SYNTHESIS OF 1,4-DIHYDROPYRIDINES BY CYCLOCONDENSATION REACTIONS

Alvils Sausiņš and Gunārs Duburs*

Institute of Organic Synthesis, Latvian SSR Academy of Sciences, Aizkraukles 21, 226006, Riga, USSR

Abstract - This review surveys the latest developments pertaining to the preparation of 1,4-dihydropyridines using Hantzsch synthesis and other cyclocondensation reactions.

The chemistry of dihydropyridines (DHP) up to the year 1980 had been reviewed in several surveys of literature[1-3]. Among the different isomers, 1,4-DHP merits special attention, the interest in these compounds increasing progressively. Investigations along these lines include the synthesis of model compounds NAD(P)H-analogues of 1,4-dihydronicotinamide - and their involvement in hydrogen transfer reactions. Recently, several review papers have appeared on the subject[4-7] including the transfer of hydrogen and other groups by chiral DHP[8,9]. Another big issue is the application of 1,4-DHP in medicine and industry. These compounds are chiefly obtained by using various modifications of Hantzsch synthesis. Most extensively studied are the calcium antagonists, whose synthesis[10] and properties[11-13] have been treated in a number of reviews. Several papers describe investigations of individual drugs[14-16] such as vasodilators and antihypertensive remedies - nifedipine, nitrendipine. Calcium transport agonists have been also found among 1,4-DHP[17-20]. 1,4-DHP possess antioxidant[21-26] (diludin is routinely used[27]), hepatoprotective[28-30], antitumour[31-33], antimutagenic[34], geroprotective[35], antiatherosclerotic[36,37], bronchodilating[38], antidiabetic[39,40], herbicidal[41-43], photosensitizing[44-46] activities. 1,4-DHP can be applied to promote drug transfer across the blood-brain barrier[47-49].

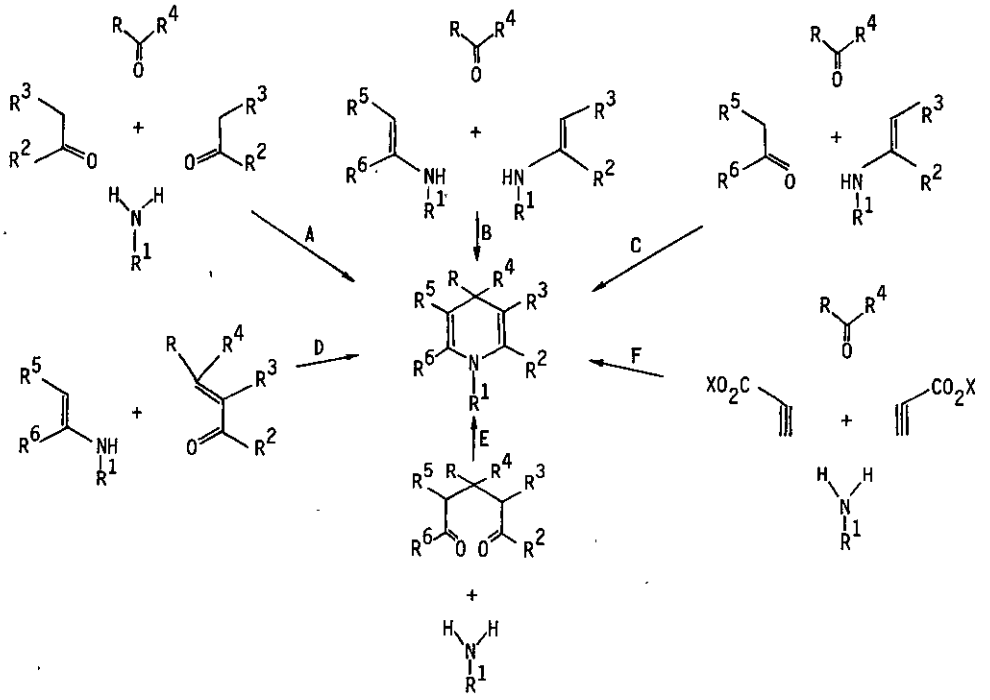
The present review paper surveys literature data on the synthesis of 1,4-dihydropyridines by way of cyclocondensation published in the years 1981-1985. Beyond the scope of this paper remain the 1,4-DHP systems with an exocyclic double bond (pyridones, pyridinethiones, pyridonimines).

1. Hantzsch Synthesis and Related Cyclocondensations

Various modifications of Hantzsch-type cyclocondensation reactions have been widely applied to prepare mono- and polycyclic 1,4-DHP, the principal pathways being outlined in scheme 1.

As the same or structurally related 1,4-DHP can be frequently obtained via different synthetic pathways, they will be discussed on the basis of their structures and not the synthetic methods used for their preparation.

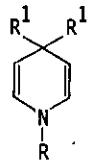
Scheme 1.



1.1.Monocyclic 1,4-Dihydropyridines

1.1.1. Substituents at Position 1

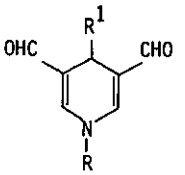
The vast majority of 1,4-DHP prepared by Hantzsch synthesis are 1-unsubstituted. Several 1-substituted α,β-unsubstituted 1,4-DHP 1 have been synthesized by method E.



1

a R = alkyl, R^1 = H[50]

b R = Me, CO_2Et, R^1 = Me[51]

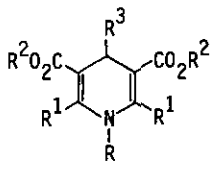


2

R = alkyl, aralkyl, $(CH_2)_nOH$, $CH_2CO_2R^2$

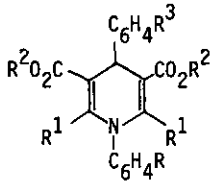
Malonodialdehyde is used as a β-dicarbonyl component in method A to form 1,4-DHP 2[52-56]. A modification of method A involving the use of amine chloride in pyridine affords 1-alkyl-1,4-DHP 3.

Aromatic amines give 1-aryl-2,6-dimethyl-1,4-DHP 4a[60] (method A) and 1-aryl-2,6-unsubstituted 1,4-DHP 4b[61] (method F). The cyclization of 1,5-diketones with hydroxylamine allows to obtain 1-hydr-



a R = R^1 = Me[57]
b R = Et, R^1 = Me[58,59]
c R = Me, R^1 = $C_6H_4R^4$ [57]

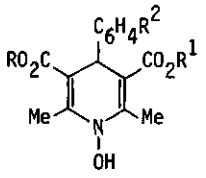
3



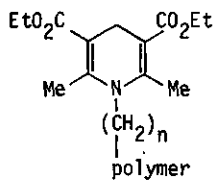
a R^1 = Me
b R^1 = H

4

oxy-1,4-DHP 5[62]. Method E has been applied to prepare 1,4-DHP 6 on a polymer matrix[63]. Polylysine ε-amino groups react with malonodialdehyde to afford 1,4-DHP in small amounts[64], in addition to aminopropenal derivatives.



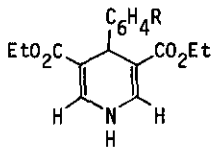
5



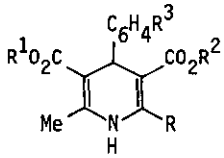
6

1.1.2. Substituents at Positions 2,6

Hantzsch synthesis generally leads to 2,6-disubstituted 1,4-DHP, the most popular being the 2,6-dimethyl derivatives. In order to prepare 2,6-unsubstituted derivatives 7[65], 4b[61], acetylene derivatives (method F) are used instead of the β-dicarbonyl component.

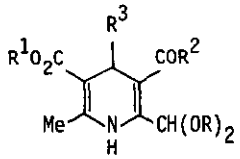


7



8

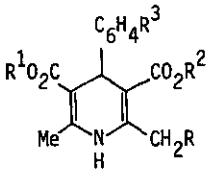
R = Et, Pr, i-Bu, CH_2Ph,



9

R^3 = aryl, heteryl
R^4 = OR^4 [69-79], NHMe[80]

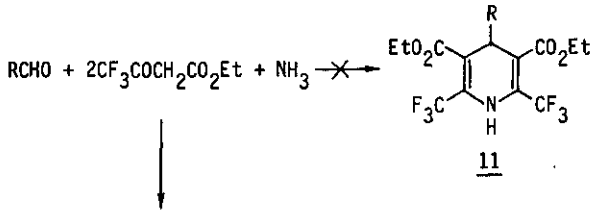
Only a few DHP carrying other alkyl groups (except for methyl) at positions 2, 6 have been prepared including 2,6-diethyl-[66] and 2,6-dicyclopropyl-1,4-DHP[67], as well as asymmetric 8[67,68]. A large number of 1,4-DHP 3,5-dicarboxylic acid derivatives 9 with acetal groups at position 2[69-80] (sometimes 2, 6[76]) have been obtained by method D (sometimes also method C). Method D or C was employed to prepare esters 10[80-94] with the aid of the corresponding substituted acetoacetic acid esters. The products obtained from trifluoroacetoacetic acid ester were assigned as 1,4-DHP 11[95] (quoted in reviews [2,3]), however analysis of their spectra revealed the structure of 2,6-dihydroxypiperidi-



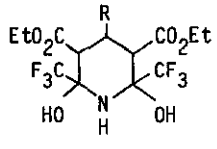
10

R = OH[80-82], O-alkyl[83], O-acyl[84,85], S-acyl[86], CH(OH)Ph[87], $O(CH_2)_nN_3$[88,89], $O(CH_2)_nNR^4R^5$ [89-92], O_2CNHR[93,94]

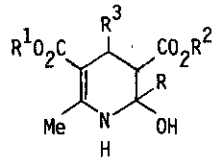
nes 12[96-98]. Depending on radical R, methods C and D yield tetrahydropyridines 13 or 1,4-DHP 14[99]. Contrary to originally held views[96,98], dihydroxypiperidines 12[43,100], as well as tetrahydropyridines 13[99] undergo dehydration to give 1,4- or 3,4-dihydro isomers depending on the reagent used.



