2-Substituted 3-Dimethylamino- and -3-cyanopropenoates in the Synthesis of Heterocyclic Systems

Branko Stanovnik

Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, P.O. Box 537, 1000 Ljubljana, Slovenia

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Contents

1. Introduction.

α-Amino and α-hydroxy acids and their derivatives play an important role in organic synthesis, especially in asymmetric synthesis as chiral synthons, chiral auxiliaries, and resolving agents [1-3].

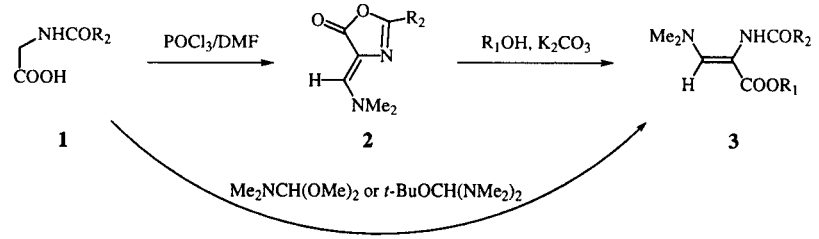
In the course of our studies of heteroaryl substituted α-amino and α-hydroxy acids and their derivatives we have prepared easily accessible 2-acylamino-3-dimethylaminopropenoates, 2-(*O*-substituted hydroxy)-3-dimethylaminopropenoates, and 2-ethenylamino-3-dimethylaminopropenoates, masked α-formyl-α-amino- and α-formyl-α-hydroxy acids, and their derivatives. They have turned out to be excellent reagents for the preparaton of a variety of heterocyclic systems with an amino or hydroxy acid structural element incorporated or partially incorporated into the newly formed heterocyclic ring [4].

2. Synthesis of 2-Acylamino-3-dimethylaminopropenoates, *O*-Substituted 2-Hydroxy-3-dimethylaminopropenoates and 2-[(2-Substituted ethenyl)amino-3-dimethylaminopropenoates.

Alkyl 2-acylamino-3-dimethylaminopropenoates (**3**) can be prepared by two methods: a) by reaction of *N*-acylglycine (**1**) with phosphorus oxychloride in *N,N*-dimethylformamide to afford 4-dimethylaminomethyliden-5(4*H*)-oxazolone (**2**) followed by alcoholysis in the presence of potassium carbonate to give **1**, or b) by treatment of **1** with *N,N*-dimethylformamide dimethyl acetal or *t*-BuOCH(NMe_2)$_2$ to give **1** in one pot procedure. Similarly, alkyl *O*-substituted 2-hydroxyacetates (**4**) when treated with *tert*-butyloxy-*bis*(dimethylamino)-methane give **5** (Scheme 1).

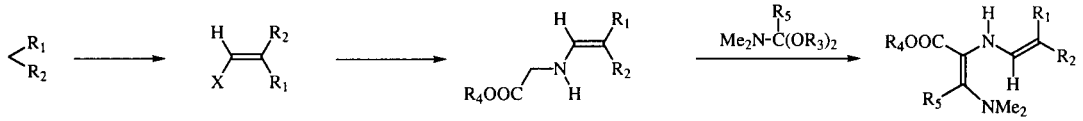
2-[(2-Substituted ethenyl)amino]-3-dimethylaminopropenoates (**9**) can be prepared from compounds with an active methylene group **6** by transformation into ethoxymethylidene- or dimethylaminomethylidene derivatives **7**. These are transformed with an alkyl glycinate into **8** and further with *N,N*-dimethylformamide dimethyl acetal into **9** (Scheme 2).

Scheme 1
Synthesis of 2-Acylamino- and *O*-Substituted 2-Hydroxy-3-dimethylaminopropenoates



	R_1	R_2	Reference
3a	Me	Ph	5,6
3b	Et	Ph	7
3c	Me	Me	8
3d	Et	Me	9
3e	Me	CF_3	8
3f	Me	OCH_2Ph	10
5a	Me	COPh	11
5b	Et	COPh	11
5c	Me	CH_2PH	11
5d	Me	Ph	11

Scheme 2
Synthesis of 2-[(2-Substituted Ethenyl)amino]-3-dimethylaminopropenoates



6 7 8 9

9	R_1	R_2	R_3	R_4	R_5	Reference
a	COOEt	COOEt	H	Me	H	12
b	COOEt	COOEt	H	Et	H	13
c	COOMe	COOMe	H	Et	H	14
d	COOEt	COPh	H	Me	H	15
e	COOEt	COPh	H	Et	H	15
f	COOEt	COMe	H	Me	H	16
g	COOMe	COMe	H	Me	H	17
h	COPh	COPh	H	Et	H	18
i	COMe	COPh	H	Et	H	19
j	COMe	COMe	H	Me	H	20
k	COOBn	COMe	H	Me	H	17
l	COOEt	Ph	H	Me	H	21
m	COOEt	CN	H	Et	H	22,23
n	COOEt	CN	Me	Me	H	23
o	COOEt	CN	Me	Et	H	23
p	COOEt	COOEt	H	Me	Me	24

3. Synthesis of Heterocyclic Systems.

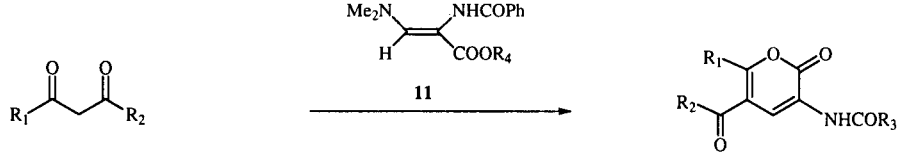
2-Acylamino- and *O*-substituted 2-hydroxy-3-dimethylaminopropenoates and their derivatives can be applied as three carbon synthons for the synthesis of a variety of monocyclic and polycyclic heterocyclic systems, in which α-amino- or α-hydroxy acid structural element is incorporated into the heterocyclic system.

3.1 Synthesis of Pyranones and Fused Pyranones.

In the reaction of 1,3-dicarbonyl compounds **10** with **11** in the presence of acetic acid 3-acylamino-2*H*-pyran-2-ones **12** are formed [25] (Scheme3).

Cyclic 1,3-dicarbonyl compounds, such as 1,3-cyclohexanedione (**14**) and its 5,5-dimethyl derivative (**16**), afford with benzyloxycarbonylamino-3-dimethylaminopropenoate (**13**), as an example, 5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-ones **15** and **17**, respectively. Phenol itself does not react, while resorcinol (**18**) and its 2-methyl derivative **20** form 2*H*-1-benzopyran-2-one derivatives **15** and **17** [26]. On the other hand, 1- (**22**) and 2-naphthol (**23**) are activated enough to give the corresponding 2*H*-naphtho[1,2-*b*]pyran-3-one **24** and 3*H*-naphtho[2,1-*b*]-pyran-2-one **25** derivatives, respectively [27]. Similarly, 2,3-dihydroxynaphthalene (**26**) produces, naphthopyra-

