HETEROCYCLES, Vol 12, No 4, 1979

POLYAZAPHENANTHRENES

Wanda Śliwa*
Institute of Organic and Physical Chemistry, Polytechnical University, 50-370 Wrocław, Poland
Henri Zamarlik
Départment de Chimie, Université de Tours, 37200 Tours, France

Abstract - Diazaphenanthrenes (DAP), including 1) DAP with two N atoms in outer rings (phenanthrolines) and in adjacent rings (benzo[h]naphthyridines), 2) DAP with two N atoms in the outer ring and 3) DAP with two N atoms in the middle ring, i.e. benzo[c]cinnoline, and also triaza- and tetrazaphenanthrenes are of interest as well for their chemistry as for their pharmacological potential.

In this paper the literature has been reviewed with respect to the synthesis and properties of these ring systems. Since the literature on 1,10-phenanthroline and its complexes is very extensive, this subject requires rather an independent treatment and will not be included here.

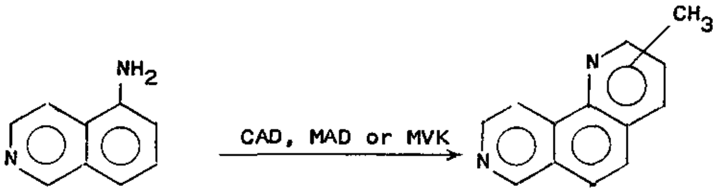
1. PHENANTHROLINES AND BENZO[h]NAPHTHYRIDINES

a) Syntheses

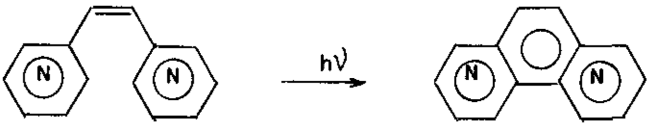
DAP are usually prepared by fusion of a pyridine ring to the carbocyclic (phenanthrolines) or heterocyclic system (benzo[h]naphthyridines) of quinolines. The classical syntheses (Skraup, Doebner-Miller, Knorr, Conrad-Limpach procedures, and other) have been reviewed (1,2). In all cyclization methods the angular, and not the linear products are formed. The improved Skraup procedure for DAP, in the presence of As_2O_5 is reported in (3).

Hamada (4,5) and Kobayashi et al. (6) synthesized DAP and methyl-DAP by the Skraup reaction of appropriate aminoquinolines with glycerine or methyl vinyl ketone (MVK) in the presence of sulfomix (H_2SO_4-SO_3-$\emptyset NO_2$), $FeSO_4$ and H_3BO_3.

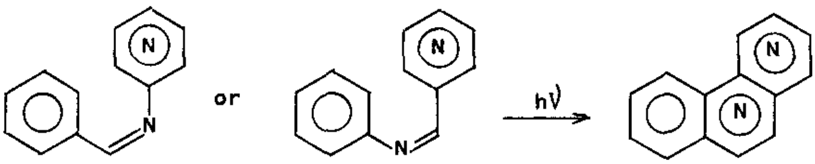
The Skraup synthesis of aminoquinolines or isoquinolines carried out with crotonaldehyde diacetate (CAD), α-methylacroleine diacetate (MAD) or MVK instead of glycerine, afforded the series of methyl-DAP, substituted with methyl group in α, β or γ positions to the N atom (7,8).
For instance:



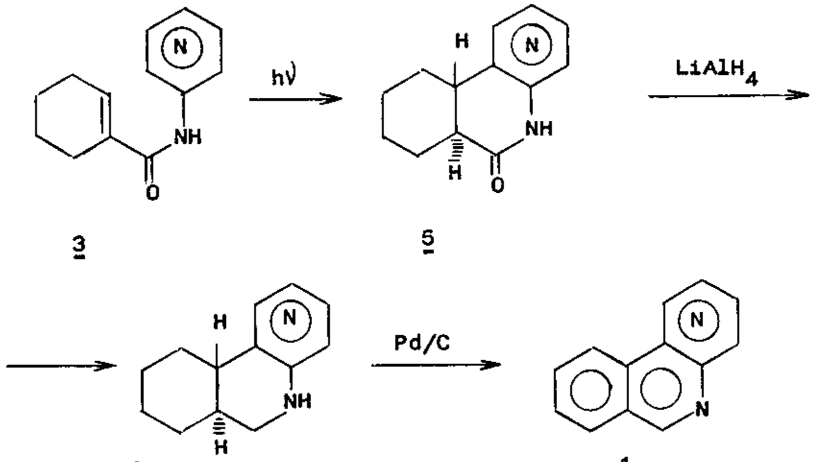
In addition to classical procedures, Perkampus et al. prepared a series of phenanthrolines and benzo[h]naphthyridines by photocyclization of dipyridylethenes (9):



and by photocyclization of benzylideneaminopyridines or pyridinalanilines (10):



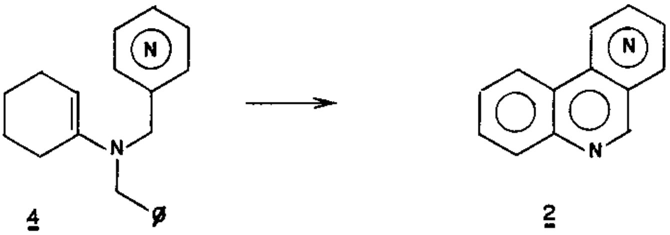
A convenient route to benzo[h]naphthyridines 1 and 2 is the photocyclization of enamides 3 and 4 described by Ninomiya et al. (11). The photocyclization of enamide 3 affords equimolar mixtures of cis and trans lactams 5, which undergo reduction with $LiAlH_4$ to give secondary amines 6 . These on heating with Pd/C yield benzo[h]naphthyridines 1 .



3 5

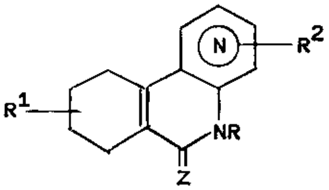
6 1

Benzo[h]naphthyridines 2 were obtained similarly:

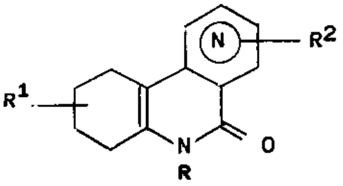


4 2

In an analogous manner Ninomiya synthesized the derivatives 7 and 8 (12)



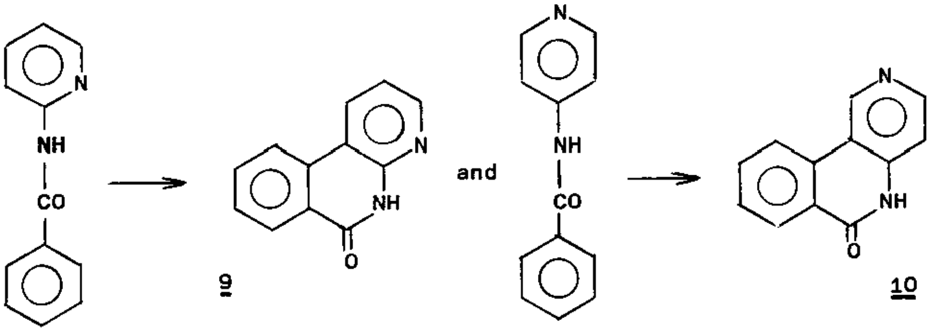
7



8

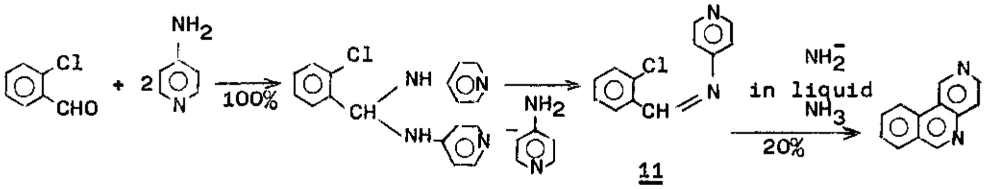
Z = H_2, O
R^1,R^2 = H, halogen, alkyl
R = H, alkyl, aryl

Photolytic Fries rearrangement of 2-benzoylamino- and 4-benzoylaminopyridines gave 4,5-DAP-6[5H]-one 9 and 2,5-DAP-6-[5H]-one 10 (13).

