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Synthesis and properties of 1-aminocyclopropane-1,2-dicarboxylic acid and compounds incorporating it

V P Krasnov, M A Korolyova, G L Levit

Contents

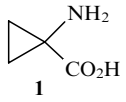
I.	Introduction	343
II.	Methods for the synthesis of 1-aminocyclo-propane-1,2-dicarboxylic acid derivatives	344
III.	Methods for the synthesis of individual stereoisomers of 1-aminocyclopropane-1,2-dicarboxylic acid	349
IV.	Properties of 1-aminocyclopropane-1,2-di-carboxylic acid derivatives	352
V.	Peptides containing 1-aminocyclopropane-1,2-dicarboxylic acid	353

Abstract. Methods for the synthesis of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives including carbo- and heterocyclic compounds and peptides are analysed. Special attention is given to methods for the synthesis of individual stereoisomers of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives based on the use of diastereoselective processes or enantiomerically pure starting compounds. The transformations of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives which yield compounds with potential biological activities are considered. The bibliography includes 87 references.

I. Introduction

Amino acid derivatives containing a cyclopropane fragment attract the attention of chemists and biochemists who endeavour to use them as starting materials for the preparation of peptide mimetics. The reviews published in the past decade [1–3] are devoted to the survey of preparation procedures and the properties of natural and synthetic cyclopropane-containing amino acids.

The simplest representative of this unique class of compounds is 1-aminocyclopropane-1-carboxylic acid (**1**), a direct precursor of ethylene biosynthesis in plants.



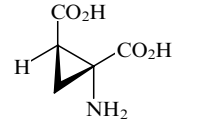
1

Some cyclopropane-containing amino acids have been isolated from natural sources. They include carnosadine [4,5] from the red seeweed *Grateloupia carnosa*, coronamic acid [6] (a component of the toxin produced by the bacteria *Pseudomonas coronafaciens*), hypoglycine A and *trans*-carboxycyclopropylglycine [7,8] from *Blighia sapinda* fruits; hypoglycine A is known to induce hypoglycemia in animals.

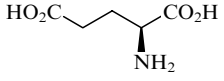
Since 1-aminocyclopropane-1,2-dicarboxylic acid derivatives belong to conformationally rigid analogues of amino acids, their incorporation into the peptide chain makes its spatial structure more rigid.[9,10] In particular, steric strain between the C=O group and the cyclopropane ring restricts the torsional rotation angle around the $C_\alpha-C(O)$ bond. The fact that changes in the conformational parameters affect the interaction of the peptide with its specific receptor [11] can be used in the study of the receptor structure and the mechanisms of its binding to the ligand.

The ability of cyclopropane-containing amino acids to fix the conformation responsible for the biological activity of various peptides affects their interactions with enzymes. For example, incorporation of 1,2,3-trisubstituted cyclopropanes into model tripeptides affords strong inhibitors of renin, the angiotensin-liberating proteolytic enzyme.[12] Studies of reactions of enzymes with peptide analogues of substrates containing cyclopropane derivatives of amino acids have shown that these fragments increase the hydrolytic stability of peptides.[13,14]

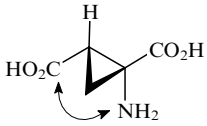
Among other derivatives of compound **1**, a special place is occupied by 1-aminocyclopropane-1,2-dicarboxylic (2,3-methanoaspartic, cycloaspartic, ∇Asp)† acid (**2**), a conformationally rigid analogue of aspartic acid. Its *Z* and *E* isomers are monoconformational analogues of 'condensed' and 'extended' conformations of glutamic acid (**3**), as regards the distance between the amino and 5-carboxy groups.



E isomer (*cis*)

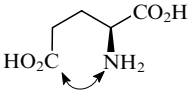


'Extended' conformation



Z isomer (*trans*)

2



'Condensed' conformation

3

Aspartic and glutamic acids play an important role in various metabolic processes occurring in living organisms. They represent neuromediators of the central nervous system [15] the functional disorder of which is related to Alzheimer's and Huntington's diseases as well as epilepsy.[16] Synthetic agonists and antagonists

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† The prefixes '1,3-methano-' and 'cyclo-' were used by Stammer [1] and Burgess [2] for the designation of cyclopropane analogues of amino acids.

of specific receptors of aspartic and glutamic acids may have therapeutic significance.

Studies of metabotropic glutamate receptors (mGluRs) which control the transmission of electrical signals from nerve cells mediated by interacting membrane proteins suggest that they are activated by L-glutamic acid in an 'extended' conformation.[17] An analysis of the biological role of these receptors is complicated due to insufficient activity, selectivity and bioaccessibility of presently known agonists and antagonists of mGluRs. Carbo- and heterocyclic compounds containing a fragment of the acid **2** are potential selective antagosists of glutamate receptors and interesting subjects for the study of structure – activity relationships.[18–22]

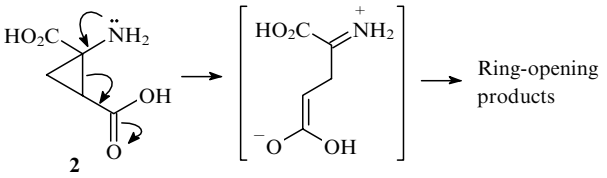
It is known also that (±)-*cis*-1-aminocyclopropane-1,2-dicarboxylic acid is an agonist of the *N*-methyl-D-aspartate receptor.[23]

The present review is devoted to surveying the methods for the synthesis of derivatives of 1-aminocyclopropane-1,2-dicarboxylic acid including miscellaneous carbo- and heterocyclic compounds and peptides. Special attention is given to the methods for the preparation of individual stereoisomers of these compounds, some of which possess pharmacological activity.

II. Methods for the synthesis of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives

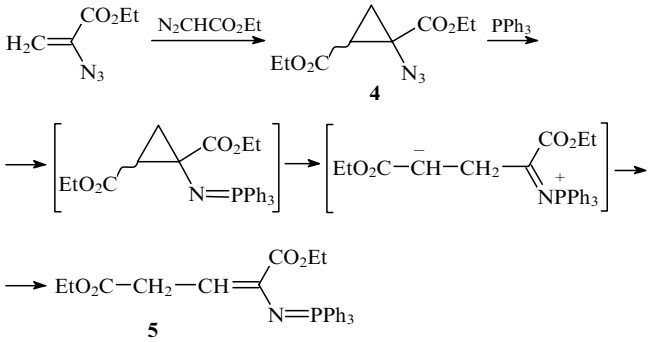
A problem in the synthesis of compound **2** is associated with the fact that the acid itself and its esters, which contain a free amino group, are unstable compounds.[1] The data from the first synthesis of acid **2** (see Ref. 24) were not confirmed by the results of subsequent investigations.[2,25–27]

The ability of the cyclopropane fragment to be involved in conjugation and to transfer the effects of the attached functional groups[28] favours push – pull reactions in 2-aminocyclopropanecarboxylic acid. Acid **2** undergoes spontaneous ring-opening as a result of which the unshared electron pair of the nitrogen atom takes part in the formation of a double bond giving rise to imines.[29,30]



2

Thus an attempt to synthesise amino acid **2** by reaction of triphenylphosphine with a mixture of *cis*- and *trans*-1-azidocyclopropane-1,2-dicarboxylates (**4**) obtained by cycloaddition of ethyl diazoacetate to α-azidoacrylate resulted in diethyl 2-triphenylphosphiniminopent-2-ene-1,5-dioate (**5**).[25]



4

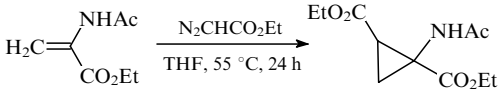
5

However, recently a series of stable compounds containing a functionalised cyclopropane ring were successfully prepared. The known methods for the synthesis of acid **2** and its derivatives can be divided into several groups, *viz.*, 1,3-dipolar cycloaddition of diazo compounds at unsaturated bonds, syntheses based on reactions of acetylenedicarboxylates with nitrogen-containing compounds, addition of sulfur ylides to dipolarophiles and intramolecular cyclisation.

1. 1,3-Dipolar cycloaddition of diazo compounds to unsaturated bonds

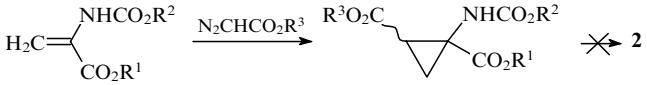
Addition of diazo compounds to alkenes, alkynes and heterocycles is a classical approach[31] widely employed in the synthesis of cyclopropane-containing amino acids.[3,13,32–38] This reaction first yields dihydropyrazoles which are decomposed upon heating or irradiation with evolution of nitrogen and closure of the cyclopropane ring.

The possibility of preparing acid **2** derivatives by addition of diazoacetates to protected α,β-dehydroalanine has been demonstrated.[39] *N*-Acetyl-α,β-dehydroalanine ethyl ester reacts with ethyl diazoacetate to give diethyl *N*-acetyl cycloaspartate (**6**) (yield 12.5%); however, the attempts to establish the configuration of the resulting stereoisomer failed.



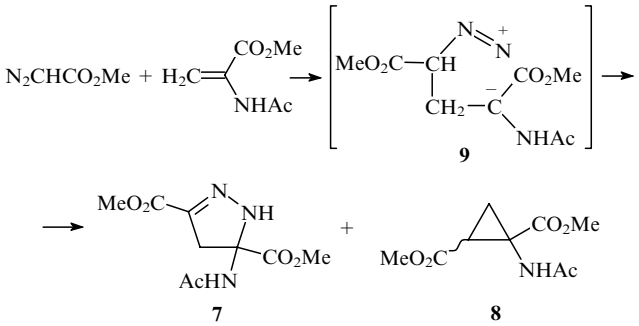
6

Cycloaddition of diazoacetates to a dehydroalanine derivative with subsequent deprotection has been undertaken by Stammer,[1] but acid **2** could not be isolated in a free state.



The low yields of acid **2** derivatives and difficulties in the isolation of the target product have stimulated further studies of reactions of alkyl diazoacetate with *N*-protected α-aminoacrylates.[40]

It was found[41] that methyl diazoacetate reacts with methyl 2-acetylaminoacrylate in dichloromethane at room temperature to give dihydropyrazole **7** (yield 60%) and a mixture of *Z* and *E* isomers of dimethyl 1-acetylaminocyclopropane-1,2-dicarboxylates (**8**) (total yield 30%). Presumably, the ring closure occurs *via* the zwitterion **9**.

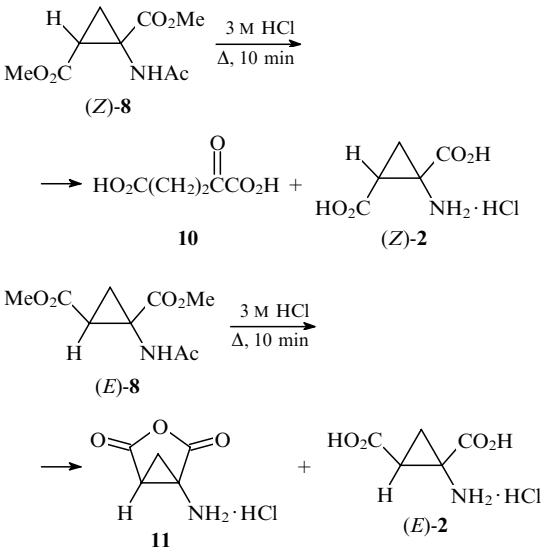


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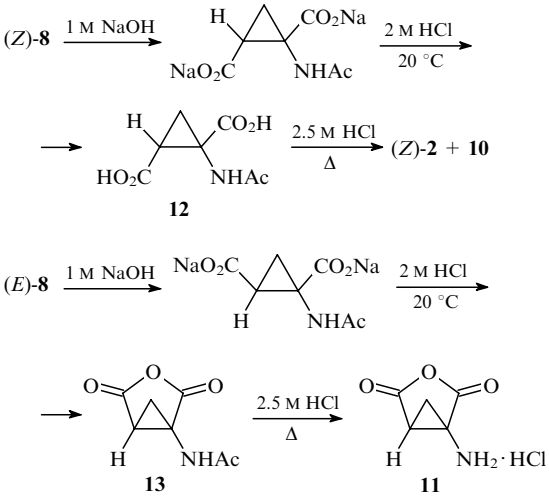
7 **8**

When the reaction is carried out in chloroform, the yields of cyclopropane derivatives increase to 70%.[42] With a twofold excess of methyl diazoacetate, the ratio of *Z*- and *E*-isomers was 1 : 3 in dichloromethane and 1 : 1 in chloroform.