11

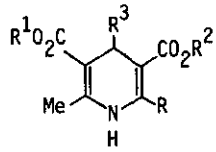


12



13

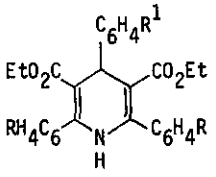
R = CF_3, CF_2CF_3, CCl_3, $C_6H_4NO_2$-4, $C_6H_4Cl_2$-3,4, C_6H_4Cl-4 (3), Ph



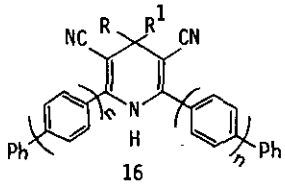
14

R = CH_2F, CHF_2, $CHCL_2$, SMe, 2-furyl, C_6H_4OMe-4, C_6H_4Me-4, Ph

Benzoylacetic acid esters do not invariably follow method A (despite reports on the synthesis of 3c[57]) and the use of method E is required for the preparation of 15[101]. A number of β-cyano-1,4-DHP 16, 17 carrying aryl groups at positions 2, 6 have been obtained.



15

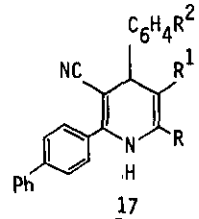


16

a $n = 0$[102]

b $n = 1$[103]

c $n = 2$[104]

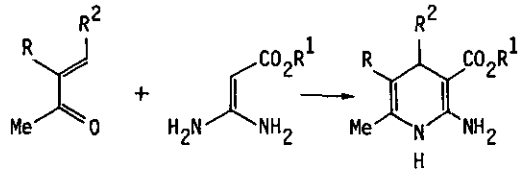


17

a R = Me, Ph; R^1 = CN, CO_2Et[105]

b $R + R^1 = (CH_2)_n$[106]

Amidinoacetic acid ester 19 used as enamine according to method D (sometimes C) yields 2-amino-1,4-DHP 20, thereby enamine 19 forms 1,4-DHP even with ketones 18 lacking the electron withdrawing R.

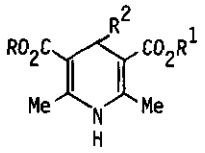


18 19 20

R^2 = aryl, heteryl
R = CO_2R^3 [77,107-111], SO_2R^3, $COMe$[107], NO_2[112], H[57,107]

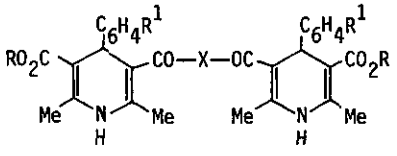
1.1.3. Substituents at Positions 3, 5

Symmetrically or, for the most part, asymmetrically substituted 1,4-DHP-3,5-dicarboxylic acid esters 21 remain in the highlight of attention, method D being claimed as the most suitable one for their synthesis[113,114].

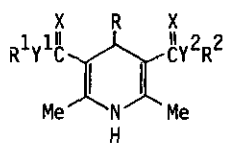


21

Apart from the readily available ethyl and methyl esters, alkyl esters containing long alkyl radicals[36,67,110,113,115,116], as well as cycloalkyl[117-122], alkenyl[24,25,29], alkynyl[29], aralkyl[123], dianhydrohexitol[124] esters have been investigated. Esters 21 were prepared whose alkyl radicals R, R^1 were partially substituted with hydroxy[125], alkoxy[29,36,67,113,115,116,126-129], acyloxy[84], alkoxycarbonyl[130], alkenyldihydroxy[118,131], alkenylthio[129], nitrato[132-134], trimethylsilyl[135-138], cyano[29,77,84,112,139,140] groups or halogens[57,84,141,142]. Aminoalkylesters 21, almost exclusively with amino groups in one of the ester radicals, have been extensively explored. Esters containing acyclic amino groups[77,140,143-159], acylated amino groups[173-176], piperidyl or piperidylalkyl[160-165], piperidinoalkyl[107,153,166], piperazinoalkyl[108,109,167-170] esters, and those carrying other nitrogen-containing heterocycles[142,171,172] have been prepared. Also known are 1,4-DHP 21, whose ester radicals R,R^1 form a macrocycle[122], and bis-1,4-DHP 22 linked via an ester or amide bridge[57,177]. Carbothiolic and carbothionic acid esters 23 have been synthesized.



22

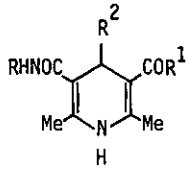


23

a X = O, Y^1=Y^2= S;
b X = O, Y^1= S, Y^2= O[178-180];
c X = S, Y^1=Y^2= O[181];
d X = Y^1=Y^2= S[182]

Amides of 1,4-DHP-3,5-dicarboxylic acids 24 and 3-acyl-1,4-DHP 25 (3,5-diformyl-1,4-DHP, see 2) were also prepared.

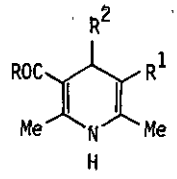
Various Hantzsch syntheses were applied to give 1,4-DHP carrying the following substituents at



24

a $R^1 = NHR$[60],

b R^1 = O-alkyl[41,42,183]



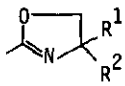
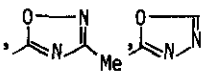
25

a R = Me, R^1 = COMe[29,60,184,185];

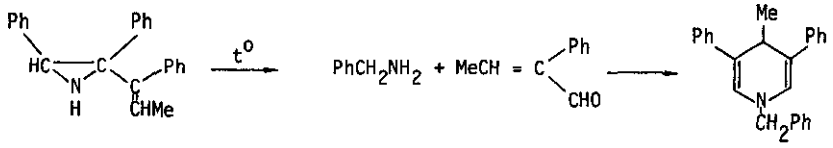
b R = Me, $R^1 = CO_2R^3$ [29,158];

c R = Me, $R^1 = CN$[29];

d R = 2-furyl, $R^1 = CO_2R^3$ [186]

positions 3 or 3, 5: CN[29,60,103-106,112,159,187,188],  [189-191],  [192], SO_2R[77,193,194], NO_2[57,112,195-197], Cl[112], $PO(OR)_2$[198-203], H[57,107,194,203].

3,5-Diphenyl-1,4-DHP 26 resulting from the thermolysis of vinylaziridine 27 is in fact formed via a variant of Hantzsch synthesis[204].

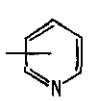
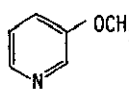
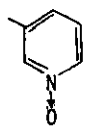


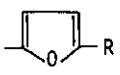
27 26

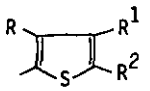
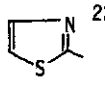
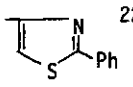
1.1.4. Substituents at Position 4

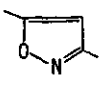
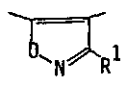
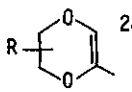
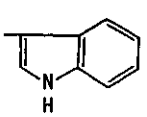
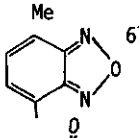
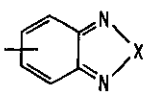
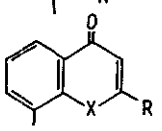
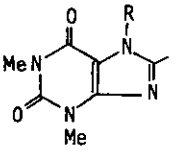
The preparation of 4-unsubstituted compounds involves either method E[24,25,50,63,120] or methods A and C with the use of formaldehyde[41,42,122,183,205,206] or hexamethylenetetramine[119,130,178-182] as the source of the former. A 4-unsubstituted 1,4-DHP was formed in the reaction of phosphorylated enamine and acrolein[203].

