The Regioselectivity of the Ring Opening of 1-Activated or Nonactivated 2-Alkoxycarbonyl or 2-Cyanoaziridines by Carbanions of the Dicarbonyl Compounds

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Received March 14, 1991

Ring opening of title compounds with alkyl malonates, acetylacetone, methyl acetylacetate, and malononitrile was studied. The regioselectivity of the opening depends on several factors. A phenyl group on C-3 favours C-3-N bond cleavage, whereas C-2-N bond cleavage is predominant with C-3-substituted or C-2-H aziridines. Cyanoaziridines are predominantly cleaved at C-3-N. The aziridine configuration at C-2 and C-3 is maintained during the cyclisation in pyrrolidones.

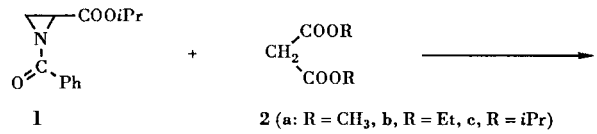
J. Heterocyclic Chem., **28**, 1757 (1991).

Many recent reports relate to the opening by hetero or carbon nucleophiles [1-10] of *N*-activated or *N*-nonactivated C-nonfunctionalized aziridines, but only a few reports deal with nucleophile opening of 2-cyano or 2-carboalkoxyaziridines [11-17]. For the purpose to develop new synthetic methods of biologically active molecules, we have examined the reaction of several 1-activated and nonactivated 2-cyano or 2-alkoxycarbonylaziridines with β-dicarbonyl compounds: alkylmalonates, malononitrile, acetylacetone, and methyl acetylacetate. Table 1 summarizes our results.

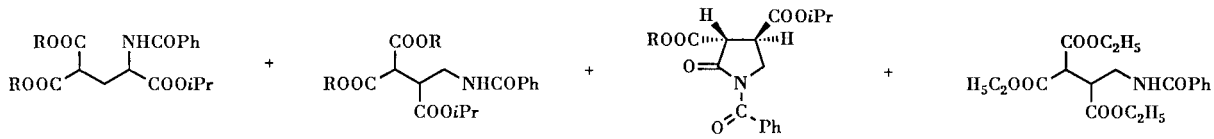
In most cases the formation of two ring-opening products is observed and in many of these reactions a cyclisation reaction into pyrrolidones is obtained. All the products have been identified by their microanalysis and their spectroscopic data (^{1}H and ^{13}C-nmr).

The reaction of *N*-benzoyl-2-carboisopropylaziridine **1** with alkyl malonates **2a-c** (Scheme 1) gives C-3-N-1 and C-2-N-1 cleavage products **3** and **4** in almost equal amounts. A part of **4** is cyclised in pyrrolidones **5**, partial *trans*-esterification is observed in the reaction with **2b**. The structures of pyrrolidones **5** are supported by the

Scheme 1

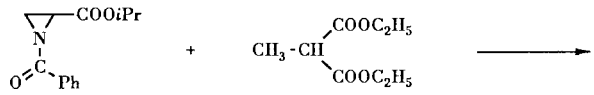


1 **2** (a: R = CH_3, b, R = Et, c, R = *i*Pr)

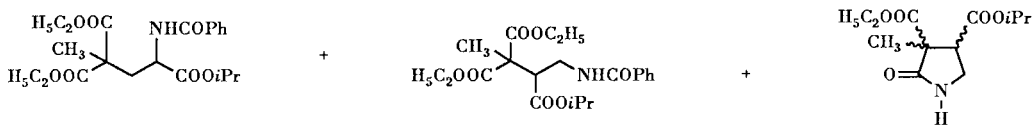


3a-c **4a-c** **5a-c** **6b**

Scheme 2



1 **7**



8 **9** **10a+b**

Table 1

No.	Aziridine	Nucleophile	Ring-opening Products C-3-N	Ring-opening Products C-2-N	Other Products	%C-3-N/C-2-N
1	1	2 $CH_2(COOR)_2$				
		2a (R = Me)	3a	4a + 5a	–	40/60
		2b (R = Et)	3b	4b + 5b	6b	44/56
		2c (R = *i*Pr)	3c	4c + 5c	–	52/48
2	1	7 CH_3-$CH(COOEt)_2$	8	9 + 10a + 10b	–	3/97
3	1	11 $CH_2(COMe)COOMe$	12	13	14	60/40
4	1	15 $CH_2(COMe)_2$	16	17	18 + 19	80/20
5	1	20 $CH_2(CN)_2$	21	22	–	15/85
6	23a *R*S**	2a	$24a_1$	25a	–	75/25
		2b	24b	25b	26 + 27a *R*S** + 27b *R*S**	75/25
7	23b *R*R**	2a	$24a_2$	–	27a *R*R**	100/0
8	28 *R*R** + *R*S**	2a	29 + 30	–	31a	100/0
9	28 *R*R** + *R*S**	32 $CH_2(COMe)CO_2Et$	–	–	33 + 31b	–
10	34a *R*S**	2a	35	36a	37a	20/80
11	34b *R*R**	2a	–	36b + 39	37b + 38	0/100
12	40	2a	41	42	–	75/25
13	40	15	43	–	44	–
14	45	2a	46 + 47	48	–	75/25
15	47	11	49	–	–	100/0

chemical shift value of methylene protons H^5 ($\delta > 3.5$ ppm) and the value of $J_{H3\text{-}H4} = 8.8$ Hz [19].

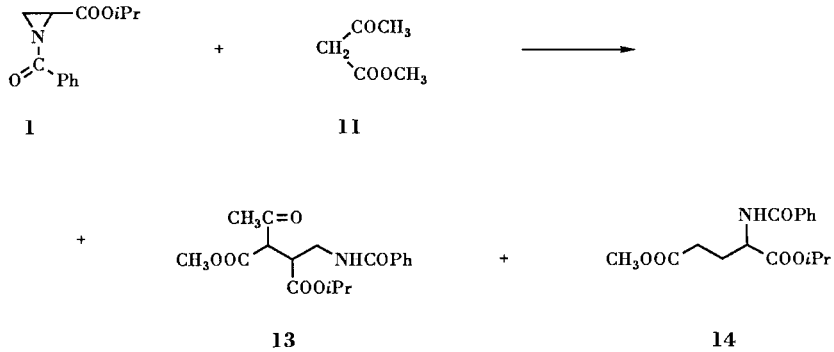
Under the same conditions, the carbanion of diethyl 2-methylmalonate **7** cleaves aziridine **1** very predominantly (97%) between C-2–N (Scheme 2); the most part of the aminoester **9** is cyclised in two isomers of the pyrrolidone **10** with a ratio of 50/50; contrary to precedent reactions the cyclised product **10** gives rise to N–C bond basic cleavage.

The reaction of aziridine **1** with methyl acetylacetate **11** (Scheme 3) gives exclusively the two opening products **12** and **13** with a ratio of 60/40, 5% of **1** is recovered unreacted.

An increase of the heating time (24 hours) gives rise to the formation of the ketonic cleavage product **14**.

A complex mixture is obtained in the reaction of the aziridine **1** with acetylacetone **15** (Scheme 4), four products have been separated by column chromatography: the

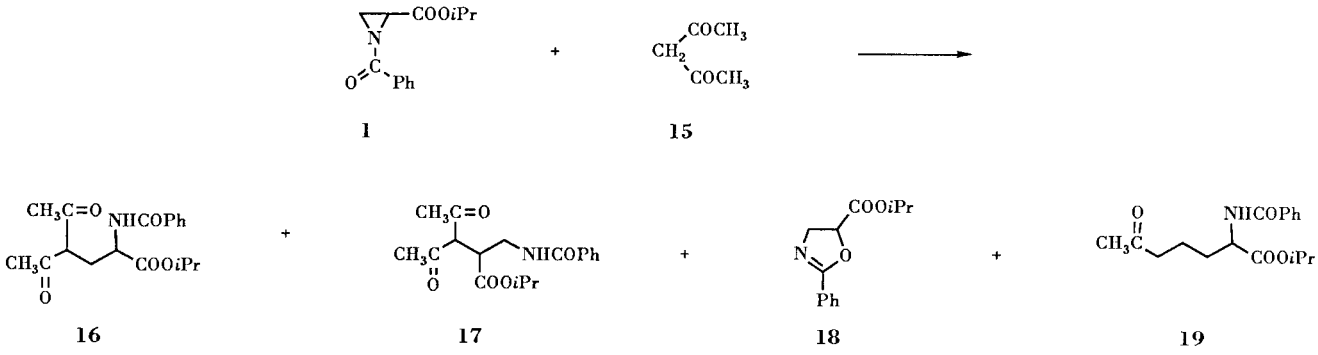
Scheme 3



1 11

12 13 14

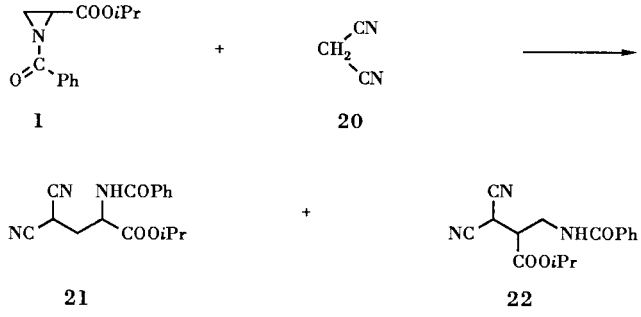
Scheme 4



derivatives **16** and **17** respectively resulting from aziridine cleavage between C-3-N and C-2-N, the oxazoline **18** rearrangement product of the aziridine **1**, and the product **19** resulting from cleavage basic of **16**; these results correspond to a cleavage ratio of C-3-N/C-2-N = 80/20.

