Tetrahedron Vol. 49, No. 47, pp. 10965-10976, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00

A New Synthesis of β-Phenylaminothioesters and β-Lactams[1] Via Base-Induced Ring-Opening of 2-Phenyl-3-Aryl-5-Phenyl-Thioisoxazolidines

Leonardo Di Nunno[a,b] and Antonio Scilimati[b]

[a]Centro CNR di Studio sulle Metodologie Innovative di Sintesi Organiche, Dipartimento di Chimica, Università di Bari, via Amendola n.173-70126 Bari, Italy.

[b]Dipartimento Farmaco-Chimico, Università di Bari, via Orabona n.4-70126 Bari, Italy.

(*Received in UK* 22 *July* 1993; *accepted* 24 *September* 1993)

Abstract: 1,3-Dipolar cycloaddition of phenyl vinyl sulfide to aryl N-phenyl, N-methyl, or N-*t*-butylnitrones affords 2-phenyl(or 2-methyl or 2-*t*-butyl)-3-aryl-5-phenylthioisoxazolidines according to the regioselectivity already known for the cycloaddition of not highly electron deficient dipolarophiles to nitrones. Treatment of 2-phenyl-3-aryl-5-phenylthioisoxazolidines with alkyllithiums (*n*-BuLi, *t*-BuLi) at -78 °C in THF gives β-phenylaminothioesters and/or the corresponding β–lactams in good yields. Complete conversion of β-aminothioesters into β-lactams can in any case be accomplished by treating them with CH_3MgI/Et_2O at 0° C. Isoxazolidine ring fragmentation to phenyl thioacetate and an imine is instead observed as the main or the exclusive pathway by performing the reaction at room temperature or in the case of N-alkyl isoxazolidines.

Decomposition of isoxazolidine derivatives by a variety of agents (acid, basic, reducing, oxidizing) is an interesting tool for the synthesis of many different compounds.[2]

As far as the basic agents are concerned, decomposition (involving a preliminary H abstraction) has been observed either on isoxazolidine salts[3] or, in the presence of electron-withdrawing groups capable of activating H abstraction from ring carbons, on isoxazolidines themselves.[4]

In the latter cases different products were observed (enamines, lactam alcohols, anils, lactam enols, etc.), depending on both the nature of activating group and the position (3 or 5) of the abstracted hydrogen.

No ring-opening following the C_4-H abstraction was observed (only epimerization was found in this case).

Recently[5] we have synthesized a number of 5-hydroxyisoxazolidines by reaction of N-phenylnitrones with the enolate ion of acetaldehyde (quantitatively generated by the known cycloreversion of the THF in the presence of *n*-BuLi at r.t.).[6] Treatment of 5-hydroxyisoxazolidines with bases (or acids) showed a further kind of decomposition involving the preliminary ring-opening of such "hemiacetalic" derivatives and then fragmentation to α,β-unsaturated aldehydes homologs of the arylaldeydes used for the synthesis of nitrones.

So, the combination of the synthesis and decomposition of 5-hydroxyisoxazolidines turned out to be an efficient procedure for the C_2-homologation of aromatic aldehydes.

Basic treatment [common bases: K_2CO_3, MeONa (the reaction mixtures were refluxed in methanol for about 1h)] did not affect 5-methoxyisoxazolidine. In fact no ring-opening (similar to 5-hydroxyisoxazolidines) was possible in this case under the cited basic conditions due to the "acetalic" character of 5-alkoxyisoxazolidines, nor the C_5-H abstraction by the base was observed, due to the deactivating[4,7] (or, at least, not sufficiently activating) effect of the adjacent oxygens. On the other hand H abstraction from the α-position of acetal derivatives is known to be difficult even with strong bases (RLi), except for some particular cases.[8] Further, the lack of reactivity of 5-methoxyisoxazolidine has been confirmed by us also in the presence of *n*-BuLi as a base (c.a. 1h under reflux).

Yet, the C_5-H abstraction from 5-alkoxyisoxazolidines could be a very interesting reaction. In fact, the subsequent N-O bond breaking affording β-aminoesters should be expected in this case, by analogy with other previous reports;[4] and β-aminoesters, in turn, are known useful precursors of azetidinones.[9]

Hence, such a reaction could constitute a new interesting approach to the synthesis of β-lactams.

So we decided to synthesize 5-phenylthioisoxazolidines owing to the known ability of the sulphur to better stabilize (compared to oxygen) an α-carbanion[10] and hence activate the α-H abstraction. In this case the formation of β–aminothioesters is expected, and these are again known precursors, just like β-aminoesters, of β-lactams.

Synthesis of 5-phenylthioisoxazolidines, as well as their ring opening (or fragmentation) in the presence of suitable bases, are thus the subject of the present paper.

RESULTS AND DISCUSSION

Synthesis of a series of 5-phenylthioisoxazolidines **1** was accomplished by cycloaddition of phenyl vinyl sulphide to a number of C-Aryl N-phenyl, N-methyl, and N-*t*-butylnitrones (Scheme 1).