Scheme 3
Synthesis of Pyranones



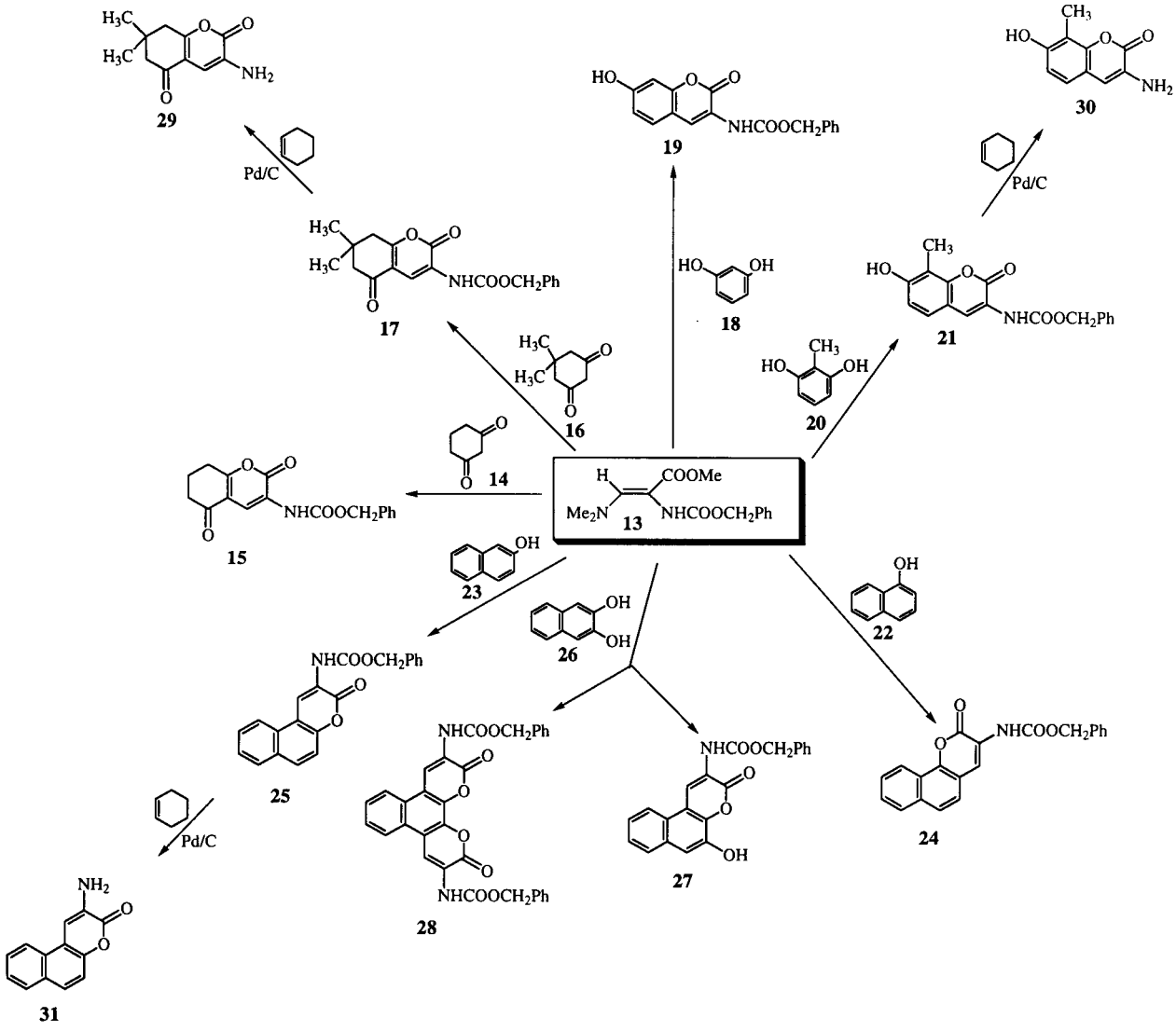
R_1	Ph	Me	Me	Me
R_2	OEt	OEt	Ph	Me

10 12

none **27** or naphthobispyranone **28**. Benzyloxacarbonyl protecting group can be easily removed by catalytic transfer hydrogenation to give free amino compounds **29**, **30**, and **31** [10] (Scheme 4).

Similarly react also heterocyclic systems with a carbonyl and an adjacent metylene group as a part of the ring system **41**, or their tautomeric hydroxy forms, such as pyrazole, pyridine, pyran, benzopyran, quinoline, pyrid-

Scheme 4
Synthesis of Pyranones Fused to Carbocyclic Systems

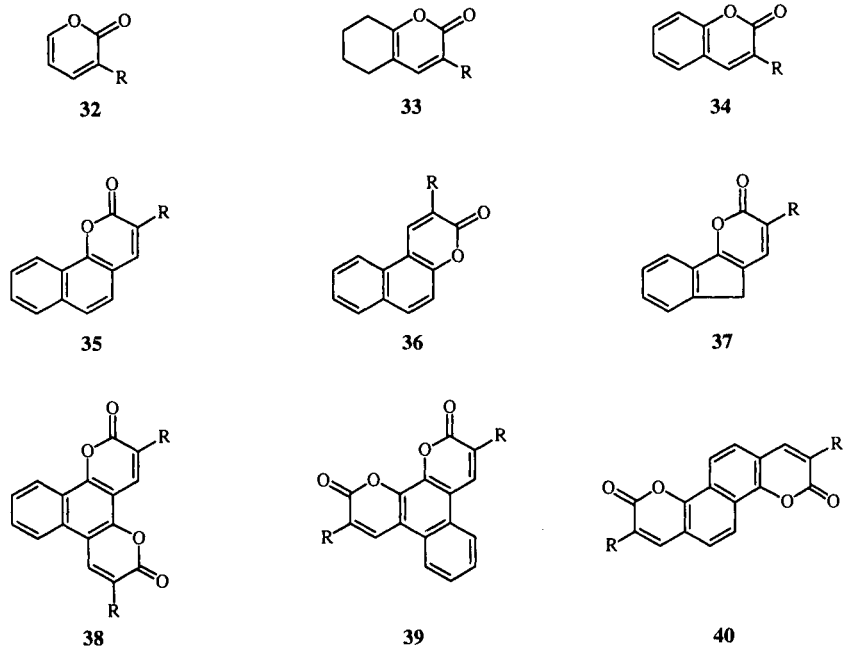


Accordingly, derivatives of the following systems have been prepared: 2*H*-pyran-2-ones **32** [8,10,25,27], 5,6,7,8-tetrahydro-2*H*-benzopyran-2-one **33** [10,15,17,20,22,27,28], 2*H*-1-benzopyran-2-one **34** [8,10,11,15,17,22,28], 2*H*-naphtho[1,2-*b*]pyran-2-one **35** [8,10,11,27,28,29], 3*H*-naphtho[2,1-*b*]pyran-3-one **36** [8,10,11,15,28,30,31], 5*H*-indano[1,2,-*b*]pyran-2-one **37** [30], 2*H*,6*H*-naphtho[1,2-*b*:-3,4-*b*']dipyran-2,6-dione **38** [30], 2*H*,11*H*-naphtho[2,1-*b*:-3,4-*b*']dipyran-2,11-dione **39** [30], and 3*H*,9*H*-naphtho[1,2-*b*:5,6-*b*']dipyran-3,9-dione **40** [30] (Scheme 5).