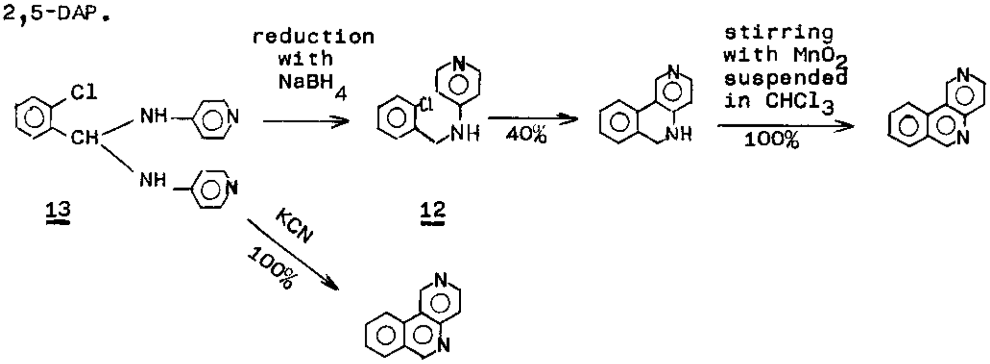


9 10

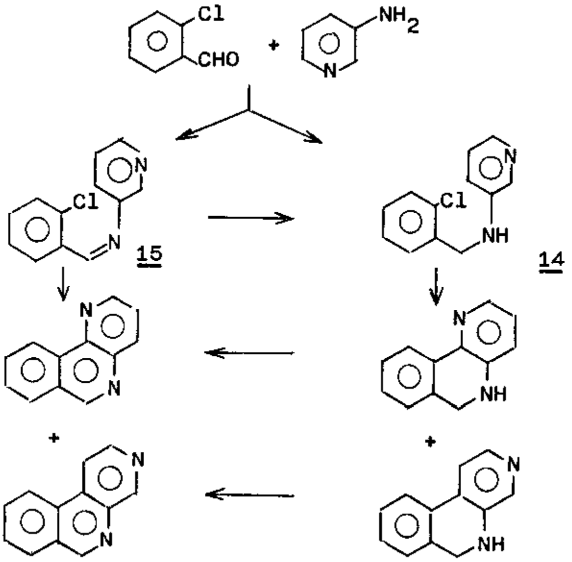
In another synthesis of benzo[h]naphthyridines the anils 11 are cyclized with excess potassium amide in liquid ammonia to give DAP (14,15)



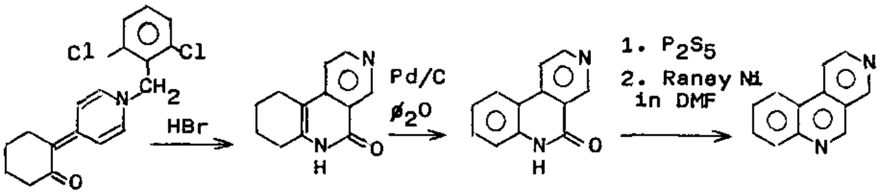
Improved yields of the naphthyne reaction are obtained when the cyclization is performed on the reduced anil 12 . There is known also direct cyclization of 13 to 2,5-DAP.



The anil 15 is obtained from 3-aminopyridine and can give 1,5-DAP or 3,5-DAP. In an alternate approach the reduced anil 14 (obtained either directly from 3-aminopyridine or from the anil 15) was treated with potassium amide in liquid ammonia to give 5,6-dihydro-1,5-DAP and 5,6-dihydro-3,5-DAP:

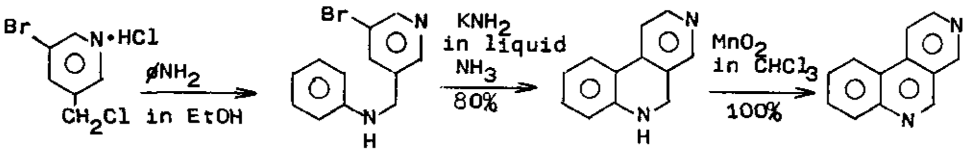


Akhtar and Jeffreys (16) synthesized 3,6-DAP in the following manner: Treatment of **16** with conc. HBr yields **17** which on heating in the presence of Pd/C undergoes dehydrogenation to give **18** , The reaction of **18** with P_2S_5 followed by the treatment with Raney nickel in the presence of DMF gives 3,6-DAP.



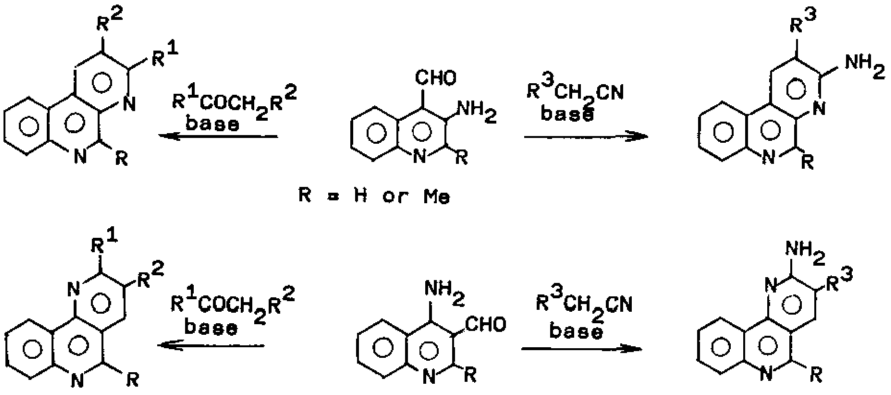
16 **17** **18**

In 1976 Kessar and coworkers reported the simpler synthesis of 3,6-DAP: 3-bromo-5-chloromethylpyridine hydrochloride treated with aniline gives **19**, which subjected to the naphthyne cyclization by KNH_2 in liquid NH_3, and then aromatized by MnO_2 gave 3,6-DAP (17).

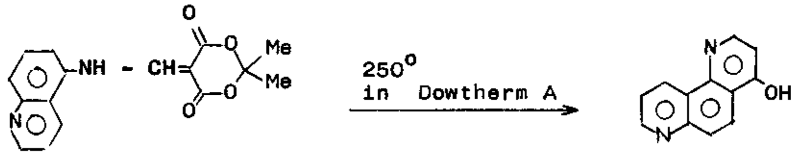


19

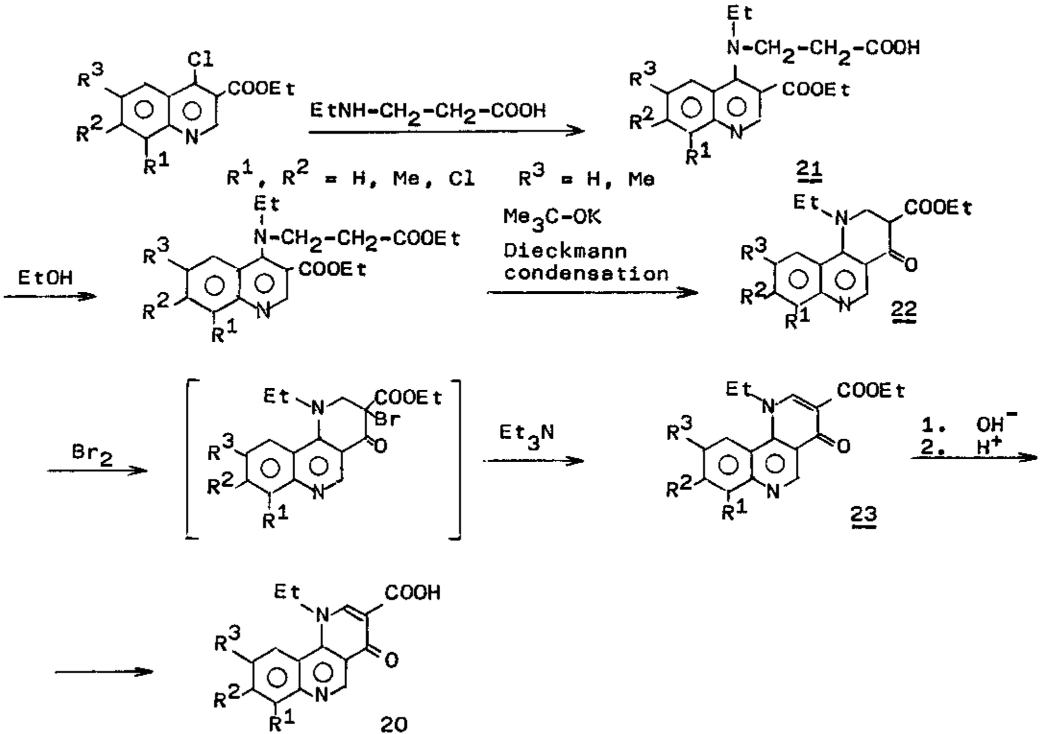
Godard et al. (18) synthesized 1,6- and 4,6-DAP by reacting o-aminoaldehydes with active methylene compounds such as $R^1COCH_2R^2$ and R^3CH_2CN (R^1 = H, Me, ø , 2-pyridyl; R^2 = H, Me, COMe, CO_2Et; R^3 = CN, $CONH_2$) in the presence of a base (piperidine or EtONa):



The hydroxy-DAP were obtained on heating cyclic malonates (19):