SCHEME 1

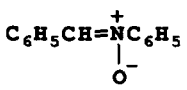
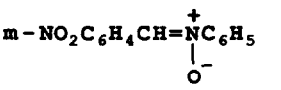
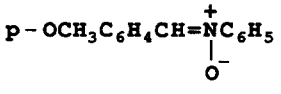
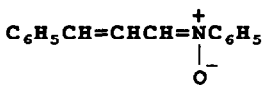
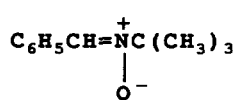
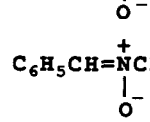
In all cases only 5-phenylthioisoxazolidines were isolated (Table 1), according to the regioselectivity generally observed in such cycloadditions when high temperatures and/or no electron-poor dipolarophiles are used.[11]

It is known, in fact, that the regioselectivity is inverted with higly electron-poor dipolarophiles (e.g., phenyl vinyl sulphone) under kinetic control (r.t.), in which case the 4-regioisomer is dominant or exclusive.[11]

As far as the stereochemistry is concerned, in all cases cis-derivatives were isolated as the main isomers, according to previous reports for other similar [3+2] cycloadditions to nitrones (e.g., cycloaddition of vinyl acetate).[12]

TABLE 1

Yields of 5-phenylthioisoxazolidines isolated from the reaction of nitrones and phenyl vinyl sulfide in toluene under reflux.

Nitrone	Yield % [a]	[cis]/[trans] [b]
	81	80 / 20
	78	90 / 10
	72	80 / 20
	70	80 / 20
	85	83 / 17
	68	54 / 46

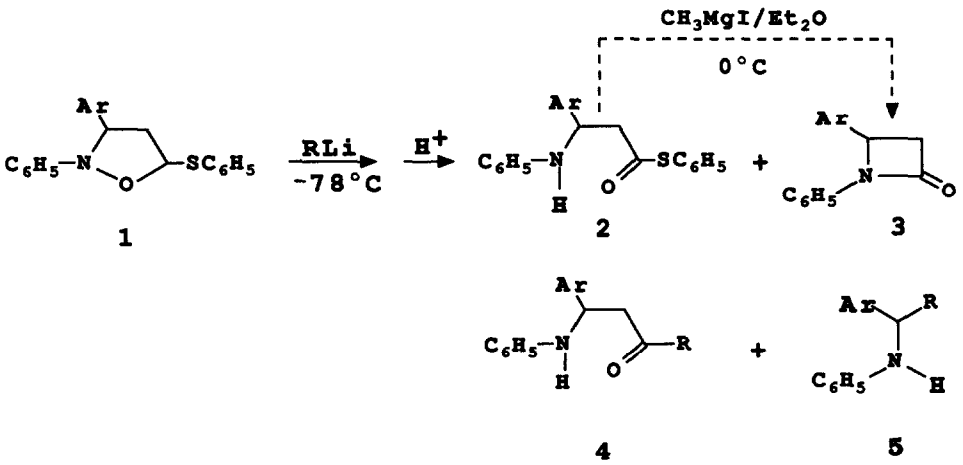
[a] The yields refer to mixtures of cis- and trans-isomers isolated by column flash chromatography. [b] The cis/trans ratio has been evaluated by ^{1}H NMR by using the signals of the 5-phenylthioisoxazolidines in the range 4.00-3.00 ppm (see Experimental).

Treatment of the so obtained 5-phenylthioisoxazolidines with bases like DBU (in THF or toluene under reflux for at least 4h), MeONa (MeOH/Δ), or LDA (in THF at -78 °C and at room temperature) did not cause appreciable decomposition.

On the contrary, the use of alkyllithiums (*n*-BuLi, *t*-BuLi) at low temperature (-78 °C) in THF gave quick decomposition of the isoxazolidine derivatives, with formation of β-aminothioesters **2** (converted in part

into the corresponding β-lactams **3**), together with little amounts (10-15 %) of other products, among which β-aminoketone **4** and an amine **5** (Scheme 2).

SCHEME 2



Except for the case of N-phenyl-3-(4-anisyl)-5-phenylthioisoxazolidine, complete conversion of β-aminothioester into β-lactams could be accomplished only by a separate treatment, by analogy with other previous reports,[9] with a Grignard reagent (CH_3MgI/Et_2O) at 0° C.

Yields of β-aminothioesters and β-lactams (overall) are rather high (Table 2), particularly with *t*-BuLi as a base (with *n*-BuLi a greater amount of aminoketones **4** is observed).

TABLE 2

Yields of β-aminothioesters and β-lactams isolated from the reaction of 5-phenylthioisoxazolidines with *t*-BuLi at -78 °C (first and second column, respectively). The overall yields of β-lactams, obtained both from the reaction of isoxazolidines with *t*-BuLi at -78 °C and the treatment of β-aminothioesters with CH_3MgI at 0 °C, are listed in the third column.

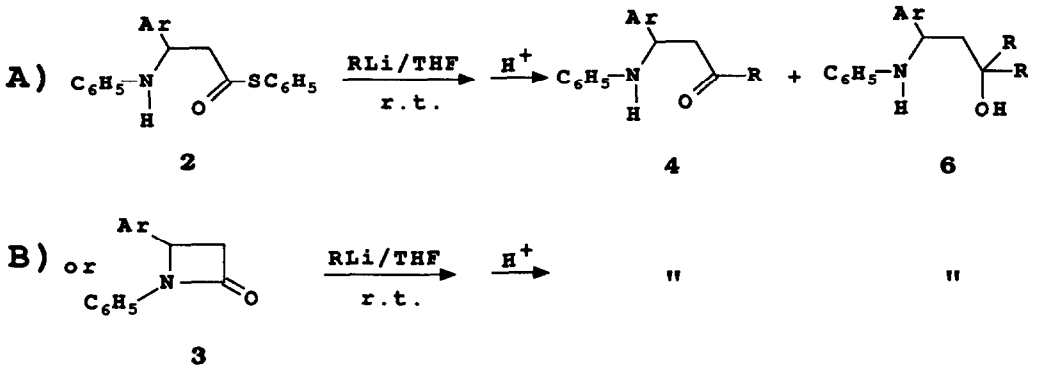
Ar	β-aminothioesters Yields (%)[a]	Yields (%) of β-lactams[a] (isolated at -78°C)	Yields (%) of β-lactams (overall)[a]
C_6H_5	70	10	77
$m-NO_2C_6H_4$	63	7	69
$p-OCH_3C_6H_4$	--	60	60
$C_6H_5CH=CH$	65	15	75

[a]The yields refer to the isolated products.