An opposite regioselectivity is observed in the reaction of malononitrile with the aziridine **1** (Scheme 5); the cleavage C-2-N product **22** is predominantly formed (C-3-N/C-2-N = 15/85).

Scheme 5

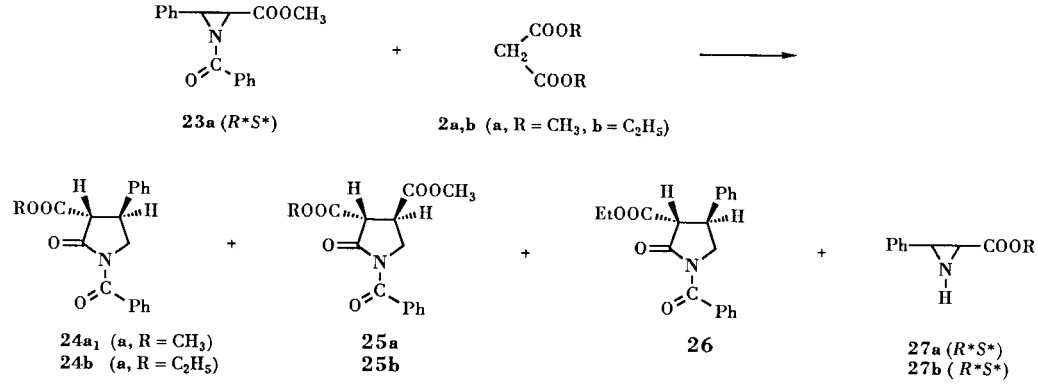


The two isomers *R*S** and *R*R** of 1-benzoyl-2-methoxycarbonyl-3-phenylaziridine **23** have been treated separately. Aziridine **23a** *R*S** reacts with alkyl malonylmalonates (Scheme 6) to give the two pyrrolidones **24** and **25** respectively formed by cyclisation of non isolated ring-opening products of C-3-N and C-2-N; the reaction is not total, a third of **23a** *R*S** is unreacted. With ethyl malonate **2b** the pyrrolidone **24b** is partly *trans*-esterified into **26** and a part (1/3) of **23a** is cleaved at the benzoyl group to give the non-substituted aziridines **27a** *R*S** and **27b** *R*S**; the ring-opening is regioselective: C-3-N/C-2-N = 75/25.

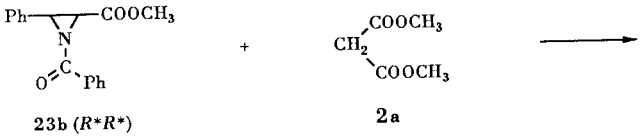
One product **24a$_2$** is only formed in the reaction between the aziridine **23b** *R*R** and methyl malonate **2a** (Scheme 7) but once again the reaction is not total; 25% of **23b** *R*R** is unreacted. The cleavage of starting aziridine **23b** at the benzoyl group leads to aziridine **27a** *R*R**.

More difficult is the reaction of *N*-non-activated aziridine **28** *R*R** + *R*S** with methyl malonate **2a** (Scheme 8). After refluxing for 4 hours in THF, **28** is unreacted; after 72 hours a complex mixture is obtained from which two solids are isolated by column chromatography. Their structures **29** and **30** have been established by ^{1}H and ^{13}C-nmr. In this reaction, unlike the others, the cyclised product formed from C-3-N bond-opening is dehydrogenized; 50% of the aziridine **28** have been recovered. Aminoester **31a**, the thermolysis product of **28**, is found as by-product.

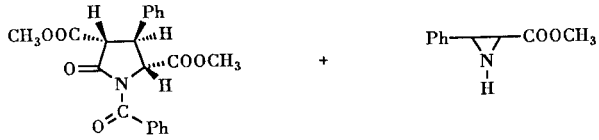
Scheme 6



Scheme 7

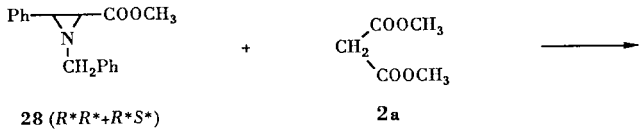


23b (R^*R^*) 2a

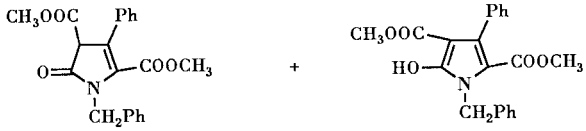


$24a_2$ 27a (R^*R^*)

Scheme 8



28 (R^*R^*+R^*S^*) 2a



29 30

+

$PhCH_2NHCH_2COOCH_3$

31a

The carbanion of ethyl acetylacetate **32** reacted with aziridine **28** $R^*R^* + R^*S^*$ to afford only a *trans*-esterified aziridine **33** accompanied by a thermolysis product **31b** (Scheme 9).

The benzyl-2-methoxycarbonylaziridine was found to be a less reactive substrate than the aziridine **28**, no reactions have been observed with methylmalonate.

The two isomers R^*S^* and R^*R^* of the aziridine **34** have been separately studied.

The aziridine **34** R^*S^*, reacting with methyl malonate **2a** (Scheme 10), gives three products separated by column chromatography; their structure of the pyrrolidone is based on ^1H and ^{13}C nmr spectra; the pyrrolidones **35** and **36a** are formed by cyclisation of the two non isolated ring-opening products of C-3-N and C-2-N bonds, **37a** by *trans*-esterification of **36a** or of its precursor. In this reaction the cleavage is regioselective and opposite of this of aziridine **23a** R^*S^*; moreover, the configuration of the carbons 2 and 3 is the same as in the pyrrolidones. The ratio C-3-N/C-2-N is 20/80.

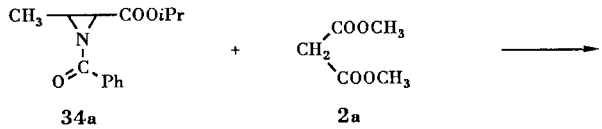
Four compounds **36b**, **37b**, **38**, and **39** result from the reaction of the aziridine **34b** R^*R^* with methyl malonate **2a** (Scheme 11); all are formed by C-2-N bond-cleavage, the normal products **36b** and **39** are partly *trans*-esterified to give **37b** and **38** so the reaction is regiospecific.

Two cyanoaziridines **40** and **45** have been studied. The reaction of **40** with methyl malonate **2a** is only regioselective with a predominant ring-opening of the C-3-N bond (Scheme 12).

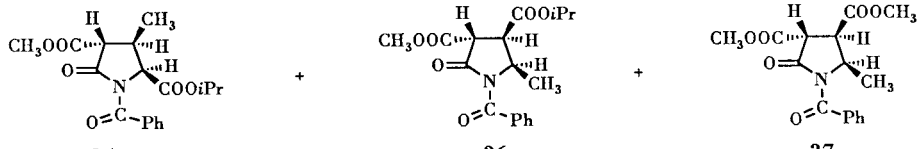
Scheme 9

28 (R^*R^*+R^*S^*) 32 33 31b

Scheme 10

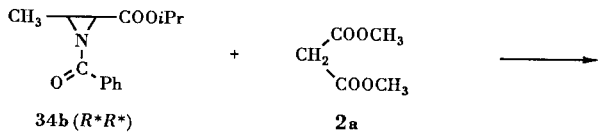


34a 2a

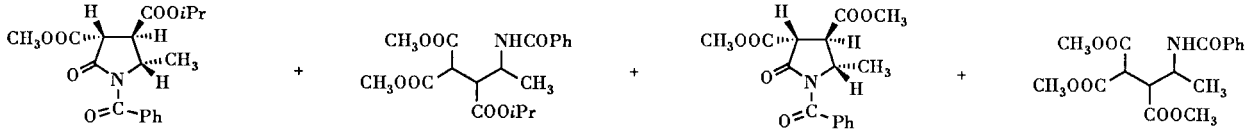


35 36a 37a

Scheme 11

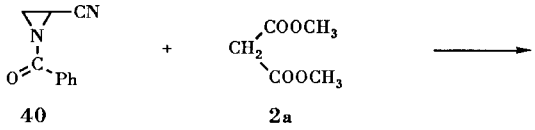


34b (R^*R^*) 2a



36b 39 37b 38

Scheme 12



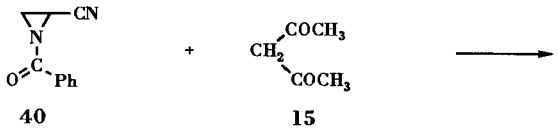
40 2a

41 42

The carbanion of acetylacetone **15** opens the cyanoaziridine **40** (Scheme 13) regiospecifically to give the product resulting of C-3-N bond opening **43**. This last one, in basic media, is partly cleaved leading to **44**.