It has been shown[43] that hydrolysis of the *Z* isomer **8** with 3 M HCl is accompanied by the formation of 2-ketoglutaric acid (**10**) (yield 60%) and (*Z*)-1-aminocyclopropane-1,2-dicarboxylic acid hydrochloride (**2**) (yield 8%). The *E* isomer **8** gives the more stable hydrochloride of anhydride **11** and the hydrochloride of the *E* isomer of acid **2** (yields 60% and 6%, respectively) under identical conditions.

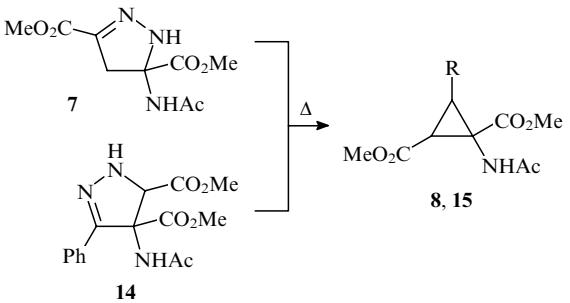


Removal of methyl protective groups in *Z* and *E* isomers of compound **8** by treatment with 1 M NaOH (22 °C, 10 h) and subsequent acidification of disodium salts to pH 5–6 give (*Z*)-1-acetylaminocyclopropane-1,2-dicarboxylic acid (**12**) and (*E*)-1-acetylaminocyclopropane-1,2-dicarboxylic acid (**13**) anhydride, respectively.



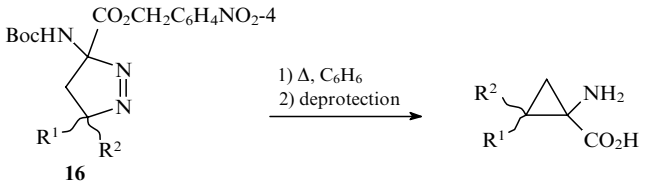
Further acidification to pH 2 and boiling of the *Z* isomer **12** affords compound (*Z*)-**2** (yield 15%) and an acyclic product **10**, whereas anhydride **11** hydrochloride is the only hydrolysis product of the *E* isomer under identical conditions.

Dihydropyrazoles **7** and **14** decompose on boiling in DMF for 40–60 min to give the corresponding *N*-acetylaminocyclopropane-1,2-dicarboxylates **8** and **15** in 50% and 40% yields, respectively.[44]



R = H (**8**), Ph (**15**).

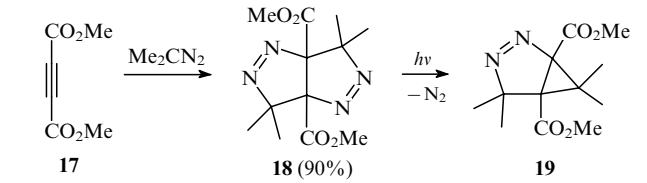
Cycloaddition of diazo compounds to *N-tert*-butoxycarbonyl-α,β-dehydroalanine *p*-nitrobenzyl ester yields dihydropyrazoles **16**. Decomposition of compounds **16** and subsequent removal of protective groups gave cyclopropane-containing amino acids that were further used for the preparation of peptides which are of interest for their use as renin inhibitors, analgetics and sweeteners.[45]



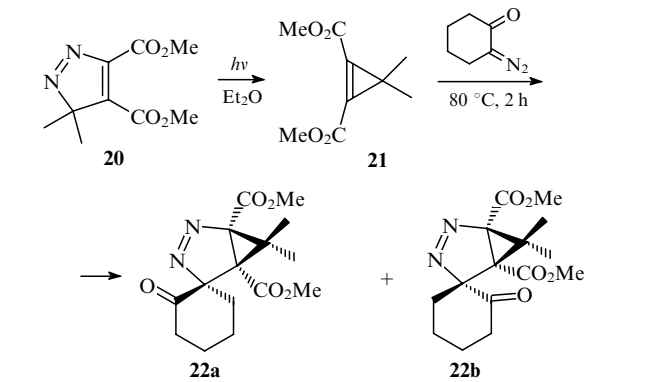
R^1, R^2 = H, Alk, Ar; Boc = CO_2Bu^t.

Heterocyclic compounds containing a fragment of 1-aminocyclopropane-1,2-dicarboxylic acid provide illustrative examples of systems with a stabilised cyclopropane fragment. In addition, their rearrangements afford products manifesting useful properties. Therefore, the development of methods for the synthesis of these compounds is attracting the attention of investigators.

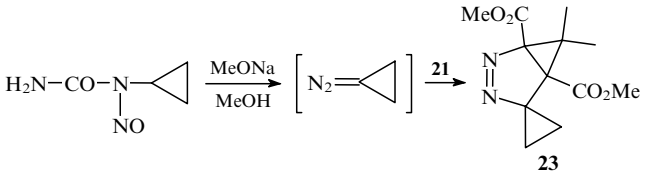
Reaction of 2-diazopropane with dimethyl acetylenedicarboxylate (**17**) gives the adduct **18** in high yield; photoirradiation of the latter results in the evolution of nitrogen and its conversion into dihydropyrazole **19**, a bicyclic derivative of the acid **2**, which represents a convenient synthon for the synthesis of cyclopropenes and dienes.[46]



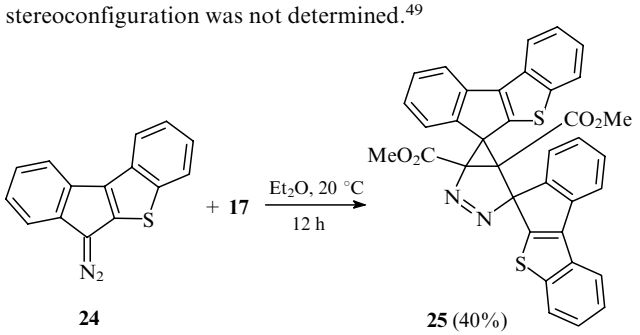
1,2-Bis(methoxycarbonyl)-3,3-dimethylcyclopropene (**21**) obtained by photolysis of 3*H*-pyrazole **20** reacts with α-diazocyclohexanone in benzene to give isomeric tricyclic adducts **22a** and **22b** in a 3 : 1 ratio (total yield 70%).[47]



A reaction of cyclopropene **21** with diazocyclopropane generated *in situ* from *N*-nitroso-*N*-cyclopropylurea under the action of sodium methoxide in methanol afforded a spirocyclic adduct **23** in 48% yield.[48]

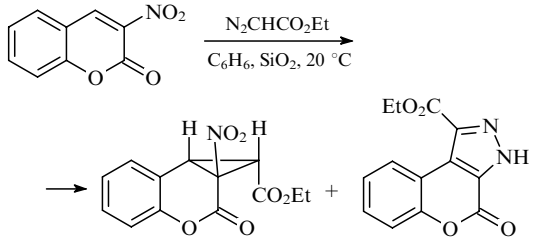


Diazoindeno[2,3-*b*]benzothiophene **24** adds to acetylenedicarboxylate **17** to give a stable polycyclic dihydropyrazole **25**; its stereoconfiguration was not determined.[49]



24 **25** (40%)

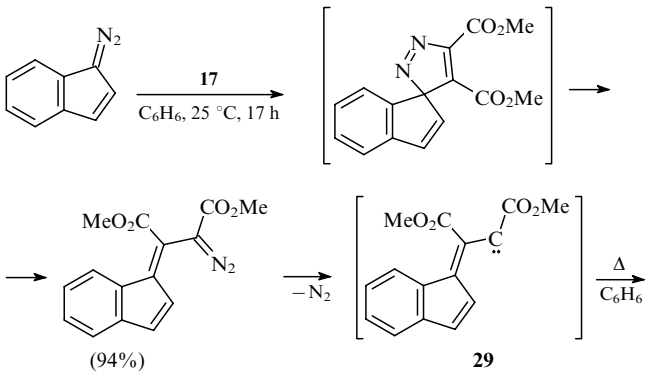
Cycloaddition of ethyl diazoacetate to 3-nitrocoumarin in the presence of silica gel yields a mixture of ethyl 4,5-benzo-1-nitro-2-oxo-3-oxabicyclo[4.1.0]hept-4-ene-7-carboxylate (**26**) and chromeno[3,4-*c*]pyrazolecarboxylate **27**.



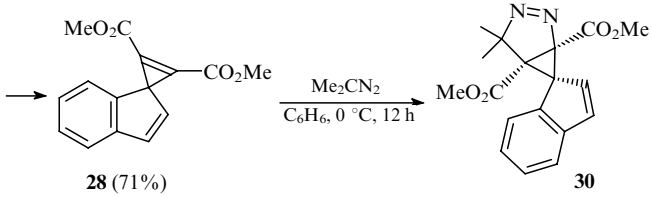
26 (58%) **27** (35%)

According to the ^{1}H NMR spectroscopic data, compound **26** is an *endo*-isomer with a *cis*-arrangement of the two protons in the cyclopropane ring and incorporates a nitro analogue of compound **2**.[50]

Spirocyclopropene **28** obtained by addition of diazoindene to dimethyl acetylenedicarboxylate (**17**) with subsequent elimination of a nitrogen molecule and cyclisation of the vinylcarbenium intermediate **29** reacts with 2-diazopropane to give a spiro derivative **30**.[51]