So, the described reaction turns out to be a new interesting isoxazolidine approach to the synthesis of both β-aminothioesters and β-lactams, alternative (concerning the latter) of other reported isoxazolidine procedures [e.g., the reductive (Ni-Raney) ring-opening of 5,5-difluoroisoxazolidines].[13]

On the other hand treatment of β-aminothioesters with RLi/THF at r.t. did not afford the expected β-lactams, but the aminoketones **4** and aminoalcohols **6** (Scheme 3A).

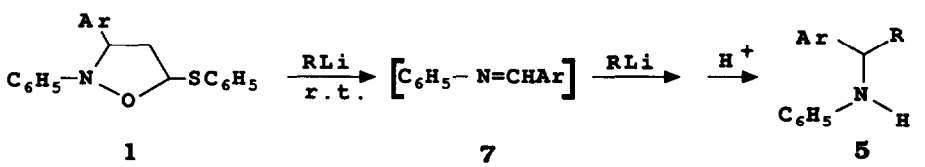
SCHEME 3



Since, however, the latter are also the products of the reaction of β-lactams with RLi under the same conditions (Scheme 3B), it is conceivable that β-lactams can actually form also in the presence of alkyllithiums but further react with them at room temperature affording in any case the aminoketones and the aminoalcohols as the final products. Accordingly, β-lactams are the main products generated in the presence of RLi when cyclization of β-aminothioesters is rapid at low temperature (-78 °C), as actually observed in the case of N-phenyl-3-(4-anisyl)-5-phenylthioisoxazolidine.

A different origin can be envisaged for the amines **5**, the imines **7** (known fragmentation products of other different 5-substituted isoxazolidines under basic conditions)[4] being the conceivable direct precursors in this case (Scheme 4).

SCHEME 4



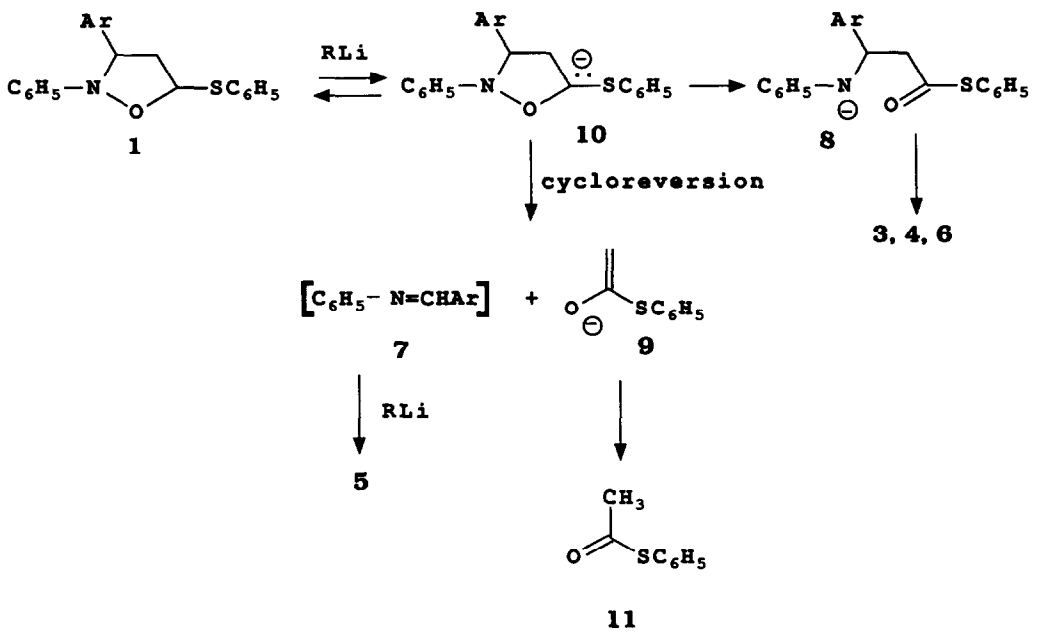
They are formed only by direct treatment with RLi of 5-phenylthioisoxazolidines (becoming the only or main products when the reaction is performed at room temperature), and not by a similar treatment of either β-aminothioesters **2** or β-lactams **3**, that both afford β-aminoketones **4** and γ-aminoalcohols **6**, as above-mentioned. Thus, fragmentation to imines **7** should involve directly 5-phenylthioisoxazolidines without the

intermediation of their preliminary ring-opening products (the β-aminothioester anion **8**). This however, is at variance with the scheme previously proposed[4] for this kind of fragmentation of isoxazolidines, for which a stepwise mechanism involving a preliminary ring-opening (similar to that affording the β-aminothioester anion) has in fact been suggested.

Thus, in the light of our findings, a different scheme should be proposed, and this, in our view, could well involve a pericyclic mechanism (-[π4s + π2s] cycloreversion) similar to that previously suggested for the conversion of THF into ethylene and the enolate ion of acetaldehyde.[6]

If so, the overall scheme of decomposition of 5-phenylthioisoxazolidines by alkyllithiums should involve two main routes (Scheme 5), both starting from a unique initial carbanion **10** generated by C_5-H abstraction.