The use of diverse synthetic variants has resulted in 4-alkyl-[52-56,58,59,64,122,178-182, 188, 202-204,207,208], 4-cycloalkyl-[208], 4-aralkyl-[59,208,209], 4-CCl_3-[210], 4-(2 ,2 -dimethoxyethyl)-[52-55], 4-(1 ,2 -dihydroxyethyl)-[211], 4-(substituted)aralkyl-[211], 4-benzoyl-1,4-DHP[211]. Most 1,4-DHP obtained by the Hantzsch synthesis contain a substituted (less frequently unsubstituted) phenyl group at position 4[36,57,60-62,65,66,68-76,80-94,99-110,112-118,121,123-129,131-139,141-151,154-158,160-182, 184-186,189-192,194,196,198-201,212-228]. The reactions conducted in an autoclave at 110-120°C have increased yield of 4-(o-substituted)-phenyl-1,4-DHP[228]. A few examples of 4-naphthyl-[57,112,191,224] and biphenylyl-1,4-DHP[74] are available. 1,4-DHP carrying the following 4-heterylsubstituents have been also prepared:

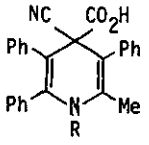
 [57,75,76,112,152,191],  [226],  [193],

 (R = H[75,76,103,152,187,191]; R = Me[152]),


(R = R^1 = R^2 = H[75,76,152,187,191]; R = R^1 = H, R^2 = Cl[152]; R = R^1 = Cl, R^2 = H[77]),

229,

229,

229,

152,

230,

28,29,

191,

67,78,79,108,111,140,153,

(X = O,S)[67,159,197],

(X = O,S)[195],

231

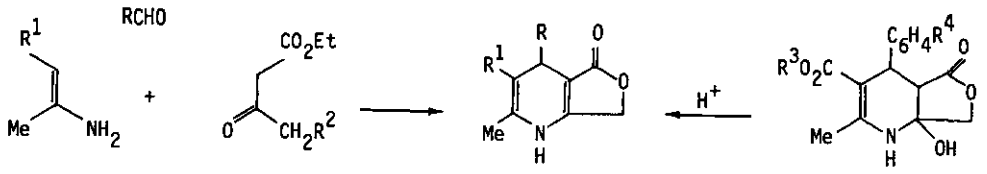
4,4-Disubstituted 1,4-DHP are formed (when ketones are applied instead of aldehydes) only in the case of 3,5-dicyano derivatives[103,188]. 1,4-DHP 1b[51] has been obtained. The preparation of 1,4-DHP 28 by method E[232] has been reported, although its structure is not adequately established.



28

1.2.Polycyclic 1,4-Dihydropyridines

1,4,5,7-Tetrahydrofuro[3,4-b]pyridines 30 can be prepared from esters 29a[80,193,233,234] or 29b[57,112,233,234] with lactone ring closure in the course of synthesis or by applying tetronic acid[233] or its derivatives[234,235]. Under mild conditions, hexahydrofuropyridines 31 are formed, which easily undergo dehydration to DHP 30[235].



29

a R^2= Cl

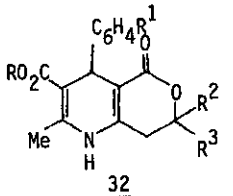
b R^2= MeCOO

30 31

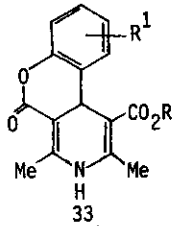
DHP 32[57,112] and 33[10] have been attained from tetrahydropyrandione and 3-acetylcoumarine derivatives, respectively.

Polycyclic 1,4-DHP 34-37 were gained on the basis of cyclic β-diketones.

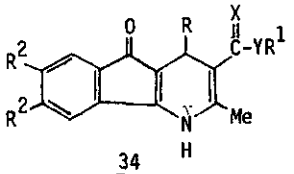
Method E may lead to a series of polycyclic 1,4-DHP 38-40 lacking electron-withdrawing groups at β-position.



32

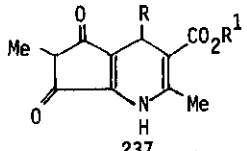


33

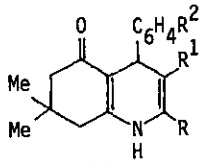


34

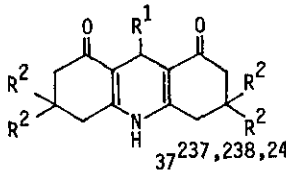
a X=Y=O[21,236];
b X=O, Y=S[179,180];
c X=S, Y=O[181];
d X=Y=S[182]



35[237]

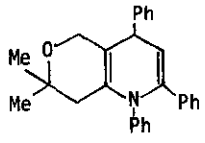


36

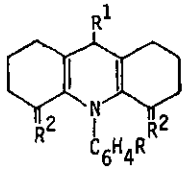


37[237,238,240]

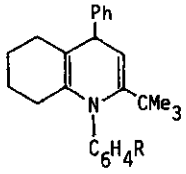
a R=Me, R^1=CO_2Et, CN[238];
b R=$C_6H_4R^2$, R^1=H[239]



38[241]

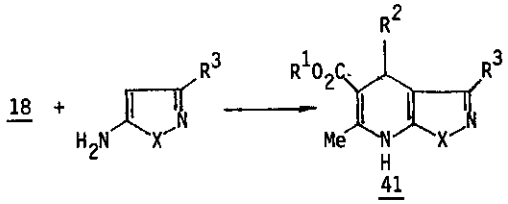


39[242,243]



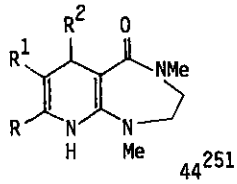
40[244]

In a number of compounds (41-48) the 1,4-DHP ring is fused with another heterocycle. Their preparation occasionally relies on novel modifications of Hantzsch synthesis, e.g. on the use of heterocyclic amines instead of enamine in method D[1] or C[245-250] and 2,4-dihydroxypyridine instead of the β-dicarbonyl species[37].

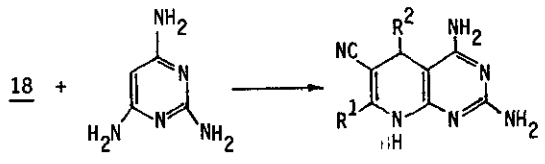


41

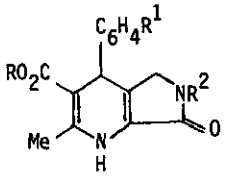
X=NR^4 [246-248]; X=O[248,249]



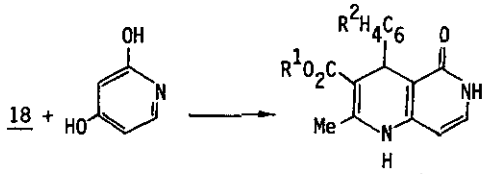
44[251]



42[250a]

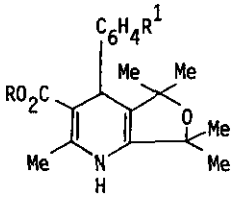


45[252]

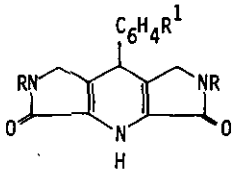


18 + HO

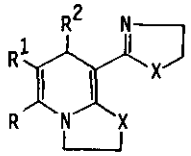
43[37]



46[252]



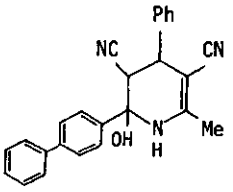
47[253]



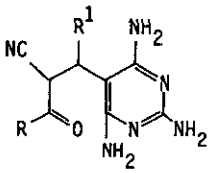
48[254]

1.3. Intermediates in Hantzsch Synthesis

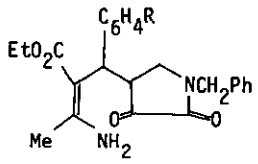
Several compounds have been isolated that can be regarded as intermediates in Hantzsch synthesis. 2,6-Dihydroxypiperidine (12[96-98]) and 2-hydroxytetrahydropyridine (13[99], 31[235] and 49[105]) derivatives result from condensation occurring without water elimination, their formation being apparently favoured by the presence of electron-acceptors at positions 2, 6. Acyclic Michael addition products 50-52 have been also isolated.



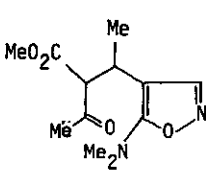
49



50[250]



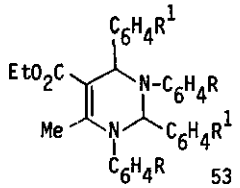
51[252]



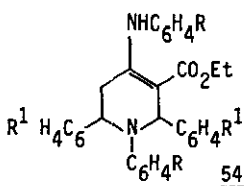
52[249]

1.4. Side Products

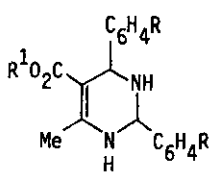
As previously noted[1], the formation of side products in Hantzsch synthesis is a rare occurrence. The presumed N-aryltetrahydropyrimidines 53[1,255,256] turned out to be in fact the 4-phenylamino-1,2,5,6-tetrahydropyridines 54[257,258]. It should be pointed out, however, that the occurrence of N-unsubstituted tetrahydropyrimidines 55 was unequivocally demonstrated in the reaction of benzaldehydes with β-dicarbonyl compounds and ammonia[185,259,260].



