Pergamon

Tetrahedron 55 (1999) 201–210

TETRAHEDRON

Reaction of Mesoionic Compounds Deriving from Cyclic N-Acyl-α-Aminoacids with N-(Phenylmethylene)benzenesulfonamide

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Received 6 August 1998; revised 15 October 1998; accepted 29 October 1998

Abstract: We studied the behaviour of bicyclic mesoionic compounds derived from the cyclodehydration of cyclic *N*-acyl-α-aminoacids **1-4** with *N*-(phenylmethylene)benzenesulfonamide **5**. The reaction affords spirocyclic β-lactams and/or imidazo-condensed products (the 1,3-dipolar cycloaddition adducts) depending on the experimental conditions and on the nature of the substituent R on the mesoionic ring. © 1998 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

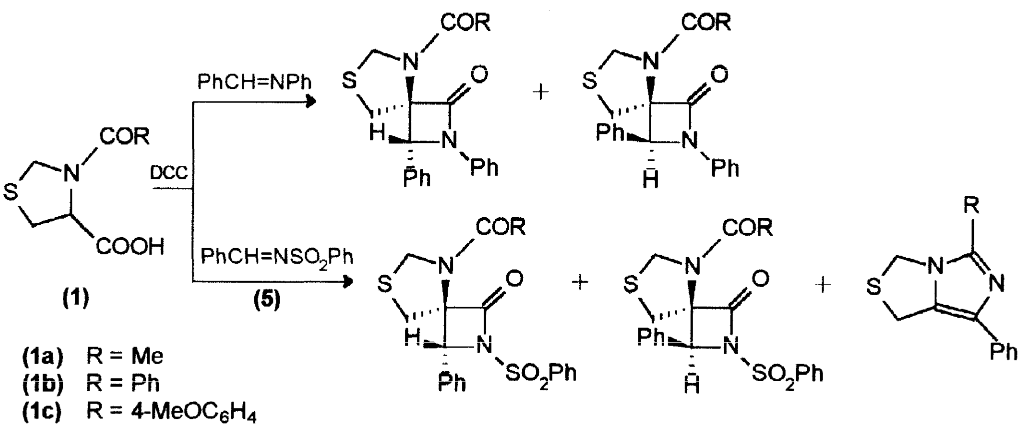
In a previous communication,[1] we reported the reactivity of bicyclic mesoionic 5H,7H-thiazolo[3,4-*c*] oxazolium-1-oxides derived from *N*-acyl-(R)-thiazolidine-4-carboxylic acids **1a-c** towards *N*-(phenyl methylene)aniline and *N*-(phenylmethylene)benzenesulfonamide **5**. The reaction of these cyclic aminoacids with *N*-(phenylmethylene)aniline, performed in a tetrahydrofuran solution at 70 °C in the presence of *N*,*N'*-dicyclohexylcarbodiimide as a dehydrating agent, led to a mixture of diastereoisomeric *N*-phenyl substituted spirocyclic β-lactams, whereas the reaction with *N*-(phenylmethylene)benzenesulfonamide **5** yielded 1H,3H-imidazo[1,5-*c*]thiazole derivatives in addition to the corresponding spirocyclic β-lactams (Scheme 1).

This different behaviour was explained by taking into account the presence of the electron-withdrawing *N*-phenylsulfonyl group that enhances C=N double bond polarization and increases the reactivity of the imine towards 1,3-dipolar cycloaddition reactions. It was estimated that the LUMO energy in the *N*-phenylsulfonyl

PII: S0040-4020(98)01026-6

substituted imine was reduced in comparison with the *N*-phenyl imine[2] and that there was a corresponding increase in the HOMO-dipole control of the cycloaddition reaction.