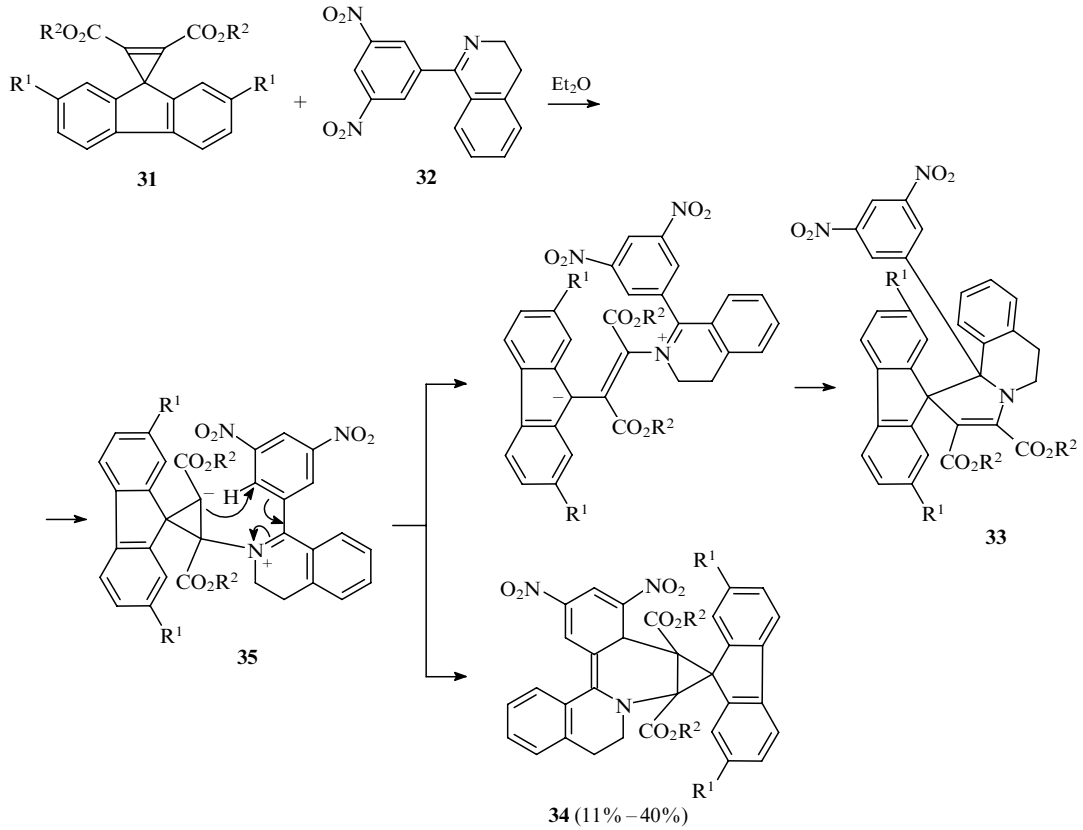
(94%) **29**



28 (71%) **30**

The reaction of substituted spirocyclopropenefluorenes **31** with 1-(3,5-dinitrophenyl)-3,4-dihydroisoquinoline (**32**) in anhydrous diethyl ether was studied.[52] In addition to the expected products (tetrahydroindolizines **33**), this reaction gave novel spiroazanorcarenefluorenes **34** formed upon intramolecular 1,6-cyclisation of the intermediate **35** (Scheme 1).

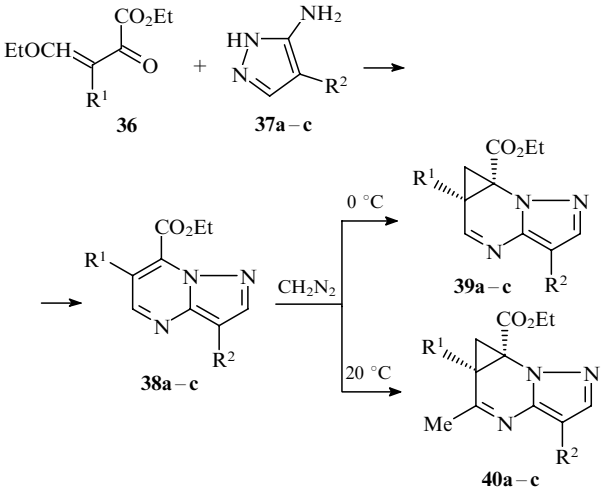
Scheme 1



R^1 = H: R^2 = Me, Et, Pr^i, Bu^t, C_6H_{13}; R^1 = Br, R^2 = Me; R^1 = Cl, R^2 = Et.

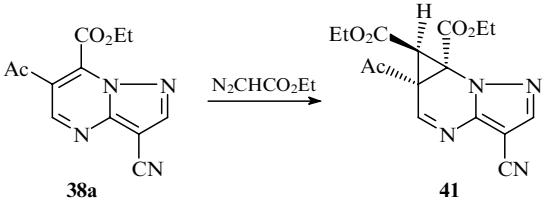
The structure of compounds **34** was established using X-ray diffraction analysis and NMR spectroscopy. Azanorcarene **34** (R^1 = H, R^2 = Me) was found to possess acidochromic properties. Its ethanolic solution has a green colour which changes to bright violet on addition of aqueous NaOH.

The addition of diazomethane to alkene fragments of heterocyclic systems was studied in the course of synthesis of substituted tricyclic nitrogen-containing compounds.[53–55] Condensation of keto acid derivatives **36** with 5-aminopyrazoles **37a–c** gave pyrazolo[1,5-*a*]pyrimidines **38a–c** which react with diazomethane at 0 °C to give 6*H*-cyclopropa[*e*]pyrazolo[1,5-*a*]dihydropyrimidines **39a–c** in 61%–100% yields. At room temperature, this reaction gives exclusively 5-methylated derivatives **40a–c**.[53]

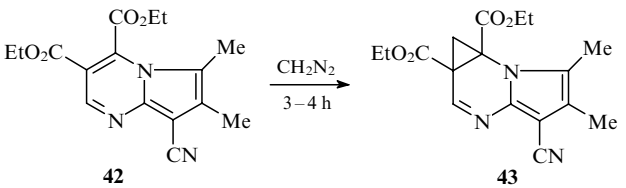


R^1 = Ac, CO_2Et; R^2 = CN (**a**), $CONH_2$ (**b**), CONHMe (**c**).

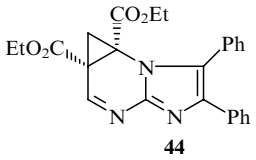
Compound **38a** (R^1 = Ac) reacts with ethyl diazoacetate in dioxane at 70 °C in the presence of copper as a catalyst to give 6-ethoxycarbonyl-6*H*-cyclopropa[*e*]pyrazolo[1,5-*a*]dihydropyrimidine **41**; its stereoconfiguration was assigned as *trans* based on the ^{1}H NMR spectroscopic data.[53]



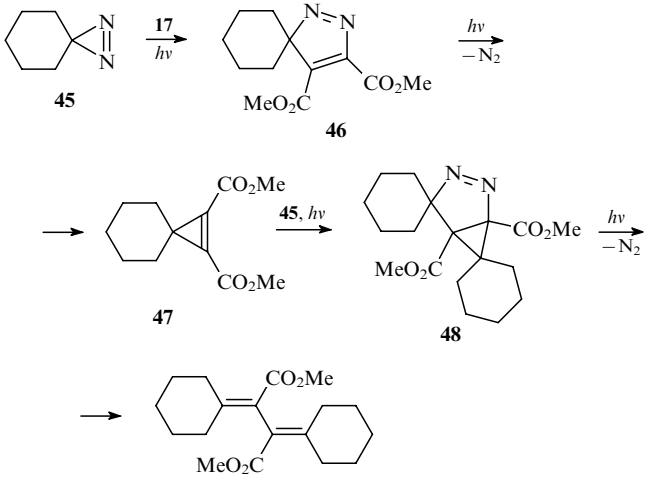
Cyclopropane derivatives of partially hydrogenated pyrrolo[1,2-*a*]pyrimidines, which can be used as catalysts in the synthesis of polyurethanes, have been synthesised. For example, diethyl 6,7-dimethyl-8-cyanopyrrolo[1,2-*a*]pyrimidine-3,4-dicarboxylate (**42**) reacts with an excess of diazomethane at room temperature to give the corresponding cyclopropane derivative of pyrrolopyrimidine **43** (yield 40%).[54]



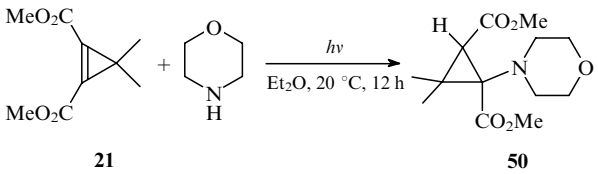
The cyclopropane derivative of imidazo[1,2-*a*]pyrimidine **44** was obtained analogously. This is representative of an interesting class of compounds which includes substances manifesting analgetic, antiinflammatory, antipyretic and anticonvulsive activities.[55]



Selective irradiation (λ = 250–350 nm) of a spiro-fused diazirine **45** and of dimethyl acetylenedicarboxylate (**17**) in dry toluene gives pyrazole **46** which is further converted into a spiro-fused cyclopropene **47** with liberation of nitrogen. The addition of a second molecule of diazirine **45** to the product formed gives cyclopropadihydropyrazole **48** (yield 12%) after column chromatography on silica gel. Further irradiation is accompanied by the cyclopropane ring opening and elimination of nitrogen, as a result of which compound **48** is converted into diene **49**.[56]



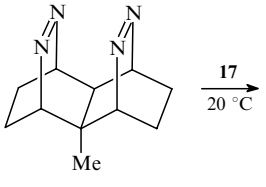
Reaction of cyclopropene **21** with morpholine in anhydrous diethyl ether under irradiation with a mercury lamp afforded morpholinocyclopropane **50**, a potential pyrethroid, as a mixture of two diastereomers as can be judged from ^{1}H NMR spectroscopic data (total yield 54%).[57]

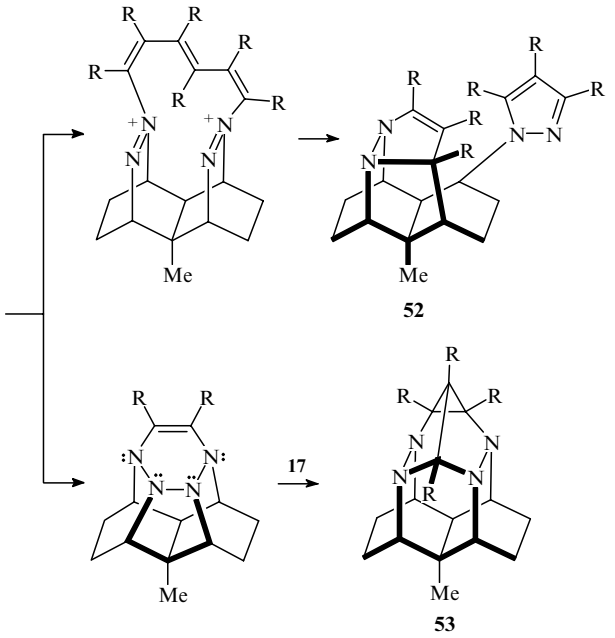


2. Reactions of acetylenedicarboxylates with other nitrogen-containing compounds

The 1-amino-1,2-dicarboxycyclopropane system can be formed as a result of reactions of electrophilic alkynes with bisdiazines.

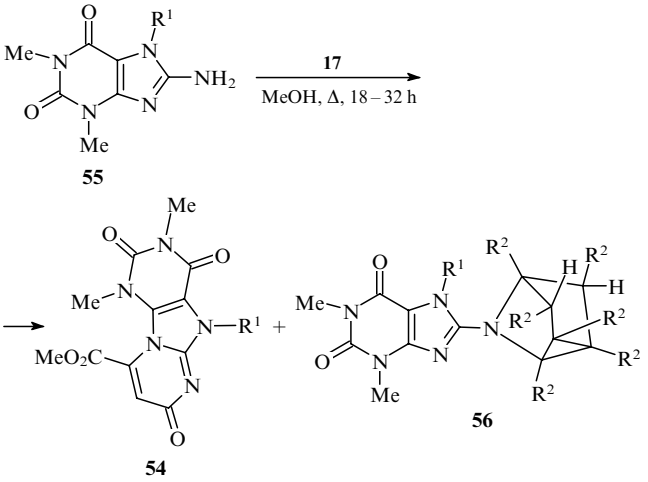
The reactivities of cyclic bisdiazines in nucleophilic cycloaddition reactions were studied in the reaction of compound **51** with acetylenedicarboxylate **17** in CH_2Cl_2 in a nitrogen atmosphere.[58, 59] In addition to a non-symmetrical 1 : 3 adduct **52**, this reaction yields a symmetrical 1 : 2 adduct **53** which incorporates 1,2-diaminocyclopropane-1,2,3-tricarboxylic acid.





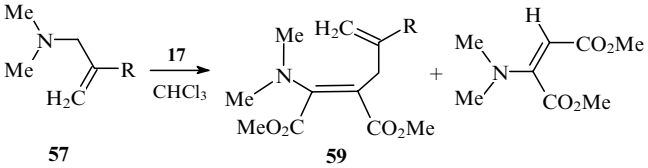
R = CO_2Me.