In these two last reactions the pyrrolidones formation is not observed.

Scheme 13

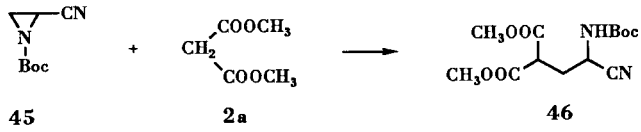


40 15

43 44

In the reaction realised with 1-carbo-*tert*-butoxy-2-cyanoaziridine **45** the results are comparable to the previous one; the substrate is ring-opened highly selectively by methyl malonate **2a** (Scheme 14) or regiospecifically by ethyl acetylacetate **11** (Scheme 15).

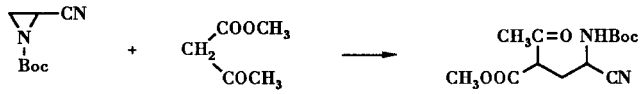
Scheme 14



45 2a 46

48 47

Scheme 15



45 11 49

Conclusion. Our results call for some remarks.

(1) Nucleophilic ring-openings of aziridinecarboxylate esters or aziridinenitriles are slow reactions, even when the ring is *N*-activated; in several studies cases, a significant amount of the aziridine is unreacted; consequently a part of the nucleophilic reagent will give by-products of autocondensation (Claisen products) and sometimes aziridine can be partly isomerised (oxazoline).

(2) The regioselectivity of the ring-opening depends on several factors. A phenyl group on C-3 increases the ability of this carbon to overlap a positive charge favouring C-3-N bond cleavage. In contrast, the cleavage C-2-N is predominant with methyl C-3-substituted-aziridines or C-3-H aziridines because of the most electrophilic character of C-2.

Cyanoaziridines are predominantly cleaved at the C-3-N bond; this result, the justification of which is most difficult, confirms other observations on the comparative reactivity of cyano and carboalkoxyaziridines.

(3) The aziridine configuration at C-2 and C-3 is maintained during the cyclisation in pyrrolidones.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded with a Perkin-Elmer 157 spectrometer. The nmr spectra were measured using tetramethylsilane as the internal standard with a Varian T 60, Bruker 1200 (200 MHz), and a JEOL FX spectrometer.

Starting aziridines were prepared according to known methods in the literature [1]. *N*-Benzoylaziridines were prepared according to the Schotten-Baumann's method: These are 1-benzoyl-2-isopropyloxycarbonyl **1** from isopropyloxycarbonylaziridine [19]; 1-benzoyl-2-methoxycarbonyl-3-phenylaziridine **23a-b** from 2-methoxycarbonyl-3-phenylaziridine *R*R** and *R*S** [20,21]; 1-benzoyl-2-isopropyloxycarbonyl-3-methylaziridine **34a-b** from 2-isopropyloxycarbonyl-3-methylaziridine [19-21]; 1-benzoyl-2-cyanoaziridine **40** from 2-cyanoaziridine [22].

1-Benzyl-2-methoxycarbonyl-3-phenyl **28** was prepared from methyl-2-bromoprop-2-enoate according to [16,23]; the two isomers of **28** were obtained in a ratio **28a/28b** = 90/10.

1-Carbo-*tert*-butoxy-2-cyanoaziridine **45** was prepared from cyanoaziridine according to [2,22].

Reaction of Aziridines **1**, **23a-b**, **28a-b**, **34a-b**, **40**, and **45** with Active Methylene Compounds.

General Procedure According to [20].

Alkyl malonate (2 equivalents) was added dropwise to a stirred suspension of sodium hydride (2.5 equivalents) in tetrahydrofuran (30 ml) and hexamethylphosphoric triamide (3 ml). The stirring was continued until evolution of gas ceased. A solution of aziridine (1 equivalent) in THF (10 ml) was then added, and the mixture was refluxed for 4 hours. After removal of the THF *in vacuo*; the residue was poured into ice water, and then extracted with ether (4 x 200 ml); the aqueous layer was then acidified with hydrochloride acid to *p*H 4. The mixture was extracted twice with ether (2 x 100 ml); the organic layers were dried over magnesium sulfate and evaporated to give crude product. Products were isolated by silica gel column chromatography.

Reaction of 1-Benzoyl-2-isopropyloxycarbonylaziridine **1** with Dimethylmalonate **2a**.

The reaction was carried out with aziridine **1** (5 g, 22 mmoles) and the crude product was purified with hexane/ethyl acetate 95/5 to give: **5a** (0.6 g, 9%), **3a** (1.4 g, 18%) and **4a** (1.3 g, 17%) respectively.

Methyl 4-(Benzoylamino)-4-isopropylcarbonyl-2-methoxycarbonylbutanoate (**3a**).

This compound was obtained as a solid, mp 53-54°; ^{1}H-nmr (deuteriochloroform): δ 1.31 (d, 6H, $CH(CH_3)_2$, J = 6), 2.21-2.89 (m, 2H, CH_2), 3.58 (t, 1H, $CH(COO)_2$, J = 7), 3.68 (s, 3H, $COOCH_3$), 3.75 (s, 3H, $COOCH_3$), 4.71-4.96 (m, 1H, CH(CO)NH), 4.83-5.28 (hept, 1H, $CH(CH_3)_2$), 7.0 (sb, 1H, NH), 7.38-7.85 (m, 5H, Ph).

Anal. Calcd. for $C_{18}H_{23}NO_7$: C, 59.17; H, 6.30; N, 3.83; O, 30.68. Found: C, 59.31; H, 6.69; N, 3.81; O, 30.88.

Methyl 4-(Benzoylamino)-3-isopropyloxycarbonyl-2-methoxycarbonylbutanoate (**4a**).

This compound was obtained as a solid, mp 86-87°; ^{1}H-nmr (deuteriochloroform): δ 1.25 (d, 6H, $CH(CH_3)_2$, J = 6), 3.23-3.60 (m, 2H, CH_2), 3.70 (s, 3H, $COOCH_3$), 3.76 (s, 3H, $COOCH_3$), 3.90 (d, 1H, $CH(COO)_2$), 4.83-5.26 (hept, 1H, $CH(CH_3)_2$), 6.90 (sb, 1H, NH), 7.30-7.86 (m, 5H, Ph).

Anal. Calcd. for $C_{18}H_{23}NO_7$: C, 59.17; H, 6.30; N, 3.83; O, 30.68. Found: C, 59.25; H, 6.42; N, 3.91; O, 30.46.

N-Benzoyl-3-methoxycarbonyl-4-isopropyloxycarbonyl-2-pyrrolidone (**5a**).

This compound was obtained as a solid, mp 109-111°; ^{1}H-nmr (deuteriochloroform): δ 1.27 (d, 6H, $CH(CH_3)_2$, J = 6), 3.75 (dd, 1H, H4, $J_{H3\text{-}H4}$ = 8.8, $J_{H4\text{-}H5a}$ = 7.5), 3.80 (s, 3H, $COOCH_3$), 3.99 (d, 1H, H3, $J_{H4\text{-}H3}$ = 8.8), 4.00 (t, 1H, H5, $J_{H5a\text{-}H5b}$ = 11.5), 4.29 (dd, 1H, H5, $J_{H5b\text{-}H4}$ = 9, $J_{H5a\text{-}H5b}$ = 11.5), 4.83-5.28 (hept, 1H, $CH(CH_3)_2$), 7.30-7.60 (m, 5H, Ph).

Anal. Calcd. for $C_{17}H_{19}NO_6$: C, 61.26; H, 5.70; N, 4.20; O, 28.82. Found: C, 61.17; H, 5.78; N, 4.02; O, 28.20.

Reaction of 1-Benzoyl-2-isopropyloxycarbonylaziridine **1** with Diethyl Malonate **2b**.

The reaction was carried out with aziridine **1** (7 g, 30 mmoles), the crude product was eluted with hexane/ethyl acetate 95/5 to give **5b** (0.7 g, 7%), **3b** (2.6 g, 22%), **4b** (2.4 g, 20%) and **6b** (0.15 g, 2%) respectively.

Ethyl 4-(Benzoylamino)-2-ethoxycarbonyl-4-isopropyloxycarbonylbutanoate (**3b**).