SCHEME 1

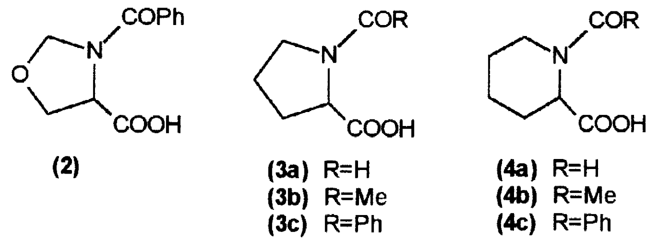


The presence of the *N*-phenylsulfonyl group also leads to complete regioselectivity in the cycloaddition reaction because the electrostatic interactions between the polarized C=N double bond and a dipole with a high local density of charge, such as mesoionic compounds, are what control the observed regiochemistry.

Another essential requirement for the 1,3-dipolar cycloaddition pathway seems to be the presence of an aryl group on C-2 of the mesoionic intermediate. When this carbon is substituted with a methyl group, only spiro β-lactams were obtained.[1]

To verify the generality of this behaviour and evaluate the factors affecting the reaction, we extended our study to other cyclic *N*-acyl-α-aminoacids (Figure 1): *N*-benzoyl-(S)-oxazolidine- 4-carboxylic acid **2**,[3] *N*-acyl-(L)-prolines **3a-c**, and *N*-acyl-(D,L)-pipecolinic acids **4a-c**. These were allowed to react with imine **5** in the presence of a dehydrating agent.

FIGURE 1

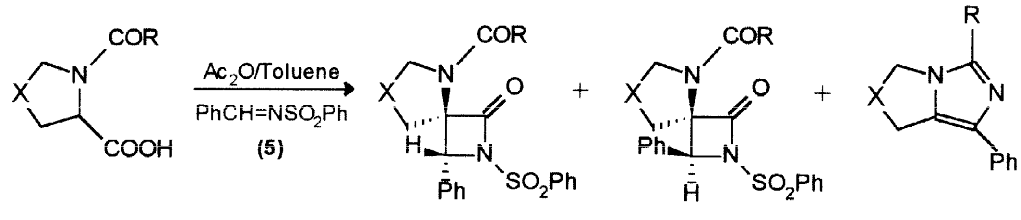


The bicyclic mesoionic compound derived from **2** is new; those derived from **3a-c** and **4a-c** were generated in acetic anhydride at 140 °C and reacted with very reactive acetylenic[4] or ethylenic[5] dipolarophiles, but their reactivity towards C=N dipolarophiles has never before been reported.

Results and discussion

The reactions between *N*-acyl-α–aminoacids **1-4** and the imine **5** were performed in toluene solution at 80 °C using 3 moles of acetic anhydride as dehydrating agent : these are generally better experimental conditions than the use of *N,N'*-dicyclohexylcarbodiimide / THF / 65 °C or acetic anhydride / 140 °C.[6] After evaporation of the solvent, the crude reaction mixture was treated with water and extracted with dichloromethane. Evaporation of the organic solvent gave a mixture of products (Scheme 2) which was separated by means of column chromatography and further purified by crystallization. The analytical, physical and spectroscopic data of the isolated products (summarized in Tables 2 and 3) made it possible to assign the structures of diastereoisomeric spiro-β-lactams **6** and **7** (which differ in terms of the relative configuration of the spiro and the benzylic carbons), and bicyclic imidazole **8**.

SCHEME 2

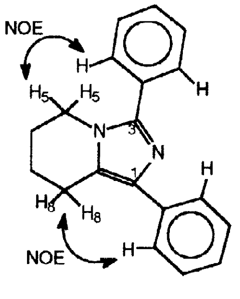


(1-4) (6) (7) (8)

			Products	Ratio	Tot.Yield (%)
(1a) (6,7a)	X = S	R = Me	**(6a):(7a):(8a)**	= 63 : 37 : 0	16
(1b) (6,7,8b)	X = S	R = Ph	**(6b):(7b):(8b)**	= 31 : 13 : 56	39
(2) (6,7c)	X = O	R = Ph	**(6c):(7c):(8c)**	= 96 : 4 : 0	13
(3b) (6,7d)	X = CH_2	R = Me	**(6d):(7d):(8d)**	= 86 : 14 : 0	37
(3c) (6,7,8e)	X = CH_2	R = Ph	**(6e):(7e):(8e)**	= 55 : 20 : 25	64
(4b) (8f)	X = $(CH_2)_2$	R = Me	**(6f):(7f):(8f)**	= 0 : 0 : 100	25
(4c) (8g)	X = $(CH_2)_2$	R = Ph	**(6g):(7g):(8g)**	= 0 : 0 : 100	53