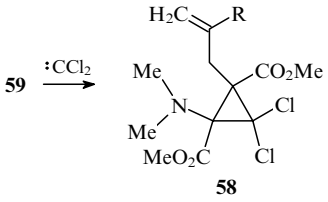
Pyrimido[1,2-*e*]purines **54** were prepared by the reaction of 7-alkyl-8-amino-1,3-dimethylxanthines (**55**) with acetylene dicarboxylate **17**. Along with compounds **54,** this reaction yields xanthines **56**, the addition products of two molecules of the alkyne **17** to the amino group of xanthine **55** followed by intramolecular cyclisation involving an additional molecule of compound **17**. The structure of compounds **56** was established by mass spectrometry and X-ray diffraction analysis.[60]



R^1 = Pr, Bu; R^2 = CO_2Me.

Reaction of allyl amines **57** with acetylenedicarboxylate **17** in chloroform gives 3,3-dichloro derivatives of 1-aminocyclopropane-1,2-dicarboxylic acid **58** as side products formed in low yields as a result of addition of dichlorocarbene, generated from chloroform, to the double bond of the enamine fragment of compound **59**.[61]

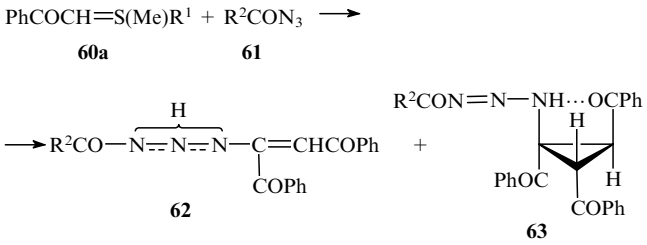




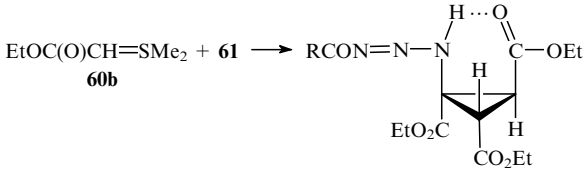
R = H (18%), Me (10%).

3. Addition of stabilised sulfur ylides to dipolarophiles

Phenacylidenesulfuranes **60a** react with acyl azides **61** in benzene at 20 °C to give 2 : 1 adducts **62** and azido analogues of 1-aminocyclopropane-1,2-dicarboxylic acid **63**. Reaction of ethyl azidoformate (**61**, R^2 = OEt) with ethoxycarbonylmethylidenedimethylsulfurane (**60b**) gives exclusively the derivative **64** (R = OEt) with a *trans*-configuration of the cyclopropane ring protons and an intramolecular hydrogen bond (^{1}H NMR spectroscopic data). Reactions of compound **60b** with benzoyl azides **61** also yield the cyclopropane derivatives **64** rather than the 2 : 1 adducts.[62]

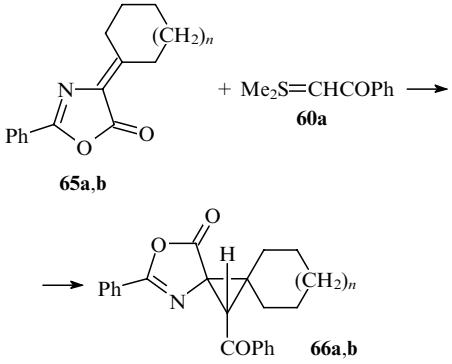


R^1 = Me, Ph; R^2 = OEt, 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-ClC_6H_4.



R = OEt (60%), 4-$MeOC_6H_4$ (25%), 4-MeC_6H_4 (57%), 4-ClC_6H_4 (32%).

Reaction of dihydrooxazolones with sulfur methylides was studied in order to prepare functionalised spirocyclopropanes that can be rearranged into non-natural amino acid derivatives upon heating.[63] 4-Cyclohexylidene- and 4-cycloheptylidene-2-phenyl-4,5-dihydrooxazol-5-ones **65a**,**b** react with phenacylidenedimethylsulfurane (**60a**, R^1 = Me) in dry THF at 0 °C to give spiro-fused cyclopropanes **66a**,**b** in 84% and 35% yields, respectively. ^{1}H NMR spectroscopic data suggest that in both cases the major isomer has a *trans*-configuration of the carbonyl groups.



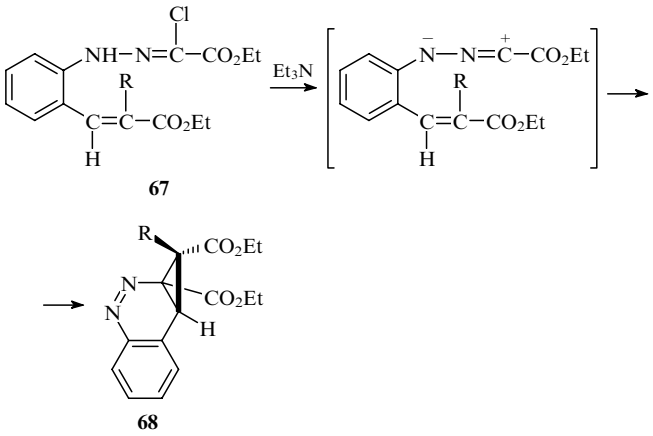
n = 1 (**a**), 2 (**b**).

Under identical conditions, reaction of dihydrooxazolone **65a** with ethoxycarbonyl methylidenedimethylsulfurane (**60b**) gives a

mixture of diastereomers (3 : 1) (^{1}H and ^{13}C NMR spectroscopic data) in a total yield of 97%.[63]

4. Intramolecular cyclisation reactions

Substituted imines undergo [2 + 1]-cycloaddition at the C=C bond to give cyclopropanes. The derivatives **67** synthesised from *ortho*-substituted anilines by diazotisation and condensation with ethyl chloroacetate were used to prepare cyclopropacinnolines **68**. The *endo*-position of the R group in the resulting compounds was established by ^{1}H NMR spectroscopy.[64]

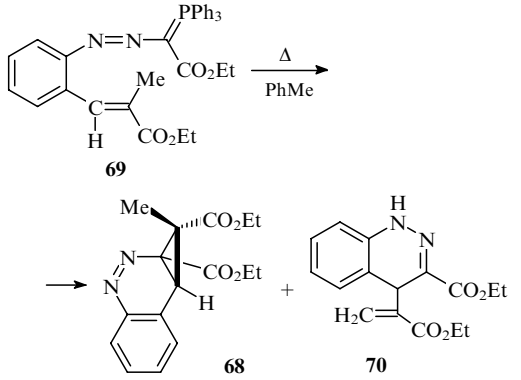


67 **68**

R = Me, Et.

Compounds **68** are interesting in that they undergo rearrangements upon boiling to give heterocyclic structures with potential biological activity.[65, 66]

Easily accessible azo-substituted phosphorus ylides are also subject to intramolecular cycloaddition at the double bond. Phosphorane **69** loses a PPh_3 group upon heating in toluene to give cyclopropacinnoline **68** (R = Me) and the product of its thermal rearrangement **70** (yields 10% and 43%, respectively).[67]



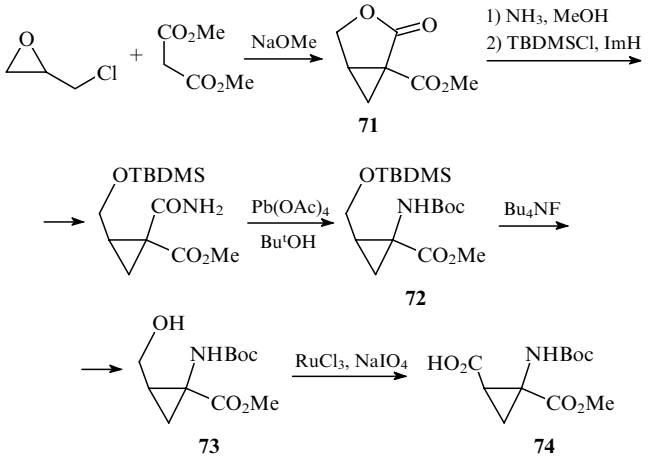
69 **68** **70**

III. Methods for the synthesis of individual stereoisomers of 1-aminocyclopropane-1,2-dicarboxylic acid

The current demand for all four cycloaspartic acid **2** diastereomers is explained by the fact that their incorporation into peptide structures changes the conformations and, as a consequence, biological activities of the peptides as regards their binding to receptors. However, the methods for the synthesis of individual stereoisomers of derivatives of compound **2** are very few in number. Some recently developed procedures for their synthesis based on diastereoselective reactions using chiral starting compounds and catalysts are considered below.

1. Syntheses based on diastereoselective reactions

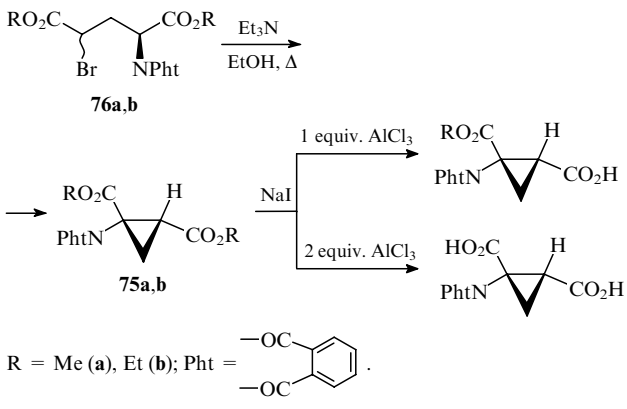
The preparation of a *trans*-isomer of an *N*-*tert*-butoxycarbonyl derivative of acid **2** has been described.[68] Methyl (1*RS*, 5*SR*)-2-oxo-3-oxabicyclo[3.1.0]hexane-1-carboxylate (**71**) was synthesised by condensation of epichlorohydrin with dimethyl malonate in the presence of freshly prepared sodium methoxide as a catalyst. Ammonolysis of bicyclic lactone **71**, protection of the free hydroxy group by reaction with *tert*-butyldimethylsilyl chloride in the presence of imidazole and subsequent Hoffmann rearrangement with lead tetraacetate in *tert*-butyl alcohol yielded *N*-Boc-protected cyclopropane **72**; selective deprotection of its hydroxy group gave alcohol **73** in 85% yield. The next step included mild oxidation of the primary alcohol in a neutral medium by *in situ* generated RuO_4 with retention of the cyclopropane ring and the protected amino group. The monomethyl ester **74** with *trans*-configuration of the carboxy groups was obtained in 60% yield. This method can also be used for the preparation of isomers with definite absolute configuration starting from optically active epichlorohydrin.



71 **72** **73** **74**

TBDMS = Bu^tMe_2Si, ImH is imidazole.

Dialkyl 1-phthalimidocyclopropane-1,2-dicarboxylates **75a**,**b** having a *trans*-configuration were prepared starting from dialkyl *N*-phthaloyl-4-bromoglutamates **76a**,**b** upon boiling in ethanol in the presence of triethylamine.[69] Under the action of 1 or 2 equiv. of $AlCl_3$ in the presence of NaI, esters **75a**,**b** are converted either into monoalkyl esters of 1-phthalimidocyclopropane-1,2-dicarboxylic acid or into a free diacid. According to X-day diffraction analysis,[69] ^{1}H NMR and ^{13}C NMR spectroscopic and GC/MS data,[70] dialkyl esters **75a**,**b** represent individual isomers with a *trans*-configuration of ester groups relative to the cyclopropane ring, although the starting bromo derivatives **76a**,**b** were used as a mixture of diastereomers.

