 (*s*, MeO); 2.90 (*dq*, *J* = 6.7, 9.3, H–C(1)); 2.64 (*m*, 1 H–C(5), 1 H–C(7)); 2.44 (*dt*, *J* = 6.8, 9.3, 9.3, 1 H–C(5)); 1.92 (*m*, 1 H–C(7)); 1.75 (*m*, 2 H–C(6)); 1.10 (*d*, *J* = 6.7, Me). ^{13}C-NMR ($CDCl_3$): 173.6 (*s*, C=O); 135.1 (*s*); 128.7 (2*d*); 128.4 (2*d*); 128.2 (2*d*); 89.2 (*d*, C(2)); 78.8 (*s*, C(7a)); 67.6 (*d*, C(3)); 52.1 (*q*, MeO); 49.7 (*t*, C(5)); 46.4 (*d*, C(1)); 37.5 (*t*, C(7)); 24.3 (*t*, C(6)); 11.2 (*q*, Me). MS: 305 (0.01, M^+), 258 (5, $[M - NO_2]^+$), 246 (30, $[MH - CO_2Me]^+$), 199 (30, $[M - NO_2 - CO_2Me]^+$), 198 (50, $[M - HNO_2 - CO_2Me]$), 184 (52, $[M - NO_2 - CO_2Me - Me]^+$), 156 (8), 128 (8), 115 (8), 97 (10), 91 (12), 77 (10). HR-MS: 258.14927 ($C_{16}H_{20}NO_2^+$, $[M - NO_2]^+$; calc. 258.14940).

*(1*R*,2R*,3*R*,7a*S*)-Methyl Hexahydro-1-methyl-2-nitro-3-phenyl-1*H-*pyrrolizine-7a-carboxylate* (**9′a**): 0.65g (43%). Oil. R_f 0.45. IR (film): 1735 (CO_2Me), 1535, 1360 (NO_2), 1595, 780, 700 (Ph). ^{1}H-NMR ($CDCl_3$): 7.31 (*m*, 3 arom. H); 7.18 (*m*, 2 arom. H); 5.50 (*dd*, *J* = 8.8, 11.0, H–C(2)); 5.08 (*d*, *J* = 8.8, H–C(3)); 3.78

(*s*, MeO); 3.06 (*dq*, *J* = 6.7, 11.1, H–C(1)); 2.75 (*dt*, *J* = 7.6, 7.6, 9.5, 1 H–C(7)); 2.70 (*ddd*, *J* = 2.7, 7.0, 9.2, 1 H–C(5)); 2.59 (*ddd*, *J* = 3.6, 8.1, 9.2, 1 H–C(5)); 2.06 (*m*, 1 H–C(6)); 1.92 (*m*, 1 H–C(6)); 1.73 (*ddd*, *J* = 7.9, 9.5, 11.9, 1 H–C(7)); 1.09 (*d*, *J* = 6.7, Me). ^{13}C-NMR ($CDCl_3$): 174.9 (*s*, C=O); 134.7 (*s*); 129.1 (2*d*); 128.7 (*d*); 128.3 (2*d*); 96.4 (*d*, C(2)); 78.7 (*s*, C(7a)); 66.1 (*d*, C(3)); 52.0 (*q*, MeO); 45.4 (*t*, C(5)); 43.5 (*d*, C(1)); 33.8 (*t*, C(7)); 27.7 (*t*, C(6)); 12.8 (*q*, Me). MS: 304 (0.1, M^+), 258 (10, $[M - NO_2]^+$), 245 (82, $[M - CO_2Me]^+$), 199 (26, $[M - NO_2 - CO_2Me]^+$), 198 (100, $[M - HNO_2 - CO_2Me]^+$), 184 (38, $[M - C_2H_6NO_4]^+$), 156 (8), 128 (8), 115 (10), 91 (20), 77 (12). HR-MS: 258.14933 ($C_{16}H_{20}NO_2^+$, $[M - NO_2]^+$; calc. 258.14940).

3.3. *Reaction of* **4–6** *with 2-Nitropropene* (**7b**). With **7b** (0.5 g, 5.7 mmol) in Et_2O and **4–6** (1.85g, 5.7 mmol) at –30°. The soln. was warmed up to r.t. and evaporated. The oily residue was fractionated by FC (AcOEt/light petroleum ether 1:9): **8b**/**8′b** 4:1 (0.7 g, 40%; R_f 0.25) and **9b**/**9′b** 9:1 (0.7g, 40%; R_f 0.5). Compounds **8b** and **9b** were isolated by further FC and **8′b** and **9′b** characterized by ^{1}H-NMR of the mixture **8b**/**8′b** and **9b**/**9′b**, resp. *(1*R*,3S*,7a*S*)-Methyl Hexahydro-1-methyl-1-nitro-3-phenyl-1H-pyrrolizine-7a-carboxylate* (**8b**): IR (film): 1735 (CO_2Me), 1530, 1370 (NO_2), 1600, 750, 720, 695 (Ph). ^{1}H-NMR ($CDCl_3$): 7.31 (*m*, 5 arom. H); 4.57 (*dd*, *J* = 6.3, 9.8, H–C(3)); 3.72 (*s*, MeO); 3.10 (*dd*, *J* = 6.3, 14.2, H–C(2) *cis* to NO_2); 2.57 (*m*, 2 H–C(5)); 2.34, 2.32 (*m* and *dd*, *J* = 9.8, 14.2, 1 H–C(7), H–C(2) *trans* to NO_2); 1.95 (*s*, Me); 1.85 (*m*, 2 H–C(6), 1 H–C(7)). ^{13}C-NMR ($CDCl_3$): 172.6 (*s*, C=O); 138.5 (*s*); 128.5 (2*d*); 128.2 (2*d*); 127.9 (*d*); 96.2 (*s*, C(2)); 82.2 (*s*, C(7a)); 61.2 (*d*, C(3)); 52.3 (*q*, MeO); 47.0 (*t*, C(5)); 45.6 (*t*, C(1)); 33.0 (*t*, C(7)); 25.3 (*t*, C(6)); 24.1 (*q*, Me).

*(1*R*,3R*,7a*R*)-Methyl Hexahydro-1-methyl-1-nitro-3-phenyl-1H-pyrrolizine-7a-carboxylate* (**8′b**): ^{1}H-NMR ($CDCl_3$): 4.55 (*dd*, *J* = 6.3, 10.0, H–C(3)); 3.73 (*s*, MeO); 2.45 (*m*, H–C(2)); 1.53 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 173.7 (*s*, C=O); 143.6 (*s*); 128.5 (2*d*); 127.2 (2*d*); 126.8 (*d*); 96.9 (*s*, C(1)); 85.0 (*s*, C(7a)); 69.7 (*d*, C(3)); 53.8 (*t*, C(5)); 52.4 (*q*, MeO); 49.9 (*t*, C(2)); 32.6 (*t*, C(7)); 27.9 (*t*, C(6)); 22.0 (*q*, Me).