Pesson and coworkers (20) synthesized analogues of the nalidixic acid **20** by condensation of the ethyl 4-chloro-quinoline-3-carboxylate with N-alkyl derivatives of β -alanine to **21** , which upon esterification and Dieckmann condensation is converted into **22**. This compound is brominated to monobromoderivative, which without isolation was reacted with tertiary aliphatic amine in order to remove HBr. The resulting **23** was hydrolyzed to give the desired acid **20**:



R^1, R^2 = H, Me, Cl R^3 = H, Me

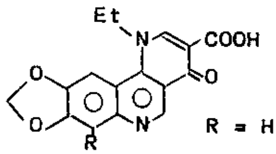
21

22

23

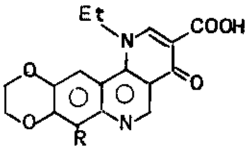
20

In analogous manner the following antibacterial compounds were synthesized (20):

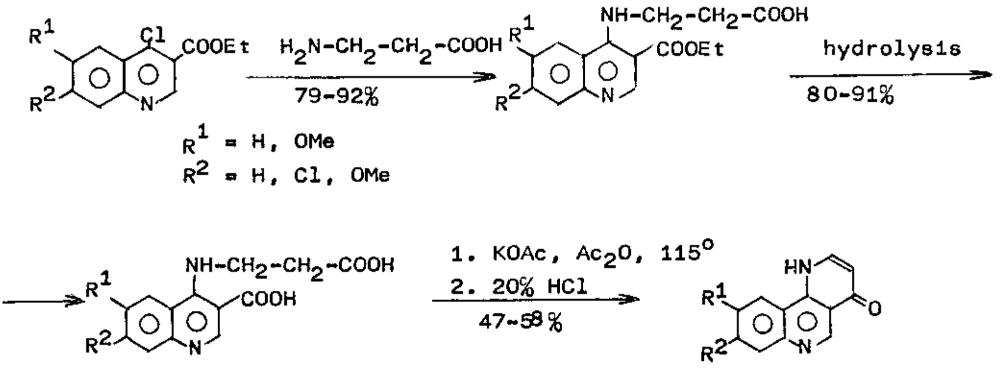


R = H, Me, Et

and

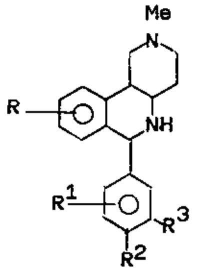


Substituted 1,6-DAP-4[1H]-ones were obtained in reaction sequence (21):



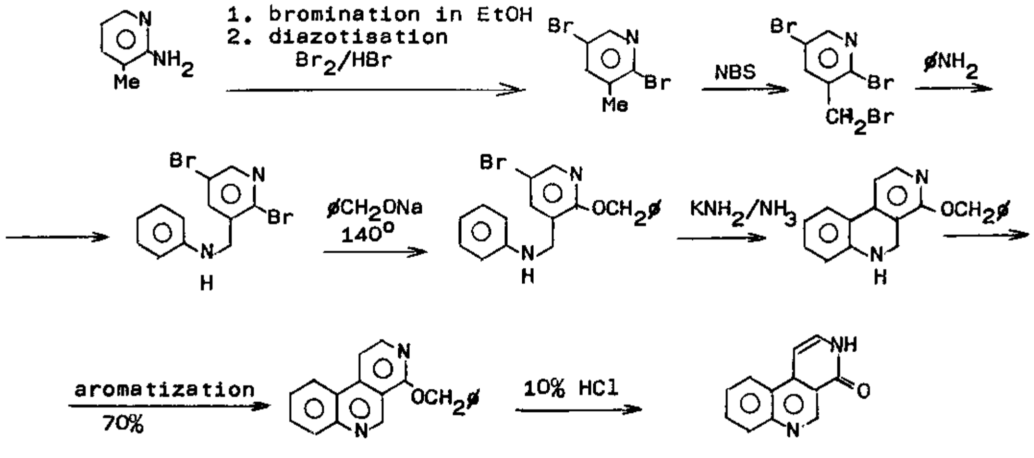
R^1 = H, OMe
R^2 = H, Cl, OMe

Ott and Suess (22) synthesized octahydro-2,5-DAP:



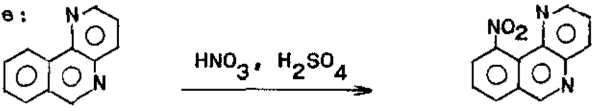
R = H, 8-OH, 9-OH, 9-OMe
R^1 = H, 2-OH, 3-Cl, 3-OH, 3-OMe
R^2 = H, NH_2, NHAc, F, Cl, Me,
R^3 = H, OMe, OH

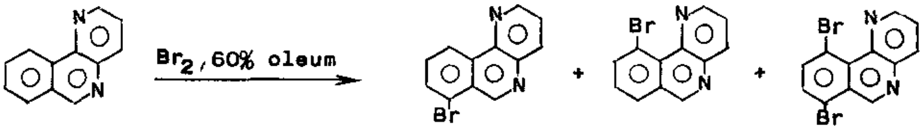
The system of 3,6-DAP is found in the alkaloids perloline and perlolidine. Among numerous syntheses of perlolidine the method described by Kessar and coworkers (17) involves the bromination of 2-amino-3-methyl-pyridine and subsequent displacement of Br atom; the product upon cyclization with KNH_2, aromatization and hydrolysis gives perlolidine:



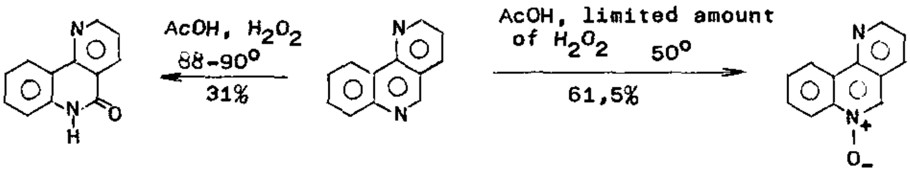
b) Reactivity

The theoretically calculated electron densities of DAP and their protonated forms, as well as localization energy and superdelocalizability values for electrophilic, nucleophilic and radical reactions are reported (23,24). The electrophilic substitution (nitration and bromination) of phenanthrolines was studied by Młochowski (25,26), and of benzo[h]naphthyridines by Śliwa (27). The results are compatible with the positions predicted by calculation of localization energy values. E.g. the nitration of 1,5-DAP yields 10-nitro-1,5-DAP, and its bromination affords a mixture of 7- and 10-monobromoderivatives and of 7,10-dibromoderivative:





The Cziczibabin amination of 4,6-DAP yields its 5-amino-derivative (5).
As an example of homolytic substitution of DAP, Młochowski (28) and Śliwa (29) investigated their methylation and t-butylation. The alkylation proceeds on the protonated DAP, the substitution taking place in α or γ positions to the N atom. The substitution positions are compatible with the calculated localization energy values for nucleophilic reactions, the alkyl radicals posessing a weakly nucleophilic character. However, in the case of t-Bu radicals, the steric features ought also be taken into account.
Phenanthrolines can be oxidized by means of permanganate in alkaline medium to corresponding diazafluorene-9-ones (30).
The literature on DAP-N-oxides is extensive due to their antibacterial and antineoplastic activities. Kobayashi et al. (6) reported the oxidation of 1,6-DAP with peracetic acid, giving 1,6-DAP-6N-oxide or 1,6-DAP-5[6H]-one:

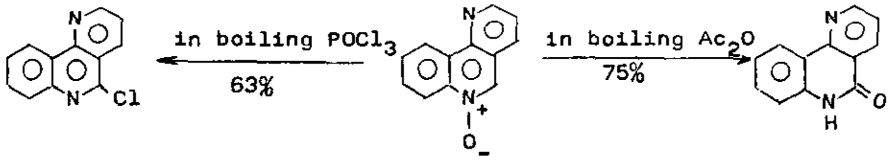


The syntheses of DAP-N-oxides have been described by Młochowski and Śliwa (31, 32). In all cases the N atom in the ,,shielded'' position is *unreactive, the* reaction proceeds on the N atom in the more accessible position. The attempts to obtain the 1-N-oxide were unsuccessful with both monoperphthalic acid, or H_2O_2 in the presence of Na_2WO_4 (6).

Also the attempts of desoxygenation of di-N-oxides in which one of the $N^+- O^-$ groups is in position 1, in order to obtain 1-N-oxide, failed. This is due to the fact, that the oxygen atom at 1-position is readily removed, owing to the steric effect of the hydrogen at 10-position (32,6).

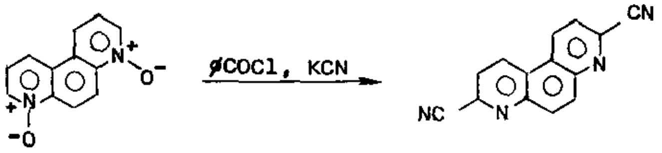
Hamada and Takeuchi investigated the oxidation of 4,6-DAP, obtaining its 4- and 6-mono-N-oxides or 4,6-di-N-oxides, depending on the reaction conditions (33).