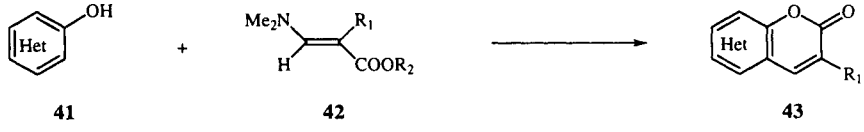
azine, tetrazolo[1,5-*b*]pyridazine, and pyrimidine derivatives, with 2-substituted 3-dimethylaminopropenoates **42** to yield pyranones fused to a heterocyclic system **43** (Scheme 6).

The following heterocyclic systems fused pyranones have been prepared: 1*H*,6*H*-pyrano[2,3-*c*]pyrazole **44** [8,10,11,31,32], 2*H*-pyrano[3,2-*c*]pyridine-2,5-dione **45** [8,10,11,15,28,31,33], 2*H*,7*H*-pyrano[2,3-*c*]pyridine-2,8-dione **46**, 2*H*,5*H*-pyrano[4,3-*b*]pyran-2,5-dione **47** [10,11,14,15,28,34], 2*H*,5*H*-pyrano[3,2-*c*]benzopyran-

Scheme 5
Pyranones and Fused Pyranones



Scheme 6
Synthesis of Pyranones Fused to a Heterocyclic System



2,5-dione **48** [8,10,11,14,15,27,28], 2*H*-pyrano[3,2-*c*]-quinoline-2,5-dione **49** [8,11,28,33], 2*H*-pyrano[2,3-*d*]-pyridazine-2,5-dione **50** [8,28,33], 8*H*-pyrano[3,2-*d*]-tetrazolo[1,5-*b*]pyridazin-8-one **51** [33], and 7*H*-pyrano[2,3-*d*]pyrimidin-7-one (**52**) [8,10,11,26,28,31] (Scheme 7).

3.2 Synthesis of Fused Pyridinones.

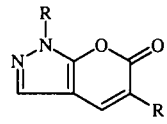
(Pyridinyl-2)acetic acid or its derivatives **53**, such as ethyl (pyridinyl-2)acetate, (pyridinyl-2)acetonitrile, and ethyl (quinolinyl-2)acetate and 2-substituted 3-dimethylaminopropenoates **42** yield by heating in acetic acid the corresponding 4*H*-quinolizin-4-ones **54** and related systems (Scheme 8).

Derivatives of the following systems have been prepared: 4*H*-quinolizin-4-one **55** [14,15,17,20,28,31,35,36], 8*H*-pyrido[1,2-*b*]pyridazin-8-one **56** [36], 8*H*-pyrido[1,2-*c*]pyrimidin-8-one **57** [36], 6*H*-pyrido[1,2-*a*]pyrazin-6-one **58** [36], and 6*H*-pyrido[1,2-*a*]pyrimidin-6-one **59** [36] (Scheme 9).

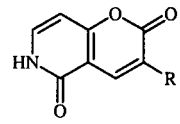
3.3 Synthesis of Fused Pyrimidinones.

Heterocyclic α-amino compounds **60**, such as 2-aminopiridines, 3-aminopyridazines, 2- and 4-aminopyrimidines, 2-aminopyrazines, 3-aminopyrazoles, 2-aminothiazoles and others, react with 2-substituted 3-dimethylaminopropenoates **42** and related compounds to form fused pyrimidinones **61** with a bridgehead nitrogen atom (Scheme 10).

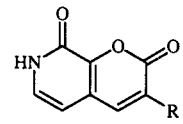
Scheme 7
Pyranones Fused to Nitrogen or Oxygen Containing Heterocycles



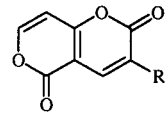
44



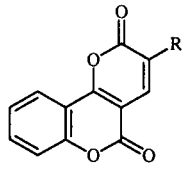
45



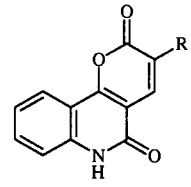
46



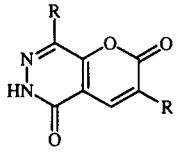
47



48



49



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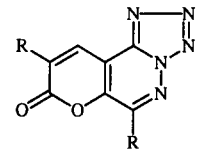
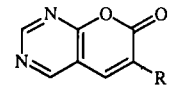


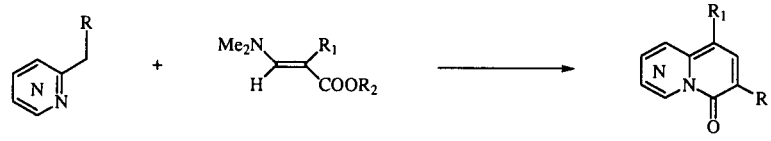
51



52

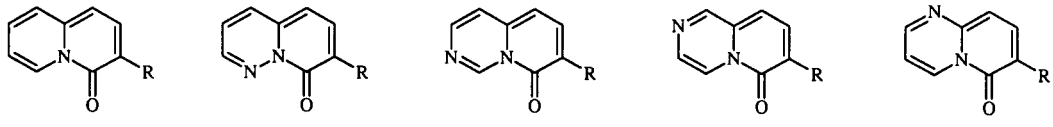
R = *N*H-Acyl, NH_2, *O*-Alkyl, OH,...

Scheme 8
Synthesis of Fused Pyridinones



53 **42** **54**

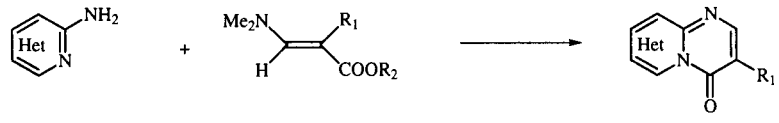
Scheme 9
Pyridinones Fused to Azole or Azine Ring



55 **56** **57** **58** **59**

R = *N*H-Acyl, NH_2, *O*-Alkyl, OH, CH_2COOMe,...

Scheme 10
Synthesis of Fused Pyrimidinones



60 42 61

Accordingly, derivatives of the following systems have been prepared: 4*H*-pyrido[1,2-*a*]pyrimidin-4-one **62** [8,13,14,17,20,22,31,37,38,39,40], 4*H*-pyrimido[1,2-*b*]-pyridazin-4-one **63** [17,37,38,40], 4*H*-pyrimido[3,4-*a*]-pyrimidin-4-one **64**, 4*H*-pyrazino[1,2-*a*]pyrimidin-4-one **65** [37,38], 4*H*-pyrimido[3,4-*a*]pyrimidin-4-one **66**, 5*H*-thiazolo[3,2-*a*]pyrimidin-4-one **67** [8,14,17,18,20,35,37,38,41], 7*H*-pyrazolo[1,5-*a*]pyrimidin-7-one **68** [13,31,37], and 7*H*-1,2,4-triazolo[1,5-*a*]pyrimidin-4-one **69** [8,37,38], and others, such as **70** and **71** (Scheme 11).