*(2*R*,3S*,7a*R*)-Methyl Hexahydro-2-methyl-2-nitro-3-phenyl-1H-pyrrolizine-7a-carboxylate* (**9b**): Oil. IR (film): 1735 (CO_2Me), 1535, 1370 (NO_2), 1600, 750, 710, 695 (Ph). ^{1}H-NMR ($CDCl_3$): 7.40 (*m*, 3 arom. H); 7.23 (*m*, 2 arom. H); 5.11 (*s*, H–C(3)); 3.74 (*s*, MeO); 3.53 (*d*, *J* = 14.6, 1 H–C(1)); 2.86 (*m*, 1 H–C(5)); 2.77 (*m*, 1 H–C(5)); 2.35 (*m*, 1 H–C(7)); 2.16 (*d*, *J* = 14.6, 1 H–C(1)); 2.12–1.84 (*m*, 2 H–C(6), 1 H–C(7)). ^{13}C-NMR ($CDCl_3$): 176.1 (*s*, C=O); 136.0 (*s*); 129.2 (2*d*); 128.7 (2*d*); 128.4 (*d*); 101.7 (*s*, C(2)); 75.6 (*s*, C(7a)); 72.3 (*d*, C(3)); 52.2 (*q*, MeO); 45.2 (*t*, C(5)); 44.3 (*t*, C(1)); 37.0 (*t*, C(7)); 27.3 (*t*, C(6)); 24.0 (*q*, Me). MS: 304 (0.1, M^+), 258 (10, $[M - NO_2]^+$), 245 (82, $[M - CO_2Me]^+$), 199 (25, $[M - NO_2 - CO_2Me]^+$), 198 (100, $[M - HNO_2 - CO_2Me]^+$), 184 (38, $[M - C_2H_6NO_4]^+$), 156 (8), 128 (8), 115 (10), 91 (20), 77 (12). HR-MS: 258.14955 ($C_{16}H_{20}NO_2^+$, $[M - NO_2]^+$; calc. 258.14940).

*(2*R*,3R*,7a*S*)-Methyl Hexahydro-2-methyl-2-nitro-3-phenyl-1H-pyrrolizine-7a-carboxylate* (**9′b**): ^{1}H-NMR ($CDCl_3$): 4.58 (*s*, H–C(3)); 3.78 (*s*, MeO); 3.36 (*d*, *J* = 14.6, 1 H–C(1)); 3.18 (*d*, *J* = 14.6, 1 H–C(1)); 2.50 (*m*, H–C(5)); 1.40 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 173.1 (*s*, C=O); 136.0 (*s*); 128.5 (*d*); 128.1 (2*d*); 127.1 (2*d*); 89.5 (*s*, C(2)); 74.7 (*s*, C(7a)); 66.6 (*d*, C(3)); 51.5 (*q*, MeO); 45.2 (*t*, C(5)); 44.8 (*t*, C(1)); 35.7 (*t*, C(7)); 26.8 (*t*, C(6)); 25.2 (*q*, Me).

3.4. *Reaction of* **4–6** *with* (E)*-β-Nitrostyrene* (**7c**). With **7c** (0.35 g, 2.5 mmol) and **4–6** (0.55 g, 2.5 mmol) at r.t. After 4 days **8c**/**9c** 2:3 was formed and separated by FC (AcOEt/light petroleum ether 1:9): *(1*R*,2S*,3R*,7a*R*)-Methyl Hexahydro-1-nitro-2,3-diphenyl-1H-pyrrolizine-7a-carboxylate* (**8c**): 0.30g (32%). R_f 0.35. M.p. 115–116° (from light petroleum ether). IR (nujol): 1720 (CO_2Me), 1530, 1370 (NO_2), 1600, 700 (Ph). ^{1}H-NMR ($CDCl_3$): 7.32 (*m*, 4 arom. H); 7.08–7.24 (*m*, 6 arom. H); 5.95 (*d*, *J* = 10.2, H–C(1)); 4.84 (*d*, *J* = 12.3, H–C(3)); 4.43 (*dd*, *J* = 10.2, 12.3, H–C(2)); 3.94 (*s*, MeO); 2.61 (*m*, 1 H–C(5)); 2.50 (*m*, 1 H–C(5), 1 H–C(7)); 1.89 (*m*, 2 H–C(6)); 1.62 (*m*, 1 H–C(7)). ^{13}C-NMR ($CDCl_3$): 173.4 (*s*, C=O); 136.2 (*s*); 134.7 (*s*); 129.3 (2*d*); 129.0 (2*d*); 128.4 (2*d*); 128.0 (*d*); 127.9 (2*d*); 127.7 (*d*); 97.6 (*d*, C(1)); 76.1 (*s*, C(7a)); 67.8 (*d*, C(3)); 53.4 (*q*, MeO); 50.8 (*t*, C(5)); 48.0 (*d*, C(2)); 32.1 (*t*, C(7)); 25.4 (*t*, C(6)). MS: 320 (100, $[M - NO_2]^+$), 307 (16, $[M - CO_2Me]^+$), 261 (71, $[M - CO_2Me - NO_2]^+$), 260 (35, $[M - HCO_2Me - NO_2]^+$), 232 (10), 217 (11), 216 (20), 193 (10), 184 (23), 178 (10), 156 (10), 155 (15), 130 (13), 129 (17), 128 (16), 118 (18), 117 (10), 115 (21), 105 (10), 104 (14), 103 (12), 92 (17), 91 (47), 83 (24), 77 (17), 41 (10), 28 (10). Anal. calc. for $C_{21}H_{22}N_2O_4$ (366.42): C 68.84, H 6.05, N 7.65; found: C 68.78, H 6.10, N 7.60.

*(1*R*,2R*,3R*,7a*S*)-Methyl Hexahydro-2-nitro-1,3-diphenyl-1H-pyrrolizine-7a-carboxylate* (**9c**): 0.44 g (48%). R_f 0.45. M.p. 104–105° (from light petroleum ether). IR (nujol): 1720 (CO_2Me), 1540, 1370 (NO_2); 1595, 740, 720, 700 (Ph). ^{1}H-NMR ($CDCl_3$): 7.28 (*m*, 10 arom. H); 6.35 (*dd*, *J* = 8.8, 11.1, H–C(2)); 5.27 (*d*, *J* = 8.8, H–C(3)); 4.30 (*d*, *J* = 11.1, H–C(1)); 3.40 (*s*, MeO); 2.78 (*m*, 1 H–C(5)); 2.67 (*m*, 1 H–C(7)); 2.51 (*m*, 1 H–C(5)); 2.17 (*m*, 1 H–C(6)); 1.90 (*m*, 1 H–C(6), 1 H–C(7)). ^{13}C-NMR ($CDCl_3$): 173.9 (*s*, C=O); 134.7 (*s*); 134.2 (*s*); 129.1 (2*d*); 128.8 (*d*); 128.7 (2*d*); 128.3 (2*d*); 127.9 (*d*); 127.0 (2*d*); 93.8 (*d*, C(2)); 79.8 (*s*, C(7a)); 65.4 (*d*, C(3)); 53.7 (*d*, C(1)); 51.7 (*q*, MeO); 44.5 (*t*, C(5)); 34.0 (*t*, C(7)); 27.5 (*t*, C(6)). MS: 320 (10, $[M - NO_2]^+$), 308 (10), 307 (40, $[M - CO_2Me]^+$), 275 (11), 273 (13), 261 (29, $[M - CO_2Me - NO_2]^+$), 260 (100, $[M - HCO_2Me -$

$NO_2]^+$), 232 (10), 217 (12), 194 (13), 193 (83), 184 (17), 178 (10), 159 (10), 156 (10), 130 (21), 129 (10), 128 (13), 118 (19), 117 (13), 116 (17), 115 (63), 105 (25), 104 (13), 103 (19), 91 (61), 89 (11), 77 (30), 65 (11), 51 (15), 41 (15), 33 (11), 28 (19). Anal. calc. for $C_{21}H_{22}N_2O_4$ (366.42): C 68.84, H 6.05, N 7.65; found: C 68.80, H 6.06, N 7.58.