DAP-N-oxides undergo reaction with Ac_2O and $POCl_3$ (6):

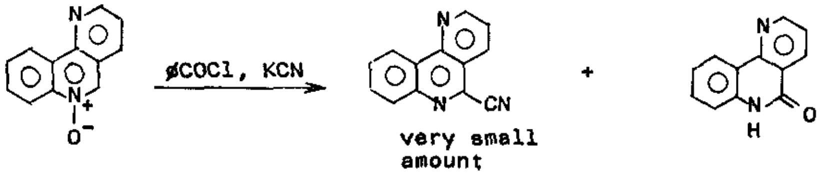


The above result shows that the only nucleophilically active position in 1,6-DAP-6-N-oxide is the α position to the $N^+- O^-$ group.

In the *Reissert reaction of phenanthroline* N-oxides, the derivatives substituted by CN group in the α-position to the $N^+- O^-$ group are formed (34). For instance:



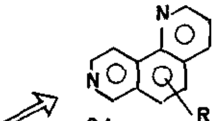
On the other hand, Kobayashi et al. (6) while investigating the Reissert reaction of 1,6-DAP-6-N-oxide obtained very small amount of 5-cyanoderivative under the usual conditions, and the product was chiefly 1,6-DAP-5[6H]-one. This fact is probably due to the influence of the N atom in the 1 position.



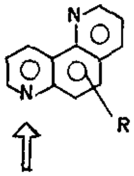
The 1,6-DAP-6-N-oxide reacted with KCN and $K_3Fe(CN)_6$ to give 1,6-DAP-5-cyano-6--N-oxide (35).

The N-methylation of DAP and methyl-DAP (36) gave biologically active N-methiodides. A series of DAP and methyl-DAP upon treatment with CH_3I in benzene yielded monomethiodides, in all cases the deshielded N atom reacting.

Analyzing the approximately determined rate constant values one can see, that the N-methylation is mainly influenced by the steric, and not by the electronic factors. The most reactive is the ,,isoquinolinic'' nitrogen atom, due to its high nucleophilicity, as well as its deshielded position, e.g. N8 in 24 is about 10 times more reactive than N7 in 25 :



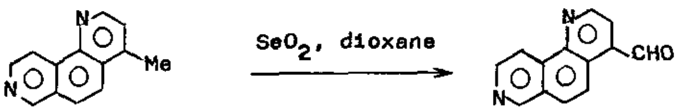
24



25

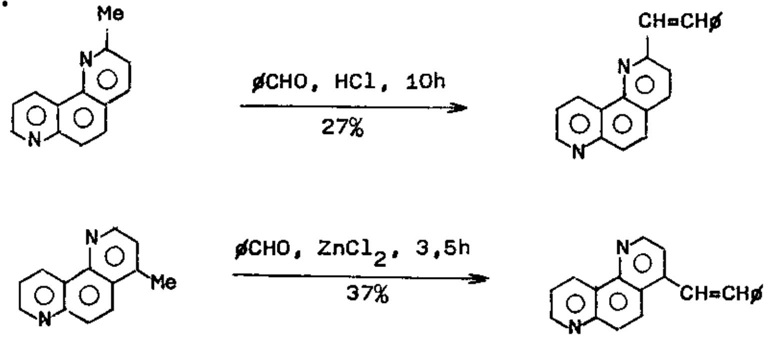
The N-methylation of 4,6-DAP is reported by Hamada et al. (5).

Methyl-DAP were oxidized with SeO_2 to give aldehydes, only methyl groups in α and γ position to the ring N atom being oxidized (8). For instance:

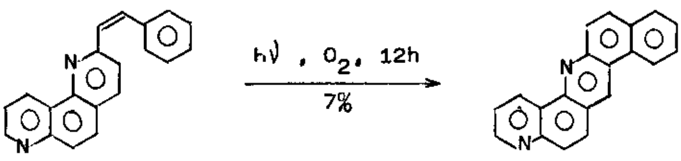


α- and γ-methyl-DAP, subjected to condensation with øCHO give styryl-DAP. The reaction was carried out in the presence of various catalysts (37).

For 1,7-DAP:

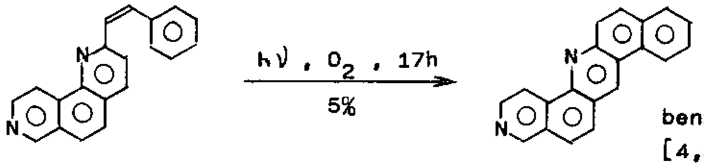


The same catalysts were used in the reaction of 2-methyl and 4-methyl-1,8-DAP. The styryl-DAP were photocyclized to give 26 and 27 (37):



benzo[a]pyrido-[3,2h] acridine

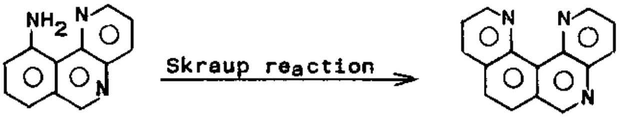
26



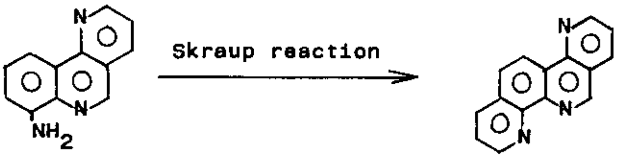
benzo[a]pyrido-[4,3h]acridine

27

Śliwa and Szulc (38) applied the Skraup synthesis to amino-DAP, obtained by reduction of nitro-DAP (27). In this way two new four-ring azaaromatic systems 28 and 29 were synthesized.



28



29

c) Properties

The dipole moments' measurements of DAP and their N-oxides are reported in (40). The pure electronic levels of the free bases and their conjugated acids were determined from the absorption fluorescence and phosphorescence spectra (41). Basara et al. performed the vibrational analysis of highly resolved phosphorescence spectra of some phenanthrolines (42). Sobczyk-Sucharda et al. (40) examined the UV spectra of DAP and their N-oxides. The IR and Raman spectra of DAP and their derivatives are discussed in (43). Bluhm et al. determined pK values and thermodynamic data of DAP from the pH and temperature dependence of the electron excitation spectra (44). Weissenfels studied spectroscopy of DAP-1,2-endiols (39).

The correlation of ^{1}H NMR chemical shifts and electron densities of DAP are described in (10,45), and of methyl-DAP in (46).

Młochowski and Śliwa (47) observed for DAP and their protonated forms the linear correlations of ^{1}H NMR chemical shifts and calculated π electron densities; similar linear correlations of ^{13}C NMR chemical shifts were found by Śliwa (48). The EPR spectra of DAP and their protonated forms are reported by Chodkowska (49), the He I photoelectron spectra of DAP are described in (50), and their mass spectra in (51).

Kato et al. (52) investigated the polarographic reduction of phenanthroline methiodides. The IR and UV spectra of 10-hydroxy-1,7 DAP and its derivatives are reported (53).

DAP have an interesting biological activity. Gupta (54) reported an antibacterial activity of DAP and their methyl- and benzylderivatives. Tuszkiewicz at al. (55) investigated antibacterial and antifungal properties of phenanthrolines and their methyl-, bromo- and $N^+ - O^-$ derivatives and found the broad activity spectrum of 1,9- and 2,7-phenanthrolines, as well as of 1,8-phenanthroline N-oxide. Benzo[h]naphthyridines, especially their N-oxides posess a broad antibacterial spectrum (48).

The 1,6- , 4,5- and 4,7-DAP, as well as the 1,8-DAP-8-N-oxide have an antineoplastic activity (24,48). The 1,6-DAP-4[1H]-ones (20,21) and the derivatives of 1,5- , 2,5- and 3,5-DAP (15) show potent and often specific antimicrobial activity. The substituted octahydro-2,5-DAP are broncholytic agents (22).

Antiinflammatory properties were found in benzonaphthyridines of the type 7 and 8 (12). The derivatives of 1,7-DAP-4,10 [1H,7H] -dione and 4,7-DAP-1,10[4H,7H] dione show a significant allergy activity (56).

3-methyl-4,7-DAP can be used as a diagnostic agent for detecting blood in body fluids (57).

Following the paper by Plakogiannis (58), who reported the antineoplastic activity of 6-methyl-1,10-phenanthroline methiodides, there appeared numerous publications on the synthesis and activity of heterocyclic methiodides. The DAP-N-methiodides,as compared with other DAP derivatives show a stronger antibacterial activity (36,48).

Młochowski and Śliwa (59) obtained the phenanthrolinic analogue of caerulomycin (4-methoxy-1,10-phenanthroline-2-aldoxime) possessing a bacteriostatic activity, however, in the synthesized oximes of DAP-aldehydes no interesting biological activity was found (8).