3.4 Synthesis of Pyrroles.

3.4.1 Substituted 3-Aminopyrrole-2,4-dicarboxylates.

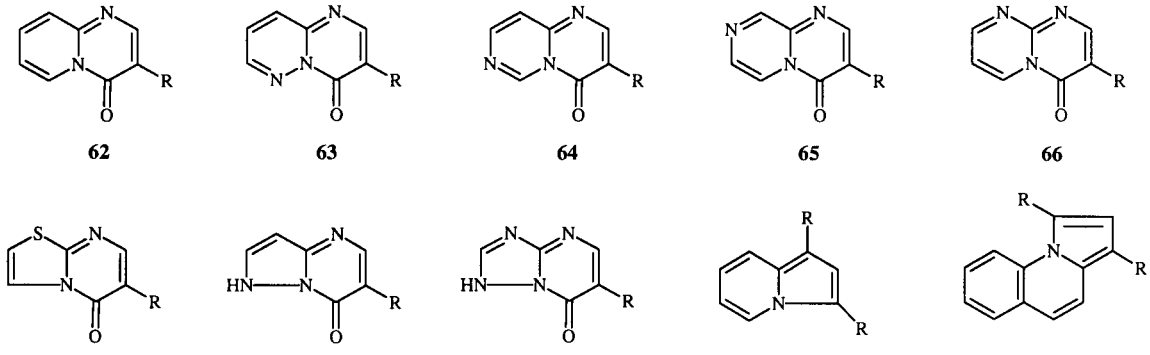
Alkyl 2-(2-alkoxycarbonyl-2-cyano-1-ethenyl)amino-3-dimethylaminopropenoates **72** undergo intramolecular cyclization, catalysed by acid, to give 3-aminopyrrole-2,4-dicarboxylates **73**. The structure of the final product is dependent upon the reaction conditions [23] (Scheme 12).

3.4.2 Pyrrole-2-carboxylates.

2-(2-Acetyl-2-benzoyl-1-ethenyl)amino-3-dimethylaminopropenoate and other alkyl 2-(2,2-*bis*(acyl)-1-ethenyl)amino-3-dimethylaminopropenoates and alkyl 2-(2-acyl-2-alkoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoates **74** cyclize by heating in various solvents to give 3,4-disubstituted- **75** and 1-acyl-3,4-disubstituted pyrrole-2-carboxylates **76** [42,43] (Scheme 13).

Methyl 2-(*N*-benzyloxycarbonyl)amino-3-dimethylaminopropenoate **78** gives with 1,3-dicarbonyl compounds **77** 5-substituted 4-acyl-1-benzyloxycarbonylpyrrole-2-carboxylate **79** [10] (Scheme 14).

Scheme 11
Pyrimidinones Fused to Azole or Azine Ring

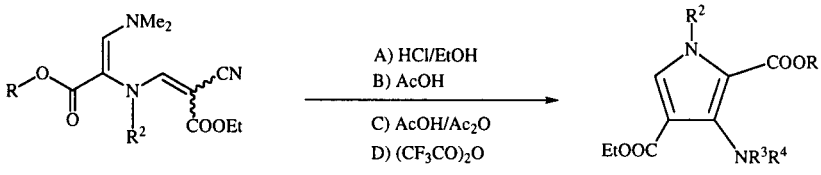


62 63 64 65 66

67 68 69 70 71

R = *N*H-Acyl, NH_2, *O*-Alkyl, OH, CH_2COOMe,...

Scheme 12
Transformations of Alkyl 2-(2-Cyano-2-ethoxycarbonylethenyl)amino-3-dimethylaminopropenoates. Synthesis of 3-Aminopyrrole-2,4-dicarboxylates

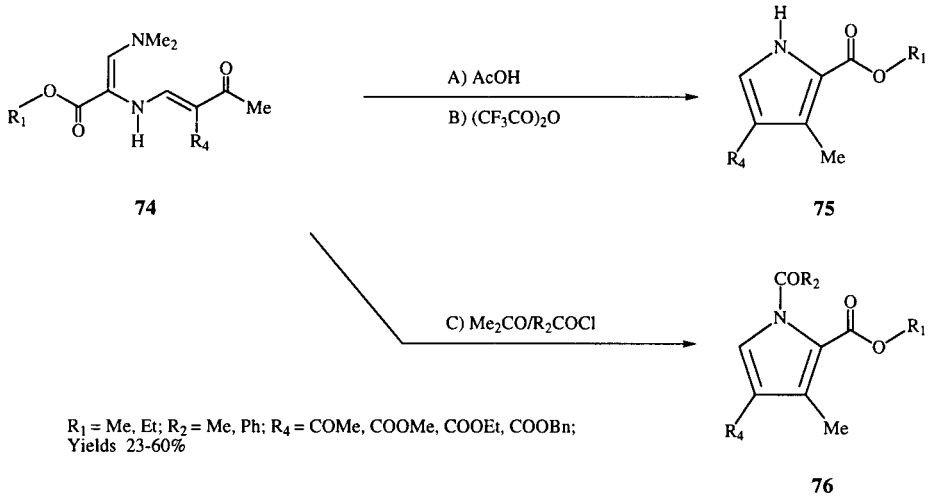


72 73

R_1 = Me, Et; R_2 = H, Me; R_3 = H, COMe; R_4 = H, COMe, $COCF_3$, CH=C(COOEt)NHCH=C(CN)COOEt; Yields 17-90%

Scheme 13

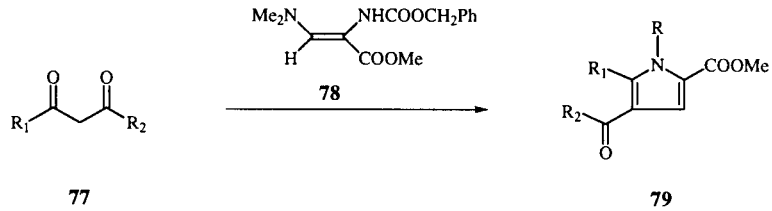
Transformations of Alkyl 2-(2-Acetyl-2-substituted-ethenyl)amino-3-dimethylaminopropenoates. Synthesis of Pyrrole-2-carboxylates



74 75 76

Scheme 14

Synthesis of 4,5-Disubstituted Pyrrole-2-carboxylates



77 78 79

79	R	R_1	R_2
a	H	Me	Me
b	H	Me	Ph
c	$COOCH_2Ph$	Me	Me

3.5 Synthesis of Imidazole-4-carboxylates.

As mentioned earlier, alkyl 2-(2,2-disubstituted 1-ethenyl)-amino-3-dimethylaminopropenoates **80** and heterocyclic compounds **81**, with an amino group attached at α-position in respect to ring nitrogen atom, form intermediates **82**, which cyclize according to path A into the corresponding azolo- and azinopyrimidinones **83**. However, when these compounds are prepared from amines in which the ring nitrogen atom is sterically hindered by a substituent attached close to the ring nitrogen atom, such as in 2-amino-6-methylpyridine, 2-amino-4-chlorobenzothiazole, and its 5-methyl derivative, the reaction resulted in the formation of imidazole derivatives **85** *via* intermediate **84**. In this manner, methyl 1-(6-methylpyridin-2-yl)-1*H*-imidazole-4-carboxylate (**86**), methyl 1-(4-chlorobenzothiazol-2-yl)-1*H*-imidazole-4-carboxylate (**87a**), and its 5-methyl derivative **87b** are formed [12] (Scheme 15).