3.5. *Reaction of* **4–6** *with (*E*)-2-Nitro-1-phenylpropene* (**7d**). With **4–6** (0.5 g, 2.0 mmol) and **7d** (0.39 g, 2.0 mmol) for 72 h at r.t.: **8d**/**9d** 9:1. The mixture was separated by FC (light petroleum ether/AcOEt 1:9): *(1*R**,2*S**,3*R**,7a*R**)-Methyl Hexahydro-1-methyl-1-nitro-2,3-diphenyl-1H-pyrrolizine-7a-carboxylate* (**8d**): 0.60g (78%). R_f 0.30. M.p. 158–159° (from ligroin). IR (nujol): 1730 (CO_2Me), 1520, 1360 (NO_2), 1595, 700 (Ph). ^{1}H-NMR ($CDCl_3$): 7.36 (*m*, 2 arom. H); 7.22 (*m*, 8 arom. H); 5.1 (*d*, *J* = 12.7, H–C(3)); 4.9 (*d*, *J* = 12.7, H–C(2)); 3.8 (*s*, MeO); 2.59 (*m*, 2 H–C(5), 1 H–C(7)); 1.78 (*m*, 1 H–C(6), 1 H–C(7)); 1.57 (*m*, 1 H–C(6)); 1.43 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 173.1 (*s*, C=O); 135.2 (*s*); 134.2 (*s*); 129.5 (2*d*); 129.1 (2*d*); 128.5 (2*d*); 128.3 (2*d*); 127.9 (*d*); 127.6 (*d*); 100.6 (*s*, C(1)); 81.6 (*s*, C(7a)); 65.2 (*d*, C(3)); 52.5 (*q*, MeO); 50.7 (*t*, C(5)); 49.8 (*d*, C(3)); 35.3 (*t*, C(7)); 24.4 (*t*, C(6)); 20.3 (*q*, Me). MS: 380 (0.5, M^+), 344 (61, $[M - NO_2]^+$), 321 (27, $[M - CO_2Me]^+$), 275 (100, $[M - CO_2Me - NO_2]^+$), 260 (28), 217 (24), 198 (32), 129 (12), 128 (14), 121 (10), 118 (15), 115 (16), 105 (10), 104 (10), 103 (10), 98.5 (19), 91 (38), 77 (13). Anal. calc. for $C_{22}H_{24}N_2O_4$ (380.44): C 69.46, H 6.36, N 7.36; found: C 69.58, H 6.37, N 7.29.

*(1*R**,2*S**,3*S**,7a*R**)-Methyl Hexahydro-2-methyl-2-nitro-1,3-diphenyl-1H-pyrrolizine-7a-carboxylate* (**9d**): 0.07 g (9%). R_f 0.60. M.p. 136–137° (from ligroin). IR (nujol): 1730 (CO_2Me), 1530, 1355 (NO_2), 1590, 695 (Ph). ^{1}H-NMR ($CDCl_3$): 7.28–7.23 (*m*, 8 arom. H); 7.06 (*m*, 2 arom. H); 4.91 (*s*, H–C(3)); 4.79 (*s*, H–C(1)); 3.61 (*s*, MeO); 3.00 (*m*, 1 H–C(5)); 2.53 (*m*, 1 H–C(5), 1 H–C(7)); 2.14 (*m*, 1 H–C(6)); 1.88 (*m*, 1 H–C(6), 1 H–C(7)); 1.76 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 174.8 (*s*, C=O); 135.5 (*s*); 133.9 (*s*); 130.4 (2*d*); 128.8 (*d*); 128.6 (2*d*); 128.4 (2*d*), 128.3 (2*d*); 127.9 (*d*); 106.0 (*s*, C(2)); 79.5 (*s*, C(7a)); 74.0 (*d*, C(3)); 60.9 (*d*, C(1)); 51.5 (*q*, MeO); 43.0 (*t*, C(5)); 35.0 (*t*, C(7)); 26.5 (*t*, C(6)); 23.0 (*q*, Me). Anal. calc. for $C_{22}H_{24}N_2O_4$ (380.44); C 69.46, H 6.36, N 7.36; found: C 69.57, H 6.41, N 7.25.

3.6. *Reaction of* **4–6** *with (*Z*)-2-Nitro-1-phenylpropene.* As described in *Exper. 3.5* for the (*E*)-isomer **7d**: crude **8d**/**9d** 1:1 (by ^{1}H-NMR).

3.7. *Reaction of* **4–6** *with α-Nitrostilbene* (**7e**). With **4–6** (0.40 g, 2.0 mmol) and **7e** (0.45 g, 2.0 mmol) for 144 h at r.t. The semisolid reaction mixture was purified by FC (AcOEt/light petroleum ether 1:9): *(1*R**,2*R**,3*S**,7a*R**)-Methyl Hexahydro-2-nitro-1,2,3-triphenyl-1H-pyrrolizine-7a-carboxylate* (**9e**): 0.77g (91%). M.p. 125–126° (from light petroleum ether). IR (nujol): 1730 (CO_2Me), 1525, 1360 (NO_2), 1595, 695 (Ph). ^{1}H-NMR ($CDCl_3$): 7.41 (*m*, 2 arom. H); 7.35 (*m*, 3 arom. H); 7.24 (*m*, 5 arom. H); 7.10 (*m*, 1 arom. H); 7.01 (*t*, 2 arom. H); 6.52 (*d*, 2 arom. H); 5.82 (*s*, H–C(3)); 5.18 (*s*, H–C(1)); 3.27 (*s*, Me); 2.94 (*dt*, *J* = 7.7, 7.7, 9.7, 1 H–C(5)); 2.86 (*dt*, *J* = 4.0, 8.7, 8.7, 1 H–C(5)); 2.64 (*ddd*, *J* = 2.5, 7.7, 10.3, 1 H–C(7)); 2.15 (*m*, 1 H–C(7)); 2.02 (*m*, 1 H–C(6)); 1.74 (*m*, 1 H–C(6)). ^{13}C-NMR ($CDCl_3$): 174.1 (*s*, C=O); 136.9 (*s*); 136.6 (*s*); 134.4 (*s*); 131.3 (2*d*); 129.5 (2*d*); 129.1 (2*d*); 128.9 (*d*); 128.7 (*d*); 128.5 (2*d*); 127.4 (3*d*); 127.1 (2*d*); 110.3 (*s*, C(2)); 81.5 (*s*, C(7a)); 73.2 (*d*, C(3)); 61.9 (*d*, C(1)); 57.3 (*q*, MeO); 46.0 (*t*, C(5)); 38.4 (*t*, C(7)); 26.4 (*t*, C(6)). MS: 396 (1, $[M - NO_2]^+$), 337 (100, $[M - CO_2Me - NO_2]^+$), 193 (12), 179 (33), 178 (11), 106 (44), 105 (43), 103 (21), 99 (15), 91 (18), 89 (16), 77 (50), 76 (16), 70 (17), 69 (21), 51 (25), 50 (15), 44 (22), 42 (12), 41 (22), 39 (12), 30 (50), 28 (30). Anal. calc. for $C_{27}H_{26}N_2O_4$ (442.51): C 73.29, H 5.92, N 6.33; found: C 73.36, H 5.98, N 6.29.