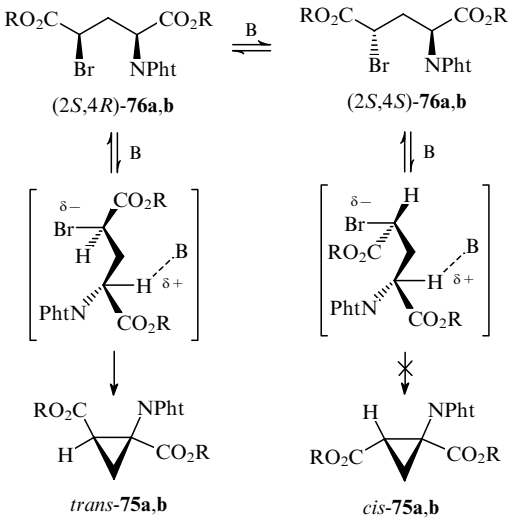


76a,**b** **75a**,**b**

R = Me (**a**), Et (**b**); Pht = .

HPLC studies have shown[70] that (2*S*,4*S*)-isomers of compounds **76** react with bases much more slowly than (2*S*,4*R*)-isomers. This reaction is accompanied by epimerisation at the C(4) atom of glutamic acid. It was suggested that the abstraction of the proton and the bromide ion follows a concerted mechanism and is similar to the E_2 mechanism. The reaction begins with an attack of the base on the proton at C(2) and the formation of a

transition state. As this reaction requires that the C(1)–C(5) atoms are coplanar in the transition state and that the *anti*-abstraction of the proton and bromide ion occur, the activation energies of the reactions of *threo*-isomers (2*S*,4*S*)-**76a**,**b** markedly exceed those of the *erythro*-isomers, presumably due to forced shielded positions of C(5)-carboxy and phthalimide groups in the transition state of *threo*-isomers. Therefore, the transformation of a mixture of diastereomers of compounds **76a**,**b** into derivatives of acid **2** is stereospecific and gives exclusively *trans*-isomers.

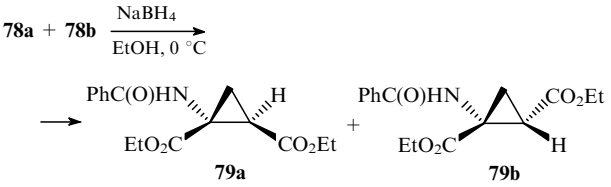


B = Et_3N, KOH.

An original method for the synthesis of derivatives of acid **2** based on diastereoselective cycloaddition of stabilised sulfur ylides to substituted 4-methylideneoxazolidin-5-ones was proposed.[26]

Treatment of compound **77** with ethyl dimethylsulfonioacetate in THF at 0 °C gives a mixture of three diastereomeric cyclopropane adducts separated by column chromatography. (1*R*,3*R*,6*R*)- and (1*S*,3*R*,6*R*)-isomers of 7-benzoyl-1-ethoxycarbonyl-4-oxo-6-phenyl-5-oxa-7-azaspiro[2.4]heptane (**78a** and **78b**) were isolated as a 9 : 1 mixture in a total yield of 55%, the yield of the diastereomerically pure product **78c** was 6%. The assignment of the stereoconfiguration of the isomers formed was carried out based on X-ray diffraction analysis and NMR spectroscopic data (Scheme 2).

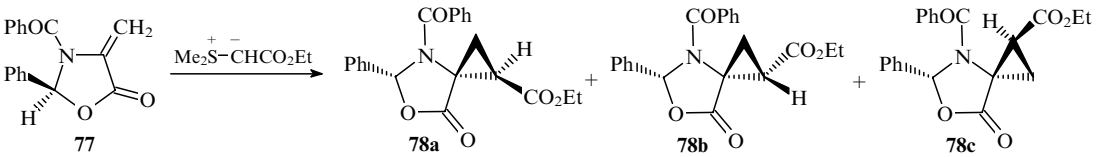
Treatment of a mixture of isomers **78a**,**b** with sodium borohydride in ethanol results in the oxazolidinone ring opening, as a result of which a mixture of diastereomers of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives **79a** and **79b** is formed in a 9 : 1 ratio.



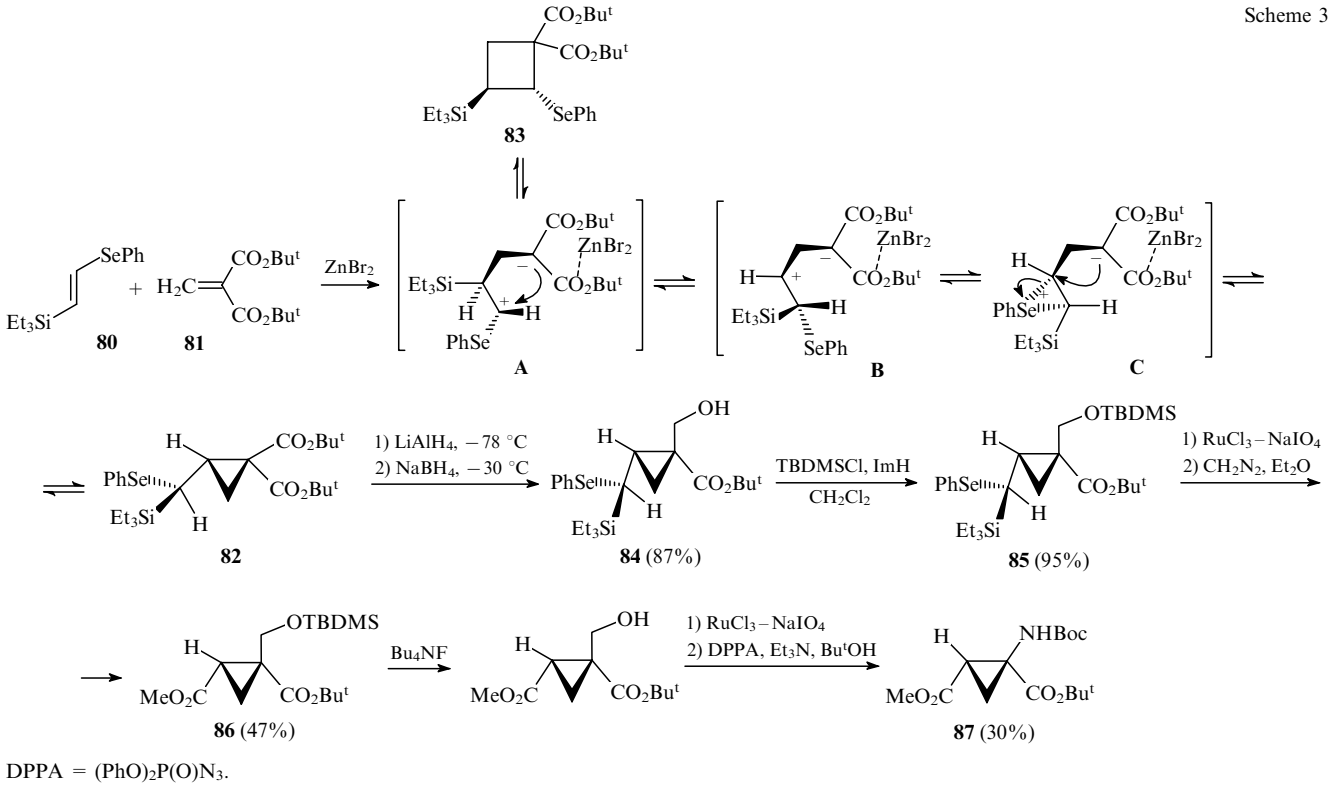
Attempts to hydrolyse the ester groups of the isomers **78a** and **78b** by treatment with 6 M HCl were unsuccessful, since this led to cyclopropane ring opening.[26]

A method for the synthesis of (*E*)-2,3-methanoaspartic acid derivatives[71] (Scheme 3) is based on the use of a chiral cyclopropane with substituents which can readily be converted into amino and carboxy functional groups. Reaction of 1-phenylseleno-2-triethylsilylethene (**80**) with di-*tert*-butyl methylidene-

Scheme 2



Scheme 3

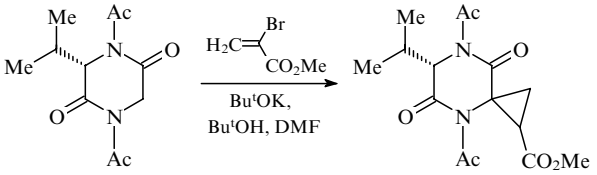


DPPA = $(PhO)_2P(O)N_3$.

malonate (**81**) in the presence of $ZnBr_2$ in CH_2Cl_2 at $-30-0$ °C gives a mixture of di-*tert*-butyl 2-[(phenylseleno)(triethylsilyl)methyl]cyclopropane-1,1-dicarboxylate (**82**) and protected cyclobutane **83** (7 : 3) in high yield. Presumably,[72] the cycloaddition mechanism is similar to that proposed[73] for vinyl ketones. The nucleophilic selenide **80** attacks the electrophilic alkene **81** activated by a Lewis acid to give the zwitterion **A**; its cyclisation gives substituted cyclobutane **83**. Intermediate **A** undergoes rearrangement to the zwitterion **B**, which can be converted into an electron-stabilised intermediate **C** containing a selenium bridge. The latter is cyclised to compound **82**; its stereochemistry was established as (*S*,*S*) or (*R*,*R*) using ^1H and ^{13}C NMR spectroscopy (Scheme 3).

Stereoselective reduction of a less shielded ester group in compound **82**, which is in the *trans*-position relative to the substituent at C(2), gave an alcohol **84**. The product **85** formed after protection of the hydroxy group in the alcohol **84** was oxidised using the $RuCl_3-NaIO_4$ system. Treatment of the acid formed with diazomethane in ether resulted in compound **86**. Removal of the protective *tert*-butyldimethylsilyl group, oxidation of the primary alcohol to an acid and its subsequent reaction with diphenyl phosphorazidate accompanied by the Curzius rearrangement and addition of *tert*-butyl alcohol to the isocyanate formed afforded dialkyl (±)-(*E*)-1-[(*N*-*tert*-butoxycarbonyl)amino]cyclopropane-1,2-dicarboxylate (**87**); its stereochemistry was established by NMR.

The diastereoselective addition of diketopiperazine **88** to the double bond of methyl 2-bromoacrylate has been described.[74] Elimination of hydrogen bromide yields the cyclic dipeptide **89** incorporating protected acid **2**.

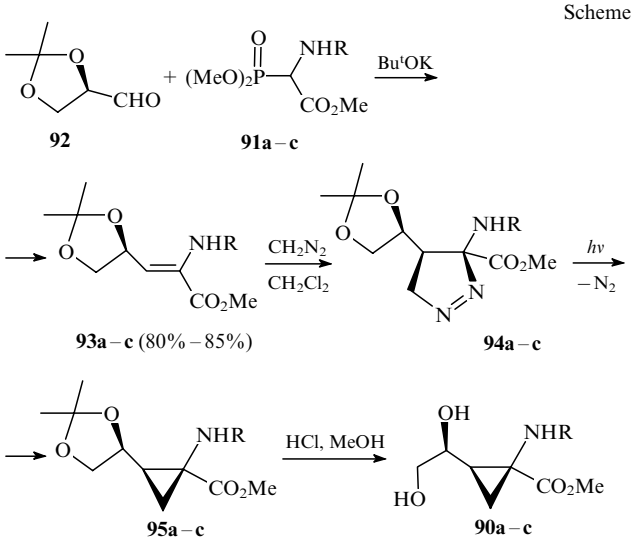


88 **89**

2. Syntheses based on the use of chiral compounds

The methods for the synthesis of individual stereoisomers of cyclopropane-containing amino acids from optically active starting compounds are often more efficient than those based on stereoselective reactions. The use of commercially available optically active synthons allows one to reduce the number of synthetic steps and to increase the yield and optical purity of the final product.