53



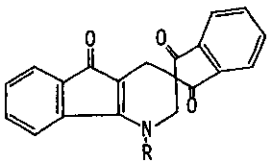
54



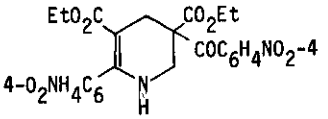
R=H, 2-NO_2;
R^1=Me, OMe, OEt

55

The formation of tetrahydropyridines with geminal carbonyl groups at position 3 - 56[261], 57[262] has been also observed.



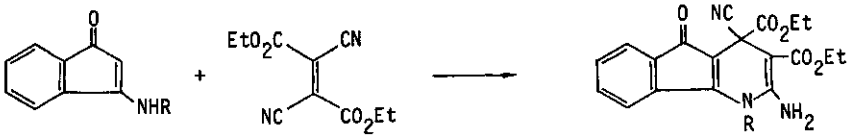
56



57

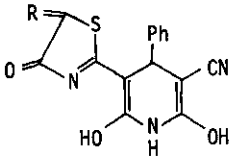
2. Other Cyclocondensations

Reaction of 3-aminoindenones with dicyanofumarates affords 1,4-DHP 58[263].

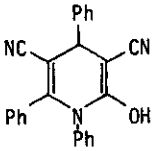


58

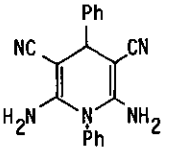
There are reports of 2-hydroxy-1,4-DHP 59[264] and 60[265-266] being formed, though their structure, in our opinion, requires further substantiation. The reaction of benzylidenemalononitrile with other nitriles affords 1,4-DHP 61[267] and 62[268-270].



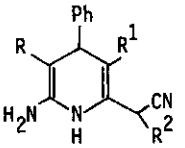
59



60



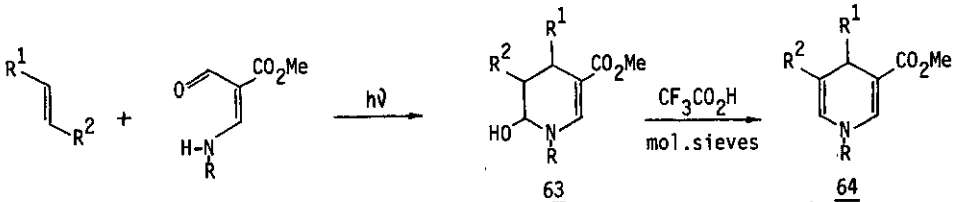
61



62

R, R^1, R^2 = CN, CO_2Et

A photochemically promoted addition of alkenes to enaminocarbaldehydes leads to tetrahydropyridines 63 that undergo dehydration to 1,4-DHP 64[271-173].

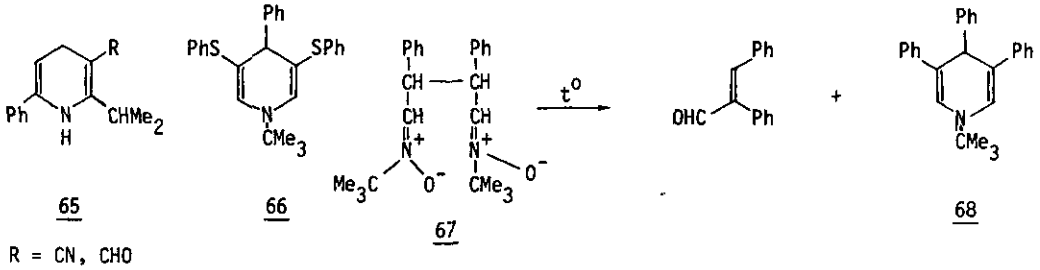


63

64

R^1, R^2 = H, Me, CO_2R^3, COMe, CN

Cycloaddition of alkenes to azabutadienes yields pyridines and also 1,4-DHP 65[274], 66[275]. The thermolysis of dinitrone 67 gives a mixture of products containing an unsaturated aldehyde and 1,4-DHP 68[276]



65 R = CN, CHO

66

67

68

REFERENCES

1. U.Eisner and J.Kuthan, Chem.Rev., 1972, 72, 1.
2. J.Kuthan and A.Kurfürst, Ind.Eng.Chem., Prod.Res.Dev., 1982, 21, 191.
3. D.M.Stout and A.J.Meyers, Chem.Rev., 1982, 82, 223.
4. N.T.Berberova and O.Yu.Okhlobystin, Khim.Geterotsikl.Soed., 1984, 1011.
5. J.Ya.Postovsky, O.N.Chupakhin, and A.J.Matern, Khim.Geterotsikl.Soed., 1984, 1299.
6. S.Yasui and A.Ohno, Bioorg.Chem., 1986, 14, 70.
7. S.Zehani and G.Gelbard, Nouv.J.Chim., 1986, 10, 511.
8. Y.Inouye, J.Oda, and N.Baba, "Asymmetric Synthesis", ed. by J.D.Morrison, Academic Press, New York, 1983, pp. 91-124.
9. R.M.Kellogg, Angew.Chem.Int.Ed.Engl., 1984, 23, 782.
10. F.Bossert, H.Meyer, and E.Wehinger, Angew.Chem.Int.Ed.Engl., 1981, 20, 762.
11. H.Meyer, Annu.Rep.Med.Chem., 1982, 17, 71.
12. R.A.Janis and D.J.Triggle, J.Med.Chem., 1983, 26, 775.
13. R.J.Miller and S.B.Freedman, Life Sci., 1984, 34, 1205.
14. M.S.Mueller, E.M.Antman, J.A.Ferst, and J.E.Muller, Pharmacotherapy, 1981, 1, 78.
15. E.M.Sorkin, S.P.Clissold, and R.N.Brodgen, Drugs, 1985, 30, 182.
16. "Nitrendipine", ed. by A.Scriabine, S.Vanov, K.Deck, Urban and Schwarzenberg, Baltimore, 1984.
17. M.Schramm, G.Thomas, R.Towart, and G.Franckowiak, Nature (London), 1983, 303, 535.
18. M.Schramm, G.Thomas, R.Towart, and G.Franckowiak, Arzneim.Forsch., 1983, 33, 1268.
19. A.M.Brown, D.L.Kunze, and A.Yatani, Nature (London), 1984, 311, 570.
20. R.P.Hof, U.T.Ruegg, A.Hof, and A.Vogel, J.Cardiovasc.Pharm., 1985, 7, 689.
21. E.Bisenieks, J.Uldrikis, I.Kirule, G.Tirzītis, and G.Duburs, Khim.Geterotsikl.Soed., 1982, 1528.

22. G.Tirzītis, I.Kirule, L.Baumane, R.Gavars, J.Stradiņš, and G.Duburs, Khim.Geterotsikl.Soed., 1984, 1120.

23. E.J.Finkelstein, E.A.Alekseev, and E.J.Kozlov, Zhurn.Organ.Khim., 1980, 792.

24. C.Pigerol, M.M.Chandavoine, and P.de Cointet de Fillain, Pat. 2435470 (Fr.); Chem.Abstr., 1981, 94, 140671.

25. C.Pigerol, M.M.Chandavoine, and P.de Cointet de Fillain, Pat. 2435496 (Fr.); Chem.Abstr., 1981, 94, 66760.

26. K.R.Molt, Pat.Appl. 70092 (Eur.); Chem.Abstr., 1983, 98, 144545.

27. A.Valdmanis, G.Duburs, and J.Sprūžs, Latvijas PSR ZA vēstis, 1977, 43.

28. Y.Inoue, T.Matsumoto, H.Niwa, K.Suzuki, and Y.Hoshide, Pat.Appl. 87156 (Eur.); Chem.Abstr., 1984, 100, 6530.

29. K.Suzuki, T.Shiraishi, Y.Yosida, T.Matsumoto, M.Iwamoto, Y.Motoyoshi, H.Niwa, and Y.Inoue, Pat. Appl. 118120 (Eur.); Chem.Abstr., 1985, 102, 45961.

30. A.Majore, T.N.Kopylova, L.Saldava, G.Duburs, Z.Ogle, and J.Uldriķis, Eksper.Med., 1982, 14, 97.

31. K.V.Honn, J.M.Onoda, C.A.Diglo, M.M.Carufel, and J.D.Taylor, Clin.Exp.Metastasis, 1984, 2, 61.

32. T.Tsuruo, H.Iida, M.Nojiri, S.Tsukagashi, and Y.Sakurai, Cancer Res., 1983, 43, 2905.

33. I.Buiķis, A.Springovičs, and G.Duburs. In: Morphologic Evaluation of Tumour Drug Resistance and Sensitivity in Chemptherapy, Zinātne, Rīga, 1983, 88 (in Russian).