3.8. *Reaction of* **4–6** *with 1-Nitrocyclopentene (*7f*).* With **7f** (0.32 g, 2.8 mmol) and **4–6** (0.62 g, 2.8 mmol) at −30°. The mixture was then warmed up to r.t. and left standing for 72 h, to give **8f**/**9f** 45:55 which were separated by FC (AcOEt/light petroleum ether 1:9): *(5*R**,5a*S**,8a*R**,8b*R**)-Methyl Decahydro-8a-nitro-5-phenylcyclopenta[*a*]pyrrolizine-8b-carboxylate* (**8f**): 0.37 g (39%). R_f 0.30. M.p. 86–87° (from ligroin). IR (nujol): 1730 (CO_2Me), 1520, 1370 (NO_2), 1600, 700 (Ph). ^{1}H-NMR ($CDCl_3$): 7.45 (*d*, 2 arom. H); 7.35 (*m*, 3 arom. H); 4.27 (*d*, *J* = 11.5, H–C(5)); 4.06 (*m*, H–C(5a)); 3.83 (*s*, MeO); 2.58 (*m*, 2 H–C((3), 1 H–C(8)); 2.46 (*m*, 1 H–C(1)); 2.11 (*ddd*, *J* = 7.2, 11.8, 13.4, 1 H–C(8)); 2.01 (*m*, 1 H–C(6)); 1.93 (*m*, 1 H–C(7)); 1.76–1.52 (*m*, 1 H–C(1), 2 H–C(2), 1 H–C(7)); 1.41 (*m*, 1 H–C(6)). ^{1}H-NMR (C_6D_6): 7.31 (*d*, 2 arom. H); 7.13 (*m*, 3 arom. H); 4.25 (*d*, *J* = 11.2, H–C(5)); 4.00 (*m*, H–C(5a)); 3.37 (*s*, MeO); 2.52 (*m*, 1 H–C(8)); 2.47–2.35 (*m*, 2 H–C(3), 1 H–C(1)); 1.96 (*ddd*, *J* = 7.3, 11.2, 14.2, 1 H–C(8)); 1.70–1.60 (*m*, 1 H–C(1), 1 H–C(6)); 1.48–1.23 (*m*, 2 H–C(2), 2 H–C(7)); 1.02 (*ddt*, *J* = 3.4, 8.3, 8.3, 13.2, 1 H–C(6)). ^{13}C-NMR ($CDCl_3$): 173.2 (*s*, C=O); 136.0 (*s*); 129.0 (2*d*); 128.4 (2*d*); 128.0 (*d*); 111.7 (*s*, C(8a)); 79.7 (*s*, C(8b)); 69.7 (*d*, C(5)); 52.4 (*q*, MeO); 50.3 (*d*, C(5a)); 49.8 (*t*, C(3)); 36.4 (*t*, C(8)); 35.6 (*t*, C(1)); 26.3 (*t*, C(7)); 26.2 (*t*, C(6)); 24.4 (*t*, C(2)). ^{13}C-NMR (C_6D_6): 172.9 (*s*, C=O); 137.3 (*s*); 129.3 (2*d*); 128.7 (2*d*); 128.5 (*d*); 111.8 (*s*, C(8a)); 80.0 (*s*, C(8b)); 69.7 (*d*, C(5)); 51.6 (*q*, MeO); 51.3 (*d*, C(5a)); 49.5 (*t*, C(3)); 36.6 (*t*, C(8)); 35.9 (*t*, C(1)); 26.5 (*t*, C(7)); 26.4 (*t*, C(6)); 24.7 (*t*, C(2)). MS: 330 (0.8, M^+), 284 (14, $[M - NO_2]^+$), 271 (69, $[M - CO_2Me]^+$), 226 (27, $[M - CO_2Me - NO_2]^+$), 225 (100,

[M – HCO_2Me – NO_2]$^+$), 224 (14), 97 (41), 196 (44), 182 (14), 104 (10), 91 (28, $C_7H_7^+$), 77 (12, $C_6H_5^+$), 41 (11), 28 (10). Anal. calc. for $C_{18}H_{22}N_2O_4$ (330.38): C 64.4, H 6.71, N 8.48; found: C 65.3, H 6.68, N 8.43.

(5R,5aR*,8aS*,8bS*)-Methyl Decahydro-5a-nitro-5-phenylcyclopenta[a]pyrrolizine-8b-carboxylate* (**9f**): 0.44 g (48%). R_f 0.45. M.p. 115–116° (from light petroleum ether). IR (nujol): 1725 (CO_2Me), 1520, 1370 (NO_2), 740, 700 (Ph). ^{1}H-NMR ($CDCl_3$): 7.32 (*m*, 3 arom. H); 7.27 (*m*, 2 arom. H); 4.81 (*s*, H–C(5)); 3.77 (*s*, MeO); 3.62 (*dd*, *J* = 4.2, 9.3, H–C(8a)); 3.22 (*dt*, *J* = 7.0, 7.0, 8.5, 1 H–C(3)); 2.71 (*dt*, *J* = 4.0, 8.2, 8.2, 1 H–C(3)); 2.66 (*m*, 1 H–C(1)); 2.51 (*dt*, *J* = 7.2, 7.2, 14.1, 1 H–C(6)); 2.19 (*dt*, *J* = 6.8, 6.8, 14.1, 1 H–C(6)); 2.12 (*m*, 1 H–C(1)); 2.03 (*m*, 1 H–C(2)); 1.94 (*m*, 1 H–C(8)); 1.76 (*m*, 1 H–C(2), 2 H–C(7)); 1.64 (*m*, 1 H–C(8)). ^{13}C-NMR ($CDCl_3$): 175.2 (*s*, C=O); 134.9 (*s*); 128.6 (2*d*); 128.5 (2*d*); 128.4 (*d*); 112.6 (*s*, C(5a)); 79.9 (*s*, C(8b)); 73.5 (*d*, C(5)); 58.5 (*d*, C(8a)); 51.7 (*q*, MeO); 45.7 (*t*, C(3)); 36.8 (*t*, C(1)); 36.3 (*t*, C(6)); 28.4 (*t*, C(8)); 26.4 (*t*, C(7)); 26.1 (*t*, C(2)). MS: 330 (0.8, M^+), 284 (23, [M – NO_2]$^+$), 271 (100, [M – CO_2Me]$^+$), 226 (28, [M – CO_2Me – NO_2]$^+$), 225 (66, [M – HCO_2Me – NO_2]$^+$), 218 (12), 217 (53), 197 (16), 196 (44), 188 (13), 174 (20), 158 (16), 157 (15), 134 (11), 129 (15), 128 (15), 105 (10), 104 (13), 103 (13), 96 (20), 91 (29, $C_7H_7^+$), 77 (16, $C_6H_5^+$), 41 (16), 28 (10). Anal. calc. for $C_{18}H_{22}N_2O_4$ (330.38): C 65.4, H 6.71, N 8.48; found: C 65.5, H 6.75, N 8.34.