Scheme 4



92 **91a–c**

93a–c (80%–85%) **94a–c**

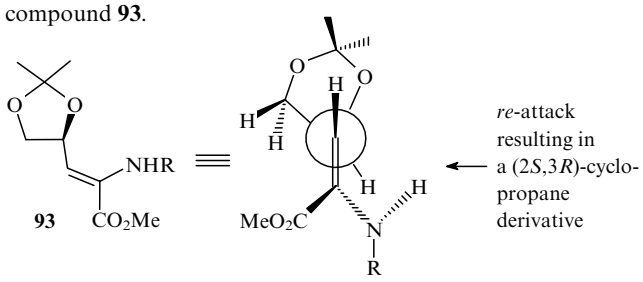
95a–c **90a–c**

R = Cbz (**a**), Boc (**b**), Ac (**c**); Cbz = $C_6H_5CH_2OC(O)$;

A method for the synthesis of methyl-(2*S*,3*R*)-*N*-benzyloxycarbonyl cycloasparaginate from chiral diols was proposed.[75,76] The Wittig–Horner condensation of phosphonates **90a–c** with isopropylidene-D-glyceraldehyde (**91**) synthesised from D-mannitol yielded (*Z*)-dehydroamino acid derivatives **92a–c** containing one chiral centre (Scheme 4).

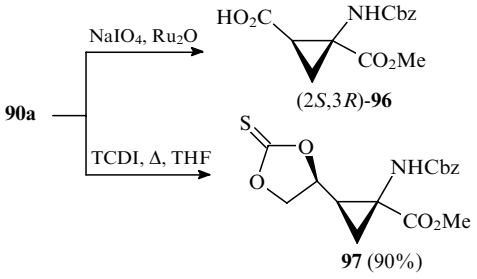
Addition of diazomethane to the double bond of intermediates **92a–c** gives dihydropyrazoles **93a–c**; their photochemical degradation affords optically pure cyclopropane derivatives **94a–c** in a quantitative yield (data from ^1H and ^{13}C NMR spectroscopy).

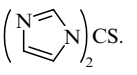
The diastereoselectivity of 1,3-dipolar cycloaddition at the double bond is explained[75] by the fact that diazomethane attacks preferably from the less shielded *re*-side of the C(2) atom of compound **93**.



Removal of the isopropylidene protective group in compounds **94a–c** is carried out under mild conditions in order to prevent cyclopropane ring opening and epimerisation of the diols formed. Treatment of derivatives **94a–c** with 5% HCl in methanol for 4–4.5 h at room temperature affords chiral diols **95a–c** in quantitative yields; the assignment of their stereoconfigurations was made based on ^1H NMR spectroscopic data. Hydrolysis performed for a longer time caused epimerisation of chiral centres of cyclopropane to yield (2*R*,3*S*)-enantiomers of the diols **95**.

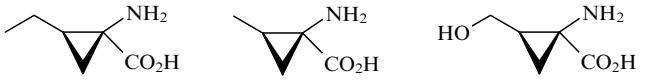
Oxidation of the diol **95a** with sodium periodate in the presence of ruthenium oxide at room temperature gives a dicarboxylic acid monoester (2*S*,3*R*)-**96** in 63% yield.[75,76]



TCDI = 

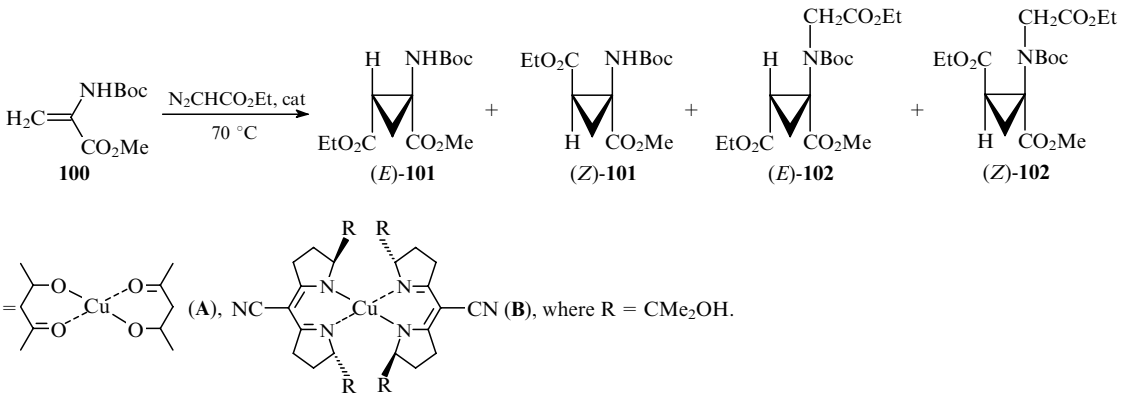
Reaction of compound **95a** with thiocarbonyldiimidazole gave (2*S*,3*R*)-thiocarbonate **97**; its absolute configuration was established unambiguously using X-ray diffraction analysis.

Other cyclopropane-containing amino acids, *viz.*, (−)-allocoronamic and (−)-allonorcoronamic acids and (−)-(*Z*)-2,3-methanohomoserine,[75,76] were synthesised starting from the diols **95**, which demonstrates the efficiency of the latter as enantiomeric synthons in the stereocontrolled synthesis of natural compounds containing a cyclopropane fragment and methano analogues of proteinogenic amino acids.



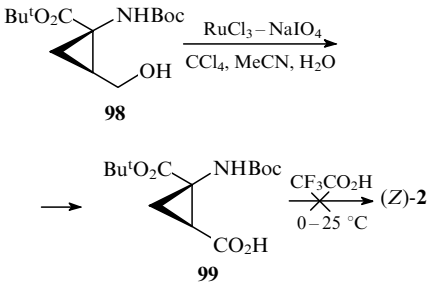
(−)-Allocoronamic acid (−)- Allonorcoronamic acid (−)-(Z)-2,3-Methanohomoserine

Scheme 5



Enantiomerically pure amino acids, which can undergo chemical transformations without loss of their optical activities, can be used as the starting compounds in the synthesis of 2,3-methano amino acid derivatives.

Thus the 2,3-cyclohomoserine derivative **98** with protected amino and carboxy groups was oxidised with $RuCl_3 - NaIO_4$ to give compound **99** (yield 51%). However, attempts at deprotection of the amino group led to the destruction of the cyclopropane ring.[2]



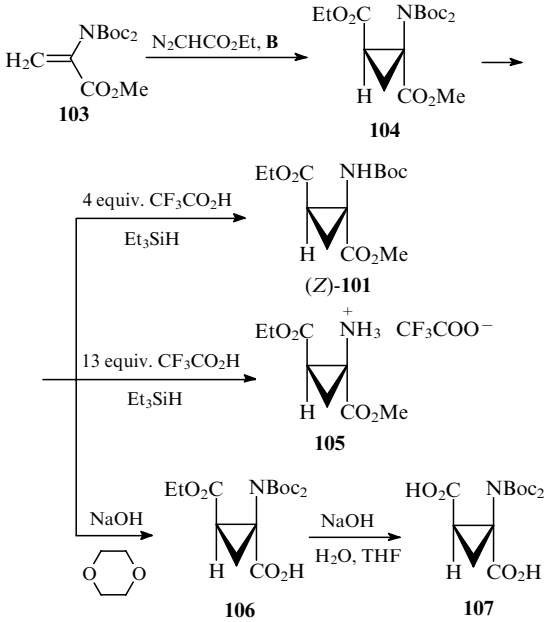
3. The use of metal complexes

Chiral metal complexes are widely used for the preparation of enantiomerically pure substituted cyclopropanes[77] including amino cyclopropanecarboxylic acids. This approach was used, in particular, for the synthesis of stereoisomers of cycloaspartic acid derivatives.

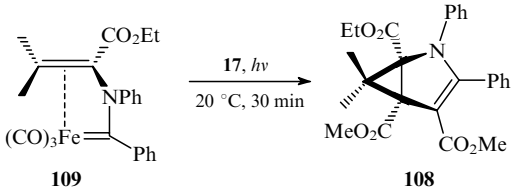
Reaction of methyl *N*-protected 2-aminoacrylate (**100**) prepared by dehydration of serine methyl ester with ethyl diazoacetate yields a mixture of four cyclopropanes which represent addition products of ethoxycarbonylcarbene at the double bond [(*E*)- and (*Z*)-**101**] and incorporation products into the N—H bond of the amino group [(*E*)- and (*Z*)-**102**] (Scheme 5).[78]

An achiral complex, copper acetylacetonate (**A**), and a chiral copper complex of hemicorrine (the Pfalz complex, **B**) were used as catalysts. *Z* Isomers of the reaction products were predominant; the use of the Pfalz complex made it possible to increase their content. The yields of substituted cyclopropanes **101** and **102** depend on both the amount of ethyl diazoacetate and the nature of the catalyst. Thus reaction of compound **100** with 1.3 equiv. of ethyl diazoacetate in the presence of catalyst **A** afforded a mixture of *E* and *Z* isomers of compounds **101** (**101a** : **101b** = 45 : 55, total yield 15%) and **102** (**102a** : **102b** = 41 : 59, total yield 8%). The reaction performed in the presence of 2.5 equiv. of ethyl diazoacetate and the Pfalz catalyst gave a mixture of *E* and *Z* isomers of compounds **101** and **102** in a 1 : 4 ratio (total yields 40% and 20%, respectively).

The methyl ester of dehydroalanine **103** with two *tert*-butoxycarbonyl groups at the nitrogen atom was synthesised in order to prevent the formation of products **102**; its treatment with an eightfold excess of ethyl diazoacetate in the presence of the Pfalz catalyst gave only the *Z* isomer of 1-[bis(*tert*-butoxycarbonyl)-amino]-2-ethoxycarbonyl-1-methoxycarbonylcyclopropane (**104**) (yield 85%). Removal of one Boc-group from compound **104** was performed by treatment with trimethylsilyl chloride in methanol – dichloromethane or with a fourfold excess of trifluoroacetic acid in the presence of triethylsilane, which gave the *Z* isomer of the derivative **101**. The same conditions were used for the cleavage of two Boc-groups from compound **104** in the presence of 13 equiv. of trifluoroacetic acid to give trifluoroacetate **105**. Saponification of the diester **104** with an alkali gave consecutively compound **106** with a free α-carboxy group and a dicarboxylic acid **107**.