This compound was obtained as a solid, mp 42-43°; ^{1}H-nmr (deuteriochloroform): δ 1.26 (t, 3H, CH_3, J = 8), 1.30 (d, 6H, $(CH_3)_2$, J = 6), 2.20-2.90 (m, 2H, CH_2), 3.56 (t, 1H, $CH(COO)_2$, J = 7), 4.12 (q, 2H, CH_2, J = 8), 4.13 (q, 2H, CH_2, J = 8), 4.70-4.96 (m, 1H, CH(COO)NH), 4.80-5.30 (m, 1H, $CH(CH_3)_2$), 7.06 (sb, 1H, NH), 7.36-7.93 (m, 5H, Ph).

Anal. Calcd. for $C_{20}H_{27}NO_7$: C, 61.06; H, 6.87; N, 3.56. Found: C, 61.13; H, 7.04; N, 3.49.

Ethyl 4-(Benzoylamino)-2-ethoxycarbonyl-3-isopropyloxycarbonylbutanoate (**4b**).

This compound was obtained as a solid, mp 50-52°; ^{1}H-nmr (deuteriochloroform): δ 1.26 (d, 6H, $(CH_3)_2$, J = 6), 1.80 (t, 3H, CH_3, J = 8), 3.23-3.93 (3m, 4H), 4.23 (q, 2H, CH_2, J = 8), 4.83-5.26 (hept, 1H, $CH(CH_3)_2$), 7.08 (sb, 1H, NH), 7.35-7.93 (m, 5H, Ph).

Anal. Calcd. for $C_{20}H_{27}NO_7$: C, 61.06; H, 6.87; N, 3.56. Found: C, 61.19; H, 6.89; N, 3.60.

N-Benzoyl-3-ethoxycarbonyl-4-isopropyloxycarbonyl-2-pyrrolidone (**5b**).

This compound was obtained as a solid, mp 64°; ^{1}H-nmr (deuteriochloroform): δ 1.1-1.4 (m, 9H, CH_3 and $(CH_3)_2$), 3.60-4.46 (m, 4H), 4.23 (q, 2H, CH_2, J = 6.8), 4.86-5.28 (hept, 1H, $CH(CH_3)_2$), 7.23-7.76 (m, 5H, Ph).

Anal. Calcd. for $C_{18}H_{21}NO_6$: C, 62.24; H, 6.00; N, 4.00. Found: C, 62.22; H, 6.31; N, 3.98.

Ethyl 4-(Benzoylamino)-2,3-diethoxycarbonylbutanoate (**6b**).

This compound was obtained as a liquid and characterized only by its ^{1}H-nmr spectrum; ^{1}H-nmr (deuteriochloroform): δ 1.33 and 1.36 (2t, 9H, $3CH_3$, J = 7), 3.33-3.36 (m, 1H), 3.76-4.06 (m, 3H, CH_2 and CH), 4.06-4.46 (m, 6H, $3CH_2$), 6.93 (sb, 1H, NH), 7.36-7.86 (m, 5H, Ph).

Reaction of 1-Benzoyl-2-isopropyloxycarbonylaziridine **1** with Diisopropyl Malonate **2c**.

The reaction was carried out with aziridine **1** (7 g, 30 mmoles). The crude product was purified with hexane/ethyl acetate 95/5 to give **5c** (0.7 g, 6.5%), **3c** (3.8 g, 30%) and **4c** (2.6 g, 21%) respectively.

Isopropyl 2-(Benzoylamino)-2,4-diisopropyloxycarbonylbutanoate (**3c**).

This compound was obtained as a solid, mp 50-52°; ^{1}H-nmr (deuteriochloroform): δ 1.23 (d, 6H, $CH(CH_3)_2$, J = 6), 2.06-2.86 (m, 2H, CH_2), 3.50 (t, 1H, $CH(COO)_2$, J = 7), 4.66-5.00 (m, 4H), 7.00 (sb, 1H, NH), 7.37-7.93 (m, 5H, Ph).

Anal. Calcd. for $C_{22}H_{31}NO_7$: C, 62.70; H, 7.36; N, 3.32; O, 26.60. Found: C, 62.56; H, 7.46; N, 3.24; O, 26.50.

Isopropyl 4-(Benzoylamino)-2,3-diisopropyloxycarbonylbutanoate (**4c**).

This compound was obtained as a solid, mp 82-83°; ^{1}H-nmr (deuteriochloroform): δ 1.26 (d, 18H, $3(CH_3)_2$, J = 6), 3.16-3.53 (m, 2H, CH_2), 3.70-3.90 (m, 2H), 4.80-5.28 (hept, 3H), 6.90 (sb, 1H, NH), 7.26-7.86 (m, 5H, Ph).

Anal. Calcd. for $C_{22}H_{31}NO_7$: C, 62.70; H, 7.36; N, 3.32; O, 26.60. Found: C, 62.43; H, 7.49; N, 3.24; O, 26.62.

N-Benzoyl-3,4-diisopropyloxycarbonyl-2-pyrrolidone (**5c**).

This compound was obtained as a solid, mp 65-67°; ^{1}H-nmr (deuteriochloroform): δ 1.30 (d, 12H, $2(CH_3)_2$, J = 6), 3.63-4.30 (m, 4H), 4.93-5.33 (hept, 2H), 7.26-7.66 (m, 5H, Ph).

Anal. Calcd. for $C_{19}H_{23}NO_6$: C, 63.15; H, 6.41; N, 3.88. Found: C, 63.54; H, 6.38; N, 3.52.

Reaction of 1-Benzoyl-2-isopropyloxycarbonylaziridine **1** with Diethyl 2-Methylmalonate **7**.

The reaction was carried out with aziridine **1** (5 g, 21 mmoles). Four compounds were separated with hexane/ethyl acetate 95/5: **8** (0.15 g, 2%), **9** (0.15 g, 2%), **10a** (0.7 g, 13%) and **9b** (0.7 g, 13%) respectively.

Isopropyl 2-(Benzoylamino)-4,4-diethoxycarbonylpentanoate (**8**).

This compound was a liquid; ^{1}H-nmr (deuteriochloroform): δ 1.03-1.06 (m, 15H), 2.20-2.76 (m, 2H, CH_2), 4.20 (q, 4H, J = 7), 4.56-5.00 (m, 1H, CHN), 4.81-5.23 (hept, 1H), 6.86-7.06 (m, 1H, NH), 7.30-8.06 (m, 5H, Ph).

Isopropyl 2-(Benzoylaminomethyl)-3,3-diethoxycarbonylbutanoate (**9**).

This compound was a liquid; ^{1}H-nmr (deuteriochloroform): δ 1.10-1.86 (m, 15H), 3.33-3.60 (m, 2H, CH_2), 3.66-4.00 (m, 1H, CH), 4.06-4.40 (m, 4H), 4.85-5.28 (hept, 1H), 6.96 (sb, 1H, NH), 7.33-7.90 (m, 5H, Ph).

3-Ethoxycarbonyl-4-isopropyloxycarbonyl-3-methyl-2-pyrrolidone (**10a**).

This compound was a liquid; ^{1}H-nmr (deuteriochloroform): δ 1.20-1.40 (m, 9H), 1.43 (s, 3H, CH_3), 3.50-4.00 (m, 3H, H5a, H5b, H4), 4.30 (q, 2H, J = 6.8), 4.83-5.26 (hept, 1H), 7.68 (sb, 1H, NH); ^{13}C-nmr: 176.0, 170.9, 169.3, 69.0, 61.6, 53.6 (C3), 48.1 (C5), 40.6 (C4), 21.7, 14.6, 14.1.

Anal. Calcd. for $C_{12}H_{19}NO_5$: C, 56.03; H, 7.39; N, 5.44; O, 31.12. Found: C, 55.14; H, 7.23; N, 5.27; O, 31.27.

3-Ethoxycarbonyl-4-isopropyloxycarbonyl-3-methyl-2-pyrrolidone (**10b**).

This compound was a liquid; ^{1}H-nmr (deuteriochloroform): δ 1.10-1.50 (m, 9H), 1.58 (s, 3H, CH_3), 3.18 (dd, 1H, H4, $J_{H4\text{-}H5a}$ = 8, $J_{H4\text{-}H5b}$ = 10), 3.66 (d, 2H, J_{gem} = 16.8, H5a, H5b), 4.16 (q, 2H, J = 6.8), 4.83-5.23 (hept, 1H), 7.66 (sb, 1H, NH); ^{13}C-nmr: 175.1, 169.9, 169.6, 68.8, 61.6, 53.6 (C3), 50.7 (C5), 42.0 (C4), 21.7, 14.6, 13.9.

Anal. Calcd. for $C_{12}H_{19}NO_5$: C, 56.03; H, 7.39; N, 5.41; O, 31.12. Found: C, 55.84; H, 7.31; N, 5.41; O, 31.14.