3.9. *Reaction of* **4**–**6** *with 1-Nitrocyclohexene* (**7g**). With **7g** (0.3 g, 3 mmol) and **4**–**6** (0.64 g, 3.0 mmol) at r.t. for 5 days; products **8g**/**9g** 36:64, which were separated by FC (AcOEt/light petroleum ether 2:98 → 10:90): *(5R*,5aS*,9aR*,9baR*)-Methyl Decahydro-9a-nitro-5-phenyl-1H-cyclopent[a]isoindole-9b-carboxylate* (**8g**): 0.31 g (30%). R_f 0.20. M.p. 129–130° (from light petroleum ether). IR (nujol): 1720 (CO_2Me), 1520, 1360 (NO_2), 740, 700, 690 (Ph). ^{1}H-NMR ($CDCl_3$): 7.27 (*m*, 3 arom. H); 7.14 (*d*, 2 arom. H); 4.61 (*d*, *J* = 12.7, H–C(5)); 3.75 (*s*, CO_2Me); 3.45 (br. *dd*, *J* = 4.8, 12.7, H–C(5a)); 2.50 (*m*, 2 H–C(3), 1 H–C(1), H_{eq}–C(9)); 2.11 (*m*, H_{ax}–C(9)); 1.67 (*m*, 1 H–C(1), 1 H–C(2), H_{eq}–C(8), 2 H–C(6)); 1.47 (*m*, H_{eq}–C(7), 1 H–C((2)); 1.27 (*m*, H_{ax}–C(7)); 1.12 (*m*, H_{ax}–C(8)). ^{1}H-NMR (C_6D_6): 7.10 (*m*, 5 arom. H); 4.53 (*d*, *J* = 12.8, H–C(5)); 3.43 (*s*, MeO); 3.40 (*dd*, *J* = 5.2, 12.8, $w_{1/2}$ = 10.4, H–C(5a)); 2.60 (br. *d*, *J* = 14.6, H_{eq}–C(9)); 2.51 (*dd*, *J* = 3.4, 5.2, H_{eq}–C(6)); 2.28 (*m*, 2 H–C(3)); 2.05 (*dt*, *J* = 3.4, 14.6, 14.6, H_{ax}–C(9)); 1.58 (*m*, H_{ax}–C(1), H_{ax}–C(6)); 1.42 (br. *d*, *J* = 12.1, H_{eq}–C(1)); 1.21 (*m*, 2 H–C(2), H_{eq}–C(8)); 1.00 (br. *d*, *J* = 7.8, H_{eq}–C(7)); 0.84 (*m*, H_{ax}–C(7), H_{ax}–C(8)). ^{13}C-NMR ($CDCl_3$): 173.1 (*s*, C=O); 135.2 (*s*); 129.9 (2*d*); 128.5 (2*d*); 128.3 (*d*); 97.3 (*s*, C(9a)); 81.0 (*s*, C(9b)); 64.7 (*d*, C(5)); 52.6 (*q*, MeO); 50.6 (*t*, C(3)); 40.5 (*d*, C(5a)); 34.8 (*t*, C(1)); 30.1 (*t*, C(9)); 24.3 (*t*, C(2)); 21.9 (*t*, C(8)); 21.4 (*t*, C(6)); 20.0 (*t*, C(7)). MS: 344 (0.8, M^+), 298 (10, [M – NO_2]$^+$), 285 (29, [M – CO_2Me]$^+$), 238 (100, [M – CO_2Me – NO_2]$^+$), 210 (10), 196 (19), 182 (11), 91 (21, $C_7H_7^+$), 77 (8, $C_6H_5^+$). Anal. calc. for $C_{19}H_{24}N_2O_4$ (344.41): C 66.20, H 7.02, N 8.01; found: C 66.12, H 7.03, N 8.01.

(5R,5aR*,9aS*,9bS*)-Methyl Decahydro-5a-nitro-5-phenyl-1H-cyclopent[a]isoindole-9b-carboxylate* (**9g**): 0.55 g (53%). R_f 0.45. M.p. 128–129° (from ligroin). IR (nujol): 1735 (CO_2Me), 1540, 1355 (NO_2), 1595, 1495, 740, 700 (Ph). ^{1}H-NMR ($CDCl_3$): 7.27 (*m*, 3 arom. H); 7.14 (*d*, 2 arom. H); 4.61 (*s*, H–C(5)); 3.79 (*s*, MeO); 3.55 (*m*, H–C(9a)); 2.76 (br. *d*, *J* = 14.6, H_{eq}–C(6)); 2.66 (*m*, 1 H–C(1), 2 H–C(3)); 2.37 (*dt*, *J* = 3.9, 14.6, 14.6, H_{ax}–C(6)); 2.10 (br. *d*, *J* = 13.7, H_{eq}–C(9)); 1.98–1.80 (*m*, 1 H–C(1), 1 H–C(2), H_{ax}–C(9)); 1.70 (*m*, 1 H–C(2)); 1.60 (*m*, H_{eq}–C(8)); 1.50 (*m*, H_{eq}–C(7)); 1.03 (br. *t*, H_{ax}–C(7), H_{ax}–C(8)). ^{1}H-NMR (C_6D_6): 7.16 (*d*, 2 arom. H); 7.06 (*m*, 3 arom. H); 4.62 (*s*, H–C(5)); 3.49 (br. *d*, *J* = 6.35, $w_{1/2}$ = 12.0, H–C(9a)); 3.33 (*s*, MeO); 2.80 (br. *d*, *J* = 14.6, H_{eq}–C(6)); 2.63 (*m*, 1 H–C(3)); 2.53 (*m*, 1 H–C(3)); 2.45 (*m*, 1 H–C(1), 1 H–C(6)); 2.01 (br. *d*, *J* = 13.7, H_{eq}–C(9)); 1.77 (*m*, H_{ax}–C(9)); 1.55 (*m*, 1 H–C(2)); 1.47 (*m*, 1 H–C(1), 1 H–C(2)); 1.31 (*m*, 1 H–C(7)); 1.22 (*m*, 1 H–C(8)); 0.95 (*m*, 1 H–C(7), 1 H–C(8)). ^{13}C-NMR ($CDCl_3$): 176.3 (*s*, C=O); 136.2 (*s*); 129.0 (2*d*); 128.6 (*d*); 128.3 (2*d*); 101.3 (*s*, C(5a)); 78.2 (*s*, C(9b)); 74.6 (*d*, C(5)); 52.5 (*q*, MeO); 47.0 (*t*, C(9a)); 45.7 (*t*, C(3)); 39.2 (*t*, C(1)); 34.1 (*t*, C(6)); 27.1 (*t*, C(2)); 21.4 (*t*, C(9)); 20.8 (*t*, C(8)); 20.1 (*t*, C(7)). ^{13}C-NMR (C_6D_6): 175.9 (*s*, C=O); 137.1 (*s*); 129.4 (2*d*); 128.7 (*d*); 128.5 (2*d*); 101.9 (*s*, C(5a)); 78.2 (*s*, C(9b)); 74.6 (*d*, C(5)); 51.7 (*q*, MeO); 47.1 (*t*, C(9a)); 45.1 (*t*, C(3)); 38.9 (*t*, C(1)); 34.2 (*t*, C(6)); 27.3 (*t*, C(2)); 21.7 (*t*, C(9)); 21.1 (*t*, C(8)); 20.5 (*t*, C(7)). Anal. calc. for $C_{19}H_{24}N_2O_4$ (344.41): C 66.2, H 7.02, N 8.01; found: C 66.31, H 6.99, N 7.96).

4. *(1S,2R,3S,6R,7aS)-Methyl Hexahydro-6-hydroxy-1-methyl-1-nitro-2,3-diphenyl-1H-pyrrolizine-7a-carboxylate* (**11**). (2*S*,4*R*)-4-Hydroxyproline methyl ester hydrochloride [16] (0.5 g, 2.7 mmol) was treated with an equimolar amount of $NaHCO_3$ in benzene and 1 ml of H_2O under vigorous stirring. After 1 h, benzaldehyde (0.6 g, 5.4 mmol) was added and the mixture stirred 2 h at r.t. Then **7d** was added (0.45 g, 2.7 mmol) and the mixture stirred for further 12 h. Evaporation left an oily residue which solidified to give 0.96 g (90%) of **11**. M.p. 202–204° (from AcOEt). $[\alpha]^{20}$ = – 67 (*c* = 0.5, $CHCl_3$). IR (nujol): 3370 (OH), 1745 (CO_2Me), 1545, 1375 (NO_2), 1495, 780, 750, 710 (Ph). ^{1}H-NMR ($CDCl_3$): 7.37 (*d*, 2 arom. H); 7.28–7.18 (*m*, 8 arom. H); 5.15 (*d*, *J* = 12.7, H–C(3)); 4.86 (*d*, *J* = 12.7, H–C(2)); 4.33 (*m*, H–C(6)); 3.86 (*s*, MeO); 2.84 (*dd*, *J* = 3.4, 10.3, H_β–C(5)); 2.69 (*d*, *J* = 13.7, H_α–C(7)); 2.58 (*d*, *J* = 10.3, 1 H, H_α–C(5)); 2.02 (*dd*, *J* = 4.1, 13.7, 1 H, H_β–C(7)); 1.86 (br. *s*, OH); 1.45 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 173.3 (*s*, C=O); 134.9 (*s*); 133.9 (*s*); 129.5 (2*d*); 129.0 (2*d*);

128.6 (2*d*); 128.4 (2*d*); 128.1 (*d*); 127.7 (*d*); 100.2 (*s*, C(1)); 80.2 (*s*, C(7a)); 70.4 (*d*, C(6)); 64.7 (*d*, C(3)); 58.1 (*t*, C(5)); 52.7 (*q*, MeO); 50.2 (*d*, C(2)); 43.6 (*t*, C(7)); 19.7 (*q*, Me). Anal. calc. for $C_{22}H_{24}N_2O_5$ (396.44): C 66.65, H 6.10, N 7.07; found: C 66.72, H 6.01, N 7.00.