SCHEME 5



The first one, observed at low temperatures, should afford the β-aminothioester anions, and, from these, β-lactams and, by further interaction with RLi, β-aminoketones and, eventually, aminoalcohols. The second route, seemingly favoured by higher temperatures and when the open form is presumably less stable due to a lower ability of the nitrogen to bear a negative charge (as in N-alkyl isoxazolidines), should afford the enolate ion of the thioester **9** (and then the thioester **11**) and the imine **7** which in turn, by reaction with RLi, gives the isolated amine **5**.

Further investigations are in progress on this point.

EXPERIMENTAL

MPS taken on a Electrothermal apparatus were uncorrected. ^1H NMR spectra were recorded on a Varian EM 390 or XL 200 spectrometer and chemical shifts are reported in parts per million (δ) from internal Me_4Si. Absolute values of the coupling constant are reported. IR spectra were recorded on a Perkin-Elmer 681 spectrometer. Thin-layer chromatography (TLC) was performed on silica gel sheets with fluorescent indicator (stratocrom SIF, Carlo Erba), the spots on the TLC were observed under ultraviolet light or were visualized with iodine vapour. Flash chromatography was conducted by using silica gel with an average particle size of 60 μm, a particle size distribution 40-63 μm and 230-400 ASTM. GC-MS analyses were performed on an HP 5995C model and microanalyses on a Elemental Analyzer mod. 1106. Carlo Erba-instrument.

Materials. Tetrahydrofuran (THF) and diethyl ether (Et_2O) from commercial source (RS, Carlo Erba) were purified by distillation (twice) from sodium wire in a N_2 atmosphere. Standardized (2.4N) *n*-butyllithium in hexane and (1.6N) *t*-butyllithium were from Aldrich Chemical Co..

All other chemicals were commercial grade further purified by distillation or crystallization prior to use.

Phenyl N-phenylnitrone, p-methoxyphenyl N-phenylnitrone, m-nitrophenyl N-phenylnitrone and cinnamal N-phenylnitrone were prepared by reacting the arylaldehyde with phenylhydroxylamine as previously described.[5] Phenyl N-methylnitrone was synthesized from benzaldehyde and methylhydroxylamine.[14] Phenyl N-*t*-butylnitrone was from Aldrich Co..

Reaction of nitrones with phenyl vinyl sulfide: general procedure

A solution of phenyl vinyl sulfide (7.2 mmole) in 20 ml of toluene is added dropwise at room temperature to a solution of nitrone (6 mmole) in 30 ml toluene, using a nitrogen-flushed, three necked flask equipped with a magnetic stirrer, a nitrogen inlet and a dropping funnel. The reaction mixture was heated under reflux for 24h. Then the solvent was evaporated under vacuum and the crude 5-penhylthioisoxazolidines obtained were purified by column flash chromatography.

Reaction of 5-phenylthioisoxazolidines with RLi at -78 °C: general procedure

11.6 ml of 1.6N *t*-BuLi (or 7.7 ml 2.4N *n*-BuLi) were added, under nitrogen atmosphere, to a stirred solution of isoxazolidine (3 mmole) in THF (30 ml) kept at -78 °C. After 1h the reaction mixture was quenched by adding aqueous NH_4Cl, the organic layer extracted with ethyl ether. The combined extracts were dried over Na_2SO_4 and evaporated under pressure, affording a residue which was chromatographed on silica gel. Elution with petrol ether/ ethyl acetate= 28/1 gave the products depicted in the Scheme 2.

Reaction of β-aminothioesters with CH_3MgI: general procedure

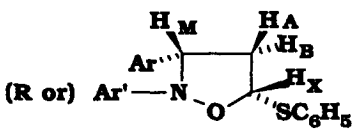
Methylmagnesium iodide (1N solution in anhydrous ethyl ether) (9mmole) was added to a solution of β-

aminothioester (3 mmole) in 100 ml of anhydrous ethyl ether cooled in an ice bath. Then the mixture was allowed to warm at room temperature and quenched (after ca 2h) with saturated aqueous ammonium chloride. Following the addition of ethyl ether and water, the organic layer was washed sequentially with water and saturated aqueous sodium chloride, then dried over anhydrous sodium sulfate and the solvent evaporated under reduced pressure to give the crude β-lactams, purified by flash chromatography on silica gel (eluent: petrol ether/ethyl acetate= 28/1).

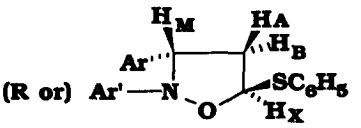
Products

As already described the 5-arylthioisoxazolidines were isolated as cis/trans mixture ranging from 4/1 to almost 1/1. So, unless otherwise indicated, the given mps and spectroscopic data refer to the above-mentioned mixtures. The following assignments of the chemical shifts and coupling constants are according to the ABMX spin system (Scheme 6).[5]

SCHEME 6



cis



trans

2,3- Diphenyl -5- phenylthioisoxazolidine: m.p. 59-61°C (CCl_4); IR(CCl_4): 3060, 3030, 1580, 1540, 1485, 905 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 8.00-6.90 (m, 15 H); 5.88(dd, J_{AX} = 4.8 Hz, J_{BX}= 5.7 Hz, H_X, trans); 5.68(dd, J_{AX}= 7.3 Hz, J_{BX}= 6.6 Hz, H_X, cis); 4.91 (t, J_{AM}= J_{BM}= 7.3 Hz, H_M, trans); 4.54(t, J_{AM}= J_{BM}= 8.3 Hz, H_M, cis); 3.29(ddd, J_{AM}=8.3 Hz, J_{AX}= 7.3 Hz, J_{AB}= 13.1 Hz, H_A, cis); 2.89(m, 2H, H_A + H_B, trans); 2.46(ddd, J_{BM}= 8.3 Hz, J_{BX}= 6.6 Hz, J_{AB}= 13.1 Hz, H_B, cis). (Found: C, 75.63; H, 5.70; N, 4.18. Calc. for $C_{21}H_{19}NOS$: C, 75.68; H, 5.71; N, 4.20; S, 9.61).