The 1,3-cycloaddition reaction was completely regioselective, with only regioisomer **8** being obtained. This structure was confirmed by N.O.E. experiments on product **8g** that revealed N.O.E. effects between H-5 and H-8 and, respectively, the *ortho* protons of the C-3 and C-1 phenyl rings (Figure 2).[7]

FIGURE 2



(8g)

The diastereoisomeric ratio of products **6** and **7** was determined on the basis of the ^{1}H-NMR analysis of the crude product mixture by evaluating integration at δ 5.4-5.6 or 5.0-5.2 for the benzylic protons of **6** and **7**, respectively. The steric hindrance between the β-lactam phenyl and the *N*-acyl groups favours the formation of diastereoisomer **6**.

The reaction completely failed with *N*-formyl-(L)-proline **3a** and *N*-formyl-(D,L)-pipecolinic acid **4a**: this behaviour is quite similar to that observed with *N*-formyl-(R)-thiazolidine-4-carboxilic acid[1] (**1**, R = H), thus confirming the influence of substituent R (present on the mesoionic ring) on the stability of the reactive intermediate.

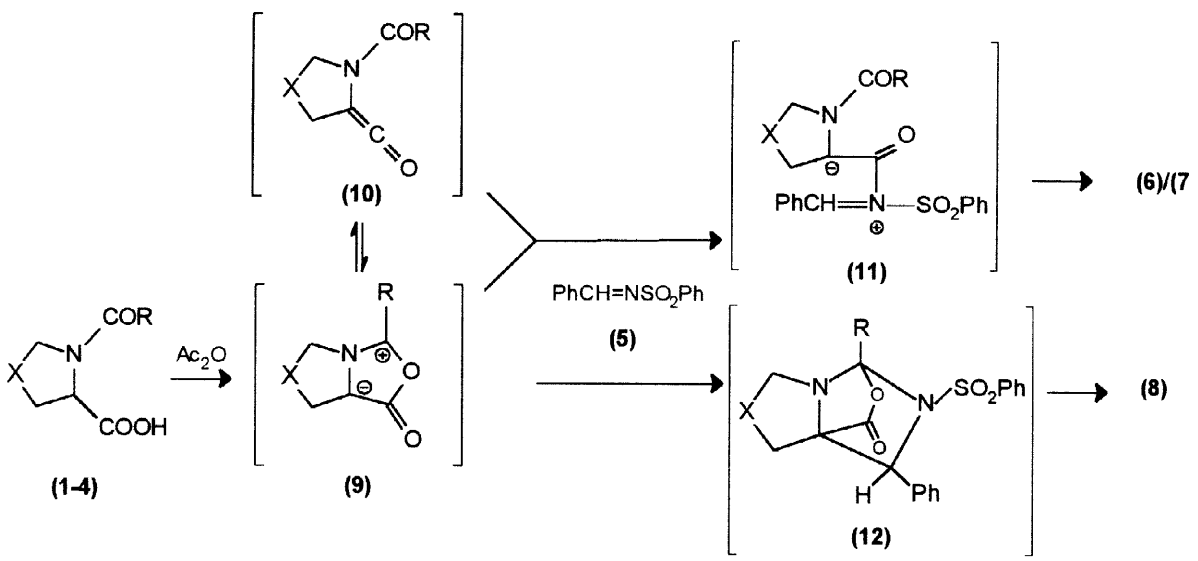
As shown in Scheme 2, the reaction affords a mixture of the two diastereoisomeric spiro-β–lactams **6** and **7** for **3b** (R = Me and X = CH_2); for **3c**, (R = Ph and X = CH_2), the bicyclic product **8** was also obtained as in the case of **1a** and **1b**.

The only products formed in the case of the *N*-benzoyl-(S)-oxazolidine-4-carboxylic acid **2** were the spiro-β-lactams with a poor total yield of 13%, the acid being recovered unchanged.