34. R.I.Goncharova, T.D.Kuzhir, G.Duburs, and J.Uldriķis, Dokl.Akad.Nauk SSSR, 1980, 255, 1483.

35. N.M.Emanuel, L.K.Obukhova, G.Duburs, G.Tirzītis, and J.Uldriķis, Dokl.Akad.Nauk SSSR, 1985, 284, 1271.

36. F.Senter, F.Bossert, H.Meyer, E.Wehinger, and H.Böshagen, Offenleg. 3222367 (BRD); Chem.Abstr., 1984, 100, 156503.

37. G.Satzinger, J.Hartenstein, K.Mannhardt, J.Kleinschrott, M.Hermann, I.Fritschi, H.D.Tauschel, B.Wagner, and G.Wolf, Offenleg. 3327650 (BRD); Chem.Abstr., 1985, 103, 71301.

38. R.W.Chapman, G.Danko, and M.I.Siegel, Pharmacology, 1984, 29, 282.

39. U.Panten, S.Zielmann, M.T.Schrader, and S.Lenzen, Naun.Schmied.Arch.Pharmacol., 1985, 328, 351.

40. W.J.Malaise and P.C.F.Mathias, Diabetologia, 1985, 28, 153.

41. F.de Reinach Hirtzbach and D.Ambrosi, Pat.Appl. 44262 (Eur.); Chem.Abstr., 1982, 97, 109876.

42. F.de Reinach Hirtzbach and D.Ambrosi, Pat.Appl. 69033 (Eur.); Chem.Abstr., 1983, 99, 22322.

43. L.F.Lee, Pat.Appl. 135491 (Eur.); Chem.Abstr., 1985, 103, 178173.

44. W.Abele, Pat.Appl. 2076985 (GB); Chem.Abstr., 1982, 96, 113566.

45. V.F.H.Chu and J.Reisenfeld, Pat. 4292394 (USA); Chem.Abstr., 1981, 95, 229334.

46. Fuji Chem.Ind., Pat. 58223147 (Jap.); Chem.Abstr., 1984, 101, 15058.

47. N.Bodor and H.H.Farag, J.Med.Chem., 1983, 26, 528.

48. N.Bodor and M.Abdel-Alim, J.Pharm. Sci., 1985, 74, 241.

49. N.Bodor and H.H.Farag, J.Pharm.Sci., 1984, 73, 385.

50. R.Lubig, P.Kusch, K.Röper, and H.Zahn, Monatsh.Chem., 1981, 112, 1313.

51. H.Hesse, S.Hünig, and H.Wenner, Ann., 1982, 2079.

52. K.Kikugawa and Y.Ido, Lipids, 1984, 19, 600.

53. K.Kikugawa, Y.Ido, and A.Mikami, J.Am.Oil Chem.Soc., 1984, 61, 1574.

54. K.Kikugawa, Y.Machida, M.Kida, and T.Kurechi, Chem.Pharm.Bull., 1981, 29, 3003.

55. K.Kikugawa, T.Maruyama, Y.Machida, and T.Kurechi, Chem.Pharm.Bull., 1981, 29, 1423.

56. K.Yoden, R.Matsuzaki, T.Iio, and T.Tabata, Yakugaku Zasshi, 1982, 102, 768.

57. G.Franckowiak, H.Böshagen, F.Bossert, S.Goldmann, H.Meyer, E.Wehinger, M.Schramm, G.Thomas, and R.Towart, Offenleg. 3130041 (BRD); Chem.Abstr., 1983, 98, 198038.

58. P.R.Ortiz de Montellano, H.S.Beilan, and K.L.Kunze, J.Biol.Chem., 1981, 256, 6708.

59. O.Augusto, H.S.Beilan, and P.R.Ortiz de Montellano, J.Biol.Chem., 1982, 257, 11288.

60. V.V.Kastron, G.Duburs, R.Vītoliņa, I.Skrastiņš, and A.Ķimenis, Khim.-Farm.Zhurn., 1985, 19, 545.

61. B.Čekavičus, A.Sausiņš, and G.Duburs, Khim.Geterotsikl.Soed., 1982, 1072.

62. M.Watanabe, K.Moto, Y.Takenato, T.Hatta, T.Hashimoto, and K.Yamada, Pat.Appl. 93945 (Eur.); Chem.Abstr., 1984, 100, 120893.

63. A.Zicmanis and R.E.Malivaiko, Latvijas PSR ZA vēstis, Chem.ser., 1982, 351.

64. K.Kikugawa, K.Takayanagi, and S.Watanabe, Chem.Pharm.Bull., 1985, 33, 5437.

65. V.Lūsis and G.Duburs, Khim.Geterotsikl.Soed., 1982, 1067.

66. P.M.Carabateas, R.P.Brundage, K.O.Gelotte, M.D.Gruett, R.R.Lorenz, C.J.Opalka, B.Singh, W.H.Thielking, G.L.Williams, and G.Y.Lesher, J.Heterocycl.Chem., 1984, 21, 1849.

67. P.Neumann, Offenleg. 2949464 (BRD); Chem.Abstr., 1980, 93, 239419.

68. E.Wehinger, H.Meyer, F.Bossert, S.Kazda, K.Stöpel, R.Towart, and W.Vater, Offenleg. 3018259 (BRD); Chem.Abstr., 1982, 96, 104101.

69. P.B.Berntsson and S.A.J.Carlsson, Pat.Appl. 2120251 (GB); Chem.Abstr., 1984, 100, 138964.

70. Fujisawa Pharm.Co., Pat. 80153768 (Jap.); Chem.Abstr., 1981, 94, 192156.

71. T.Miyano, K.Suzuki, N.Harada, and A.Asai, Pat.Appl. 63359 (Eur.); Chem.Abstr., 1983, 98, 160590.

72. Y.Sato, Pat.Appl. 2026471 (GB); Chem.Abstr., 1980, 93, 186175.

73. Y.Sato, Offenleg. 2756226 (BRD); Chem.Abstr., 1978, 89, 109132.

74. T.Teraji and Y.Sato, Offenleg. 2935772 (BRD); Chem.Abstr., 1980, 93, 204462.

75. Y.Sato, Offenleg. 2940833 (BRD); Chem.Abstr., 1980, 93, 225094.

76. Y.Sato, Offenleg. 2629892 (BRD); Chem.Abstr., 1977, 86, 189726.

77. H.Kühnis, Offenleg. 3445356 (BRD); Chem.Abstr., 1985, 103, 178176.

78. A.Vogel, Offenleg. 3305577 (BRD); Chem.Abstr., 1984, 100, 51576.

79. J.Dixon and A.C.Tinker, Pat.Appl. 80220 (Eur.); Chem.Abstr., 1983, 99, 175596.

80. H.Kühnis, Pat.Appl. 111453 (Eur.); Chem.Abstr., 1984, 101, 151762.

81. Banyu Pharm.Co., Pat. 6054364 (Jap.); Chem.Abstr., 1985, 103, 123361.

82. Banyu Pharm.Co., Pat. 6092265 (Jap.); Chem.Abstr., 1985, 103, 215178.

83. P.B.Berntsson, S.A.J.Carlsson, J.O.Gaarder, and B.R.Ljung, Pat.Appl. 31801 (Eur.); Chem.Abstr., 1981, 95, 169004.

84. H.Meyer, E.Wehinger, F.Bossert, and D.Scherling, Arzneim.Forsch., 1983, 33, 106.

85. H.Meyer, D.Scherling, and W.Karl, Arzneim.Forsch., 1983, 33, 1528.

86. S.Goldmann, M.Schramm, G.Thomas, and R.Gross, Offenleg. 3412947 (BRD); Chem.Abstr., 1986, 104, 109606.

87. Nissan Chem.Ind., Pat. 6064962 (Jap.); Chem.Abstr., 1985, 103, 87776.

88. D.Alker, P.E.Cross, and S.F.Campbell, Pat.Appl. 119050 (Eur.); Chem.Abstr., 1985, 102, 24492.

89. S.F.Campbell, P.E.Cross, and J.K.Stubbs, Pat.Appl. 89167 (Eur.); Chem.Abstr., 1984, 100, 6351.

90. S.F.Campbell, P.E.Cross, and J.K.Stubbs, Pat.Appl. 60674 (Eur.); Chem.Abstr., 1983, 98, 34509.

91. S.F.Campbell, P.E.Cross, and J.K.Stubbs, Pat. 4515799 (USA); Chem.Abstr., 1985, 103, 87879.

92. S.F.Campbell, J.K.Stubbs, and P.E.Cross, Pat.Appl. 100189 (Eur.); Chem.Abstr., 1984, 101, 7031.

93. Banyu Pharm. Co., Pat. 59152373 (Jap.); Chem.Abstr., 1985, 102, 113304.

94. T.Miyano, K.Suzuki, S.R.Ushijima, and S.Nakagawa, Pat.Appl. 101023 (Eur.); Chem.Abstr., 1984, 101, 23346.

95. R.Balicki and P.Nantka-Namirski, Acta Polon Pharm., 1974, 31, 261.

96. B.Singh and G.Y.Lesher, J.Heterocycl.Chem., 1980, 17, 1109.

97. N.V.Barmenkova, In: Synthesis and Properties of Biologically Active Compounds. Abstracts of the 7th Young Scientists Conf., Zinātne, Rīga, 1981, 22 (in Russian).