2-Phenyl-3-(4-methoxyphenyl)-5-phenylthioisoxazolidine: m.p. 105-106°C; IR(KBr): 3060, 2980, 1610, 1600, 1580, 1530, 1440, 1250, 745, 690 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.70-6.88(m, 14H); 5.87 (dd, J_{AX}= 5.3 Hz, J_{BX}= 6.0 Hz, H_X, trans); 5.68(dd, J_{AX}= 7.4 Hz, J_{BX}= 6.3 Hz, H_X, cis); 4.85(t, J_{AM}= 7.2 Hz, H_M, trans); 4.45(t, J_{AM}= J_{BM}= 8.3 Hz, H_M, cis); 3.86(s, 3H, trans); 3.82(s, 3H, cis); 3.25(ddd, J_{AM}= 8.3 Hz, J_{AX}= 7.4 Hz, J_{AB}= 13.2 Hz, H_A, cis); 2.87(m, 2H, H_A+H_B, trans); 2.43(ddd, J_{BM}= 8.3 Hz, J_{BX}= 6,3 Hz, J_{AB}= 13.2 Hz, H_B, cis). (Found: C, 72.70; H, 5.79; N, 3.86. Calc. for $C_{22}H_{21}NO_2S$: C, 72.73; H, 5.78; N, 3.86; S, 8.81).

2-Phenyl-3-cinnamal-5-phenylthioisoxazolidine: 60-62 °C; IR(CCl_4): 3060, 2980, 1605, 1580, 1530, 1445,

1250, 750 cm^{-1}; ^1H NMR($CDCl_3$, δ): 7.71-7.00(m, 15H); 6.69(d, J= 15.9 Hz, 1H, PhCH=, cis); 6.42(dd, J= 15.9 Hz, 7.6 Hz, 1H, =CH-, cis); the latter two signals almost entirely cover the doublet and the doublet of doublets due to -CH=CH- belonging to the trans isoxazolidine, having the following chemical shifts: [6.65(d, J= 16.0 Hz, 1H, PhCH=); 6.37(dd, J= 16.0 Hz, 7.6 Hz, 1H, =CH)]; 5.85(dd, J_{AX}= 5.4 Hz, J_{BX}= 6.7 Hz, H_X, trans); 5.69 (dd, J_{AX}= 7.5 Hz, J_{BX}= 6.2Hz, H_X, cis); 4.52(m, H_M, trans); 4.22(m, H_M, cis); 3.10(dt, J_{AM}= J_{AX} = 7.5 Hz, J_{AB} = 13.2 Hz, H_A, cis); 2.65(m, 2H, H_A+H_B, trans); 2.37(dt, J_{BM}= J_{BX}= 6.2 Hz, J_{AB}= 13.2 Hz). (Found: C, 76.85; H, 5.81; N, 3.92. Calc. for $C_{23}H_{21}NOS$: C, 76.88; H, 5.85; N, 3.90; S, 8.91).

2-Phenyl-3-(3-nitrophenyl)-5-phenylthioisoxazolidine: 86-87 °C; IR(CCl_4): 3080, 3040, 2960, 2920, 1600, 1530, 1470, 1440, 1350 cm^{-1}; ^1H NMR($CDCl_3$, δ): 8.40-6.90 (m, 14H); 5.84(t, J_{AX}= J_{BX}= 5.8 Hz, H_X, trans); 5.66(t, J_{AX}= J_{BX}= 7.0 Hz, H_X, cis); 5.01(t, J_{AM}= J_{BM}= 7.0 Hz, H_M, trans); 4.74(dd, J_{AM}= 8.8 Hz, J_{BM} = 6.3 Hz, H_M, cis); 3.30(ddd, J_{AM}= 8.8 Hz, J_{AX}= 7.0 Hz, J_{AB}= 13.0 Hz, H_A, cis); 3.10-2.76(m, 2H, H_A+H_B, trans); 2,36(dt, J_{BM}= J_{BX}= 7.0 Hz, J_{AB}= 13.0 Hz, H_B, cis). (Found: C, 66.65; H, 4.78; N, 7.40. Calc. for $C_{21}H_{18}N_2O_3S$: C, 66.67; H, 4.76; N, 7.41; S, 8.47).

cis 2-Methyl-3-phenyl-5-phenylthioisoxazolidine: oil; IR(CCl_4): 3100, 3000, 3000, 2800, 1455, 1370, 1100 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.62-7.20(m, 10H); 5.69(dd, J_{AX}= 8.2 Hz, J_{BX}= 5.4 Hz, H_X); 3.48(t, J_{AM}= J_{BM}= 8.2 Hz, H_M); 3.20(dt, J_{AM}= J_{AX}= 8.2 Hz, H_A); 2.66(s, 3H); 2.38(ddd, J_{BM}= 8.2 Hz, J_{BX}= 5.4 Hz, J_{AB} = 13.4 Hz, H_B). trans 2-Methyl-3-phenyl-5-phenylthioisoxazolidine: oil; IR(CCl_4): 3100, 3000, 3000, 2800, 1455, 1370, 1100 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.60-7.20 (m, 10H); 5.63(dd, J_{AX}= 5.4 Hz, J_{BX}= 7.8 Hz, H_X); 3.74(t, J_{AM}= J_{BM} = 8.0 Hz, H_M); 2.90-2.63 (m, 2H, H_A+H_B); 2.74(s, 3H). (Found: C, 70.89; H, 7.22; N, 5.18. Calc. for $C_{16}H_{17}NOS$: C,70.85; H,6.27; N, 5.17; S, 11.81).