When R = Me or Ph and X = $(CH_2)_2$, (**4b** and **4c**), only the 1,3-cycloaddition products (**8f** and **8g**, respectively) were obtained: ^{1}H-NMR analysis of the crude reaction mixture did not reveal the presence of any spiro-β-lactams.

As indicated in Scheme 3, the spirocyclic β-lactams **6** and **7** are the result of a nucleophilic attack of the imine nitrogen on the carbonyl carbon of the mesoionic compound **9**, or its ketene valence tautomer **10**. In both cases, the attack gives the same zwitterionic intermediate **11** which undergoes ring closure to afford **6** and **7**. The phenyl group present on the imine carbon can stabilize the positive charge, and so the zwitterionic intermediate may isomerize its double C=N bond to the *cis* form thus preferentially affording the thermodynamically more stable β-lactam **6** (phenyl and *N*-acyl groups *trans* to each other).[8]

SCHEME 3

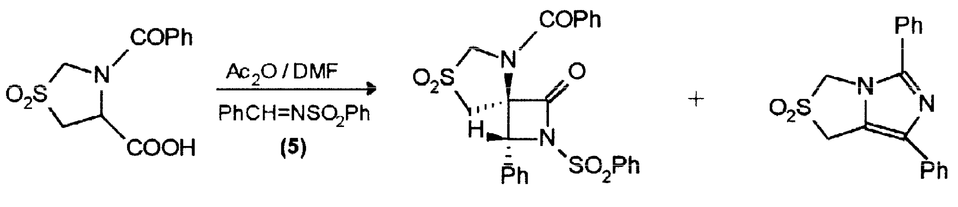


Products **8** are derived from a 1,3-dipolar cycloaddition between the mesoionic compound **9** and the C=N double bond of imine **5**, giving a tricyclic adduct **12** that loses carbon dioxide and benzenesulfinic acid, and thus leads to the imidazo-condensed products **8**.

It can be deduced from our results that the reaction pathway is influenced by various factors. The first is the electronic effect of the R group: the greater stabilization of the mesoionic ring allowed by the phenyl group, in comparison with methyl and hydrogen, led the reaction to follow the 1,3-dipolar cycloaddition pathway leading to products **8** and gave the best yields. However, the effect of the R group is mediated by the ring size of the α-aminoacid. For X = $(CH_2)_2$ and R = Me or R = Ph, **4b** or **4c**, the reaction only gave the bicyclic adducts **8f** and **8g**, unlike **1a** and **3b** which only gave spiro-β-lactams, and **1b** and **3c** which gave a mixture of both kinds of products. The reduced strain present in the mesoionic compounds derived from **4b** and **4c** (due to fusion to a larger ring), and their consequent stabilization, favour the 1,3-dipolar cycloaddition mechanism and thus the formation of the bicyclic adducts.

The reaction is also influenced by the nature of the X group: the presence of a heteroatom such as oxygen or sulfur on the α-amino acid ring lowers the total yield of the reaction. To verify whether this is due to the destabilizing electronic effect of the heteroatom electron pairs on mesoionic stability, we oxidized the *N*-benzoyl-(R)-thiazolidine-4-carboxylic acid **1b** to the *N*-benzoyl-(R)-thiazolidine-4-carboxylic acid 1,1-dioxide **13** and allowed the result to react with the imine **5** in DMF solution (for reasons of solubility) in the presence of acetic anhydride as dehydrating agent. The reaction led to a mixture of the spiro-β-lactam **14** and the bicyclic adduct **15** with a ratio of 45:55 and a total yield of 22% (Scheme 4).

SCHEME 4



(13) **(14)** **(15)**

This result, which is comparable with that obtained using **1b**, showed that the low reaction yields obtained with α-amino acids containing heteroatoms are not due to negative electronic effects on the stability of the intermediate, but probably to greater ring rigidity and a consequently greater difficulty in forming the corresponding bicyclic mesoionic compound.

Finally, the influence of the solvent and reaction temperature on the product ratio was tested for the reaction between **3c** and **5**, because this provided the best yields and all of the products. The product ratio was not influenced by solvent polarity, but was greatly affected by the reaction temperature (see Table 1).