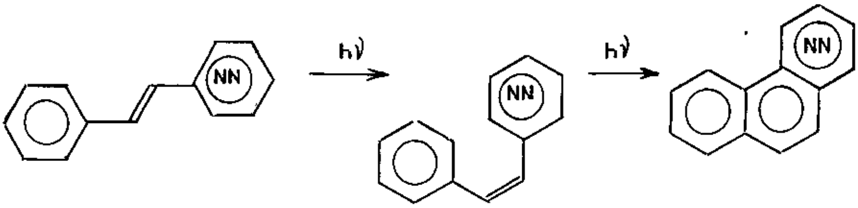
DAP are inhibitors of photosynthetic electron transport (60). Perloline and perlolidine inhibit rumen fermentation (61), 4,7-DAP inhibits the phalloidin poisoning (62), and 1,7 DAP is an inhibitor for metapyrocatechase (63).

2. DAP WITH TWO N ATOMS IN THE OUTER RING

Munslow and Delia in a paper of 1976 reviewed the synthesis and properties of 2,4- and 1,3-DAP (64).

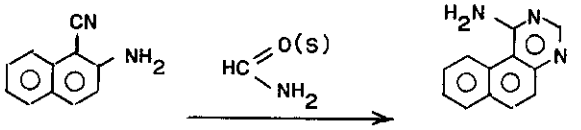
a) Syntheses

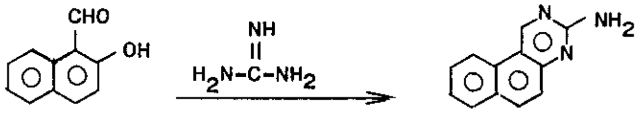
Six isomeric DAP with two N atoms in the outer ring were obtained by photocyclodehydrogenation of styryldiazines in the yield of 10-59% (65); this method proved to be easier than the classical synthesis, e.g. (66). The photocyclodehydrogenation is preceeded by cis-trans photoisomerisation:



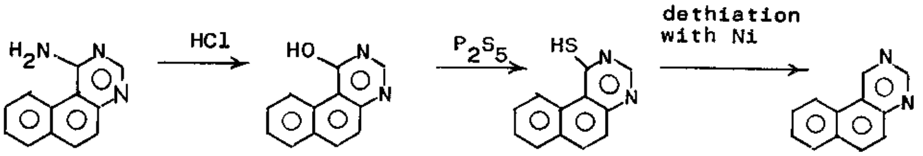
2,4-DAP

2,4-DAP are usually synthesized by condensation of naphthalene derivatives with simple nitrogen compounds, for instance (67):

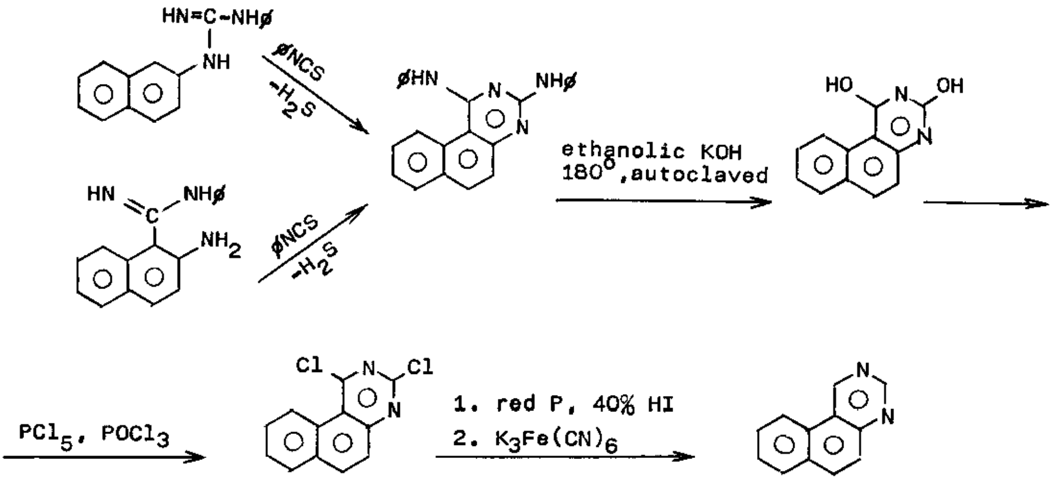




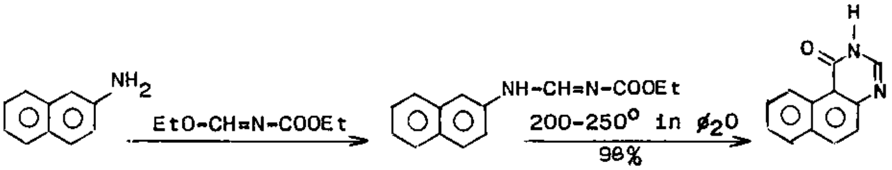
To achieve the deamination of 1-amino-(or 3-amino)-2,4-DAP, the following reaction was carried out (67):



Dymek and Sybistowicz (68) synthesized 2,4-DAP in the following reaction:

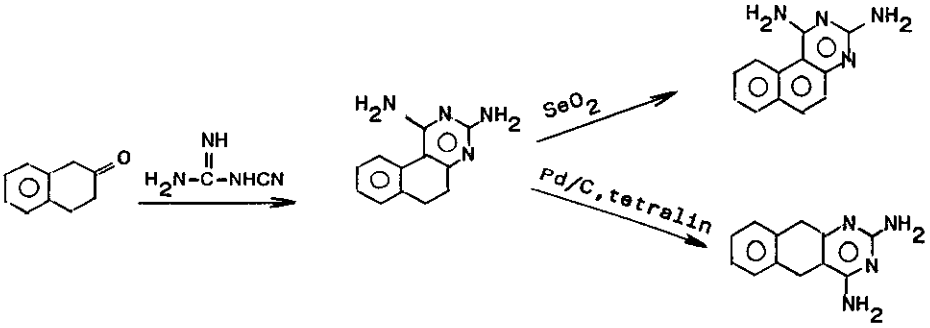


Gompper et al. (69) reacted 2-naphthylamine with EtO-CH=N-COOEt, and heated the resulting formamidine to obtain 2,4-DAP-1 (2H)-one:

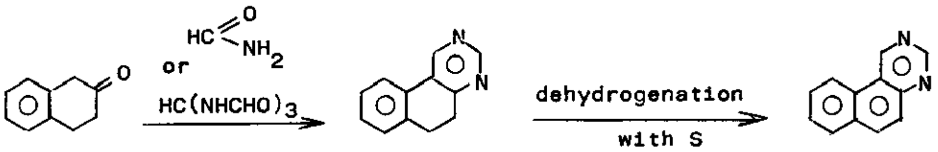


Among other methods of the synthesis of 2,4-DAP system, there ought to be mentioned the condensation of o-aminonitriles with cyanamide (70) and thermal cyclization of bis(2-naphthyl)-biguanidide hydrochlorides (71).

In addition to the fully aromatic 2,4-DAP there exist also a number of their 5,6-dihydroderivatives; they are usually synthesized by the condensation of an appropriate 2-tetralone with cyanoguanidine (72). The 1,3-diamino-5,6-dihydro-2,4-DAP can be oxidized with SeO$_2$ (70). However, when this compound was dehydrogenated under disproportionation conditions in the presence of tetralin and 10% Pd/C catalyst, the aromatization did not take place but an interesting rearrangment to the linear 2,4-diamino-5,10-dihydro-1,3-diazaanthracene was found to occur (72).



Koyama et al. (73) reacted 2-tetralone with formamide or HC(NHCHO)$_3$ to obtain 5,6-dihydro-2,4-DAP, which upon dehydrogenation with sulfur gave 2,4-DAP:

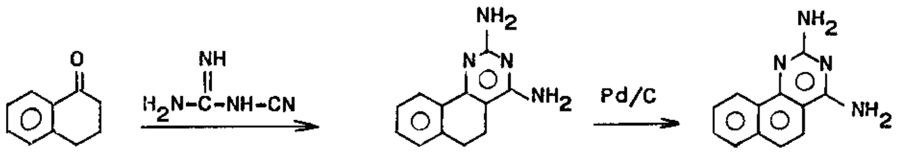


The 2,4-DAP system has been incorporated into the steroidal skeleton (74).

1,3-DAP

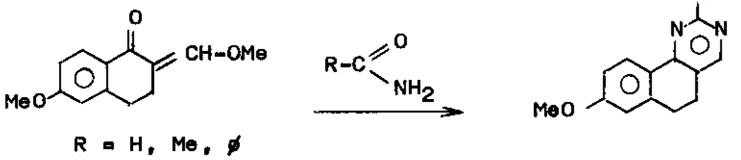
For the synthesis of these compounds there is often used the condensation of 1-tetralone with nitrogen compounds. Koyama et al. (73) carried out the reaction of 1-tetralone with $HC(NHCHO)_3$ in an analogous manner as in the case of 2-tetralone, obtaining 1,3-DAP.