2-*t*-Butyl-3-phenyl-5-phenylthioisoxazolidine: mp 77-78 °C (petrol ether, cis isomer), 69-71 °C (50% cis/trans mixture); IR (KBr): 2973, 1582, 1473, 1362, 1222, 1053, 1024, 942, 745, 692 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.60-7.20 (m, 10H); 5.59 (m, 1H, trans isomer); 5.53 (dd, J_{AX}= 7.1 Hz, J_{BX}= 5.5 Hz, H_X, cis isomer); 4.35 (t, J_{AM}= J_{BM}= 7.7 Hz, H_M, trans isomer); 4.01 (t, J_{AM}= J_{BM}= 8.5 Hz, H_M, cis isomer); 3.08 (ddd, J_{AX}= 7.1 Hz, J_{AM}= 8.5 Hz, J_{AB}= 13.4 Hz, H_A, cis isomer); 2.75-2.50 (m, 2H, H_A+H_B, trans isomer); 2.28 (ddd, J_{BX}= 5.5 Hz, J_{BM}= 8.5 Hz, J_{AB}= 13.4 Hz, H_B, cis isomer); 1.08 (s, 9H, trans isomer); 1.03 (s, 9H, cis isomer). MS (70 eV) m/z (%) 313 (M^+, 26), 226 (13), 225 (75), 177 (23), 148 (19), 121 (26), 120 (40), 117 (27), 116 (13), 115 (69), 109 (18), 105 (43), 104 (21), 103 (13), 91 (28), 77 (28), 72 (38), 65 (18), 57 (100), 56 (17), 41 (46). (Found: C, 72.85; H, 7.40; N, 4.45. Calc. for $C_{19}H_{23}NOS$: C, 72.84; H, 7.35; N, 4.47; S, 10.22).

3-(N-phenylamine)-3-phenyl-phenylthiopropanoate: mp 63-64 °C; IR(KBr): 3400, 3040, 2980, 1690, 1610, 1325, 1300, 1215, 1050, 990, 745, 720, 700, 690 cm^{-1}; ^1H NMR($CDCl_3$, δ): 7.60-7.08 (m, 12H); 6.80-6.55 (m, 3H); 4.93 (t, J= 6.6 Hz, 1H); 4.80-4.45 (bs, NH: exchange with D_2O); 3.14 (d, J= 6.6 Hz, 2H). MS (70 eV) m/z (%) 333 (M^+, 16), 183 (14), 182 (100), 109 (11), 104 (26), 77 (32). (Found: C, 75.65; H, 5.70; N, 4.21. Calc. for $C_{21}H_{19}NOS$: C, 75.68; H, 5.71; N, 4.20; S, 9.61).

2-Phenyl-2-(N-phenylamine)-ethyl *t*-butylketone: oil; IR (neat): 3400, 3035, 2980, 1695, 1610, 1508, 1370, 1320, 1085 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.60-6.40 (m, 10H); 4.89(t, J= 6.2 Hz, 1H); 4.50-4.30 (bs, NH: exchange with D_2O); 3.00 (d, J= 6.2 Hz, 2H); 1.04 (s, 9H). MS (70 eV) m/z (%) 281 (M^+, 26), 222 (16), 183 (14), 182 (100), 181 (14), 180 (18), 77 (18), 57 (14). (Found: C, 81.14; H, 8.14; N, 4.95. Calc. for $C_{19}H_{23}NO$: C, 81.14; H, 8.18; N, 4.98).

N-Phenyl N-(1-phenyl-2,2-dimethylpropyl)-amine: oil; IR (neat): 3400, 3030, 2980, 1610, 1510, 1370, 1320, 1080, 715 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.34-7.00 (m, 7H); 6.63-6.47 (m, 3H); 4.40-4.10 (bs, NH : exchange with D_2O); 4.05 (s, 1H); 1.00 (s, 9H). MS (70 eV) m/z (%) 239 (M^+, 5), 183 (15), 182 (100), 104 (18), 77 (23). (Found: C, 85.35; H, 8.80; N, 5.86. Calc. for $C_{17}H_{21}N$: C, 85.36; H, 8.79; N, 5.86).

1,4-diphenylazetidin-2-one: mp 135-136°C; IR (neat): 3040, 2965, 2930, 2860, 1740, 1600, 1505, 1460, 1385 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.43-7.00 (m, 10H); 5.00 (dd, J= 5.7 Hz, 2.7 Hz, 1H); 3.55 (dd, J=15.2 Hz, 5.7 Hz, 1H); 2.93 (dd, J= 15.2 Hz, 2.7 Hz, 1H). MS (70 eV) m/z (%) 223 (M^+,16), 180 (19), 104 (100), 78 (12), 77(26), 51 (12). (Found: C, 80.72; H, 5.81; N, 6.25. Calc. for $C_{15}H_{13}NO$: C, 80.72; H, 5.83; N, 6.28).

3-(N-Phenylamine)-3-cinnamal-phenylthiopropanoate: oil; IR(neat): 3400, 1698, 1601, 1505, 1478, 746, 691 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.66-6.63 (m, 16H); 6.29 (m, 1H); 4.64 (m, 1H); 4.20-3.80 (bs, NH: exchange with D_2O); 3.09 (dd, J= 6.2 Hz, 1.9 Hz, 2H). (Found: C, 76.85; H, 5.83; N, 3.86. Calc. for $C_{23}H_{21}NOS$: C, 76.88; H, 5.85; N, 3.90; S, 8.91).