Table 1

T (°C)	Yield (%)		
	6e	**7e**	**8e**
80	35	13	16
100	21	7	56
120	--	--	70

When the reaction temperature was increased, the product ratio changed towards the formation of the bicyclic imidazo adduct **8e**. At 80 °C, products **6e**,**7e** and **8e** are formed by means of the two distinct mechanisms discussed above. Products **6e** and **7e** are completely stable in solution at this temperature. Only above 100 °C is their transformation into the corresponding imidazo product **8e** observed. At 120 °C, this transformation is complete for *trans* diastereoisomer **6e**, whereas for *cis* isomer **7e**, it is necessary to heat to nearly 180 °C and for longer times. This fact, which is due to greater steric hindrance, further confirms the previously proposed mechanism[1] of this transformation: an intramolecular attack of the *N*-acyl oxygen on the lactam carbonyl followed by a rearrangement leading to the same tricyclic intermediate **12**. As it is common to all of the other spiro-β-lactams, this behaviour could be used to obtain only imidazo derivatives **8** or also spiro-β-lactams **6** and **7** from the reaction.

Our attempts to find the experimental conditions necessary to obtain only these latter products failed: at temperatures of less than 80 °C, the reactions performed with acetic anhydride did not proceed; with *N*,*N'*-dicycloexylcarbodiimide in tetrahydrofuran at room temperature, the major product was the adduct between the *N*-acyl-α-aminoacids and the *N*,*N'*-dicycloexylcarbodiimide.[1]

The possibility of synthesising spiro-β-lactams **6** and **7** by other routes was also tested. The first attempt made use of a one-pot procedure[9] for the preparation of ketenes from carboxylic acids, with *N*-[[(chlorosulfinyl)oxy]methylene]-*N*-methylmethanaminium chloride being used as dehydrating agent. The preparation of ketene **10** from **1b** and its reaction with imine **5** was carried out in dichloromethane solution at 0-25 °C: products **6b** and **7b** were obtained, but their total yield was only 15%. Another attempt to obtain spiro-β-lactams was made through the condensation[10] of the imine **5** and the ester enolate of substrate **1c**, but the reaction carried out with LDA in tetrahydrofuran at –78 °C was completely unsuccessful.

In conclusion, our conditions remain the best for obtaining this new class of spiro-β–lactams whose biological activity will be the subject of further study.

EXPERIMENTAL

General Methods. Melting points were measured using a Büchi apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded by means of a Bruker AC 300 spectrometer. Infrared spectroscopy was performed using a Perkin-Elmer 298 spectrophotometer.

Compounds **1a**[1], **1b**[1], **2**[3], **3b**[11], **3c**[4a], **4b**[4c], **4c**[12], **5**[1] were prepared according to the reported methods.

***N*-Benzoyl-(R)-thiazolidine-4-carboxylic acid 1,1-dioxide 13:** Compound **13** was prepared using Clarke's method[13] to give 45% of a colorless solid, m.p. 180 °C (iPrOH/iPr$_2$O); $[\alpha]_D^{20}$ -125.5° (c = 1, acetone); ^{1}H-NMR (CDCl$_3$): δ 3.6 (d, 2H, S-CH$_2$-C), 4.5 (m, 2H, S-CH$_2$-N), 5.0 (broad, 1H, COOH), 5.7 (m, 1H, CH), 7.3-7.5 (m, 5H, aromatic); IR: 1145, 1330, 1610, 1760 cm^{-1}.

General procedure for the reactions of 1-4 with 5. Acetic anhydride (30 mmol) was added dropwise, under nitrogen, to a stirred solution of **1-4** (10 mmol) in toluene (20 ml). The mixture was heated at 80 °C for 1 h, and then a solution of imine **5** (10 mmol) in toluene (10 ml) was added dropwise and the heating continued for 24-30 h. After evaporation of the solvent, the residue was taken up in dichloromethane (50 ml) and the solution was washed with 10% sodium bicarbonate (2 x 20 ml) and water. The organic phase was dried (Na$_2$SO$_4$) and the solvent evaporated off. The crude mixture was separated using column chromatography (silica gel, toluene/ethyl acetate: 95:5). The products were recrystallized and identified by means of analytical and spectroscopic data (Tables 2 and 3).