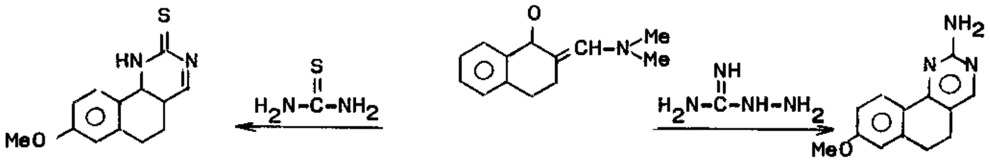
2,4-Diamino-1,3-DAP was prepared according to the equation (72):



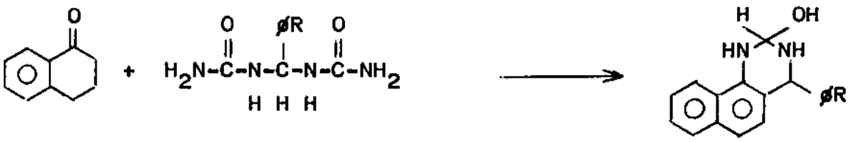
In this reaction no linear compound resulted.

The following syntheses of 1,3-DAP system were carried out by Taylor and coworkers (75):

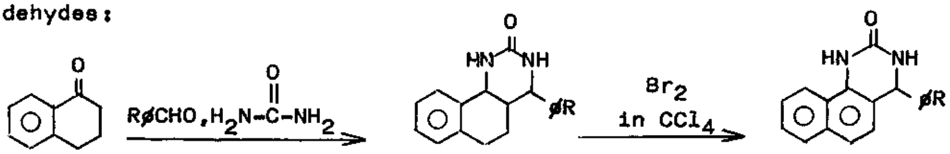




A series of 1,2,3,4-tetrahydro-1,3-DAP was prepared by reacting 1-tetralone with arylidenebis-ureas (76):



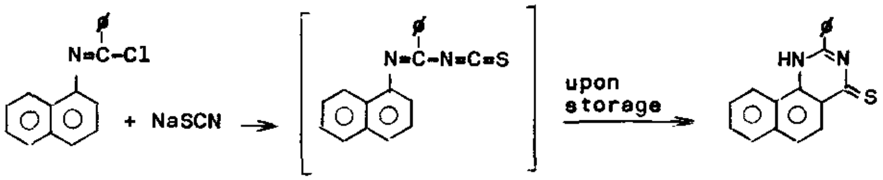
Mamaev and Sedova (77) condensed 1-tetralone and urea with the series of aromatic aldehydes:

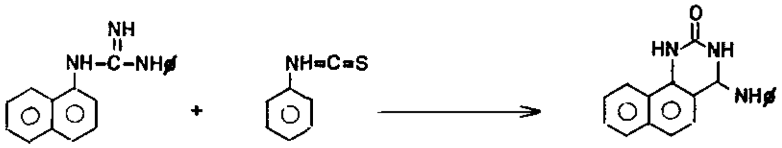


For the dehydrogenation, instead of bromine, other agents can be used, e.g. chloranil, NBS or Pd/C (78).

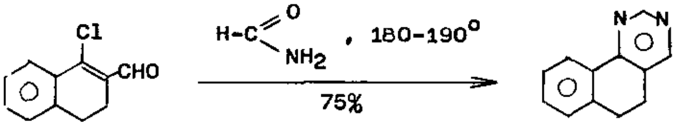
Reacting 1-naphthylamine with EtO-CH=N-COOEt under similar conditions as in the case of 2-naphthylamine, 1,3-DAP-4[3H]-one was formed (69).

The following reactions of naphthalene derivatives were carried out (79):





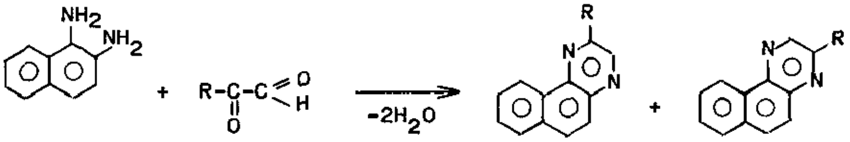
5,6-Dihydro-1,3-DAP can be prepared in the reaction (78):



The method of the incorporation of the 1,3-DAP system into the steroidal structure has been reported (80).

1,4- and 2,3-DAP

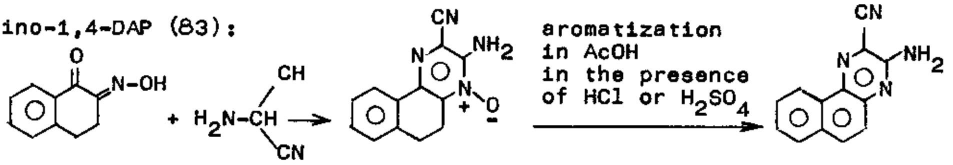
In the condensation of 1,2-diaminonaphthalene with unsymmetrically substituted α-dicarbonyl compounds, two isomeric 2- and 3-substituted 1,4-DAP have been formed (81):



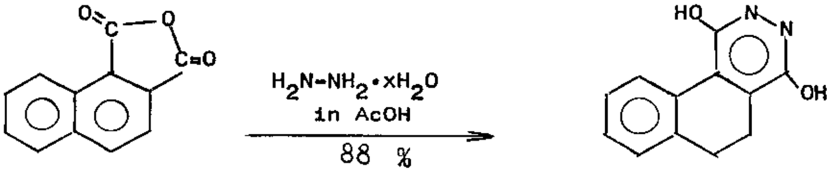
R = COOH, -CHO, -CH=N-NHø etc.

1,2-Diaminonaphthalene sulfate reacts with 2-hydroxyiminoacetophenone to give 2-phenyl- and 3-phenyl-1,4-DAP (82).

Condensation of 2-oximino-1-tetralone with aminomalonitrile afforded 2-cyano-3-amino-5,6-dihydro-1,4-DAP-4-N-oxide, which upon aromatization yielded 2-cyano-3-amino-1,4-DAP (83):



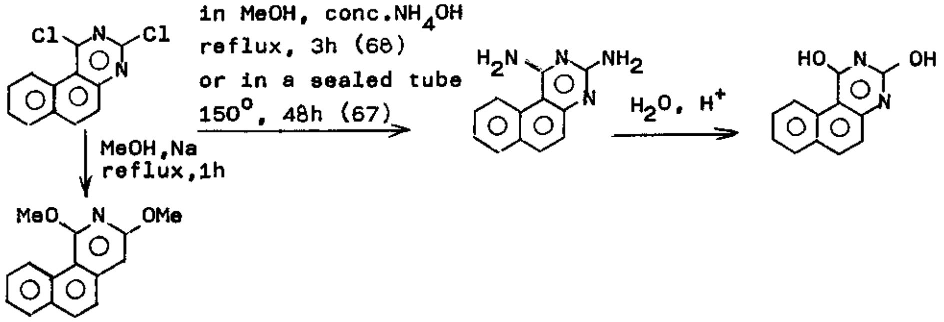
The 2,3-DAP system was obtained in the reaction of naphthalene-1,2-dicarboxylic acid anhydride with hydrazine hydrate (84):



b) Reactivity

2,4-DAP

The following reactions of 1,3-dichloro-2,4-DAP were reported (67,68):

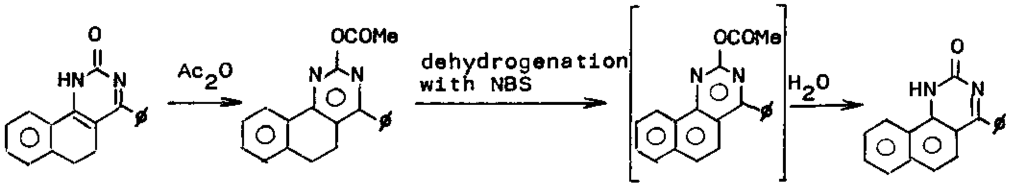


3-Hydroxy-2,4-DAP can be converted directly into 3-amino-2,4-DAP upon treatment with øO-P(O)$(NH_2)_2$. This method obviates the usual requirement for chlorination or thiation prior to amination (85).