2-Cinnamal-2-(N-phenylamine)-ethyl *t*-butylketone: oil; IR (neat): 3400, 1700, 1600, 1500, 1475, 748 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.60-6.60 (m, 11H); 6.30 (m, 1H); 4.65 (m, 1H); 4.20-3.90 (bs, NH: exchange with D_2O); 2.96 (dd, J= 5.9 Hz, 1.6 Hz, 2H); 1.12 (s, 9H). MS (70 eV) m/z (%) 307 (M^+, 1), 279 (21), 167 (42), 150 (11), 149 (100), 71 (11), 70 (10), 57 (22), 41 (17). (Found: C, 82.06; H, 8.15; N, 4.55. Calc. for $C_{21}H_{25}NO$: C, 82.08; H, 8.14; N, 4.56).

N-Phenyl N-(1-cinnamal-2,2-dimethylpropyl)-amine : oil; IR (neat): 3400, 1600, 1505, 1480, 750, 690 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.55-6.99 (m, 8H); 6.67-6.48 (m, 3H); 6.18 (dd, J= 15.9 Hz, 6.9 Hz, 1H); 4.20-4.00 (bs, NH : exchange with D_2O); 3.67 (dd, J = 6.9 Hz, 1.5 Hz, 1H); 1.03 (s, 9H); MS (70 eV) m/z (%) 265 (M^+, 2), 209 (17), 208 (100), 130 (16), 115 (21), 91 (21), 77 (15). (Found: C, 86.02; H, 8.69; N, 5.28. Calc. for $C_{19}H_{23}N$: C, 86.04; H, 8.68; N, 5.28).

1-Phenyl-4-Cinnamalazetidin-2-one: oil; IR (neat): 3074, 2950, 1753, 1654, 1600, 1500, 1479, 800, 749, 692 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.55-6.80 (m, 11H); 6.25 (m, 1H); 4.65 (m, 1H), 3.38 (m, 1H); 2.90 (m, 1H). MS (70 eV) m/z (%) 249 (M^+, 29), 131 (11), 130 (100), 129 (53), 128 (19), 115 (26), 77 (18), 51 (11). (Found: C, 81.90; H, 6.02; N, 5.61. Calc. for $C_{17}H_{15}NO$: C, 81.93; H, 6.02; N, 5.62).

3-(N-Phenylamine)-3-(4-methoxyphenyl)-phenylthiopropanoate: oil; IR(CCl_4): 3400, 1700, 1605, 1476, 746,

690 cm^{-1}; ^1H NMR($CDCl_3$, δ): 7.40-6.50 (m, 14H); 4.83 (t, J= 6.5 Hz, 1H); 4.15-3.90 (bs, NH: exchange with D_2O); 3.77 (s, 3H); 3.09 (d, J= 6.5 Hz, 2H). (Found: C, 72.70; H, 5.80; N, 3.88. Calc. for $C_{22}H_{21}NO_2S$: C,72.73; H, 5.78; N, 3.86; S, 8.81).

2-(4-methoxyphenyl)-2-(N-phenylamine)-ethyl *t*-butylketone: oil; IR(neat): 3400, 1701, 1600, 1503, 1475, 750 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.40-6.50 (m, 9H); 4.78 (t, J= 6.2 Hz, 1H); 4.25-3.80 (bs, NH: exchange with D_2O); 3.75 (s, 3H); 2.96 (d, J= 6.2 Hz, 2H); 1.00 (s, 9H). MS (70 eV) m/z (%) 311 (M^+, 26), 213 (16), 212 (100), 134 (16), 104 (15), 85 (20), 77 (16), 57 (83), 41 (14). (Found: C, 77.14; H, 8.06; N, 4.51. Calc. for $C_{20}H_{25}NO_2$: C, 77.17; H, 8.04, N, 4.50).

1-Phenyl-4-(4-methoxyphenyl)-azetidin-2-one: oil; IR (neat): 3080, 1735, 1660, 1600, 1500, 1480, 800, 753, 693 cm^{-1}; ^1H MNR ($CDCl_3$, δ): 7.40-6.50 (m, 9H); 4.94 (dd, J= 5.6 Hz, 2.5 Hz, 1H); 3.80 (s, 3H); 3.51 (dd, J= 15.2 Hz, 5.6 Hz, 1H); 2.90 (dd, J= 15.2 Hz, 2.5 Hz, 1H). MS (70 eV) m/z (%) 253 (M^+, 10), 135 (11), 134 (100), 119 (16), 91 (12), 77 (13). (Found: C, 75.90; H, 5.94; N, 5.53. Calc. for $C_{16}H_{15}NO_2$: C, 75.89; H, 5.93; N, 5.53).

3-(N-Penylamine)-3-(3-nitrophenyl)-phenylthiopropanoate: oil; IR ($CHCl_3$): 3402, 2965, 2872, 1703, 1603, 1525, 1375, 1325, 1262, 1087, 1026, 803, 750, 692 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.30-6.40 (m, 14H); 4.85 (t, J= 6.0 Hz, 1H); 4.30-4.00 (bs, NH: exchange with D_2O); 2.97 (d, J= 6.0 Hz, 2H). (Found: C, 66.67; H, 4.71; N, 7.40. Calc. for $C_{21}H_{18}N_2O_3S$: C, 66.67; H, 4.76; N, 7.41; S, 8.47).