Reaction of 1-Benzoyl-2-isopropyloxycarbonylaziridine **1** with Methyl Acetylacetate **11**.

The reaction was carried out with aziridine **1** (5 g, 22 mmoles) with a reflux for 4 hours. The crude product, purified with hexane/ethyl acetate 75/25, gave two compounds **12** (2.6 g, 35%) and **13** (1.65 g, 25%).

When the reaction mixture was refluxed for 24 hours, three products were obtained: **12**, **13** (**12** + **13** = 49%) and **14** (10%).

Isopropyl 2-(Benzoylamino)-4-methoxycarbonyl-5-oxopentanoate (**12**).

This compound was obtained as a solid, mp 72-73°; ^{1}H-nmr (deuteriochloroform): δ 1.30 (d, 6H, J = 6), 2.26 (s, 3H, $COCH_3$), 1.93-2.56 (m, 2H, CH_2), 3.71 (s, 3H, CO_2CH_3), 3.73 (t, 1H, J = 6), 4.53-4.83 (m, 1H), 4.83-5.26 (hept, 1H), 6.90-7.03 (m, 1H, NH), 7.36-7.90 (m, 5H, Ph); ^{13}C-nmr: 202.1, 170.8, 169.5, 167.1, 133.2-126.8, 69.6, 55.8, 52.4, 50.8, 30.1, 29.3, 21.4.

Anal. Calcd. for $C_{18}H_{23}NO_6$: C, 61.89; H, 6.59; N, 4.01; O, 27.50. Found: C, 61.95; H, 6.49; N, 4.06; O, 27.50.

Isopropyl 2-(Benzoylaminomethyl)-3-methoxycarbonyl-4-oxopentanoate (**13**).

This compound was obtained as a solid, mp 70°; ^{1}H-nmr (deuteriochloroform): δ 1.27 (d, 6H, J = 6), 2.33 (s, 3H, $COCH_3$), 3.36-3.91 (m, 3H), 3.71 (s, 3H, $COOCH_3$), 4.00 (d, 1H, J = 8), 4.83-5.28 (hept, 1H), 6.85 (sb, 1H, NH), 7.36-7.83 (m, 5H, Ph).

Anal. Calcd. for $C_{18}H_{23}NO_6$: C, 61.89; H, 6.59; N, 4.01; O, 27.50. Found: C, 61.60; H, 6.47; N, 4.14; O, 27.27.

Isopropyl 2-(Benzoylamino)-4-methoxycarbonylbutanoate (**14**).

This compound was obtained as a solid, mp 74-75°; ^{1}H-nmr (deuteriochloroform): δ 1.30 (d, 6H, J = 6), 2.06-2.66 (m, 4H), 3.66 (s, 3H, OCH_3), 4.66-5.30 (m, 2H), 7.16 (sb, 1H, NH), 7.33-7.96 (m, 5H, Ph); ^{13}C-nmr: 173.6, 171.5, 167.2, 133.9-127.1, 69.5, 52.4, 51.8, 30.2, 27.4, 21.7.

Anal. Calcd. for $C_{16}H_{21}NO_5$: C, 62.54; H, 6.84; N, 4.56; O, 26.05. Found: C, 62.30; H, 6.77; N, 4.30; O, 26.15.

Reaction of 1-Benzoyl-2-isopropyloxycarbonylaziridine **1** with Acetylacetone **15**.

The reaction was carried out with aziridine **1** (7 g, 30 mmoles) and the reaction was refluxed for 6 hours. The crude product was purified with hexane/ethyl acetate 75/25 to give four compounds:

18 (0.4 g, 8%), **16** (2.8 g, 30%), **17** (0.9 g, 9%) and **19** (0.6 g, 7%) respectively.

Isopropyl 2-(Benzoylamino)-4-acetyl-5-oxohexanoate (**16**).

This compound was obtained as a solid, mp 98°; ^{1}H-nmr (deuteriochloroform): δ 1.20 (d, 6H, J = 6), 2.16 (s, 3H, $COCH_3$), 2.25 (s, 3H, $COCH_3$), 2.33-2.90 (m, 2H, CH_2), 3.96 (t, 1H, J = 7), 4.53-5.50 (m, 1H), 4.83-5.20 (hept, 1H), 6.83 (sb, 1H, NH), 7.30-7.86 (m, 5H, Ph).

Anal. Calcd. for $C_{18}H_{23}NO_5$: C, 64.86; H, 6.90; N, 4.20; O, 24.02. Found: C, 64.85; H, 6.93; N, 4.33; O, 24.06.

Isopropyl 2-(Benzoylamino)-4-acetyl-5-oxohexanoate (**17**).

This compound was obtained as a solid, mp 80-82°; ^{1}H-nmr (deuteriochloroform): δ 1.26 (d, 6H, J = 6), 2.30 (s, 6H, $COCH_3$), 3.30-3.80 (m, 2H), 4.20 (d, 1H, J = 8), 4.83-5.23 (hept, 1H), 6.83 (sb, 1H, NH), 7.33-7.86 (m, 5H, Ph).

Anal. Calcd. for $C_{18}H_{23}NO_5$: C, 64.86; H, 6.90; N, 4.20; O, 24.02. Found: C, 64.98; H, 6.99; N, 4.07; O, 23.75.

5-Isopropyloxycarbonyl-2-phenylΔ^2-oxazoline (**18**).

This compound was obtained as a solid, mp 66-67°; ^{1}H-nmr (deuteriochloroform): δ 1.30 (d, 6H, J = 6), 4.2-5.0 (m, 4H), 7.30-7.90 (m, 5H, Ph); ^{13}C-nmr: 170.16, 164.18, 128.40, 75.95, 69.45, 59.45, 21.70.

Anal. Calcd. for $C_{13}H_{15}NO_3$: C, 66.95; H, 6.40; N, 6.01; O, 20.60. Found: C, 66.80; H, 6.40; N, 6.12; O, 20.68.

Isopropyl 2-(Benzoylamino)-5-oxohexanoate (**19**).

This compound was obtained as a solid, mp 60-61°; ^{1}H-nmr (deuteriochloroform): δ 1.30 (d, 6H, J = 6), 2.15 (s, 3H, CH_3CO), 1.80-2.80 (2m, 4H), 4.00-4.83 (m, 1H), 4.83-5.30 (hept, 1H), 7.13 (sb, 1H, NH), 7.30-7.93 (m, 5H, Ph); ^{13}C-nmr: 208.3, 171.6, 167.3, 133.8-127.1, 69.5, 52.4, 39.6, 30.0, 26.0, 21.5.

Anal. Calcd. for $C_{16}H_{21}NO_4$: C, 65.97; H, 7.21; N, 4.81; O, 21.99. Found: C, 66.26; H, 7.21; N, 4.58; O, 22.04.

Reaction of 1-Benzoyl-2-isopropyloxycarbonylaziridine **1** with Malononitrile **20**.

The reaction was carried out with aziridine **1** (3.5 g, 15 mmoles). The crude product was purified with hexane/ethyl acetate 90/10 to give two compounds **21** (0.15 g, 3%) and **22** (0.85 g, 19%) respectively.

Isopropyl 2-(Benzoylamino)-4,4-dicyanobutanoate (**21**).

This compound was obtained as a liquid; ^{1}H-nmr (deuteriochloroform): δ 1.33 (d, 6H, J = 6), 2.20-3.03 (m, 2H, CH_2), 4.20 (t, 1H, J = 7), 4.73-5.46 (m, 2H), 7.32-7.66 (sb, 1H, NH), 7.60-8.06 (m, 5H, Ph).

Isopropyl 2-(Benzoylaminomethyl)-3,3-dicyanopropanoate (**22**).

This compound was obtained as a solid, mp 98-99°; ^{1}H-nmr (deuteriochloroform): δ 1.26 (d, 6H, J = 6), 3.50-3.80 (m, 2H), 4.96 (d, 1H, J = 4.8), 4.80-5.43 (hept, 1H), 7.40-8.04 (m, 5H, Ph), 8.2 (sb, 1H, NH); ^{13}C-nmr (acetone-d_6): 173.1, 172.7, 139.5-132.3, 124.7, 124.4, 75.0, 50.69, 44.1, 28.0, 26.0.

Anal. Calcd. for $C_{16}H_{17}N_3O_3$: C, 64.21; H, 5.68; N, 14.04; O, 16.05. Found: C, 63.93; H, 5.68; N, 14.30; O, 16.04.

Reaction of *R*S** 1-Benzoyl-2-methoxycarbonyl-3-phenylaziridine **23a** with Methyl Malonate **2a**.

The reaction was carried out with aziridine **23a** *R*S** (4.22 g, 15 mmoles). The reaction mixture was refluxed 6 hours in tetrahydrofuran. The crude product was purified with hexane/ethyl acetate 90/10 to give **24a$_1$** (1.5 g, 27%) and **25a** (0.5 g, 9%) respectively.