98. R.Balicki and P.Nantka-Namirski, Pol.J.Chem., 1981, 55, 2439.

99. A.J.G.Baxter, J.Dixon, K.J.Gould, T.McInally, and A.C.Tinker, Pat.Appl. 125803 (Eur.); Chem. Abstr., 1985, 102, 203874.

100. L.F.Lee, Pat.Appl. 133612 (Eur.); Chem.Abstr., 1986, 104, 19514.

101. B.Čekavičus, A.Sausiņš, R.Zolotoyabko, and G.Duburs, Latvijas PSR ZA vēstis, Chem.ser., 1985, 77.

102. C.Seoane, F.L.Soto, P.Zamorano, and M.Quintero, J.Heterocycl.Chem., 1981, 18, 309.

103. S.Marchalin and J.Kuthan, Coll.Czech.Chem.Commun., 1983, 48, 3112.

104. S.Marchalin and J.Kuthan, Coll.Czech.Chem.Commun., 1985, 50, 1962.

105. S.Marchalin and J.Kuthan, Coll.Czech.Chem.Commun., 1983, 48, 3123.

106. S.Marchalin and J.Kuthan, Coll.Czech.Chem.Commun., 1984, 49, 1395.

107. H.Meyer, E.Wehinger, F.Bossert, K.Stöpel, and W.Vater, Arzneim.Forsch., 1981, 31, 1173.

108. K.Meguro, M.Aizawa, T.Sohda, Y.Kawamatsu, and A.Nagaoka, Chem.Pharm.Bull., 1985, 33, 3787.

109. K.Meguro and A.Nagaoka, Pat.Appl. 138505 (Eur.); Chem.Abstr., 1985, 103, 142011.

110. E.Wehinger, H.Meyer, and A.Knorr, Offenleg. 3208628 (BRD); Chem.Abstr., 1984, 100, 22581.

111. A.Vogel, Pat.Appl. 2086901 (GB); Chem.Abstr., 1982, 97, 109882.

112. G.Franckowiak, H.Böshagen, F.Bossert, S.Goldman, H.Meyer, E.Wehinger, J.Stoltefuss, M.Schramm, G.Thomas, and R.Towart, Offenleg. 3206671 (BRD); Chem.Abstr., 1983, 98, 215488.

113. W.Teller, Offenleg. 3313383 (BRD); Chem.Abstr., 1985, 102, 95544.

114. W.Teller, W.Köbernick, A.Haaf, P.Naab, and M.Preiss, Offenleg. 3312216 (BRD); Chem.Abstr., 1985, 102, 95543.

115. H.Meyer, F.Bossert, E.Wehinger, K.Stöpel, and W.Vater, Arzneim.Forsch., 1981, 31, 407.

116. E.Wehinger, F.Bossert, H.Meyer, A.Heise, S.Kazda, K.Stöpel, and W.Vater, Pat. 635078 (Switz.); Chem.Abstr., 1983, 99, 53613.

117. Maruko Pharm.Co., Pat. 59216873 (Jap.); Chem.Abstr., 1985, 103, 22467.

118. S.Ohno, K.Mizukoshi, A.Iwakura, O.Komatsu, K.Ichihara, T.Kenzi, and T.Morishima, Offenleg. 3238705 (BRD); Chem.Abstr., 1983, 99, 88063.

119. G.Tirzītis, I.Preisa, J.Uldriķis, A.Zīdermane, G.Duburs, and E.Bisenieks, Pat. 882498 (Belg.); Chem.Abstr., 1981, 94, 156764.

120. M.Fushimi, N.Baba, J.Oda, and Y.Inouye, Bull.Inst.Chem.Res., Kyoto Univ., 1980, 58, 357.

121. E.Bisenieks, M.Vēveris, G.Duburs, J.Polis, J.Uldriķis, N.Barmenkova, and A.Ķimenis, Offenleg. 3314362 (BRD); Chem.Abstr., 1985, 102, 78733.

122. M.Watanabe, M.Fushimi, N.Baba, J.Oda, and Y.Inouye, Agric.Biol.Chem., 1985, 49, 3533.

123. L.Weidolf, K.J.Hoffmann, S.Carlsson, and K.O.Borg, Acta.Pharm.Suec., 1984, 21, 209.

124. P.Stoss and M.Leitold, Offenleg. 3248548 (BRD); Chem.Abstr., 1985, 102, 149715.

125. Maruko Pharm.Co., Pat. 58201764 (Jap.); Chem.Abstr., 1984, 100, 138968.

126. Bayer AG, Pat. 900511 (Belg.); Chem.Abstr., 1985, 103, 6242.

127. Teijin Ltd., Pat. 6094963 (Jap.); Chem.Abstr., 1985, 103, 123371.

128. E. Wehinger, H.Meyer, F.Bossert, W.Vater, R.Towart, K.Stöpel, and S.Kazda, Offenleg. 2935451 (BRD); Chem.Abstr., 1981, 95, 42922.

129. Yoshitomi Pharm.Ind., Pat. 57200364 (Jap.); Chem.Abstr., 1982, 98, 215491.

130. J.Uldriķis, G.Duburs, A.Zīdermane, A.Dauvarte, E.Bisenieks, and G.Tirzītis, Latvijas PSR ZA vēstis, Chem.ser., 1983, 122.

131. S.Ohno, S.Mizukoshi, O.Komatsu, K.Ichihara, and Y.Nakamura, Pat. 60149563 (Jap.); Chem.Abstr., 1986, 104, 50796.

132. K.Hatayama, A.Nakazato, T.Ogawa, S.Ito, and J.Sawada, Pat.Appl. 92936 (Eur.); Chem.Abstr., 1984, 100, 68180.

133. Taisho Pharm., Pat.Appl., 8303616 (Neth.); Chem.Abstr., 1985, 103, 87782.

134. T.Ueda, D.Morino, and K.Takimoto, Pat.Appl., 127150 (Eur.); Chem.Abstr., 1985, 102, 131924.

135. R.Tacke, A.Bentlage, W.S.Sheldrick, L.Ernst, R.Towart, and K.Stöpel, Z.Naturf., B, 1982, 37, 443.

136. R.Tacke, A.Bentlage, R.Towart, and E.Möller, Eur.J.Med.Chem.-Chim.Ther., 1983, 18, 155.

137. R.Tacke, A.Bentlage, R.Towart, and W.Vater, Offenleg. 2837477 (BRD); Chem.Abstr., 1980, 93, 71946.

138. C.Materne and H.Betzing, Offenleg. 2915355 (BRD); Chem.Abstr., 1981, 94, 139948.

139. S.Goldmann, H.Böshagen, J.Stoltefuss, M.Schramm, G.Thomas, and S.Kazda, Offenleg. 3207982 (BRD); Chem.Abstr, 1983, 99, 212422.

140. A.Vogel, Offenleg. 3320616 (BRD); Chem.Abstr., 1984, 101, 7162.

141. G.S.Poindexter and D.L.Temple, Offenleg. 3512995 (BRD); Chem.Abstr., 1986, 104, 88595.

142. T.Tanaka, K.Nagami, S.Tamada, and K.Nakagawa, Offenleg. 3331808 (BRD); Chem.Abstr., 1984, 101, 54938.

143. R.Martin Perez, Pat. 491466 (Span.); Chem.Abstr., 1982, 96, 104100.

144. B.Aristegui and J.Juan, Pat. 503958 (Span.); Chem.Abstr., 1982, 97, 162837.

145. Yamanouchi Pharm.Co., Pat. 8085563 (Jap.); Chem.Abstr., 1981, 94, 47144.

146. Yamanouchi Pharm.Co., Pat. 8231663 (Jap.); Chem.Abstr., 1982, 97, 6157.

147. T.Shibanuma, M.Iwanami, M.Fujimoto, T.Takenaka, and M.Murakami, Chem.Pharm.Bull., 1980, 28, 2609.

148. K.Araki, H.Ao, K.Aihara, and T.Kimura, Pat.Appl. 8201185 (PCT Int.); Chem.Abstr., 1982, 97, 92145.

149. Yoshitomi Pharm.Ind., Pat. 57200386 (Jap.); Chem.Abstr., 1983, 98, 215490.

150. Yoshitomi Pharm.Ind., Pat. 58157785 (Jap.); Chem.Abstr., 1984, 100, 138958.

151. Yoshitomi Pharm.Ind., Pat. 58159461 (Jap.); Chem.Abstr., 1984, 100, 51460.

152. Yoshitomi Pharm.Ind., Pat. 5951281 (Jap.); Chem.Abstr., 1984, 101, 110746.

153. Yoshitomi Pharm.Ind., Pat. 5978186 (Jap.); Chem.Abstr., 1984, 101, 151862.

154. Yoshitomi Pharm.Ind., Pat. 57167967 (Jap.); Chem.Abstr., 1983, 98, 107166.

155. H.Yamaguchi, Y.Odamiya, H.Kanno, and K.Sunakawa, Pat.Appl. 128010 (Eur.); Chem.Abstr., 1985, 102, 220754.

156. Teijin Ltd., Pat. 6097955 (Jap.); Chem.Abstr., 1985, 103, 196011.

157. P.B.Berntsson, S.A.J.Carlsson, and B.R.Ljung, Pat.Appl. 95451 (Eur.); Chem.Abstr., 1984, 100, 103187.

158. Yamanouchi Pharm.Co., Pat. 8262258 (Jap.); Chem.Abstr., 1982, 97, 127516.

159. P.Neumann, Offenleg. 2949491 (BRD); Chem.Abstr., 1980, 93, 239420.

160. K.Muto, T.Kuroda, A.Karasawa, K.Yamada, and N.Nakamizo, Pat.Appl. 106275 (Eur.); Chem.Abstr., 1984, 101, 110742.

161. K.Muto, M.Watanabe, T.Hatta, T.Sugaya, Y.Takemoto, and N.Nakamizo, Pat.Appl. 63365 (Eur.); Chem.Abstr., 1983, 98, 160591.