2-(3-Nitrophenyl)-2-(N-phenylamine)-ethyl *t*-butylketone: oil; IR ($CHCl_3$): 3385, 2960, 2925, 2894, 1701, 1602, 1525, 1376, 1325, 1260, 1081, 1025, 804, 748, 691 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.40-6.50 (m, 9H); 4.76 (t, J= 5.8 Hz, 1H); 4.40-4.00 (bs, NH: exchange with D_2O); 2.90 (d, J= 5.8 Hz, 2H); 1.01 (s, 9H). MS (70 eV) m/z (%) 326 (M^+, 13), 281 (3), 241 (8), 228 (16), 227 (100), 207 (12), 181 (21), 180 (10), 118 (3), 77 (10), 57 (24), 41 (13). (Found: C, 69.90; H, 6.73; N, 8.56. Calc. for $C_{19}H_{22}N_2O_3$: C, 69.94; H, 6.75; N, 8.59).

1-Phenyl-4-(3-nitrophenyl)-azetidin-2-one: oil; IR (KBr): 3058, 2964, 2928, 2869, 1740, 1601, 1500, 1477, 1366, 1261, 1222, 1146, 1018, 1078, 801, 751, 690 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.50-6.60 (m, 9H); 4.88 (dd, J= 5.6 Hz, 2.6 Hz, 1H); 3.50 (dd, J= 15.1 Hz, 5.6 Hz, 1H); 2.82 (dd, J= 15.1 Hz, 2.6 Hz, 1H). (Found: C, 67.18; H, 4.49; N, 10.44. Calc. for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.48; N, 10.45).

N-t-Butyl N-(1-phenyl-2,2-dimethylpropyl)-amine: oil; IR (CCl_4): 3420, 3020, 2985, 1580, 1475, 1390, 1370, 1260 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.60-7.20 (m, 5H); 4.00-3.70 (bs, NH: exchange with D_2O); 3.40 (s, 1H); 0.90 (s, 9H); 0.84 (s, 9H). MS (70 eV) m/z (%) 219 (M^+, 2), 204 (1), 162 (43), 106 (100), 105 (9), 91 (12), 79 (10), 57 (11), 41 (19).

N-Methyl N-(1-phenyl-2,2-dimethylpropyl)-amine: oil; IR (CCl_4): 3425, 3020, 2980, 1578, 1475, 1385, 1375, 1260 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 7.50-7.20 (m, 5H), 4.15-4.00 (bs, NH: exchange with D_2O); 3.20 (s,

1H); 2.20 (s, 3H); 0.89 (s, 9H). MS (70 eV) m/z (%) 177 (M^+, 5), 162 (8), 106 (100), 105 (10), 91 (13), 79 (23), 57 (10), 41 (20).

Spectroscopic and analytical data of diphenyl disulfide and phenyl thioacetate were compared with autentical samples.

Acknowledgements: We thank the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (Rome) for partial support of this research.

REFERENCES

1. Presented in part at the "Third International Symposium on Carbanion Chemistry", Gallipoli (Italy), June 14-18 **1992**.
2. Takeuchi, Y.; Furusaki, F. *Advances in Heterocyclic Chemistry* (Katritzky A.R. and Boulton A.J. Ed.), **1977**, *21*, 207-251, Academic Press, New York.
3. Liguori, A.; Sindona, G.; Uccella, N. Tetrahedron **1984**, *40*, 1901-1906, and references given.
4. Joucla, M.; Hamelin, J.; Carrié, R. *Tetrahedron* **1974**, *30*, 1121-1126.
5. Di Nunno, L.; Scilimati, A. *Tetrahedron* **1991**, *47*, 4121-4132.
6. Bates, R.B.; Kroposki, L.M.; Potter, D.E. *J.Org.Chem.* **1972**, *37*, 560-562; Tomboulian, P.; Amick, D.; Beare, S.; Dumke, K.; Hart, D.; Hites, R.; Metzger, A.; Nowak, R. *ibid.* **1973**, *38*, 322-325; Jung, M.E.; Blum, R.B. *Tetrahedron* **1977**, 3791-3794.
7. Bordwell, F.G.; Van Der Puy, M.; Vanier, N.R. *J.Org.Chem.* **1976**, *41*, 1883-1885, *ibid.* 1885-1886.
8. Berlin, K.D.; Rathore, B.S.; Peterson, M. *J.Org.Chem.* **1965**, *30*, 226-228.
9. Hart, D.J.; Ha, D.-C. *Chem.Rev.* **1989**, *89*, 1447; Isaac, N.S. *Chem.Soc.Rev.* **1976**, *5*, 181.
10. Bordwell, F.G.; Bares, J.E.; Bartmess, J.E.; Drucker, G.E.; Gerhold, J.; McCollum, G.J.; Van Der Puy, M.; Vanier, N.R.; Matthews, W.S. *J.Org.Chem.* **1977**, *42*, 326-332; Abbotto, A.; Bradamante, S.; Pagani, G.A. *ibid.* **1993**, *58*, 449-455.
11. Sims, J.; Houk, K.N. *J.Am.Chem.Soc.* **1973**, *95*, 5798-5800; Koizumi, T.; Hirai, H.; Yoshii, E.; *J.Org.Chem.* **1982**, *47*, 4004-4005; Dalla Croce, P.; La Rosa, C.; Stradi, R.; Ballabio, M. *J.Heterocyclic Chem.* **1983**, *20*, 519-521; Burdisso, M.; Gandolfi, R.; Grunanger, P. *Tetrahedron* **1989**, *45*, 5579-5594.
12. Cum, C.; Aversa, M.C.; Uccella, N. *Gazz.Chim.Ital.* **1968**, *98*, 782-794.
13. Purrington, S.T.; Shen, K.-W. *Tetrahedron Lett.* **1992**, 3289-3292.
14. du Pont de Nemours, E.I. and Co., Belgian Patent 614730; *Chem.Abstr* **1962**, *57*, 16484.