1-Ethoxycarbonyl-4,5-bis(methoxycarbonyl)-6,6-dimethyl-2,3-diphenyl-2-azabicyclo[3.1.0]hex-3-ene (**108**), a chiral derivative of the acid (*E*)-**2**, was prepared in 62% yield using a photoinduced reaction of the *N*-vinylaminocarbene iron complex **109** with acetylenedicarboxylate **17**.[79]

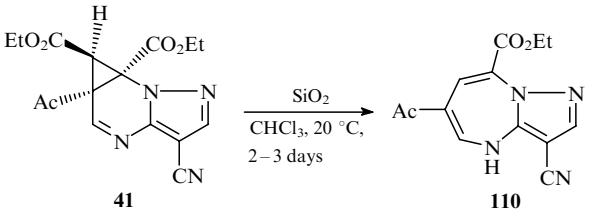


IV. Properties of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives

Rearrangements of compounds **40** and **41,** which yield diazepines with potential biological activities, have been studied.[80, 81]

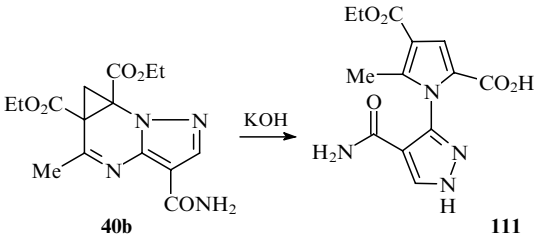
Thus compound **41** is converted into diazepine **110** in the presence of silica gel in chloroform; this reaction is accompanied

by the cleavage of one ethoxycarbonyl group (^{1}H and ^{13}C NMR data).[80]



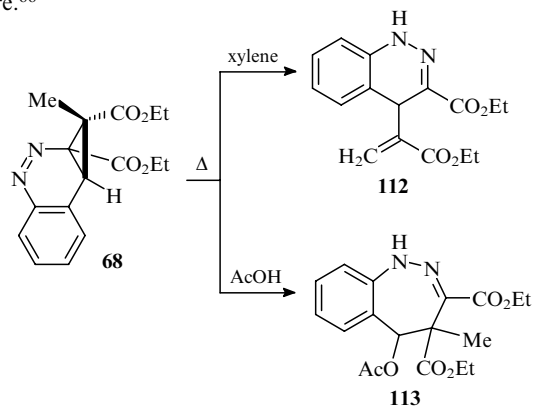
41 **110**

Treatment of diethyl ester **40b** (R^1 = CO_2Et) with ethanolic KOH leads to profound rearrangement of the molecule and the formation of substituted pyrazolylpyrrole **111** by cyclopropane ring opening.[81]

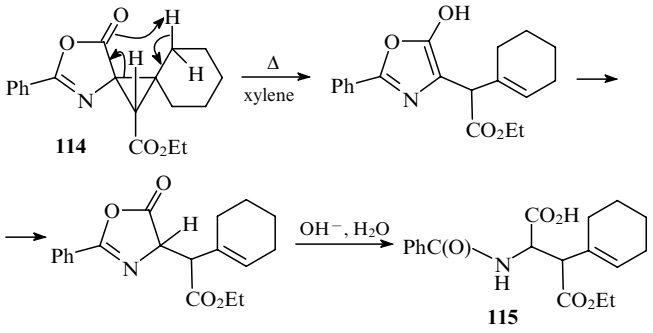


40b **111**

Boiling of 1,1*a*-bis(ethoxycarbonyl)-1-methyl-1*a*,7*b*-dihydrocyclopropa[*c*]cinnoline (**68**, R = Me) in xylene affords a 1,4-dihydrocinnoline derivative **112** in 60% yield,[65] while boiling in acetic acid gives an individual isomer of an acetoxydiazepine derivative **113** (yield 60%) with a non-established spatial structure.[66]

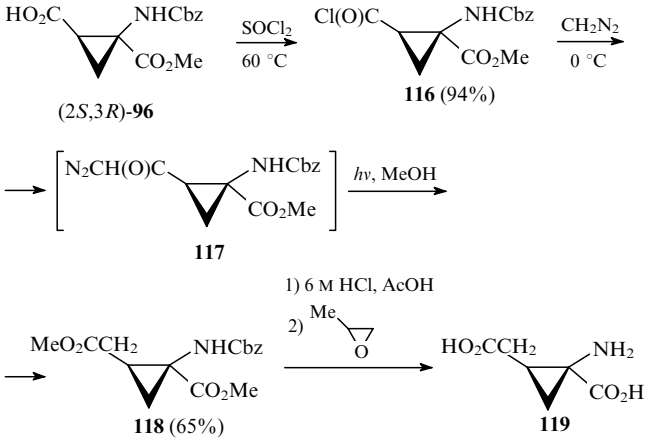


Thermolysis of spirocyclopropane **114** in boiling xylene and subsequent alkaline hydrolysis yield a mixture of stereoisomers of amino acid **115** of unknown configuration.[63]



Protected (*Z*)-cycloaspartic acid (2*S*,3*R*)-**96** was used as an optically pure starting compound in enantioselective synthesis of (−)-(*Z*)-2,3-methano-L-glutamic acid.[82]

The reaction of acid **96** with thionyl chloride in toluene gives acid chloride **116**; treatment of the latter with diazomethane in ether afforded the corresponding diazo ketone **117**. Photolysis of compound **117** in methanol was accompanied by the Wolff rearrangement resulting in methyl ester **118**. Subsequent hydrolysis of the ester **118** with 6 M HCl in the presence of several drops of glacial acetic acid (90 °C, 6 h) and treatment with propylene oxide at 35 °C gave a free amino acid **119** in quantitative yield.



V. Peptides containing 1-aminocyclopropane-1,2-dicarboxylic acid

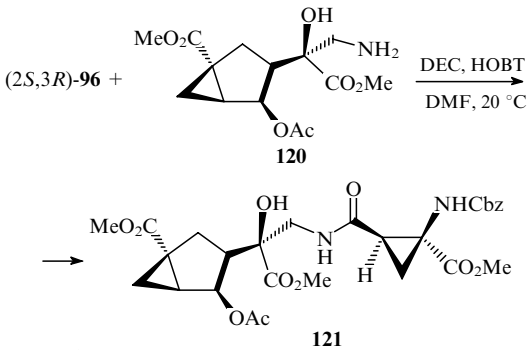
The synthesis of peptides containing 1-aminocyclopropane-1,2-dicarboxylic acid having a sweet taste has been described.[83]

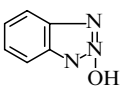
The yields of di- and tripeptides containing a residue of acid **2** prepared by oxidation of peptides containing (±)-(*Z*)-2,3-methanohomoserine with sodium periodate in the presence of $RuCl_3$ are given below.[84]

Peptide	Yield (%)
Boc-∇Asp-L-Phe-OMe	8
Bz-∇Asp-L-Phe-OMe	59
CF_3CO-∇Asp-L-Phe-OMe	82
Ac-∇Asp-L-Phe-OMe	36
Boc-Gly-∇Asp-OMe	45
Bz-Gly-∇Asp	51
Bz-Gly-∇Asp-Gly-OMe	42
Bz-Gly-∇Asp-L-Phe-OMe	62

The possibility of removal of *N*-protective groups from peptides where cycloaspartic acid is not terminal and the presence of free carboxy groups in the side chain allow incorporation of these short fragments into more complex peptides.

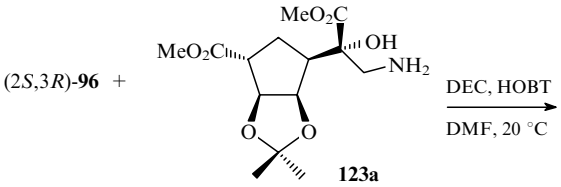
Condensation of the (2*S*,3*R*)-isomer of acid **96** with amine **120** in the presence of 1-(3-dimethylaminopropyl)-3-ethylcarbodi-



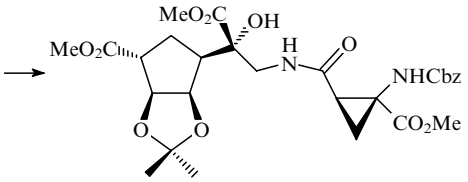
HOBT =  ; DEC = $Me_2N(CH_2)_3N{=}C{=}NEt$.

imide (DEC) as an activating reagent and 1-hydroxybenzotriazole (HOBT) as a catalyst affords a conformationally rigid dipeptide **121** (yield 64%).[85]

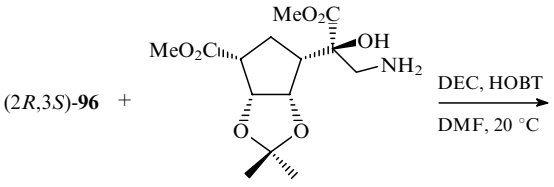
Dipeptide analogues **122a**,**b** were synthesised [86] by a reaction of enantiomers of acid **96** with chiral α-substituted isoserine derivatives **123a**,**b**.



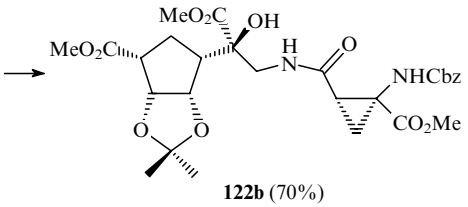
123a



122a (72%)

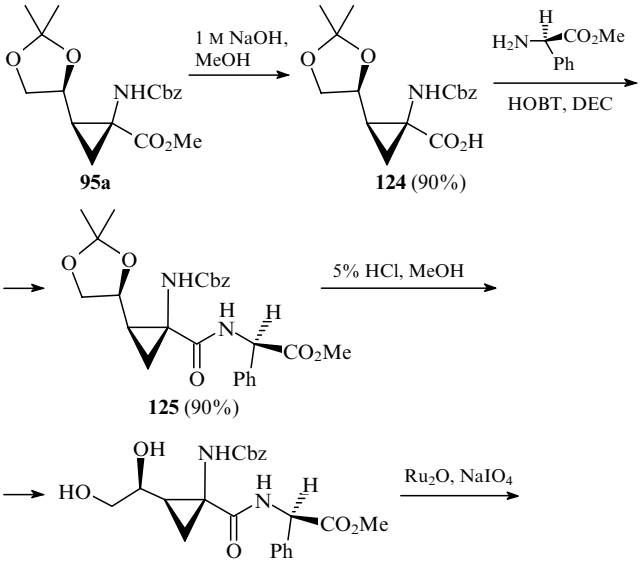


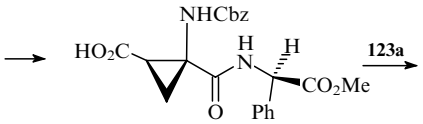
123b



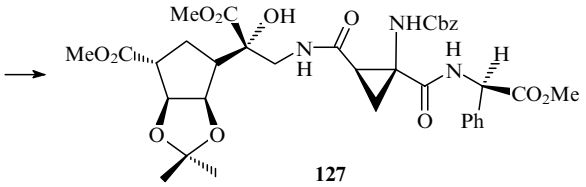
122b (70%)

Reaction of (1*S*,2*R*,4′*S*)-1-[*N*-(benzyloxycarbonyl)amino]-2-(2,2-dimethyl-1,3-dioxolan-4-yl)cyclopropanecarboxylic acid (**124**), obtained by saponification of the ester **95a** with 1 M methanolic NaOH, with the methyl ester of (*R*)-phenylglycine yields the dipeptide **125**. Removal of isopropylidene protection in the peptide **125** with 5% HCl in methanol and subsequent oxidation of the diol affords product **126**. Condensation of compound **126** with α-substituted isoserine derivative **123a** afforded the tripeptide **127**.[86]





126 (64%)



127

In addition to conformational rigidity, incorporation of a cycloaspartic fragment into a peptide chain results in the introduction of an additional lateral carboxy group, which may affect the binding of the peptide to the active site of an enzyme or a receptor. Some peptides containing cycloaspartic acid act as analgesics and renin inhibitors and manifest antiviral activities against the hepatitis C virus.[87] They can also be used as sweeteners.[45]

* * *

1-Aminocyclopropane-1,2-dicarboxylic acid occupies a special place in the series of 2,3-methano amino acids, firstly because it represents a structural analogue of glutamic and aspartic acids which play a crucial role in various metabolic processes occurring in living organisms. Despite the instability of this amino acid, original approaches to the synthesis of its numerous derivatives some of which possess physiological activity have been developed. The use of modern synthetic approaches has made it possible to develop elegant procedures for the synthesis of individual stereoisomers of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives based on diastereoselective reactions and the use of readily available enantiomeric starting compounds. Conformationally rigid peptides containing 1-aminocyclopropane-1,2-dicarboxylic acid play the role of molecular 'probes' in the study of biochemical processes. At the same time, the potentialities of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives in the study of mechanisms of biochemical reactions and the synthesis of physiologically active compounds have not been completely exhausted. Further progress in this branch of amino acid chemistry is expected in the near future.