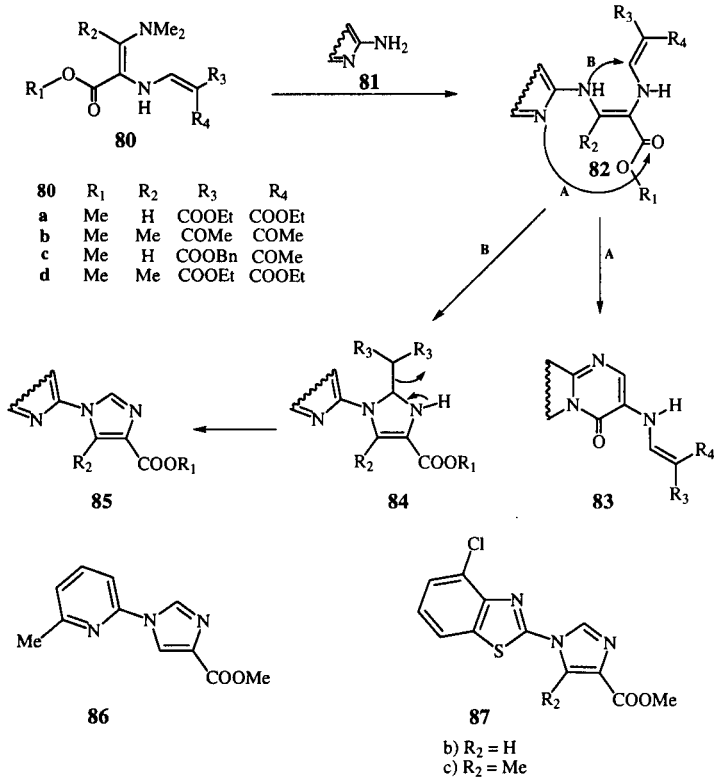
3.6 Synthesis of Pyrazoles.

4-(1-Dimethylaminoethylidene)-2-phenyl-5(4*H*)-oxazolone (**88**), prepared from hippuric acid and *N,N*-dimethylacetamide as an intermediate in preparation of the corresponding propenoates, gives by hydrolysis 2-benzoylamino-2-oxobutanoate (**89**). In the reaction with hydrazines the corresponding 1-substituted 4-benzoylamino-3-methylpyrazol-5(2*H*)-ones (**90**) are formed. In some cases the hydrazones **91** can be isolated as intermediates [44] (Scheme 16).

In the case of 2-(2-benzoyl-2-ethoxycarbonyl-1-ethnyl)amino-3-dimethylaminopropenoate (**92**) two concurrent reactions take place, in which 2-(2-benzoyl-2-ethoxycarbonyl-1-ethnyl)amino-3-heteroarylhydrazino)propenoates (**93**) and/or 4-ethoxycarbonyl-1-heteroaryl-3-phenylpyrazoles (**94**) are formed [45] (Scheme 17).

Scheme 15

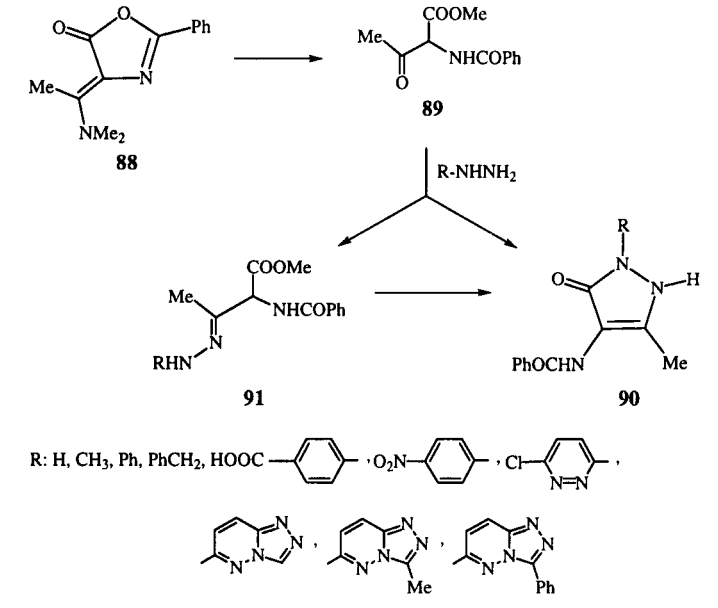
Transformations of 2-(2,2-Disubstituted-ethenyl)amino-3-dimethylaminopropenoates. Synthesis of 1-Heteroaryl-imidazole-4-carboxylates.



80	R_1	R_2	R_3	R_4
a	Me	H	COOEt	COOEt
b	Me	Me	COMe	COMe
c	Me	H	COOBn	COMe
d	Me	Me	COOEt	COOEt

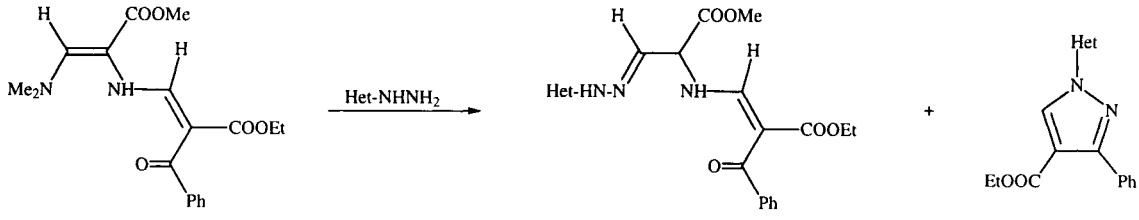
Scheme 16

Transformations of Methyl 2-Benzoylamino-3-oxobutanoate. Synthesis of Pyrazole Derivatives.



Scheme 17

Synthesis of Pyrazole-4-carboxylates



92 93 94

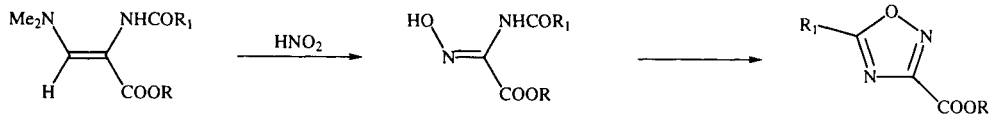
3.7 Synthesis of 1,2,4-Oxadiazoles.

By treatment of 2-acylamino-3-dimethylaminopropenoates (**95**) with nitrous acid at 0°C the corresponding oximes **96** are formed, which cyclize into 5-substituted 1,2,4-oxadiazole-3-carboxylates **97** [7,46] (Scheme 18).

Recently, a considerable interest arose also in the synthesis of azaaplysinopsins and their analogs [47]. In this connection a new method for the construction of the fused imidazole ring connected to oxazolone ring through a conjugated double bond in a single step is represented by

Scheme 18

Synthesis of 1,2,4-Oxadiazoles



95 96 97

R = Me, Et

R_1 = Me, Ph, 2-Chlorophenyl, 4-Chlorophenyl, 4-Methylphenyl, *etc.*

3.8 Synthesis of Aplysinopsins and Azaaplysinopsins.

Aplysinopsins (**98**) and azaaplysinopsins (**99**) are interesting class of compounds because of their biological properties [47]. 2-(2,2-Disubstituted ethenylamino)-3-dimethylaminopropenoates can be successfully employed in the synthesis of these compounds. For example, ethyl 2-[(2-acetyl-2-methoxy(or benzyloxy)carbonylethenyl)-amino]-3-dimethylaminopropenoates (**100**) react with indole (**101**) to form intermediates **102**. These, when treated with hydrazine, give intermediates **103**, from which aplysinopsin (**104**) is formed by cyclization with urea. Alternatively, the same type of compounds can be obtained also from indole (**101**) and 5-dimethylaminomethylenehydantoin (**106**), prepared from hydantoin (**105**) and *N,N*-dimethylformamide dimethyl acetal, in good yields [48] (Scheme 19).

the reaction of 4-(2-bromo-1-dimethylaminoethylidene)-2-phenyl-5(4*H*)-oxazolone (**111**) with *N,N*-dimethyl-*N'*-heteroarylformamidines (**110**) in acetonitrile or *N,N*-dimethylformamide [48] (Scheme 20). The method is an extension of the previously described synthesis of fused imidazo[1,2-*x*]azines from *N,N*-dimethyl-*N'*-heteroarylformamidines and α-halo ketones [50-53].