162. K.Schönafinger, R.Bayerle, P.A.Martorana, M.Just, and H.Bohn, Offenleg. 3303066 (BRD); Chem. Abstr., 1985, 102, 95550.

163. Teijin Ltd., Pat. 6092266 (Jap.); Chem.Abstr., 1985, 103, 215179.

164. M.Watanabe, K.Moto, T.Sugaya, T.Kuroda, T.Hashimoto, K.Yamada, and N.Nakamizo, Pat.Appl. 106276 (Eur.); Chem.Abstr., 1984, 101, 110743.

165. Yoshitomi Pharm.Ind., Pat. 58216158 (Jap.); Chem.Abstr., 1984, 100, 174672.

166. K.Araki, H.Ao, J.Inui, and K.Aihara, Pat.Appl. 88903 (Eur.); Chem.Abstr., 1984, 100, 85591.

167. K.Meguro and A.Nagaoka, Pat.Appl. 94159 (Eur.); Chem.Abstr., 1984, 100, 209872.

168. K.Meguro and A.Nagaoka, Pat.Appl. 8304023 (PCT Int.); Chem.Abstr., 1984, 100, 120900.

169. Takeda Chem.Ind., Pat. 6048970 (Jap.); Chem.Abstr., 1985, 103, 87773.

170. T.S.Zumin, C.Casagrande, F.deMarchi, and M.Nicola, Pat.Appl. 97821 (Eur.); Chem.Abstr., 1984, 101, 55114.

171. Akteibolag Haessle, Pat. 5852286 (Jap.); Chem.Abstr., 1983, 99, 70571.

172. Yoshitomi Pharm.Ind., Pat. 81140989 (Jap.); Chem.Abstr., 1982, 96, 199719.

173. T.Fujikura, N.Ito, Y.Matsumoto, M.Asano, and T.Takenaka, Pat.Appl. 151006 (Eur.); Chem.Abstr., 1985, 103, 196015.

174. K.Yasuda, R.Ochi, T.Seki, M.Saito, M.Kobayashi, T.Shibata, A.Izumi, and T.Ishimori, Pat. 60136558 (Jap.); Chem.Abstr., 1986, 104, 109478.

175. C.Sunkel Letelier, M.Pau de Casa-Juana Minoz, P.R.Statkov, and D.Straumann, Pat.Appl. 8402132 (PCT Int.); Chem.Abstr., 1984, 101, 191700.

176. T.Watanabe, K.Momoi, T.Hiraiwa, S.Ono, J.Nakano, K.Nanun, and H.Takagi, Pat. 60215684 (Jap.); Chem.Abstr., 1986, 104, 109644.

177. S.Goldmann and A.Knorr, Pat.Appl. 52300 (Eur.); Chem.Abstr., 1982, 97, 127513.

178. B.Vīgante, J.Ozols, G.Duburs, J.Beilis, E.Belash, and V.Prezhdo, Khim.Geterotsikl.Soed., 1982, 219.

179. Inst.Org.Synth.Acad.Sci.LatvSSR, Pat. 80124761 (Jap.); Chem.Abstr., 1981, 94, 83961.

180. B.Vīgante, J.Ozols, R.Vītoliņa, G.Sileniece, A.Ķimenis, and G.Duburs, Offenleg. 2909852 (BRD); Chem.Abstr., 1981, 94, 15579.

181. B.Vīgante, J.Ozols, G.Duburs, E.Belash, and J.Beilis, Khim.Geterotsikl.Soed., 1984, 210.

182. B.Vīgante, J.Ozols, M.I.Terekhova, E.S.Petrov, G.Duburs, E.Liepiņš, and G.Rozentāle, Khim. Geterotsikl.Soed., 1986, 491.

183. D.Ambrosi and H.F.deReinach, Pat. 210190 (DDR); Chem.Abstr., 1984, 101, 186152.

184. V.Lūsis, A.Zandersons, D.Muceniece, and G.Duburs, Khim.Geterotsikl.Soed., 1983, 508.

185. K.Görlitzer and D.Buß, Arch.Pharm., 1984, 1029.

186. M.W.Gittos and M.Speding, Pat.Appl. 2137622 (GB); Chem.Abstr., 1985, 102, 95549.

187. R.Balicki, H.B.Blaszczak, and P.Nantka-Namirski, Acta Polon.Pharm., 1980, 37, 1.

188. J.Kuthan, J.Palecek, B.Svobodova, and M.Sramek, Chem.Prum., 1980, 30, 473.

189. Bristol-Myers Co., Pat. 896727 (Belg.); Chem.Abstr., 1984, 100, 156620.

190. Bristol-Myers Co., Pat.Appl. 8301672 (Neth.); Chem.Abstr., 1985, 102, 149254.

191. G.S.Poindexter and D.L.Temple, Pat. 4414213 (USA); Chem.Abstr., 1984, 100, 121050.

192. K.Schönafinger, H.Bohn, J.Melitta, and P.Martorana, Offenleg. 3247118 (BRD); Chem.Abstr., 1984, 101, 191701.

193. M.Zimmermann and H.Kühnis, Pat.Appl. 83315 (Eur.); Chem.Abstr., 1983, 99, 139790.

194. B.L.Feringa, J.Chem.Soc., Chem.Commun., 1985, 466.

195. S.Goldmann, G.Franckowiak, M.Schramm, G.Thomas, and R.Gross, Offenleg. 3311005 (BRD); Chem. Abstr., 1985, 102, 62091.

196. F.R.Heiker, J.Stoltefuss, G.Franckowiak, M.Schramm, G.Thomas, and R.Gross, Offenleg. 3326384 (BRD); Chem.Abstr., 1985, 103, 178575.

197. A.Vogel and G.Bormann, Offenleg. 3438884 (BRD); Chem.Abstr., 1985, 103, 178263.

198. Nippon Shinyaku Co., Pat. 59161382 (Jap.); Chem.Abstr., 1985, 102, 132271.

199. Nissan Chem.Ind., Pat. 6069089 (Jap.); Chem.Abstr., 1985, 103, 142188.

200. K.Seto, S.Tanaka, and R.Sakoda, Pat.Appl. 141222 (Eur.); Chem.Abstr., 1985, 103, 178452.

201. K.Seto, S.Tanaka, and R.Sakoda, Pat.Appl. 196243 (Eur.); Chem.Abstr., 1985, 103, 196243.

202. A.Yu.Alikin, M.P.Sokolov, F.G.Liorber,A.I.Razumov, T.V.Zykova, and V.V.Zykova, Zhurn.Obshch. Khim., 1981, 51, 547.

203. A.Yu.Alikin, M.P.Sokolov, F.G.Liorber, A.J.Razumov, T.V.Zykova, V.V.Zykova, and I.N.Suleimanova, Zhurn.Obshch.Khim., 1981, 556.

204. M.E.M.Attia, Y.Gelas-Mialhe, and R.Vessiere, Canad.J.Chem., 1983, 61, 2126.

205. Y.Suzuki and K.Tani, Bunseki Kagaku, 1980, 29, 849; Chem.Abstr., 1981, 94, 186303.

206. Y.Suzuki and K.Tani, Bunseki Kagaku, 1985, 34, 55; Chem.Abstr., 1985, 102, 105424.

207. S.P.C.Cole, R.A.Whitney, and G.S.Marks, Mol.Pharmacol., 1981, 20, 395.

208. G.S.Marks, D.T.Allen, C.T.Johnston, E.P.Sutherland, K.Nakatsu, and R.A.Whitney, Mol.Pharmacol., 1985, 27, 459.

209. C.Materne, Offenleg. 3021958 (BRD); Chem.Abstr., 1982, 96, 122639.

210. J.Koenig, O.Uhlova, F.Weichet, J.Helfert, and M.Vanecek, Pat. 192407 (Czech.); Chem.Abstr., 1982, 96, 68842.

211. D.A.Claremon and D.E.McClure, Pat.Appl. 139221 (Eur.); Chem.Abstr., 1985, 103, 178181.

212. P.Berntsson and R.E.Carter, Acta Pharm.Suec., 1981, 18, 221.

213. Kanebo Ltd., Pat. 80124760 (Jap.); Chem.Abstr., 1981, 95, 24815.

214. LEK Tovarna Farmacevtskih in Kemicnih Izdelkov, Pat.Appl. 820360 (Neth.); Chem.Abstr., 1983, 99, 38373.

215. S.Goldmann and W.Geiger, Angew.Chem., 1984, 96, 301.

216. B.Loev, F.R.Shroff, and R.Desai, Pat. 4500527 (USA); Chem.Abstr., 1985, 102, 184980.

217. J.J.Boldwin, R.Hirschmann,E.L.Engelhardt, and G.S.Ponticello, J.Med.Chem., 1981, 24, 628.

218. V.Kastron, G.Duburs, R.Vītoliņa, A.Ķimenis, M.Selga, N.V.Kondratenko, L.M.Yagupolsky, D.Tirzīte, Yu.A.Fialkov, and S.V.Shelezhenko, Khim.-Farm.Zhurn., 1982, 16, 1322.