5. *Substrates* **12**/**13**. 5.1. *(1*R*,3*R*,7a*R*)-Methyl Tetrahydro-3-(4-methoxyphenyl)-1-phenyl-1*H,*3*H-*pyrrolo[1,2-*c*]*oxazole-7a-carboxylate* (**12**) *and (1*R*,3*S*,7a*S*)-Methyl Tetrahydro-3-(4-methoxyphenyl)-1-phenyl-1*H,*3*H-*pyrrolo[1,2-*c*]*oxazole-7a-carboxylate* (**13**). Reaction of proline methyl ester hydrochloride (1.0 g, 6.0 mmol) and 4-methoxybenzaldehyde (1.63 g, 12.0 mmol) as described for the synthesis of **4**–**6** gave **12**/**13** 65:35. ^{1}H-NMR ($CDCl_3$): 7.49 (*d*, 0.7 H, arom. H); 7.44 (*m*, 1.3 H, arom. H); 7.32 (*d*, 0.7 H, arom. H); 7.16 (*d*, 1.3 H, arom. H); 6.85 (*d*, 1.3 H, arom. H); 6.76 (*d*, 0.7 H, arom. H); 6.37 (*s*, 0.65 H, H–C(3)); 5.63 (*s*, 0.35 H, H–C(3)); 5.21 (*s*, 0.35 H, H–C(1)); 4.94 (*s*, 0.65 H, H–C(1)); 3.76 (*s*, 1.05 H, MeO); 3.71 (*s*, 1.95 H, MeO); 2.70 (*q*, 0.65 H, H–C(5)); 2.53 (*m*, 2 H, 1.35 H–C(5), 0.65 H–C(7)); 2.26 (*m*, 0.65 H, H–C(7)); 1.88–1.75 (*m*, 1.65 H, 1.3 H–C((6), 0.35 H–C(7)); 1.68 (*m*, 0.35 H, H–C(6)); 1.48 (*m*, 0.35 H, H–C(6)); 1.36 (*ddd*, 0.35 H, H–C(7)).

5.2. *Reaction of* **12**/**13** *with (*E*)-2-Nitro-1-phenylpropene* (**7d**). According to *3.1*, with **7d** (0.66 g, 4.0 mmol) and **12**/**13** (1.2 g, 4.0 mmol) at r.t. for 6 d: **14**/**15** 1:1 which were separated by FC (AcOEt/light petroleum ether 2:98 → 15:85): *(1*R*,2*S*,3*R*,7a*R*)-Methyl Hexahydro-3-(4-methoxyphenyl)-1-methyl-1-nitro-2-phenyl-1H-pyrrolizine-7a-carboxylate* (**14**): 0.74 g (45%). M.p. 158–159° (from light petroleum ether). IR (nujol): 1735 (CO_2Me), 1530 (NO_2), 1610, 1580, 700 (Ph). ^{1}H-NMR ($CDCl_3$): 7.28 (*d*, 2 arom. H); 7.21 (*m*, 5 arom. H); 6.78 (*d*, 2 arom. H), 5.03 (*d*, J = 12.8, H–C(3)); 4.86 (*d*, J = 12.8, 1 H–C(2)); 3.85 (*s*, CO_2Me); 3.73 (*s*, MeO); 2.61 (*m*, 2 H–C(5), 1 H–C(7)); 1.78 (*m*, 1 H–C(6), 1 H–C(7)); 1.57 (*m*, H–C(6)); 1.43 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 173.1 (*s*, C=O); 159.0 (*s*, *C*OMe); 134.2 (*s*); 130.6 (2*d*); 129.1 (2*d*); 128.5 (2*d*); 127.5 (*d*); 127.2 (*s*); 113.6 (2*d*); 100.5 (*s*, C(1)); 81.5 (*s*, C(7a)); 64.6 (*d*, C(3)); 55.0 (*q*, MeO); 52.5 (*q*, CO_2Me); 50.7 (*t*, C(5)); 50.0 (*d*, C(2)); 35.3 (*t*, C(7)); 24.4 (*t*, C(6)); 20.3 (*q*, Me). Anal. calc. for $C_{22}H_{24}N_2O_4$ (380.44): C 69.46, H 6.36, N 7.36; found: C 69.58, H 6.37, N 7.29.

*(1*R*,2*S*,3*S*,7a*R*)-Methyl Hexahydro-3-(4-methoxyphenyl)-2-methyl-2-nitro-1-phenyl-1H-pyrrolizine-7a-carboxylate* (**15**): 0.74 g (45%). Oil. IR (film): 1720 (CO_2Me), 1530, 1375 (NO_2), 1600, 720, 700 (Ph). ^{1}H-NMR ($CDCl_3$): 7.31 (*m*, 5 arom. H); 7.26 (*m*, 2 arom. H); 7.14 (*m*, 2 arom. H), 4.92 (*s*, H–C(3)); 4,87 (*s*, H–C(1)); 3.80 (*s*, MeO); 3.68 (*s*, CO_2Me); 3.08 (*ddd*, 1 H–C(5)); 2.63 (*m*, 1 H–C(5)); , 1 H–C(7)); 2.20 (*m*, 1 H–C(6)); 1.94 (*m*, 1 H–C(6), 1 H–C(7)); 1.82 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 174.7 (*s*, C=O); 159.8 (*s*, *C*OMe); 133.9 (*s*); 130.3 (2*d*); 129.8 (2*d*); 128.2 (2*d*); 127.8 (*d*); 127.2 (*s*); 113.7 (2*d*); 105.7 (*s*, C(2)); 79.4 (*s*, C(7a)); 73.8 (*d*, C(3)); 60.0 (*d*, C(1)); 55.1 (*q*, MeO); 51.6 (*q*, CO_2Me); 44.0 (*t*, C(5)); 35.3 (*t*, C(7)); 26.4 (*t*, C(6)); 22.9 (*q*, Me).

6. *Substrate* **16**. 6.1. *(1*R*,3*R*,7a*R*)-Methyl Tetrahydro-3-(4-nitrophenyl)-1-phenyl-1*H,*3*H-*pyrrolo[1,2-*c*]*oxazole-7a-carboxylate* (**16**). Reaction of proline methyl ester hydrochloride (1.0 g, 6.0 mmol) and 4-nitrobenzaldehyde (1.63 g, 12 mmol) as described for the synthesis of **4**–**6** gave a mixture of oxapyrrolizidines, from which **16** was isolated. ^{1}H-NMR ($CDCl_3$): 8.29 (*d*, 2 arom. H); 8.20 (*d*, 2 arom. H); 7.80 (*d*, 2 arom. H); 7.51 (*d*, 2 arom. H); 6.56 (*s*, H–C(3)); 5.17 (*s*, H–C(1)); 3.21 (*s*, MeO); 2.74 (*m*, 2 H–C(5), 1 H–C(7)); 2.65 (*m*, 1 H–C(7)); 1.84 (*m*, 2 H–C(6)). ^{13}C-NMR ($CDCl_3$): 171.2 (*s*, C=O); 147.9 (*s*); 147.5 (*s*); 146.1 (*s*); 143.7 (*s*); 127.6 (2*d*); 126.3 (2*d*); 123.6 (2*d*); 123.3 (2*d*); 96.3 (*d*, C(3)); 85.7 (*d*, C(1)); 83.1 (*s*, C(7a)); 51.2 (*q*, MeO); 49.4 (*t*, C(5)); 34.1 (*t*, C(7)); 24.3 (*t*, C(6)).