N-Benzoyl-3,5-dimethoxycarbonyl-4-phenyl-2-pyrrolidone (**24a$_1$**).

This compound was obtained as a solid, mp 111-112°; ^{1}H-nmr (deuteriochloroform): δ 3.65-3.88 (m, 1H, H), 3.71 (s, 3H, $COOCH_3$), 3.72 (s, 3H, $COOCH_3$), 4.08 (dd, 1H, J_{H4-H3} = 9, J_{H4-H5} = 7.5), 5.01 (d, 1H, J = 7.5), 7.45-8.12 (m, 10H, Ph); ^{13}C-nmr: 170.3, 169.3, 167.5, 137.6-127.2, 63.8, 57.0, 53.2, 52.8, 44.5.

Anal. Calcd. for $C_{21}H_{19}NO_6$: C, 66.14; H, 4.98; N, 3.67; O, 25.19. Found: C, 66.03; H, 4.93; N, 3.63; O, 25.10.

N-Benzoyl-3,4-dimethoxycarbonyl-5-phenyl-2-pyrrolidone (**25a**).

This compound was obtained as a solid, mp 130-132°; ^{1}H-nmr (deuteriochloroform): δ 3.37 (d, 1H, H3, J_{H3-H4} = 9), 3.77 (s, 3H, CO_2CH_3), 3.88 (s, 3H, CH_3), 3.93 (dd, 1H, H4, J_{H4-H3} = 9, J_{H4-H5} = 7.5), 5.57 (d, 1H, H5, J_{H5-H4} = 7.5), 7.42-8.02 (m, 10H, Ph); ^{13}C-nmr: 170.5, 169.4, 167.9, 167.4, 133.8-127.4, 61.5, 53.2, 52.7, 52.5, 48.2.

Anal. Calcd. for $C_{21}H_{19}NO_6$: C, 66.14; H, 4.98; N, 3.67; O, 25.19. Found: C, 65.70; H, 4.17; N, 3.63; O, 24.74.

Reaction of *R*S** 1-Benzoyl-2-methoxycarbonyl-3-phenylaziridine **23a** with Ethyl Malonate **2b**.

The reaction was carried out with aziridine **23a** *R*S** (6 g, 21 mmoles). The reaction mixture was refluxed 6 hours in tetrahydrofuran. The crude product was purified with hexane/ethyl acetate 10/90 to give five products: **24b** and **25b** (2.1 g, 24%), **26** (1.5 g, 17%), **27a** *R*S** (0.5 g, 16%), **27b** *R*S** (0.9 g, 22%) respectively. The two isomers **24b** + **25b** were obtained as a solid product in a 63/37 ratio calculated from ^{1}H-nmr; they were not separated.

N-Benzoyl-3-ethoxycarbonyl-5-methoxycarbonyl-4-phenyl-2-pyrrolidone (**24b**).

This compound had ^{1}H-nmr (deuteriochloroform): δ 1.23 (t, 3H, CH_3, J = 6), 3.73 (s, 3H, $COOCH_3$), 3.76 (d, 1H, H3, J_{H3-H4} = 8.5), 3.93-4.55 (m, 3H), 5.03 (d, 1H, H5, J_{H5-H4} = 7.5), 7.40-7.90 (m, 10H, Ph).

N-Benzoyl-3-ethoxycarbonyl-4-methoxycarbonyl-5-phenyl-2-pyrrolidone (**25b**).

This compound had ^{1}H-nmr (deuteriochloroform): δ 1.26 (t, 3H, CH3, J = 7), 3.73 (s, 3H, $COOCH_3$), 3.74-4.46 (m, 4H), 5.55 (d, 1H, H5, J_{H5-H4} = 7.5), 7.26-7.86 (m, 10H, Ph).

Anal. Calcd. for (**24b** + **25b**) $C_{22}H_{21}NO_6$: C, 66.83; H, 5.31; N, 3.54; O, 24.30. Found: C, 66.79; H, 5.42; N, 3.49; O, 24.02.

N-Benzoyl-3,5-diethoxycarbonyl-4-phenyl-2-pyrrolidone (**26**).

This compound was obtained as a solid, mp 123-124°; ^{1}H-nmr (deuteriochloroform): δ 1.25 (t, 6H, J = 7), 3.76 (d, 1H, H3, J_{H3-H4} = 8.5), 3.96-4.43 (m, 5H), 5.01 (d, 1H, H5, J_{H5-H4} = 7.5), 7.40-7.88 (m, 10H, Ph).

Anal. Calcd. for $C_{23}H_{23}NO_6$: C, 67.48; H, 5.62; N, 3.42; O, 23.47. Found: C, 67.25; H, 5.32; N, 3.35; O, 23.68.

*R*S** 2-Methoxycarbonyl-3-phenylaziridine (**27a**).

This compound was obtained as a solid, mp 72-73°; ^{1}H-nmr (deuteriochloroform): δ 1.83 (sb, 1H, NH), 3.0 (d, 1H, H2, J = 6.6), 3.43 (d, 1H, H3, J = 6.6), 3.5 (s, 3H, $COOCH_3$), 7.30 (s, 5H, Ph).

Anal. Calcd. for $C_{10}H_{11}NO_2$: C, 67.79; H, 6.21; N, 7.90; O, 18.07. Found: C, 67.45; H, 6.29; N, 7.61; O, 18.34.

*R*S** 2-Ethoxycarbonyl-3-phenylaziridine (**27b**).

This compound was obtained as a solid, mp 62-63°; the ^{1}H-nmr data are the same as those described in the literature [21].

Reaction of *R*R** Benzoyl-2-methoxycarbonyl-3-phenylaziridine **23b** with Methyl Malonate **2a**.

The reaction was carried out with aziridine **23b** *R*R** (4.22 g, 15 mmoles). The reaction mixture was refluxed 6 hours in tetrahydrofuran. The crude product was purified with hexane/ethyl acetate 90/10 to give **24c** (0.9 g, 15%) and **27a** *R*R** (0.8 g, 30%) respectively.

N-Benzoyl-3,5-dimethoxycarbonyl-4-phenyl-2-pyrrolidone (**24c**).

This compound was obtained as a solid, mp 161-162°; ^{1}H-nmr (deuteriochloroform): δ 3.35 (s, 3H, CH_3), 3.76 (s, 3H, $COOCH_3$), 4.40 (d, 1H, H3, $J_{H3\text{-}H4}$ = 1.8), 4.41 (d, 1H, H5, J = 6.2), 5.05 (dd, 1H, H4, J = 1.8, J = 6.2, H4), 7.26-7.35 (m, 10H, Ph); ^{13}C-nmr: 168.8, 168.7, 167.5, 167.1, 138.1-126.6, 61.6, 52.1, 51.5, 51.2, 42.5.

Anal. Calcd. for $C_{21}H_{19}NO_6$: C, 66.14; H, 4.98; N, 3.83. Found: C, 66.15; H, 5.23; N, 3.60.

*R*R** 2-Methoxycarbonyl-3-phenylaziridine (**27a**).

This compound was obtained as a liquid; ^{1}H-nmr (deuteriochloroform): δ 1.95 (sb, 1H, NH), 2.58 (d, 1H, H2, J = 2.5), 3.25 (d, 1H, H3, J = 2.5), 3.75 (s, 3H, $COOCH_3$), 7.33 (s, 5H, Ph). The ^{1}H-nmr data are compared with those described in literature for 2-ethoxycarbonyl-3-phenylaziridine *R*R** [21].

Reaction of *R*R** + *R*S** Benzyl-2-methoxycarbonyl-3-phenylaziridine **28** with Methyl Malonate **2a**.

The reaction was carried out with a mixture of two isomers of the aziridine **28** *R*S**/*R*R** = 90/10 (9 g, 33 mmoles). The reaction mixture was refluxed 72 hours in tetrahydrofuan; the crude product was purified with hexane/ethyl acetate 90/10 to give **30** (1.8 g, 16%), a mixture of **30** and **29** (0.2 g, 2%) and **31a** respectively.

1-Benzyl-3,5-dimethoxycarbonyl-4-phenylpyrrolone (**29**).

This compound was not isolated; it was identified by its spectral data; ^{1}H-nmr (deuteriochloroform): δ 3.58 (s, 3H, $COOCH_3$), 3.65 (s, 3H, $COOCH_3$), 3.92 (s, 1H, C3-H), 5.00 (s, 2H, CH_2-N), 6.7-7.6 (m, 10H, Ph).

N-Benzyl-1-hydroxy-2,4-dimethoxycarbonyl-4-phenylpyrrole (**30**).