Reaction of 1b with 5 and *N*-[[(chlorosulfinyl)oxy]methylene]-*N*-methylmethanaminium chloride.
A solution of *N*-[[(chlorosulfinyl)oxy]methylene]-*N*-methylmethanaminium chloride (4.2 mmol), freshly prepared using the method of Palomo,[14] in anhydrous dichloromethane (10 ml), was added to a solution of **1b** (0.5 g, 2.1 mmol) in anhydrous dichloromethane (10 ml) at 0-5 °C. After stirring at this temperature for 15 min, **5** (0.51 g, 2.1 mmol) was added, followed by the dropwise addition of anhydrous Et$_3$N (0.7 ml, 5 mmol) in dichloromethane (2 ml). The resulting mixture was stirred at r.t. for 24 h, then it was quenched with water and extracted with dichloromethane. The combined organic extract was dried (Na$_2$SO$_4$) and evaporated under reduced pressure. The residue was purified using column chromatography (silica gel, toluene/ethyl acetate: 95:5). Products **6b** and **7b** were obtained with a respective yield of 11% and 4%.

TABLE 2. Yields, Physical and Analytical Data of Products 6 – 15

N°	Yield (%)[a]	m.p. (°C) (cryst. solv.)	Molecular Formula	Elemental Analysis (%)		
				C	H	N
				Found (Required)		
6a	10	Ref.1	Ref.1	Ref.1		
7a	6	Ref.1	Ref.1	Ref.1		
6b	12	Ref.1	Ref.1	Ref.1		
7b	5	Ref.1	Ref.1	Ref.1		
8b	22	Ref.1	Ref.1	Ref.1		
6c	12.5	189-190 d.	$C_{24}H_{20}N_2O_5S$	64.15	4.46	6.02
		(iPrOH)		(64.27	4.49	6.25)
7c	0.5	204-206 d.	$C_{24}H_{20}N_2O_5S$	64.04	4.18	6.01
		(trichloroethylene)		(64.27	4.49	6.25)
6d	32	185-186 d.	$C_{20}H_{20}N_2O_4S$	62.28	5.14	7.07
		(iPrOH)		(62.48	5.24	7.29)
7d	5	199-200 d.	$C_{20}H_{20}N_2O_4S$	62.38	5.10	7.17
		(iPrOH)		(62.48	5.24	7.29)
6e	35	181-183 d.	$C_{25}H_{22}N_2O_4S$	66.98	4.69	6.15
		(iPrOH)		(67.25	4.96	6.27)
7e	13	198-200 d.	$C_{25}H_{22}N_2O_4S$	67.00	4.90	6.16
		(iPrOH)		(67.25	4.96	6.27)
8e	16	222-224	$C_{18}H_{16}N_2$	82.94	5.91	10.55
		(iPrOH)		(83.04	6.19	10.76)
8f	25	160-161	$C_{14}H_{16}N_2$	79.01	7.29	12.99
		(iPrOH)		(79.24	7.54	13.20)
8g	53	178-180	$C_{19}H_{18}N_2$	83.05	6.48	10.11
		(iPr_2O/iPrOH)		(83.21	6.56	10.21)
14	10	184-185 d.	$C_{24}H_{20}N_2O_6S_2$	57.91	4.00	5.49
		(iPrOH)		(58.06	4.03	5.64)
15	12	222-223	$C_{17}H_{14}N_2O_2S$	65.61	4.45	8.92
		(AcOEt)		(65.80	4.51	9.03)

a) Yield of pure isolated products.