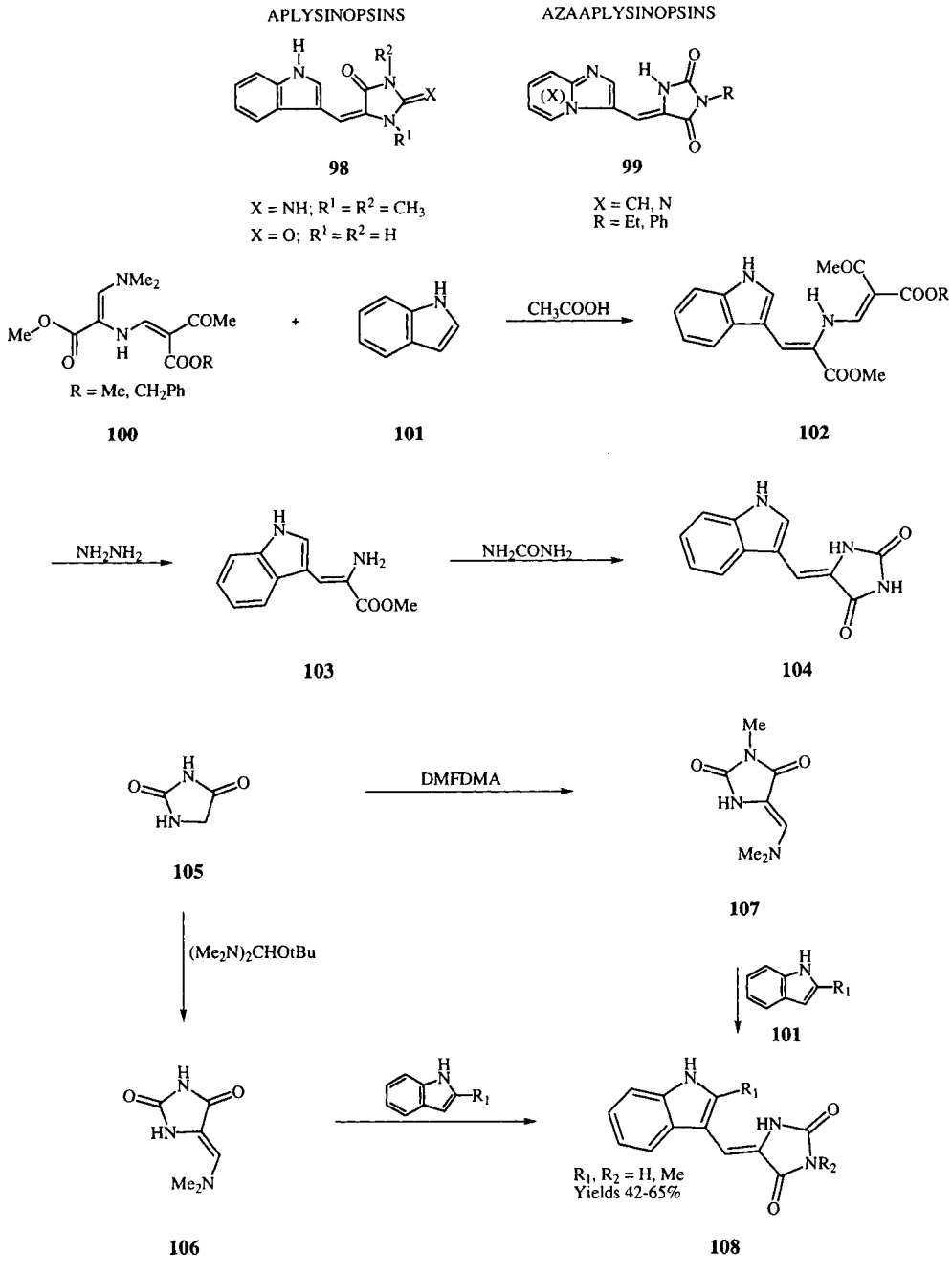
4. Synthesis and Transformations of 2-Acylamino-3-cyanopropenoates.

Dimethylamino group in alkyl (*Z*)-2-acylamino-3-dimethylaminopropenoates **116** can be easily replaced by a cyano group to give the corresponding (*E*)-2-acylamino-3-cyanopropenoates **117** in good yields [9,54,55] (Scheme 21).

They are useful reagents for preparation of several polyfunctional 5- and 6-membered heterocycles, such as pyrrols **118**, pyrimidines **119** and **120**, and pyridazines

Scheme 19

Application of 2-(2-Acyl-2-alkoxycarbonylethenyl)amino-3-dimethylaminopropenoates and 5-Dimethylaminomethylenehydantoins in the Synthesis of Aplysinopsins