This compound was obtained as a solid, mp 116-117°; ^{1}H-nmr (deuteriochloroform): δ 3.62 (s, 3H, $COOCH_3$), 3.78 (s, 3H, $COOCH_3$), 5.40 (s, 2H, CH_2-N), 6.70-7.60 (m, 10H, Ph), 9.40 (s, 1H, OH); ^{13}C-nmr: 164.96, 160.74, 153.70, 141.05, 136.90-124.6, 105.2, 100.50, 50.09, 48.20; ir (deuteriochloroform): ν 1745 (COO), 1665 (C=C), 3300-3400 (OH) cm^{-1}.

Anal. Calcd. for $C_{21}H_{19}NO_5$: C, 69.04; H, 5.20; N, 3.83; O, 21.91. Found: C, 68.41; H, 5.33; N, 3.71; O, 21.18.

Methyl 2-(*N*-Benzylamino)ethanoate (**31a**).

The ^{1}H-nmr data are identical with those described in the literature [22]; ^{1}H-nmr (deuteriochloroform): δ 2.65 (sb, 1H, NH), 3.40 (s, 2H, CH_2-COOR), 3.68 (s, 3H, $COOCH_3$), 3.80 (s, 2H, CH_2-Ph), 7.21 (s, 5H, Ph).

Reaction of (*R*R** + *R*S**) Benzyl-2-methoxycarbonyl-3-phenylaziridine **28** with Ethyl Acetylacetate **32**.

The reaction was carried out with a mixture of two isomers of the aziridine **28**, *R*R**/*R*S** = 90/10 (7 g, 26 mmoles). The reaction mixture was refluxed 72 hours in tetrahydrofuran. The crude product was purified with hexane/ethyl acetate 90/10 to give **33** (0.8 g, 12%) and **31b** (0.5 g, 10%) respectively.

1-Benzyl-2-ethoxycarbonyl-3-phenylaziridine (**33**).

This compound was obtained as a liquid; ^{1}H-nmr (deuteriochloroform): δ 0.90 (t, 3H, COOEt, J = 7), 2.60 (d, 1H, H2, $J_{H2\text{-}H3}$ = 6.6), 3.06 (d, 1H, H3, J = 6.6), 3.75 (AB, 2H, N-CH_2, J = 13), 3.98 (q, 2H, COOEt, J = 7), 7.20-7.46 (m, 5H, Ph). The ^{1}H-nmr data are compared with those described in literature for 1-benzyl-2-methoxycarbonyl-3-phenylaziridine (**23**).

Ethyl 2-(*N*-Benzylamino)ethanoate (**31b**).

This compound was obtained as a liquid; ^{1}H-nmr (deuteriochloroform): δ 1.25 (t, 3H, COOEt, J = 7), 2.13 (sb, 1H, NH), 3.50 (s, 2H, CH_2-COO), 3.77 (s, 2H, CH_2Ph), 4.15 (q, 2H, COOEt, J = 7), 7.22 (s, 5H, Ph); ^{13}C-nmr: 172.30, 139.36-128.27, 60.68, 53.10, 49.9, 14.16.

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.39; H, 7.77; O, 16.58. Found: C, 68.18; H, 7.50; O, 16.45.

Reaction of *R*S** Benzoyl-2-isopropyloxy-3-methylaziridine **34a** with Methyl Malonate **2a**.

The reaction was carried out with aziridine **34a** *R*S** (7 g, 28 mmoles). The reaction mixture was refluxed 6 hours in tetrahydrofuran; the crude product was purified with hexane/ethyl acetate 90/10 to give **35** (0.6 g, 6%), **36a** (1.7 g, 17%) and **37a** (0.6 g, 7.5%) respectively.

N-Benzoyl-5-isopropyloxycarbonyl-4-methyl-3-methoxycarbonyl-2-pyrrolidone (**35**).

This compound was obtained as a solid, mp 85-86°; ^{1}H-nmr (deuteriochloroform): δ 1.30 (d, 6H, $CH(CH_3)_2$, J = 6), 1.38 (d, 3H, C4-CH_3, $J_{H4\text{-}CH3}$ = 6), 2.56-3.06 (m, 1H, H4), 3.60 (d, 1H, H3, $J_{H3\text{-}H4}$ = 8.8), 3.80 (s, 3H, $COOCH_3$), 4.41 (d, 1H, H5, $J_{H5\text{-}H4}$ = 7), 4.83-5.31 (hept, 1H, $CH(CH_3)_2$), 7.23-7.76 (m, 5H, Ph).

Anal. Calcd. for $C_{18}H_{21}NO_6$: C, 62.25; H, 6.05; N, 4.03; O, 27.66. Found: C, 61.90; H, 6.11; N, 3.85; O, 27.85.

N-Benzoyl-3-isopropyloxycarbonyl-5-methyl-3-methoxycarbonyl-2-pyrrolidone (**36a**).

This compound was obtained as a solid, mp 54-56°; ^{1}H-nmr (deuteriochloroform): δ 1.30 (d, 6H, $CH(CH_3)_2$, J = 6), 1.58 (d, 3H, C5-CH_3, J = 6), 3.33 (dd, 1H, H4, $J_{H4\text{-}H3}$ = 8.8, $J_{H4\text{-}H5}$ = 7), 3.81 (s, 3H, $COOCH_3$), 3.90 (d, 1H, H3, $J_{H3\text{-}H4}$ = 8.8), 4.31-4.75 (m, 1H, H5), 4.83-5.31 (hept, 1H, $CH(CH_3)_2$), 7.21-7.73 (m, 5H, Ph).

Anal. Calcd. for $C_{18}H_{21}NO_6$: C, 62.25; H, 6.05; N, 4.03. Found: C, 61.78; H, 6.07; N, 4.07.

N-Benzoyl-5-methyl-3,4-dimethoxycarbonyl-2-pyrrolidone (**37a**).

This compound was obtained as a solid, mp 78-79°; ^{1}H-nmr (deuteriochloroform): δ 1.30 (d, 6H, $CH(CH_3)_2$, J = 6), 1.58 (d, 3H, C5-CH_3, J = 6), 3.50 (dd, 1H, H4, $J_{H4\text{-}H3}$ = 8.8, $J_{H4\text{-}H5}$ = 7), 3.81 (s, 3H, $COOCH_3$), 3.95 (d, 1H, H3, $J_{H3\text{-}H4}$ = 8.8), 4.31-4.75 (m, 1H, H5), 4.83-5.31 (hept, 1H, $CH(CH_3)_2$), 7.21-7.73 (m, 5H, Ph).

Anal. Calcd. for $C_{16}H_{19}NO_6$: C, 59.81; H, 5.96; N, 4.36. Found: C, 60.22; H, 5.46; N, 4.19.

Reaction of *R*R** Benzoyl-2-isopropyloxy-3-methylaziridine **34b** with Methyl Malonate **2a**.

The reaction was carried out with aziridine **34b** *R*R** (8 g, 32 mmoles). The reaction mixture was refluxed 6 hours in tetrahydrofuran; the crude product was purified with hexane-ethyl acetate 85/15 to give **36b** (2.4 g, 24%), **37b** (1.9 g, 18.5%), **38** (0.8 g, 7%) and a mixture of **38** and **39** in a ratio 40/60.

N-Benzoyl-5-isopropyloxycarbonyl-5-methyl-3-methoxycarbonyl-2-pyrrolidone (**36b**).

This compound was obtained as a solid, mp 54-55°; ^{1}H-nmr (deuteriochloroform): δ 1.30 (d, 6H, $CH(CH_3)_2$, J = 6), 1.38 (d, 3H, C5-CH_3, J = 6.8), 3.83 (s, 3H, $COOCH_3$), 3.92 (dd, 1H, H4, J_{H4-H3} = 11.3, J_{H4-H5} = 8.4), 4.18 (d, 1H, H3, J = 11.3), 4.78-5.36 (m, 2H, H5 and CH), 7.38-7.65 (m, 5H, Ph).

Anal. Calcd. for $C_{18}H_{21}NO_6$: C, 62.24; H, 6.05; N, 4.03. Found: C, 61.83; H, 5.98; N, 4.73.

N-Benzoyl-5-methyl-3,4-dimethoxycarbonyl-2-pyrrolidone (**37b**).

This compound was obtained as a solid, mp 121-122°; ^{1}H-nmr (deuteriochloroform): δ 1.35 (d, 3H, C5-CH_3, J = 6.8), 3.80 (s, 6H, $COOCH_3$), 3.92 (dd, 1H, H4, J_{H4-H3} = 11.3, J_{H4-H5} = 8.4), 4.18 (d, 1H, H3, J = 11.3), 4.98 (qd, 1H, H5, J = 8.4), 7.29-7.60 (m, 5H, Ph).

Anal. Calcd. for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.32; N, 4.38; O, 30.09. Found: C, 60.25; H, 5.30; N, 4.26; O, 29.86.

Methyl 4-Benzoylamino-2,3-dimethoxycarbonylpentanoate (**38**).