6.2. *Reaction of* **16** *with (*E*)-2-Nitro-1-phenylpropene* (**7d**). Nitroolefin **7b** (0.5 g, 3.0 mmol) and **16** (1.0 g, 3 mmol) were mixed neat in a 50-ml flask, and the solid mixture was fused at 100° (oil bath) under Ar. After 2 h, an orange sticky oil was obtained and purified by FC (20% AcOEt/light petroleum ether: **17**/**18** 4:1: *(1*R*,2*S*,3*R*,7a*R*)-Methyl Hexahydro-1-methyl-1-nitro-3-(4-nitrophenyl)-2-phenyl-1H-pyrrolizine-7a-carboxylate* (**17**): 0.90g (70%). M.p. 145–146°. IR (nujol): 1735 (CO_2Me), 1535, 1375 (NO_2), 1520, 1320 (arom. NO_2), 1600, 1500, 850, 755, 710 (ArH). ^{1}H-NMR ($CDCl_3$): 8.02 (*d*, 2 arom. H); 7.48 (*d*, 2 arom. H); 7.14 (*s*, 5 arom. H); 5.10 (*d*, J = 12.7, H–C(3)); 4.84 (*d*, J = 12.7, H–C(2)); 3.78 (*s*, MeO); 2.56 (*m*, 2 H–C(5), 1 H–C(7)); 1.69 (*m*, 1 H–C(7), 1 H–C(6)); 1.53 (*m*, 1 H–C(6)); 1.35 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 172.6 (*s*, C=O); 147.3 (*s*); 142.9 (*s*); 133.4 (*s*); 130.3 (2*d*); 128.9 (2*d*); 128.7 (2*d*); 127.9 (*d*); 123.4 (2*d*); 100.5 (*s*, C(1)); 81.5 (*s*, C(7a)); 64.5 (*d*, C(3)); 52.5 (*q*, MeO); 50.6 (*t*, C(5)); 50.3 (*d*, C(2)); 35.0 (*t*, C(7)); 24.3 (*t*, C(6)); 20.3 (*q*, Me). Anal. calc. for $C_{22}H_{23}N_3O_6$ (425.44): C 62.11, H 5.45, N 9.88; found: C 62.10, H 5.42, N 10.00.

*(1*R*,2*S*,3*S*,7a*R*)-Methyl Hexahydro-2-methyl-2-nitro-3-(4-nitrophenyl)-1-phenyl-1H-pyrrolizine-7a-carboxylate* (**18**): 0.22 g (17%). M.p. 131–132° (from ligroin). IR (nujol): 1720 (CO_2Me), 1535, 1360 (NO_2), 1510, 1340 (arom. NO_2), 1595, 1500, 760, 695 (Ph). ^{1}H-NMR ($CDCl_3$): 8.20 (*d*, 2 arom. H); 7.50 (*d*, 2 arom. H); 7.20 (*m*, 5 arom. H); 5.08 (*s*, H–C(3)); 4.83 (*s*, H–C(1)); 3.72 (*s*, MeO); 2.93 (*m*, 1 H–C(5)); 2.56 (*m*, 1 H–C(5), 1 H–C(7)); 2.30 (*m*, 1 H–C(6)); 1.98 (*m*, 1 H–C(6)); 1.91 (*m*, 1 H–C(7)); 1.83 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 174.6 (*s*, C=O); 149.1 (*s*); 143.3 (*s*); 133.1 (*s*); 130.2 (2*d*); 129.1 (2*d*); 128.4 (2*d*); 128.3 (*d*); 123.5 (2*d*); 107.4 (*s*, C(2));

79.3 (*s*, C(7a)); 71.9 (*d*, C(3)); 59.4 (*d*, C(1)); 51.7 (*q*, MeO); 42.1 (*t*, C(5)); 34.1 (*t*, C(7)); 26.5 (*t*, C(6)); 22.9 (*q*, Me). Anal. calc. for $C_{22}H_{23}N_3O_6$ (425.44): C 62.11, H 5.45, N 9.88; found: C 62.05, H 5.40, N 9.97.

7. *Substrates* **19/20**. 7.1. *(1*R*,3*R*,7a*R*)*-tert-*Butyl Tetrahydro-1*H,*3*H-*pyrrolo[1,2-*c*]oxazole-7a-1,3-diphenyl-carboxylate* (**19**) *and (1*R*,3*S*,7a*S*)*-tert-*butyl Tetrahydro-1,3-diphenyl-1*H,*3*H-*pyrrolo[1,2-*c*]oxazole-7a-carboxylate* (**20**). Reaction of proline *tert*-butyl ester hydrochloride (1.0 g, 5.8 mmol) and benzaldehyde (1.23 g, 11.6 mmol) as described for the synthesis of **4–6** gave **19/20** 1:1. ^{1}H-NMR ($CDCl_3$): 7.65–7.15 (*m*, 10 arom. H); 6.42 (*s*, 0.5 H, H–C(3)); 5.75 (*s*, 0.5 H, H–C(3)); 5.21 (*s*, 0.5 H, H–C(1)); 5.02 (*s*, 0.5 H, H–C(1)); 2.70 (*m*, 0.5 H); 2.56 (*m*, 1.5 H); 2.34 (*m*, 0.5 H); 1.82 (*m*, 1.5 H); 1.55 (*s*, 4.5 H, *t*-Bu); 1.40 (*m*, 0.5 H); 0.99 (*s*, 4.5 H, *t*-Bu). ^{13}C-NMR ($CDCl_3$): 174.0, 170.6 (2*s*, C=O); 139.2, 138.5 (2*s*); 137.3, 136.2 (2*s*); 129.5 (*d*); 128.8 (*d*); 128.1 (*d*); 128.0 (*d*); 127.9 (*d*); 127.3 (*d*); 126.7 (*d*); 126.6 (*d*); 126.1 (*d*); 125.9 (*d*); 96.6, 93.4 (2*d*); 86.1, 83.2 (2*d*); 82.2, 81.3 (2*s*); 80.9, 79.6 (2*s*); 49.7, 48.8 (2*t*); 34.9, 32.1 (2*t*); 27.9, 27.8 (2*q*, *Me*$_3$C); 27.1, 23.2 (2*t*).

7.2. *Reaction of* **19/20** *with (*E*)-β-Nitrostyrene* **7c**. According to *3.1*, with **7c** (0.30 g, 2.0 mmol) and **19/20** (0.69 g, 2.0 mmol) at r.t. for 144 h: *(1*R*,2*S*,3*R*,7a*R*)*-tert-*Butyl Hexahydro-1-nitro-2,3-diphenyl-1H-pyrrolizine-7a-carboxylate* (**21c**): 0.72 g (88%). M.p. 107–108° (from light petroleum ether). IR (nujol): 1720 (CO_2(*t*-Bu)), 1530, 1360 (NO_2), 1600, 1580, 710, 690 (Ph). ^{1}H-NMR ($CDCl_3$): 7.29 (*m*, 4 arom. H); 7.15 (*m*, 6 arom. H); 5.76 (*d*, *J* = 10.2, H–C(1)); 4.83 (*d*, *J* = 12.2, H–C(3)); 4.34 (*dd*, *J* = 10.2, 12.2, H–C(2)); 2.59 (*m*, 1 H–C(5)); 2.45 (*m*, 1 H–C(5), 1 H–C(7)); 1.84 (*m*, 2 H–C(6)); 1.60 (*s*, *t*-Bu); 1.45 (*m*, H–C(7)). ^{13}C-NMR ($CDCl_3$): 171.8 (*s*, C=O); 136.7 (*s*); 135.2 (*s*); 129.4 (*d*); 129.2 (2*d*); 129.0 (2*d*); 128.3 (2*d*); 127.9 (2*d*); 127.6 (*d*); 98.1 (*d*, C(1)); 82.4 (*s*, C(7a), Me$_3$*C*); 67.8 (*d*, C(3)); 50.7 (*t*, C(5)); 48.3 (*d*, C(2)); 31.9 (*t*, C(7)); 28.0 (3*q*, *Me*$_3$C); 25.3 (*t*, C(6)). Anal. calc. for $C_{24}H_{28}N_2O_4$ (408.50): C 70.57, H 6.91, N 6.86; found: C 70.64, H 6.85, N 6.96.