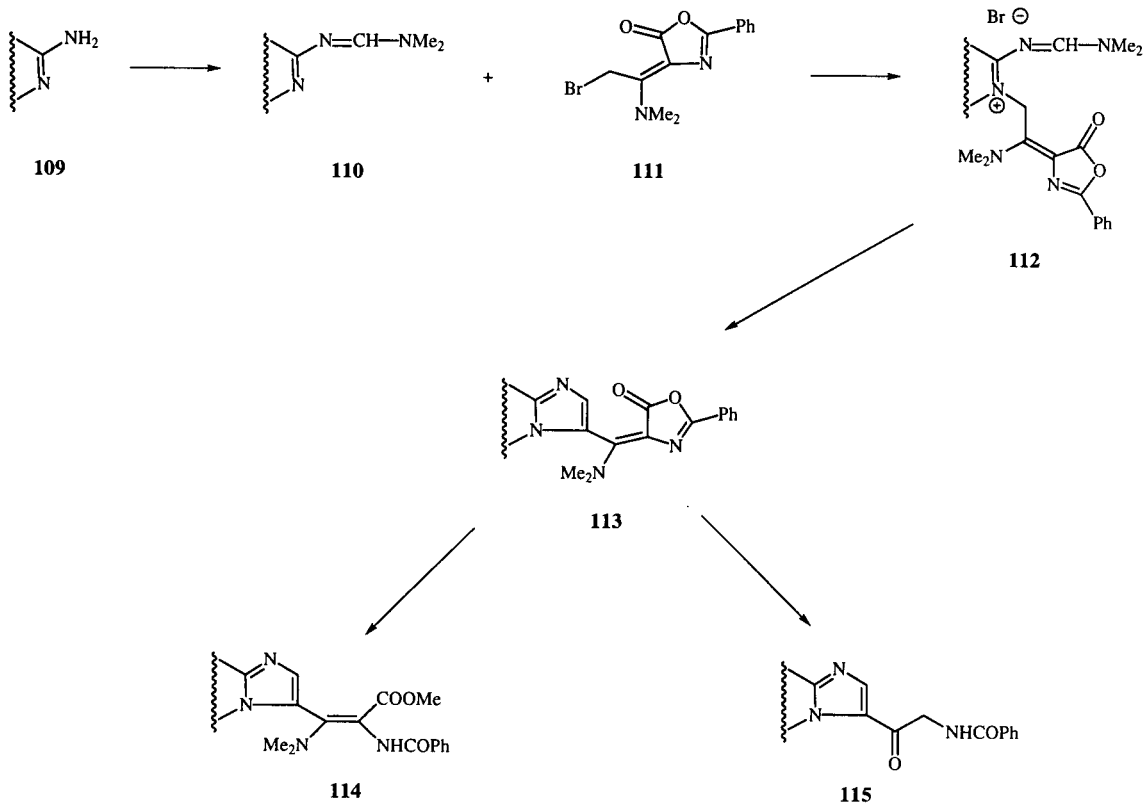


121. 1,3-Dipolar cycloadditions of diazomethane, nitrile oxides, and nitrile imines yield the corresponding 3,4-disubstituted pyrazolecarboxylates **122** and **123**, isoxazolecarboxylates **124**, and 2,4,5-trisubstituted pyrazole-3-carboxylates **125** [54,55] (Scheme 22).

Chiral 3-dimethylaminopropenoate analogs, derived from L-pyroglutamic acid, 5-substituted tetrahydrofuran-2-ones, and pyrrolidin-2-ones, can be utilized for the preparation of chiral 3-heteroaryl-2-amino- and -2-hydroxy acid derivatives [56-59].

Scheme 20

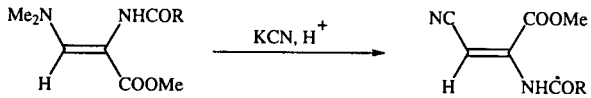
Synthesis of Azaaplysinopsin Derivatives



109 110 111 112 113 114 115

Scheme 21

Synthesis of Alkyl 2-Acylamino-3-cyanopropenoates



116 **117**

1a R = Me
1b R = Ph

2a R = Me
2b R = Ph

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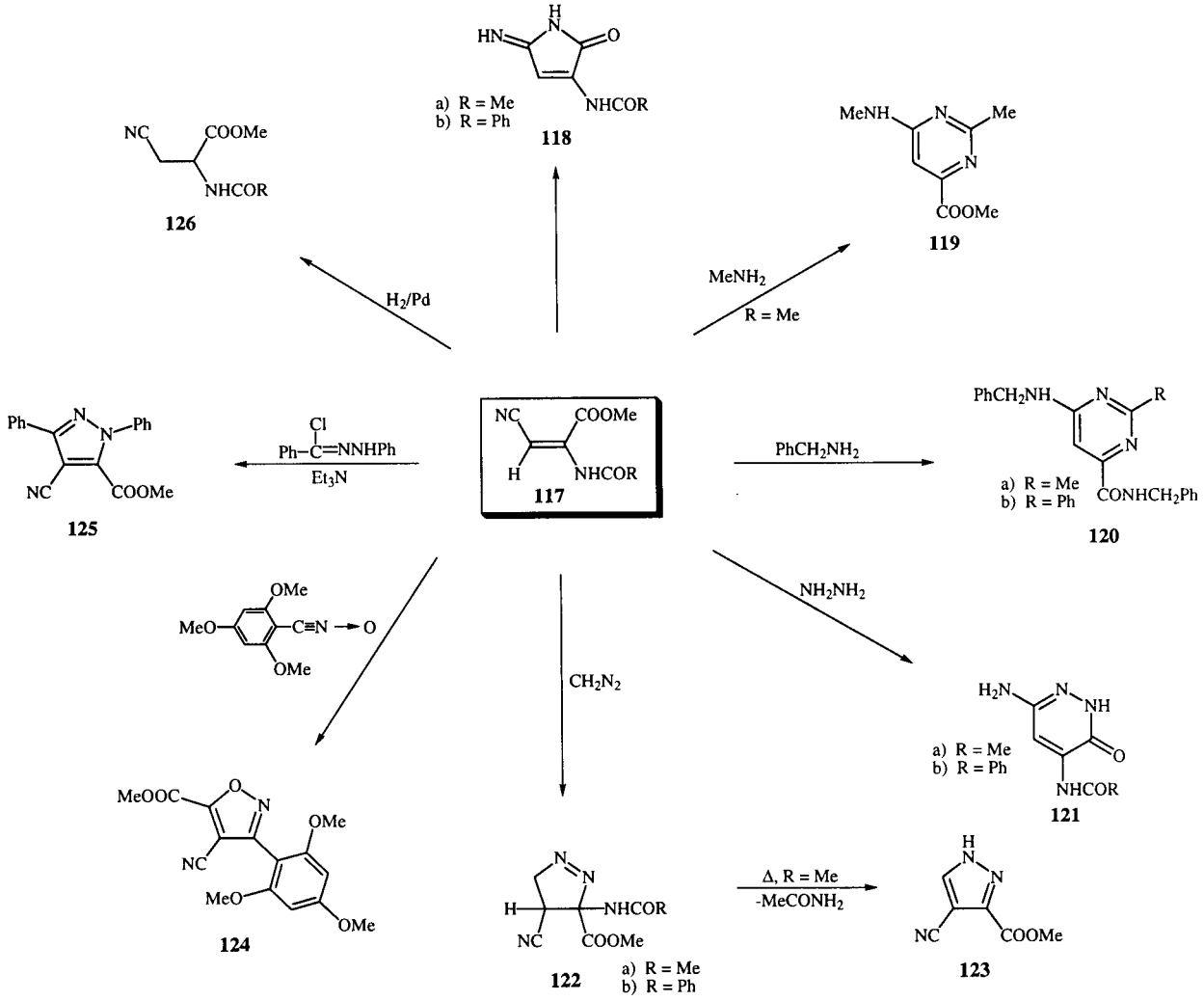
Scheme 22

Transformations of Alkyl 2-Acylamino-3-dimethylaminopropenoates



5. REFERENCES AND NOTES

[*] e-mail: branko.stanovnik@uni-lj.si

[1] R. M. Williams, Synthesis of Optically Active α-Amino Acids, Pergamon Press, Oxford, 1989.

[2a] R. O. Duthaler, *Tetrahedron*, **50**, 1539 (1994); [b] I. Wagner and H. Musso, *Angew. Chem.*, **95**, 827 (1983); [c] U. Schmidt, A. Lieberknecht, and J. Wild, *Synthesis*, 1159 (1988).

[3] J. Mulzer, Basic Principles of EPC Synthesis in Stereoselectie Synthesis, Methods of Organic Chemistry (Houben-Weyl), 4th Ed, Vol **1**, G. Helmchen, ed, Thieme Vellag, Stuttgart, 1996, p 75.

[4] For reviews see: [a] B. Stanovnik, Methyl 2-Benzoylamino-3-dimethylaminopropenoate in the Synthesis of Heterocyclic Systems in Progress in Heterocyclic Chemistry, Vol **5**, H. Suschitzky and E. F. V. Scriven, eds, Pergamon Press, Oxford, 1993, pp 34-53; [b] B. Stanovnik, *Molecules*, **1**, 123 (1996).