This compound was obtained as a solid, mp 71-72°; ^{1}H-nmr (deuteriochloroform): δ 1.30 (d, 3H, CH_3, J = 6), 3.43 (dd, 1H, C*H*-$COOCH_3$, J = 3, J = 10), 3.70 (s, 3H, $COOCH_3$), 3.76 (s, 3H, $COOCH_3$), 3.83 (s, 3H, $COOCH_3$), 3.95 (d, 1H, C*H*$(COOCH_3)_2$, J = 10), 4.00-4.40 (m, 1H, C*H*-NH), 6.93 (sb, 1H, NH), 7.36-7.90 (m, 5H, Ph).

Anal. Calcd. for $C_{17}H_{21}NO_7$: C, 58.11; H, 5.98; N, 3.98; O, 31.90. Found: C, 58.08; H, 6.24; N, 4.07; O, 31.71.

Methyl 4-Benzoylamino-3-isopropyloxycarbonyl-2-methoxycarbonylpentanoate (**39**).

This compound was not isolated but identified by the ^{1}H-nmr spectrum of the mixture of **38** + **39**; ^{1}H-nmr (deuteriochloroform): δ 1.26 (d, 6H, $CH(CH_3)_2$, J = 6), 1.30 (d, 3H, CH_3, J = 6), 3.43 (dd, 1H, CH-COO*i*Pr, J = 3, J = 10), 3.66 (s, 3H, $COOCH_3$), 3.76 (s, 3H, $COOCH_3$), 3.95 (d, 1H, $CH(COOCH_3)_2$, J = 10), 4.00-4.40 (m, 1H, CH-NH), 4.83-5.28 (hept, 1H, $CH(CH_3)_2$), 7.00 (sb, 1H, NH), 7.36-7.83 (m, 5H, Ph).

Reaction of Benzoyl-2-cyanoaziridine **40** with Methyl Malonate **2a**.

The reaction mixture was carried out with aziridine **40** (8 g, 46 mmoles). The reaction mixture was refluxed in tetrahydrofuran for 4 hours. The oily crude product was purified with hexane/-ethyl acetate 75/25 to give **41** (3.3 g, 38%) and **42** (1.1 g, 13%) respectively.

Methyl 4-Benzoylamino-4-cyano-2-methoxycarbonylbutanoate (**41**).

This compound was obtained as a solid, mp 71-73°; ^{1}H-nmr (deuteriochloroform): δ 2.63 (dd, 2H, CH_2, J = 7, J = 8), 3.56-3.70 (m, 1H, $CH(COOCH_3)_2$), 3.71 (s, 3H, $COOCH_3$), 3.78 (s, 3H, $COOCH_3$), 5.30-5.60 (m, 1H, CHNH), 7.33-7.93 (m, 6H, Ph and NH).

Anal. Calcd. for $C_{15}H_{16}N_2O_5$: C, 59.21; H, 5.26; N, 9.21; O, 26.31. Found: C, 59.46; H, 5.37; N, 9.15; O, 26.17.

Methyl 4-Benzoylamino-3-cyano-2-methoxycarbonylbutanoate (**42**).

This compound was obtained as a solid, mp 120-121°; ^{1}H-nmr (deuteriochloroform): δ 3.81 (s, 6H, $COOCH_3$), 3.40-3.94 (m, 3H), 4.25 (d, 1H, $CH(COOCH_3)_2$, J = 6), 7.43-8.05 (m, 5H, Ph), 8.91 (sb, 1H, NH).

Anal. Calcd. for $C_{15}H_{16}N_2O_5$: C, 59.21; H, 5.26; N, 9.21; O, 26.31. Found: C, 59.50; H, 5.43; N, 9.04; O, 26.11.

Reaction of Benzoyl-2-cyanoaziridine **40** with Acetylacetone **15**.

The reaction was carried out with aziridine **40** (3 g, 17 mmoles). The reaction mixture was refluxed in tetrahydrofuran for 4 hours. The crude product was purified with hexane/ethyl acetate 80/20 to give **43** (1 g, 21%) and **44** (1.2 g, 30%) respectively.

4-Acetyl-2-benzoylamino-5-oxohexanenitrile (**43**).

This compound was obtained as a solid, mp 113-114°; ^{1}H-nmr (deuteriochloroform): δ 2.26 (s, 6H, $COCH_3$), 2.23-3.00 (m, 2H, CH_2), 3.98 (t, 1H, $CH(COCH_3)_2$, J = 7), 4.90-5.55 (m, 1H, C*H*-NH), 7.35-7.66 (m, 6H, Ph and NH).

Anal. Calcd. for $C_{15}H_{16}N_2O_3$: C, 66.17; H, 5.88; N, 10.03; O, 17.03. Found: C, 65.88; H, 5.59; N, 10.27; O, 17.64.

2-Benzoylamino-5-oxohexanenitrile (**44**).

This compound was obtained as a solid, mp 89-90°; ^{1}H-nmr (deuteriochloroform): δ 1.95-2.38 (m, 2H, CH_2CO), 2.18 (s, 3H, $COCH_3$), 2.66-2.88 (m, 2H, C3-CH_2), 5.06 (dd, 1H, C2-H, J = 7, J = 14), 7.33-7.95 (m, 6H, Ph and NH).

Anal. Calcd. for $C_{13}H_{14}N_2O_2$: C, 67.82; H, 6.08; N, 12.17; O, 13.91. Found: C, 67.80; H, 6.12; N, 12.35; O, 14.21.

Reaction of Carboterbutoxy-2-cyanoaziridine **45** with Methyl Malonate **2a**.

The reaction was carried out with aziridine **45** (3 g, 18 mmoles). The reaction mixture was refluxed in tetrahydrofuran for 4 hours. The crude product was purified with hexane-ethyl acetate 85/15 to give **46** (0.25 g, 3.5%), **48** (0.8 g, 12%) and **47** (1.8 g, 28%) respectively.

Methyl 4-(Carboterbutoxycarbonyl)amino-4-cyano-2-methoxycarbonylbutanoate (**46**).

This compound was obtained as an oily product; ^{1}H-nmr (deuteriochloroform): δ 1.50 (s, 9H, *t*-Bu), 2.46 (t, 2H, CH_2, J = 7), 3.60 (t, 1H, $CH(COOMe)_2$, J = 7), 3.83 (s, 6H, $COOCH_3$), 4.50-4.90 (m, 1H, CH-NH), 5.25 (sb, 1H, NH).

Anal. Calcd. for $C_{13}H_{20}N_2O_6$: C, 52.00; H, 6.66; N, 9.33; O, 32.00. Found: C, 51.46; H, 6.73; N, 9.38; O, 31.98.

N-Carbo-*tert*-butoxycarbonyl-4-cyano-3-methoxycarbonyl-2-pyrrolidone (**47**).

This compound was obtained as an oily product; ^{1}H-nmr (deuteriochloroform): δ 1.60 (s, 9H, *t*-Bu), 2.46-2.98 (m, 2H), 3.85 (s, 3H, $COOCH_3$), 3.50-4.00 (m, 1H, H-C3), 4.95 (m, 1H, H-C5).

Anal. Calcd. for $C_{12}H_{16}N_2O_5$: C, 53.73; H, 5.97; N, 10.44. Found: C, 53.34; H, 6.00; N, 10.31.

N-Carbo-*tert*-butoxycarbonyl-4-cyano-3-methoxycarbonyl-2-pyrrolidone (**48**).

This compound was obtained as a solid, mp 93-94°; ^{1}H-nmr (deuteriochloroform): δ 1.56 (s, 9H, *t*-Bu), 3.76-4.26 (m, 4H), 3.86 (s, 3H, $COOCH_3$).

Anal. Calcd. for $C_{12}H_{16}N_2O_5$: C, 53.73; H, 5.97; N, 10.44. Found: C, 53.26; H, 5.86; N, 10.12.

Reaction of Carbo-*tert*-butoxy-2-cyanoaziridine **45** with Methyl Acetylacetate **11**.

The reaction was carried out with aziridine **45** (3 g, 18 mmoles). The reaction mixture was refluxed in tetrahydrofuran for 4 hours. The crude product was purified with hexane/ethyl acetate 80/20 to give the sole compound **49** (1.6 g) in 32% yield.

Methyl 2-Acetyl-4-(carbo-*tert*-butoxycarbonyl)amino-4-cyanobutanoate (**49**).

This compound was a solid, mp 65-66°; ^{1}H-nmr (deuteriochloroform): δ 1.50 (s, 9H, *t*-Bu), 2.06-2.63 (m, 2H, CH_2), 2.33 (s, 3H, $COCH_3$), 3.73 (t, 1H, $CH(COOCH_3)_2$, J = 7), 3.83 (s, 3H, $COOCH_3$), 4.30-4.90 (m, 1H, CH-N), 5.56 (d, 1H, NH, J = 9).

Anal. Calcd. for $C_{13}H_{20}N_2O_5$: C, 54.92; H, 7.04; N, 9.85; O, 28.17. Found: C, 54.33; H, 6.92; N, 9.78; O, 28.42.

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