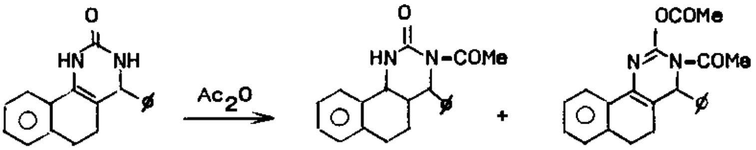
1,3-DAP

The acetylation of 4-phenyl-5,6-dihydro-1,3-DAP-2[1H]-one and its di- and tetrahydroderivatives has found to be dependent upon the degree of hydrogenation (86):

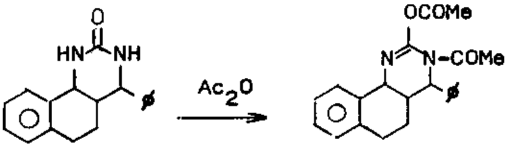
1)



2)

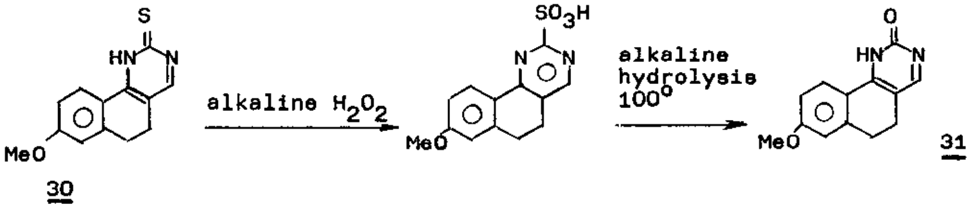


3)

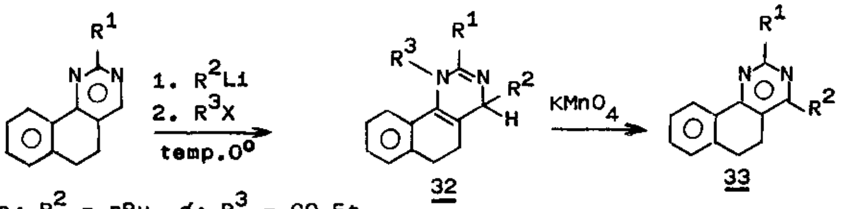


Upon treatment of 4-hydroxy-1,3-DAP with P_4S_{10}, the OH group is replaced by SH (87).

The oxidation of the thione 30 with H_2O_2 to the 2-sulfinic acid, followed by aqueous alkaline hydrolysis to give 31 proceeds as follows (75,88):



Organolithium addition to 5,6-dihydro-1,3-DAP, followed by quenching with either ethyl chloroformate or hydrogen chloride gas, gives in high yield the dihydrocompound 32 , which can be oxidized to 33 (89):



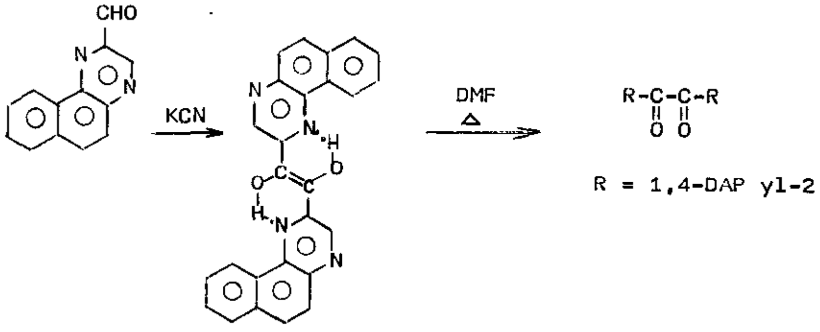
R^1 = H,Me; R^2 = nBu, ø; R^3 = CO_2Et

1,4- and 2,3-DAP

The oxidation of 1,4-DAP with performic acid yielded a mixture of mono- and di-N-oxides; in order to obtain only di-N-oxide, peracetic acid had to be used (90).

The oxidation of 2-phenyl and 3-phenyl-1,4-DAP with monoperphthalic acid afforded mono-N-oxides, the reaction taking place, as usually, at the deshielded N atom (82).

The reaction of 2-formyl-1,4-DAP with KCN gives 34 , which on heating in DMF can be converted into diketone (81):



34

R = 1,4-DAP yl-2

Kobe et al. (84) accomplished the dehydrogenation of 5,6-dihydro-2,3-DAP and of its derivatives with bromine and NaOAc in AcOH.

c) Properties

The data of phosphorescence polarization of 1,4-DAP are reported in (91), and the fluorescence spectra of its heteroexcimers with electron donors - in (92). The chemiluminescence quantum yields of 2,3-dihydro-2,3-DAP-1,4-dione were measured (93).

There was observed, that DAP with two N atoms in ortho position caused skin irritation (65). A number of 1,3- and 2,4-DAP derivatives were synthesized in order to screen their physiological activity. Dihydro-1,3- and 2,4-DAP were obtained as the analogues of primethamine, a dihydrifolate reductase inhibitor (64). 1,3-Diamino-2,4-DAP derivatives were synthesized as potential folic acid antagonists and antitumor agents (72).

Amino-1,3- and 2,4-DAP are used as antifoggants for silver halide photographic materials and as stabilizers for silver halide emulsion (64,94). 1,4-DAP derivatives are applied in the production of plastics, used as freeze drying photochromic filters (95).

3. BENZO[c]CINNOLINE

a) Syntheses

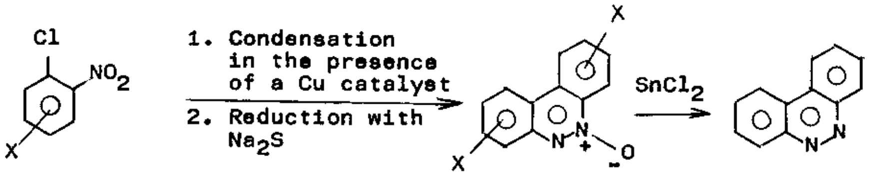
The synthetic approaches to benzo[c]cinnoline (BC) can be classified as:

1) cyclization of diphenyl derivatives with the formation of the N-N bond

2) cyclization of azobenzenes with the formation of the C-C bond

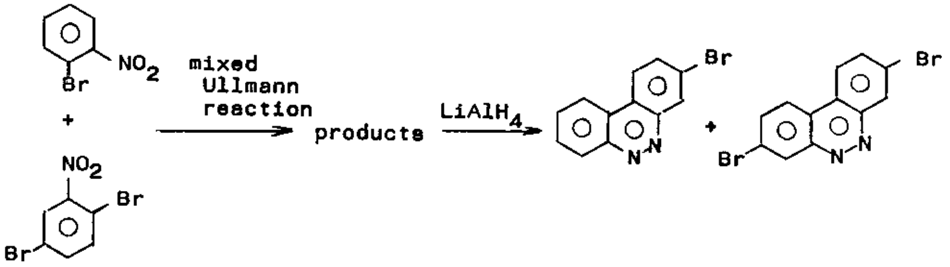
1) cyclization of diphenyl derivatives

BC can be obtained in the Ullmann reaction, from o-chloronitrobenzene (substituted or not) and by the subsequent reduction of the resulting 2,2'-dinitrodiphenyl, for instance (96):



X = halogen, alkyl

Instead of fusion there can be used DMF as a medium (97). An example of a mixed Ullmann reaction is (98):

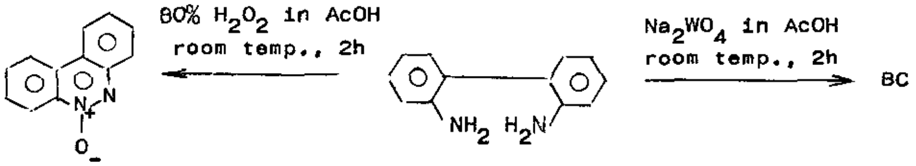


Reduction of 2,2'-dinitrodiphenyl can be carried out with hydrogen in the presence of Raney Ni or Pd/C, as well as in the presence of $Fe(CO)_5$ and CO (99), with either 100% hydrazine hydrate or hydrazine hydrate and EtOH (100), with Zn + NaOH (101), with Li in THF (102) or $LiAlH_4$ (103), as well as with $NaAlH_2(OCH_2CH_2OMe)_2$ and $(EtO)_3P$ (104).

The partial reduction of 2,2'-dinitrodiphenyl e.g. with NaHS yields BC-mono-N--oxide (105). The reduction of alkyl-2,2'-dinitrodiphenyls, resulting in alkyl--BC is described in (106), and the reduction of amino- and hydroxydinitrodiphenyls in (107).

BC and its N-oxide (substituted or not) can also be obtained by the reduction of 2-amino-2-nitro-diphenyl or its derivatives (98, 108, 109).

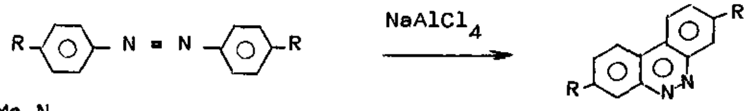
Sometimes the synthesis of BC by reduction of 2,2'-dinitrodiphenyl is impossible the substituents during the reaction being removed or reduced, e.g. nitro- and chloroderivatives cannot be obtained in this way. In such cases there is used oxidation of 2,2'-diaminodiphenyl with peracetic acid or with sodium perborate (103):



BC can be also obtained from 2,2'-diaminodiphenyl by diazotisation (110), or from 2,2'-diazidediphenyl or its derivatives (111). Reaction of 3-trifluoromethylnitrobenzene with sodium amide yields 3,8-ditrifluoromethyl-BC-N-oxide (112).