TABLE 3. Spectroscopic Data of Products 6 – 15

N°	^{1}H-NMR (CDCl$_3$) δ from TMS, J (Hz)	^{13}C-NMR (CDCl$_3$) δ from TMS	IR (cm^{-1})
6a	Ref.1	Ref.1	Ref.1
7a	Ref.1	Ref.1	Ref.1
6b	Ref.1	Ref.1	Ref.1
7b	Ref.1	37.5(S-CH_2-C);51.3(S-CH_2-N);72.4(CH); 79.8(C_{sp});160.5-162.3(2CO).	Ref.1
8b	Ref.1	Ref.1	Ref.1
6c	3.5,4.1(AB syst.,J=10.7,2H,O-CH_2-C); 4.88,4.92 (AB syst.,J=3.8,2H,O-CH_2-N); 5.6(s,1H,CH);7.3-7.7(m,13H,aromatic);8.05(d,2H, aromatic).	65.0(CH);70.0(O-CH_2-C);75.8(C_{sp}); 81.6 (O-CH_2-N);164.8-167.8(2CO).	1670 1805
7c	4.35,4.42(AB syst.,J=10.8,2H,O-CH_2-C); 4.65(s, 2H,O-CH_2-N);5.3 (s,1H,CH);6.8(d,2H,aromatic); 7.1-7.7(m,11H,aromatic); 8.05(d,2H,aromatic).	71.1(CH);72.9(O-CH_2-C);75.9(C_{sp}); 80.7 (O-CH_2-N);166.3-169.4(2CO).	1640 1805
6d	1.3-2.0(m,4H,C-CH_2CH_2-C_{sp}); 2.05(s,3H,CH_3); 3.35-3.45(m,2H,C-CH_2-N); 5.4(s,1H, CH); 7.2-7.7(m,8H,aromatic); 8.0(d,2H,aromatic).	22.6(CH_3); 23.3(C-CH_2-C); 29.4(C-CH_2-C_{sp});48.6(C-CH_2-N); 66.4(CH); 78.0(C_{sp}); 167.0-169.5(2CO).	1650 1810
7d	1.4-1.95(m,4H,C-CH_2CH_2-C_{sp}); 2.15(s,3H,CH_3); 3.4(m,2H,C-CH_2-N); 5.0(s,1H,CH); 7.2-7.7(m,8H, aromatic); 8.0(d,2H,aromatic).	21.6(CH_3); 23.5(C-CH_2-C); 34.5(C-CH_2-C_{sp});48.3(C-CH_2-N); 72.4(CH); 78.0(C_{sp}); 165.4-168.8(2CO).	1640 1805
6e	1.5-1.65(m,2H,C-CH_2-C); 1.7-2.1(m,2H,C-CH_2-C_{sp});3.4-3.55(m,2H,C-CH_2-N);5.6(s,1H,CH);7.3-7.7(m,13H,aromatic);8.1(d,2H,aromatic).	24.2(C-CH_2-C); 30.4(C-CH_2-C_{sp});51.1(C-CH_2-N); 65.7(CH); 78.6(C_{sp}); 167.3-169.6(2CO).	1640 1780
7e	1.9-2.1(m,2H,C-CH_2-C); 2.3-2.45(m,2H,C-CH_2-C_{sp});3.15-3.25(m,2H,C-CH_2-N);5.15(s,1H,CH); 6.75(d,2H,aromatic); 7.1-7.3(m,11H,aromatic); 8.1(d,2H,aromatic).	23.9(C-CH_2-C); 34.3(C-CH_2-C_{sp});50.3(C-CH_2-N); 72.1(CH); 78.2(C_{sp}); 165.5-169.7(2CO).	1640 1780
8e	2.75(m,2H,C-CH_2-C); 3.1(t,2H,C-CH_2-C=); 4.2 (m,2H,C-CH_2-N); 7.2 -7.8 (m, 10H, aromatic).	23.3(C-CH_2-C); 27.9(C-CH_2-C=); 47.8(C-CH_2-N).	1580 1600
8f	1.8-1.9(m,2H,C-CH_2-C); 2.0-2.1(m,2H,C-CH_2-C); 2.4(s,3H,CH_3); 3.0(t,2H,C-CH_2-C=); 4.1(t,2H, C-CH_2-N); 7.3-7.6(m,5H,aromatic).	--------------------	725 1600
8g	1.9-2.1(m,4H,C-CH_2CH_2-C); 3.1(t,2H,C-CH_2-C=); 4.1(t,2H, C-CH_2-N); 7.2-7.5(m,6H,aromatic);7.7(d, 2H, H-*ortho* C-3 Ph);7.8(d,2H, H-*ortho* C-1 Ph).	20.3(C-CH_2-C=);23.0-23.2(C-CH_2CH_2-C); 45.0(C-CH_2-N).	725 1600
14	3.05,3.4(AB syst.,J=14.1,2H,SO_2-CH_2-C); 4.45, 4.55(AB syst.,J=10.8,2H,SO_2-CH_2-N); 5.65(s,1H, CH);7.3-7.8(m,13H,aromatic);7.95(d,2H,aromatic).	49.5(SO_2-CH_2-C);64.3(SO_2-CH_2-N);65.8 (CH);74.6(C_{sp}).	1340 1660 1800
15	4.65(s,2H,SO_2-CH_2-C); 5.2(s,2H,SO_2-CH_2-N); 7.3-7.8(m,10H,aromatic).	50.0(SO_2-CH_2-C); 64.4(SO_2-CH_2-N).	710 1340 1600