219. V.V.Kastron, G.J.Dubur, V.D.Shatz, and L.M.Yagupolsky, Arzneim.Forsch., 1985, 35(1), 668.

220. V.J.Parinov, A.G.Odinec, A.P.Gilev, G.J.Dubur, D.H.Muceniece, J.J.Ozol, V.D.Shatz, M.P.Gavars, and B.A.Vigante, Arzneim.Forsch., 1985, 35(1), 808.

221. V.V.Kastron, R.Vītoliņa, G.Duburs, M.Selga, G.Zariņš, N.V.Kondratenko, V.I.Popov, A.A.Kolomeitsev, and L.M.Yagupolski, Demande 2509727 (Fr.); Chem.Abstr., 1983, 99, 139778.

222. G.D.Hartman and B.T.Phillips, Pat. 4532237 (USA); Chem.Abstr., 1985, 103, 196110.

223. G.D.Hartman, B.T.Phillips, and W.Halczenko, J.Org.Chem., 1985, 50, 2423.

224. G.D.Hartman, W.Halczenko, and B.T.Phillips, J.Org.Chem., 1985, 50, 2427.

225. D.C.Remy, S.W.King, D.Cochran, J.P.Springer, and J.Hirshfield, J.Org.Chem., 1985, 50, 4120.

226. J.R.Shroff and B.Loev, Pat. 4478834 (USA); Chem.Abstr., 1985, 102, 62211.

227. S.Ozaki and H.Watanabe, Pat. 6056956 (Jap.); Chem.Abstr., 1985, 103, 160398.

228. Y.Watanabe, K.Shiota, T.Hoshiko, and S.Ozaki, Synthesis, 1983, 761.

229. C.Materne, Offenleg. 3022030 (BRD); Chem.Abstr., 1981, 96, 8553.

230. N.R.Natale and D.A.Quincy, Synth.Commun., 1983, 13, 817.

231. B.Jarimowicz, Acta Pol.Pharm., 1981, 38, 201.

232. A.A.Hamed, A.Essawy, A.F.Shaban, and J.A.G.El-Karim, Rev.Roum.Chim., 1983, 28, 623.

233. H.Kühnis, Pat.Appl. 111455 (Eur.); Chem.Abstr., 1984, 101, 191875.

234. S.Goldmann, F.Bossert, M.Schramm, G.Thomas, and R.Gross, Offenleg. 3311003 (BRD); Chem.Abstr., 1985, 102, 45915.

235. K.Görlitzer, U.Bartke, S.Goldmann, M.Schramm, G.Thomas, and R.Gross, Offenleg. 3343658 (BRD); Chem.Abstr., 1985, 102, 45915.

236. V.Lūsis, D.Muceniece, A.Zandersons, I.Mažeika, and G.Duburs, Khim.Geterotsikl.Soed., 1984, 393.

237. R.Vītoliņa, E.Stankeviča, E.Grinstein, and A.Dreimane, Khim.-Farm.Zhurn., 1981, 15, 39.

238. E.Grinstein, A.Dreimane, E.Liepiņš, and E.Stankeviča, Latvijas PSR ZA vēstis, Chem.ser., 1980, 722.

239. L.I.Markova and T.D.Kazarinova, In: Nucleophilic Reactions of Carbonyl Compounds. Saratov University Press (In Russian), 1985, 45.

240. H.Iida, Y.Yuasa, and C.Kibayashi, J.Chem.Soc., Chem.Commun., 1981, 114.

241. S.A.Shumakov, V.A.Kaminsky, and M.N.Tilichenko, Khim.Geterotsikl.Soed., 1985, 89.

242. V.A.Kaminsky, N.V.Krugliakova, I.I.Maltsev, and M.N.Tilichenko, Khim.Geterotsikl.Soed., 1981, 95.

243. N.N.Minaeva, V.A.Kaminsky, and M.N.Tilichenko, Khim.Geterotsikl.Soed., 1984, 1393.

244. V.A.Kaminsky, T.V.Zabolotnova, T.V.Novikova, and M.N.Tilichenko, Khim.Geterotsikl.Soed., 1983, 1664.

245. I.Adachi, T.Yamamori, M.Ueda, and M.Doteuchi, Offenleg. 3432985 (BRD); Chem.Abstr., 1985, 103, 87869.

246. I.Adachi, T.Yamamori, and M.Ueda, Pat.Appl. 157260 (Eur.); Chem.Abstr., 1986, 104, 88537.

247. Shionogi and Co., Pat. 5965089 (Jap.); Chem.Abstr., 1984, 101, 171243.

248. Shionogi and Co., Pat. 59152386 (Jap.); Chem.Abstr., 1985, 102, 113473.

249. T.Yamamori, Y.Hiramatu, K.Sakai, and I.Adachi, Tetrah., 1985, 41, 913.

250. a) R.Troschütz, Arch.Pharm., 1984, 317, 709; b) Takeda Chem.Ind., Pat. 59225188 (Jap.); Chem. Abstr., 1985, 103, 22612.

251. H.Meyer, Ann., 1981, 1545.

252. Y.Sato, Y.Shimoji, H.Fujita, H.Mizano, and S.Kumakura, Yakugaku Zasshi, 1978, 98, 448.

253. C.A.Snyder, M.A.Thorn, J.E.Klijanowicz, and P.L.Southwick, J.Heterocycl.Chem., 1982, 19, 603.

254. H.Meyer, Ann., 1981, 1523.

255. J.G.Erickson, J.Am.Chem.Soc., 1945, 67, 1382.

256. N.S.Kozlov and V.V.Zhigulev, Proceed.Perm.Agricultural Inst., 1965, 29, 49 (In Russian).

257. R.Haller, R.Kohlmorgen, and W.Hänsel, Arch.Pharm., 1974, 307, 418.

258. A.Sausiņš, B.Čekavičus, V.Lūsis, and G.Duburs, Khim.Geterotsikl.Soed., 1980, 493.

259. K.Görlitzer and D.Buß, Arch.Pharm., 1981, 314, 938.

260. K.Görlitzer and D.Buß, Arch.Pharm., 1981, 314, 949.

261. H.Möhrle, S.Dörnbrack, and H.J.Novak, Monatsh.Chem., 1981, 112, 1417.

262. B.Čekavičus, A.Sausiņš, R.Zolotoyabko, E.Liepiņš, I.Mažeika, and G.Duburs, Khim.Geterotsikl. Soed., 1986, 501.

263. H.Möhrle and H.J.Novak, Arch.Pharm., 1982, 315, 1042.

264. K.U.Sadek, A.E.Mourad, A.E.Abd-Elhafeez, and M.H.Elnagdi, Synthesis, 1983, 739.

265. N.M.Abed, E.A.A.Hafez, I.Elsakka, and M.H.Elnagdi, J.Heterocycl.Chem., 1984, 21, 1261.

266. G.E.H.Elgemeie, S.A.Elees, I.Elsakka, and M.H.Elnagdi, Z.Naturf., B, 1983, 38, 639.

267. Z.A.Kandeel, K.M.Hasan, N.A.Ismail, and M.H.Elnagdi, J.Prakt.Chem., 1984, 326, 248.

268. S.H.Fahmy, S.O.Abd Allah, and R.M.Mohareb, Synthesis, 1984, 976.

269. L.Fuentes, J.J.Vaquero, and J.L.Soto, Synthesis, 1982, 320.

270. N.M.Abed, N.S.Ibrahim, S.M.Fahmy, and M.H.Elnagdi, Org.Prep.Proced.Int., 1985, 17, 107.

271. L.F.Tietze and K.Brüggemann, Angew.Chem.Int.Ed.Engl., 1982, 21, 539.

272. L.F.Tietze, A.Bergmann, and K.Brüggemann, Tetrah.Lett., 1983, 22, 3579.

273. L.F.Tietze and A.Bergmann, Angew.Chem,Int.Ed.Engl., 1985, 24, 127.

274. Y.Nomura, Y.Takeuchi, S.Tomada, and M.M.Ito, Bull.Chem.Soc.Japan, 1981, 54, 2779.

275. M.Komatsu, S.Takamatsu, U.Masatoshi, Y.Shinji, and O.Yoshiki, J.Org.Chem., 1984, 49, 2691.

276. F.de Sarlo, A.Brandi, and A.Guarna, J.Chem.Soc., Perkin Trans. 1, 1982, 1395.

Received, 17th June, 1987