7.3. *Reaction of* **19/20** *with (*E*)-2-Nitro-1-phenylpropene* **7d**. According to *3.1*, with **7d** (0.42g, 2.6 mmol) and **19/20** (0.68 g, 2.6 mmol) at –30°: *(1*R*,2*S*,3*R*,7a*R*)*-tert-*Butyl Hexahydro-1-methyl-1-nitro-2,3-diphenyl-1H-pyrrolizine-7a-carboxylate* (**21d**): 0.86g (78%). M.p. 115–116° (from ligroin). IR (nujol): 1720 (CO_2 (*t*-Bu)), 1540, 1375 (NO_2), 1600, 1580, 700, 680 (Ph). ^{1}H-NMR ($CDCl_3$): 7.36 (*d*, 2 arom. H); 7.27–7.17 (*m*, 8 arom. H); 5.08 (*d*, *J* = 12.5, H–C(3)); 4.90 (*d*, *J* = 12.5, H–C(2)); 2.61 (*m*, 2 H–C(5)); 2.51 (*m*, 1 H–C(7)); 1.84 (*m*, 1 H–C(7)); 1.66 (*m*,1 H–C(6)); 1.55 (*s* and *m*, *t*-Bu, 1 H–C(6)); 1.53 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 171.4 (*s*, C=O); 135.6 (*s*); 134.5 (*s*); 129.6 (2*d*); 129.1 (2*d*); 128.8 (*d*); 128.5 (2*d*); 128.2 (2*d*); 127.8 (*d*); 127.5 (*d*); 100.3 (*s*, C(1)); 82.3 (*s*, C(7a)); 81.7 (*s*, Me$_3$*C*); 65.3 (*d*, C(3)); 50.8 (*d*, C(2)); 50.4 (*t*, C(5)); 35.6 (*t*, C(7)); 28.0 (*q*, *Me*$_3$C); 24.3 (*t*, C(6)); 20.0 (*q*, Me). MS: 375 (1, $[M - NO_2]^+$), 321 (20), 275 (100), 269 (20), 198 (21), 91 (12, $C_7H_7^+$), 77 (6, $C_6H_5^+$), 44 (10), 41 (18), 28 (15). Anal. calc. for $C_{25}H_{30}N_2O_4$ (422.52): C 71.07, H 7.16, N 6.63; found: C 71.06, H 7.25, N 6.63.

REFERENCES

[1] D. J. Robins, *Nat. Prod. Rep.* **1995**, *12*, 413, and ref. cit. therein; 'Natural Occurring Pyrrolizidine Alkaloids', Ed. A. F. M. Rizk, CRC Press, Boston, 1991; A. R. Mattocks, 'Chemistry and Toxicology of Pyrrolizidine Alkaloids', Academic Press, London, 1986.

[2] W. M. Dai, Y. Nagao, E. Fujita, *Heterocycles* **1990**, *30*, 1231.

[3] A. Murray, G. R. Proctor, P. J. Murray, *Tetrahedron* **1996**, *52*, 3757.

[4] R. A. Pilli, D. Russowsky, *J. Org. Chem.* **1996**, *61*, 3187.

[5] S. E. Denmark, A. Thorarensen, *J. Org. Chem.* **1994**, *59*, 5672.

[6] a) O. Tsuge, S. Kanemasa, in 'Advances in Heterocyclic Chemistry', Ed. A. R. Katritzy, Academic Press, New York, 1989, Vol. 45, p. 231; b) M. Joucla, J. Mortier, J. Hamelin, L. Toupet, *Bull. Soc. Chim. Fr.* **1988**, 143.

[7] H. Ardill, R. Grigg, J. F. Malone, V. Sridharan, W. A. Thomas, *Tetrahedron* **1994**, *50*, 5067, and ref. cit. therein; F. Orsini, F. Pelizzoni, M. Forte, M. Sisti, P. Gariboldi, *J. Heterocycl. Chem.* **1988**, *25*, 1665.

[8] M. F. Aly, M. I. Younes, S. A. M. Metwally, *Tetrahedron* **1994**, *50*, 3159; K. Amornraksa, R. Grigg, H. Q. N. Gunaratne, J. Kemp, K. J. Shridharan, *J. Chem. Soc., Perkin Trans. 1* **1987**, 2285.

[9] D. Seebach, M. Missbach, G. Calderari, M. Eberle, *J. Am. Chem. Soc.* **1990**, *112*, 7625, and ref. cit. therein; 'Nitroalkanes and Nitroalkenes in Synthesis', Ed. A. G. M. Barrett; W. R. Bowman, S. W. Jackson, *Tetrahedron* **1990**, *46*, 7313; G. Rosini, R. Ballini, *Synthesis* **1988**, 833; G. W. Kabalka, R. S. Varma, *Org. Prep. Proceed. Int.* **1987**, *19*, 283; A. G. M. Barrett, G. G. Graboski, *Chem. Rev.* **1986**, *86*, 751; D. Seebach, E. W. Colvin, F. Lehr, T. Weller, *Chimia* **1979**, *33*, 1.

[10] O. Tsuge, S. Kanemasa, S. Takenaka, *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3321.

[11] H. Benhaoua, J.-C. Piet, R. Danion-Bougot, L. Toupet, R. Carrie, *Bull. Soc. Chim. Fr.* **1987**, 325.

[12] A. Padwa, Y. Y. Chen, U. Chiacchio, W. Dent, *Tetrahedron* **1985**, *41*, 3529.

[13] F. Felluga, P. Nitti, G. Pitacco, E. Valentin, *J. Chem. Soc., Perkin Trans. 1* **1992**, 2335.
[14] G. Pitacco, A. Pizzioli, A. Valentin, *Synthesis* **1996**, 242.
[15] G. Bianchi, R. Gandolfi, in '1,3-Dipolar Cycloadditions Chemistry', Ed. A. Padwa, Wiley, New York, 1984, Vol. 2, Chapt. 14.
[16] T. Sato, Y. Kugo, E. Nakaumi, H. Ishibashi, M. Ikeda, *J. Chem. Soc., Perkin Trans. 1* **1995**, 1801.
[17] N. Ono, A. Kamimura, T. Kawai, A. Kaji, *J. Chem. Soc., Chem. Commun.* **1987**, 1550.
[18] I. Fleming, 'Frontier Orbitals and Organic Chemical Reactions', John Wiley & Sons, London, 1982.
[19] G. D. Buckley, C. W. Scaife, *J. Am. Chem. Soc.* **1947**, 1471.
[20] F. Boberg, G. R. Schultze, *Chem. Ber.* **1957**, *90*, 1215.
[21] D. N. Robertson, *J. Org. Chem.* **1960**, *25*, 47.
[22] E. J. Corey, H. Estreicher, *J. Am. Chem. Soc.* **1978**, *100*, 6294.