REFERENCES AND NOTES

1. Dalla Croce, P.; Ferraccioli, R.; La Rosa, C. *Tetrahedron* **1995**, *51*, 9385.
2. Bonati, L.; Ferraccioli, R.; Moro, G. *J. Phys. Org. Chem.* **1995**, *8*, 452.
3. Only the *N*-benzoyl derivative of 1,3-oxazolidine-4-carboxylic acid is known: Conti, S.; Cossu, S.; Giacomelli, G.; Falorni, M. *Tetrahedron* **1994**, *50*, 13493. Any attempt to synthesize the *N*-acetyl derivative was unsuccessful.
4. For *N*-acyl-L-prolines see for example: a) Anderson, W.K.; Corey, P.F. *J. Med. Chem.* **1977**, *20*, 812; b) Yebdri, O.; Texier, F. *J. Heter. Chem.* **1986**, *23*, 809. For *N*-acyl-(D,L)-pipecolinic acids see for example: c) Pizzorno, M.T.; Albonico, S.M. *J. Org. Chem.* **1977**, *42*, 909; d) Uchida, T.; Tsubokawa, S.; Harihara, K.; Matsumoto, K. *J. Heter. Chem.* **1978**, *15*, 1303.
5. For *N*-acyl-L-prolines see for example: a) Okano, T.; Uekawa, T.; Morishima, N.; Eguchi, S. *J. Org. Chem.* **1991**, *56*, 5259. For *N*-acyl-(D,L)-pipecolinic acids see for example: b) Benages, I.A.; Albonico, S.M. *J. Org. Chem.* **1978**, *43*, 4273.
6. To compare the present results with those obtained with **1a-c**,[1] we repeated the reaction of **1a,b** with **5** in toluene solution and acetic anhydride as dehydrating agent.
7. The reversed regioisomer should show only N.O.E. effect between H-5 and the *ortho* protons of the C-3 phenyl ring. The assignment of the *ortho* protons of the two phenyl rings is a consequence of the observed N.O.E. effects with the independently assigned H-5 and H-8.
8. Hegedus, L.S.; Montgomery, J.; Narukawa, Y.; Snustad, D.C. *J. Am. Chem. Soc.* **1991**, *113*, 5784.
9. Singh, S.P.; Mahajan, A.R.; Prajapati, D.; Sandhu, J.S. *Synthesis* **1991**, 1026.
10. Hart, D.J.; Ha, D. *Chem. Rev.* **1989**, *89*, 1447.
11. Applewhite, T.H.; Niemann, C. *J. Am. Chem. Soc.* **1959**, *81*, 2212.
12. Burgstahler, A.W.; Aiman, C.E. *J. Org. Chem.* **1960**, *25*, 489.
13. Ratner, S.; Clarke, H.T. *J. Am. Chem. Soc.* **1937**, *59*, 200.
14. Arrieta, A.; Aizpurua, J.M.; Palomo, C. *Tetrahedron Lett.* **1984**, *25*, 3365.