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References

1. C H Stammer *Tetrahedron* **46** 2231 (1990)
2. K Burgess, K-K Ho, D Moye-Sherman *Synlett* 575 (1994)
3. A Alami, M Calmes, J Daunis, R Jacquier *Bull. Soc. Chim. Fr.* **130** 5 (1993)
4. T Wakamiya, H Nakamoto, T Shiba *Tetrahedron Lett.* **25** 4411 (1984)
5. T Wakamiya, Y Oda, H Fujita, T Shiba *Tetrahedron Lett.* **27** 2143 (1986)
6. A Ichihara, K Shiraishi, S Sakamura *Tetrahedron Lett.* 365 (1979)
7. S R Landor, Ph D Landor, M Kalli *J. Chem. Soc., Perkin Trans. 1* 2921 (1983)
8. N Kurokawa, Y Ohfune *Tetrahedron Lett.* **26** 83 (1985)
9. K Burgess, K-K Ho, B M Pettitt *J. Am. Chem. Soc.* **117** 54 (1995)
10. K Burgess, Ch-Y Ke *J. Org. Chem.* **61** 8627 (1996)
11. D Lim, K Burgess *J. Am. Chem. Soc.* **119** 9632 (1997)
12. S F Martin, R E Austin, C J Oalmann, W R Baker, S L Condon, E deLara, S H Rosenberg, K P Spina, H H Stein, J Cohen, H D Kleinert *J. Med. Chem.* **35** 1710 (1992)

13. C Mapelli, L F Elrod, E M Holt, C H Stammer *Tetrahedron* **45** 4377 (1989)
14. C Mapelli, L F Elrod, F L Switzer, C H Stammer *Biopolymers* **28** 123 (1989)
15. L B Piotrovskii *Khim.-Farm. Zh.* **21** 773 (1987) [a]
16. R L Johnson, J F Koerner *J. Med. Chem.* **31** 2057 (1988)
17. T Knöpfel, R Kuhn, H Allgeier *J. Med. Chem.* **38** 1417 (1995)
18. K Yamanoi, Y Ohfune *Tetrahedron Lett.* **29** 1181 (1988)
19. K Shimamoto, Y Ohfune *Tetrahedron Lett.* **30** 3803 (1989)
20. R Pellicciari, B Natalini, M Marinozzi *Tetrahedron Lett.* **31** 139 (1990)
21. K Shimamoto, M Ishida, H Shinozaki, Y Ohfune *J. Org. Chem.* **56** 4167 (1991)
22. O N Zefirova, N S Zefirov *Zh. Org. Khim.* **36** 1273 (2000) [b]
23. L I Deiko, K V Varlygo, in *Fiziologiya i Biokhimiya Glutamatergicheskikh Sinapsov* (Physiology and Biochemistry of Glutamatergic Synapses) (Ed. Yu E Mandel'shtam) (Leningrad: Nauka, 1989) p. 25
24. G A Kraus, H Kim, P J Thomas, D E Metzler, C M Metzler, J E Taylor *Synth. Commun.* **20** 2667 (1990)
25. E C Taylor, B H Hu *Synth. Commun.* **26** 1041 (1996)
26. S G Pyne, K Schafer, B W Skelton, A H White *Aust. J. Chem.* **51** 127 (1998)
27. R Beumer, C Bubert, C Cabrele, O Vielhauer, M Pietzsch, O Reiser *J. Org. Chem.* **65** 8960 (2000)
28. L A Yanovskaya, V A Dombrovskii, A Kh Khusid, in *Tsiklopropany s Funktsional'nymi Gruppami* (Cyclopropanes with Functional Groups) (Ed. V F Kucherov) (Moscow: Nauka, 1989) p. 106
29. J G Cannon, J E Garst *J. Org. Chem.* **40** 182 (1975)
30. L Dechoux, E Doris *Tetrahedron Lett.* **35** 2017 (1994)
31. R Huisgen *Angew. Chem.* **75** 604 (1963)
32. I Bregovec, T Jakovčić *Monatsh. Chem.* **103** 288 (1972)
33. T Hyama, M Kai *Tetrahedron Lett.* **23** 2103 (1982)
34. J M Bland, C H Stammer, K I Varughese *J. Org. Chem.* **49** 1634 (1984)
35. C Cativiela, M D Diaz de Villegas, E Melendez *Tetrahedron* **42** 583 (1986)
36. J Bland, A Shah, A Bortolussi, C H Stammer *J. Org. Chem.* **53** 992 (1988)
37. A M P Koskinen, L Muñoz *J. Org. Chem.* **58** 879 (1993)
38. H M L Davies, P R Bruzinski, D H Lake, N Kong, M J Fall *J. Am. Chem. Soc.* **118** 6897 (1996)
39. H Horikawa, T Nishitani, T Iwasaki, I Inoue *Tetrahedron Lett.* **24** 2193 (1983)
40. N A Anisimova, T Ya Paperno, L I Deiko, in *Sintez, Struktura i Khimicheskie Prevrashcheniya Organicheskikh Soedinenii Azota: Nitrozosoedinenii, Aminov i Aminokislot* (Synthesis, Structure and Chemical Conversions of Organic Compounds of Nitrogen: Nitroso Compounds, Amines and Amino Acids) (Ed. N A Solov'ev) (Leningrad: A I Gertsen Russian State Pedagogical University, 1991) p. 97
41. N A Anisimova, G A Berkova, L I Deiko *Zh. Obshch. Khim.* **68** 1165 (1998) [c]
42. N A Anisimova, G A Berkova, L I Deiko, V P Pozdnyakov *Zh. Obshch. Khim.* **69** 1529 (1999) [c]
43. N A Anisimova, G A Berkova, L I Deiko *Zh. Obshch. Khim.* **72** 93 (2002) [c]
44. N A Anisimova, L I Deiko, G A Berkova *Zh. Org. Khim.* **35** 160 (1999) [b]
45. WO PCT 8 500 809; *Chem. Abstr.* **103** 215 811 (1985)
46. M Franck-Neumann, D Martina, C Dietrich-Buchecker *Tetrahedron Lett.* 1763 (1975)
47. M Franck-Neumann, C Buchecker *Angew. Chem.* **85** 259 (1973)
48. M A Kuznetsov, I D Kuchuk *Zh. Org. Khim.* **33** 1628 (1997) [b]
49. S Mataka, T Ohshima, M Tashiro *J. Org. Chem.* **46** 3960 (1981)
50. A Bojilova, I Videnova, C Ivanov, N A Rodios, A Terzis, C P Raptopoulou *Tetrahedron* **50** 13023 (1994)
51. A Padwa, S I Goldstein *Can. J. Chem.* **62** 2506 (1984)
52. Y Tan, S A Ahmed, H Dürr, V Huch, A Abdel-Wahab *Chem. Commun.* 1246 (2001)
53. T Kurihara, K Nasu, F Ishimori, T Tani *J. Heterocycl. Chem.* **18** 163 (1981)
54. T Kurihara, K Nasu, Y Adachi *J. Heterocycl. Chem.* **20** 81 (1983)
55. T Kurihara, K Nasu, J Byakuno, T Tani *Chem. Pharm. Bull.* **30** 1289 (1982)
56. H Gstach, H Kisch *Chem. Ber.* **115** 2586 (1982)
57. M Franck-Neumann, M Miesch, H Kempf *Tetrahedron* **44** 2933 (1988)
58. G Fischer, D Hunkler, H Prinzbach, G Rihs, H Fritz *Tetrahedron Lett.* **25** 2459 (1984)
59. K Exner, G Fischer, N Bahr, E Beckmann, M Lugan, F Yang, G Rihs, M Keller, D Hunkler, L Knothe, H Prinzbach *Eur. J. Org. Chem.* 763 (2000)
60. T Ueda, Y Kawabata, N Murakami, S Nagai, J Sakakibara, M Goto *Chem. Pharm. Bull.* **39** 270 (1991)
61. A L Schwan, J Warkentin *Can. J. Chem.* **66** 1686 (1988)
62. E Van Loock, G L'abbé, G Smets *Tetrahedron* **28** 3061 (1972)
63. O Tsuge, M Noguchi, H Moriyama *Heterocycles* **19** 1823 (1982)
64. L Garanti, A Vigevani, G Zecchi *Tetrahedron Lett.* 1527 (1976)
65. L Garanti, G Zecchi *J. Heterocycl. Chem.* **15** 509 (1978)
66. L Garanti, G Zecchi *J. Chem. Soc., Perkin Trans. 1* 1195 (1979)
67. A Alemagna, P Del Buttero, E Licandro, S Maiorana *Gazz. Chim. Ital.* **111** 285 (1981)
68. L Wick, C Tamm, T Boller *Helv. Chim. Acta* **78** 403 (1995)
69. V Kh Kravtsov, V N Biyushkin, T I Malinovskii, V P Krasnov, T V Matveeva *Dokl. Akad. Nauk SSSR* **311** 622 (1990) [d]
70. V P Krasnov, M A Korolyova, T V Matveeva, E A Zhdanova, A N Grishakov, N A Klyuev *Izv. Akad. Nauk, Ser. Khim.* 619 (2001) [e]
71. S Yamazaki, T Inoue, T Hamada, T Takada, K Yamamoto *J. Org. Chem.* **64** 282 (1999)
72. S Yamazaki, M Tanaka, T Inoue, N Morimoto, H Kumagai, K Yamamoto *J. Org. Chem.* **60** 6546 (1995)
73. S Yamazaki, M Tanaka, A Yamaguchi, S Yamabe *J. Am. Chem. Soc.* **116** 2356 (1994)
74. X A Zhang, M M Campbell, D W Brown *Chem. Res. Chin. Univ.* **8** 377 (1992)
75. J M Jiménez, J Rifé, R M Ortuño *Tetrahedron: Asymmetry* **7** 537 (1996)
76. J M Jiménez, J Rifé, R M Ortuño *Tetrahedron: Asymmetry* **6** 1849 (1995)
77. M P Doyle, M N Protopopova *Tetrahedron* **54** 7919 (1998)
78. K El Abdioui, J Martinez, P Viallefont, Y Vidal *Bull. Soc. Chim. Belg.* **106** 425 (1997)
79. R Aumann, B Trentmann, C Krüger, F Lutz *Chem. Ber.* **124** 2595 (1991)
80. T Kurihara, E Kawasaki, K Nasu *Heterocycles* **20** 1913 (1983)
81. T Kurihara, T Tani, K Nasu, M Inoue, T Ishida *Chem. Pharm. Bull.* **29** 3214 (1981)
82. J M Jiménez, R M Ortuño *Tetrahedron: Asymmetry* **7** 3203 (1996)
83. M Tamura, J A Park, C H Stammer *Pept. Chem.* 705 (1998)
84. E Godier-Marc, D J Aitken, H-P Husson *Tetrahedron Lett.* **38** 4065 (1997)
85. M Díaz, R M Ortuño *Tetrahedron: Asymmetry* **7** 3465 (1996)
86. M Díaz, J M Jiménez, R M Ortuño *Tetrahedron: Asymmetry* **8** 2465 (1997)
87. WO PCT 0 009 558; *Chem. Abstr.* **132** 175 808 (2000)

[a] — *Pharm. Chem. J. (Engl. Transl.)*
[b] — *Russ. J. Org. Chem. (Engl. Transl.)*
[c] — *Russ. J. Gen. Chem. (Engl. Transl.)*
[d] — *Dokl. Chem. (Engl. Transl.)*
[e] — *Russ. Chem. Bull., Int. Ed. (Engl. Transl.)*