[5] B. Stanovnik, J. Svete, M. Tišler, L. Žorž, A. Hvala, and I. Simonič, *Heterocycles*, **27**, 903 (1988).

[6] Japan kokai 75 58.063; *Chem. Abstr.*, **83**, P193075y (1975).

[7] M. Kmetič and B. Stanovnik, *J. Heterocyclic Chem.*, **32**, 1563 (1995).

[8] L. Kralj, A. Hvala, J. Svete, L. Golič, and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 247 (1997).

[9] L. Pizzioli, J, Svete, and B. Stanovnik, to be published.

[10a] R. Toplak, J. Svete, B. Stanovnik, and S.Golič Grdadolnik, *J. Heterocyclic Chem.*, **36**, 225 (1999); [b] S. Rečnik, R. Toplak, J. Svete, L. Pizzioli, and B. Stanovnik, *J. Heterocyclic Chem.*, submitted for publication.

[11] J. Smodiš and B. Stanovnik, *Tetrahedron*, **54**, 9799 (1998).

[12] L. Selič and B. Stanovnik, *J. Heterocyclic Chem.*, **35**, 1527 (1998).

[13] G. Soršak, A. Sinur, L. Golič, and B. Stanovnik, *J. Heterocyclic Chem.*, **32**, 921 (1995).

[14] G. Soršak, S. Golič Grdadolnik, and B. Stanovnik, *ACH-Models Chem.*, **135**, 613 (1998).

[15] S. Strah, S. Golič Grdadolnik, and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 263 (1997).

[16] R. Toplak, M. Zucchiati, S. Golič Grdadolnik, and B. Stanovnik, *Heterocycles*, **50**, 853 (1999).

[17] L. Selic, S. Golič Grdadolnik, and B. Stanovnik, *Helv. Chim. Acta*, **80**, 2418 (1997).

[18] G. Soršak, S. Golič Grdadolnik, and B. Stanovnik, *J. Heterocyclic Chem.*, **35**, 1275 (1998).

[19] M. Malesič, A. Krbavčič, A. Golobič, L. Golič, and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 1757 (1997).

[20] L. Selič and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 813 (1997).

[21] L. Selič and B. Stanovnik, to be published.

[22] L. Selič, S. Golič Grdadolnik, and B. Stanovnik, *Heterocycles*, **49**, 133 (1998).

[23] L. Selič and B. Stanovnik, *Helv. Chim. Acta*, **81**, 1634 (1998).

[24] L. Selič, S. Golič Grdadolnik, and B. Stanovnik, *Heterocycles*, **45**, 2349 (1997).

[25] J. Svete, Z. Čadež, B. Stanovnik, and M. Tišler, *Synthesis*, 70 (1990).

[26] B. Stanovnik, J. Svete, and M. Tišler, *J. Heterocyclic Chem.*, **26**, 1273 (1989).

[27] B. Ornik, Z. Čadež, B. Stanovnik, and M. Tišler, *J. Heterocyclic Chem.*, **27**, 1021 (1990).

[28] R. Toplak, L.Selič, G. Soršak, and B. Stanovnik, *Heterocycles*, **45**, 555 (1997).

[29] B. Ornik, B. Stanovnik, and M.Tišler, *J. Heterocyclic Chem.*, **29**, 1241 (1992).

[30] B. Ornik, B. Stanovnik, and M. Tišler, *J. Heterocyclic Chem.*, **29**, 831 (1992).

[31] M. Kušar, J. Svete, and B. Stanovnik, *J. Heterocyclic Chem.*, **33**, 1041 (1996).

[32] B. Stanovnik, J. Svete, and M. Tišler, *J. Heterocyclic Chem.*, **26**, 1273 (1989).

[33] M. Kmetič, B. Stanovnik, M. Tišler, and T. Kappe, *J. Heterocyclic Chem.*, **35**, 1331 (1993).

[34] B. Stanovnik, L. Golič, P. Kmecl, B. Ornik, J. Svete, and M. Tišler, *J. Heterocyclic Chem.*, **28**, 1961 (1991).

[36] A.Čopar, B. Stanovnik, and M. Tišler, *Bull. Soc. Chim. Belg.*, **100**, 533 (1991).

[37] B. Stanovnik, H. van de Bovenkamp, J. Svete, A. Hvala, I. Simonič, and M. Tišler, *J. Heterocyclic Chem.*, **27**, 359 (1990).

[38] R. Toplak, J. Svete, S. Golič Grdadolnik, and B. Stanovnik, *Collect. Czech Chem. Commun.*, **64**, 177 (1999).

[39] S. Strah, A. Golobič , L. Golič, and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 1511 (1997).

[40] L. Selič, S. Strah, R. Toplak, and B. Stanovnik, *Heterocycles*, **47**, 1017 (1998).

[41] M. Malešič, A. Krbavčič, and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 813 (1997).

[42] M. Malešič, A. Krbavčič, A. Golobič, L. Golič, and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 1757 (1997).

[43] L. Selič and B. Stanovnik, *Synthesis*, 479 (1999).

[44] U. Bratušek, A. Hvala, and B. Stanovnik, *J. Heterocyclic Chem.*, **35**, 1281 (1998).

[45] S. Strah and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 1629 (1997).

[46] M. Kmetič and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 1705 (1997).

[47] J. M. Chezal, G. Delmas, S. Mavel, H. Elakmaoui, J. Metin, A. Diez, Y. Blache, A. Gueiffier, M. Rubiralta, J. C. Teulade, and O. Chavignon, *J. Org. Chem.*, **62**, 4085 (1997).

[48] R. Jakše, K. Lampič, V. Krošelj, L. Selič, G. Soršak, J. Svete, and B. Stanovnik, to be published.

[49] U. Bratušek, A. Hvala, and B. Stanovnik, *J. Heterocyclic Chem.*, **35**, 971 (1998).

[50] S. Podergajs, B. Stanovnik, and M. Tišler, *Synthesis*, 263 (1984).

[51] A. Čopar, B. Stanovnik, and M. Tišler, *J. Heterocyclic Chem.*, **30**, 1577 (1993).

[52] L. Jukić, U. Bratušek, M. Škof, J. Svete, and B. Stanovnik, *Khim. Geterats. Soed.*, 1510 (1996).

[53] M. Škof, J. Svete, and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 83 (1997).

[54] L. Pizzioli, B. Ornik, J. Svete, and B. Stanovnik, *Helv. Chim. Acta*, **81**, 231 (1998).

[55] R. Toplak, J. Svete, and B. Stanovnik, to be published.

[56] M. Škof, J. Svete, B. Stanovnik, S. Golič Grdadolnik, and L. Selič, *Helv. Chim. Acta*, **81**, 2332 (1998).

[57] M. Škof, J. Svete, and B. Stanovnik, *Heterocycles*, **51**, 1051 (1999).

[58] M. Škof, J. Svete, M. Kmetič, B. Stanovnik, and S. Golič Grdadolnik, *Eur. J. Org. Chem.*, 1581 (1999).

[59] M. Škof, J. Svete, and B. Stanovnik, *J. Heterocyclic Chem.*, submitted for publication.