2) cyclization of azobenzenes

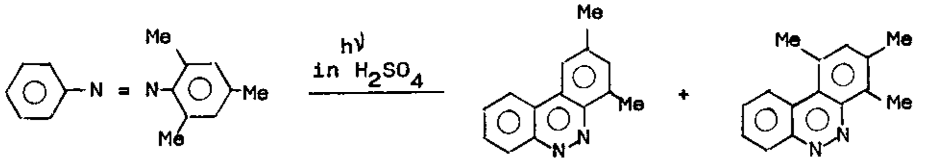
The second route of the synthesis of BC systems is the cyclodehydrogenation of azobenzenes, for instance with $NaAlCl_4$:



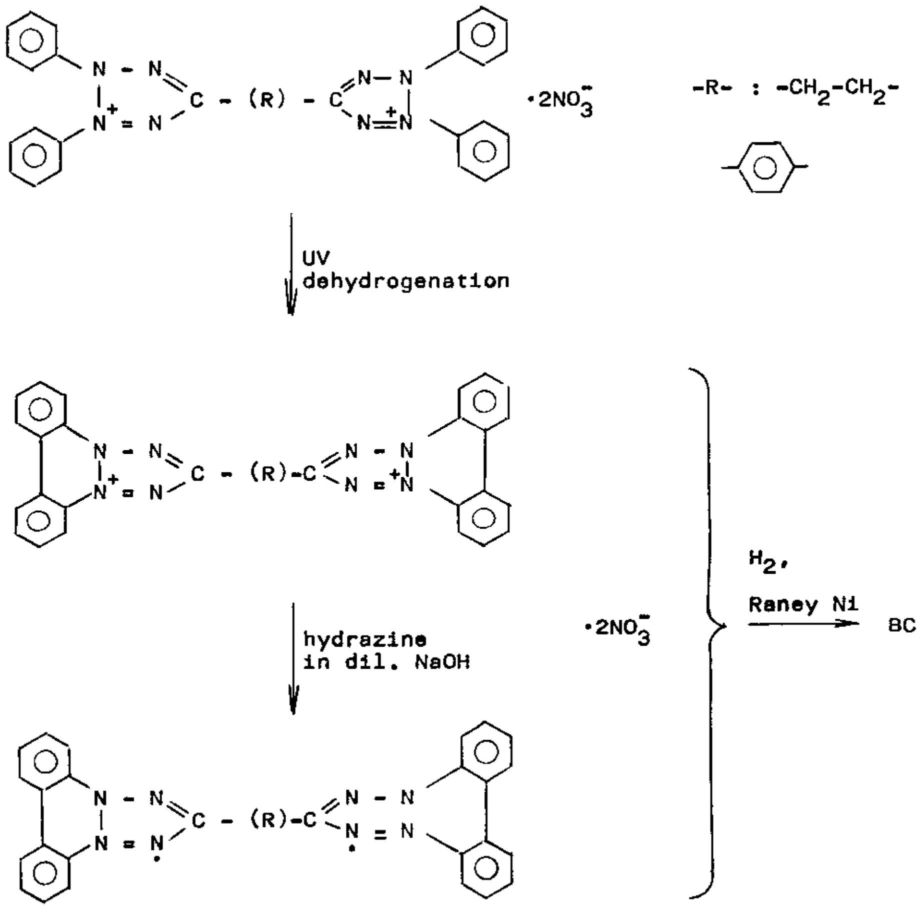
R = H, Me, Me_2N

Azobenzene in EtOH and 24N H_2SO_4 exposed to sunlight is photochemically dehydrogenated to BC (117). The photochemical cyclodehydrogenation of azobenzenes to BC can also be carried out in the presence of Lewis acid, e.g. $FeCl_3$, $AlCl_3$, $SnCl_4$ (118, 119).

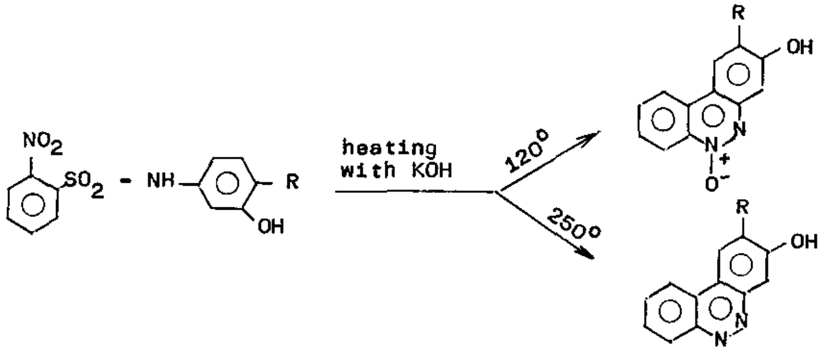
2,4,6-Trimethyloazobenzene underwent photochemical cyclodehydrogenation in sulfuric acid, with the loss of one and migration of another methyl group (120):



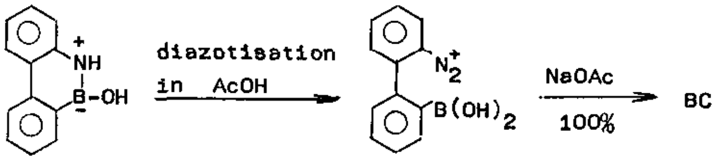
The following sequence of reactions results in BC (121):



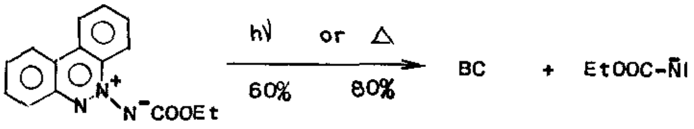
A convenient synthesis of hydroxy-BC and methyl-hydroxy-BC, as well as of their N-oxides was reported by Waldau (122):



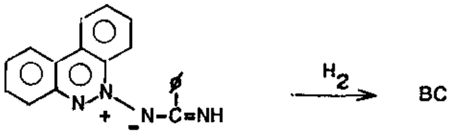
BC can also be readily obtained from dihydroazoboracompounds (123):



Among the synthetic approaches to BC there ought also to be mentioned its syntheses from ylides by their thermolysis or photolysis (e.g. 124,125):



as well as by their dehydrogenation, e.g. (125):



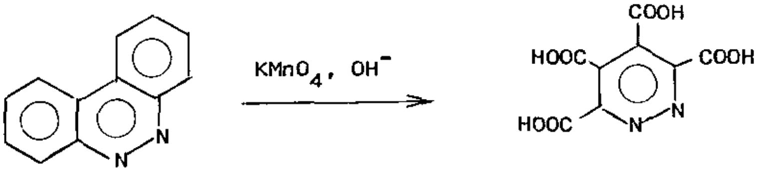
b) Reactivity

Reactions of BC can be classified as follows:

1. oxidation
2. reduction
3. substitution
4. formation of ylides and their reactions
5. formation of metal complexes

1. Oxidation

The electron density in the middle ring of BC is increased due to the presence of two nitrogen atoms, thus this ring is resistant against oxidation, and susceptible to reduction, e.g. the reaction of BC with permanganate results in the oxidation of two outer rings (126):



BC is oxidized with peracetic acid to mono- or di-N-oxide, depending on the reaction conditions (100, 127). The oxidation of methyl-BC is described in (116) and of nitro-BC in (128).

Studying oxidation of bromo-BC there was found, that N atom in the peri position to Br does not undergo oxidation owing to the steric factors; bromo-BC with the Br atom in the position 4 give 6-N-oxides, and not 5-N-oxides (129). For the same reason 4,7-dibromo-BC does not undergo oxidation (98). By oxidation of BC with ozone, its tetraozonide was obtained (130).

BC-di-N-oxide was reduced to BC with triethylphosphite, or with hydrogen in the presence of Raney nickel or Adams catalyst (131). Tanikaga (132) studied the photoreduction of BC-N-oxide to BC in various solvents.

2. Reduction

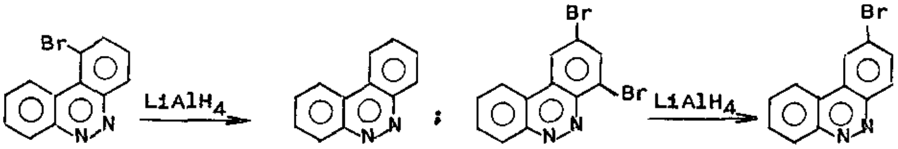
The N-N bond in the middle ring of BC is more susceptible to reduction than both outer rings, thus the hydro-BC cannot be obtained by direct hydrogenation, but by other methods, e.g. by cyclization of the appropriate phenylhydrazones (133).

Benzo[c]cinnolinic system is rather stable, however, under drastic conditions the N-N bond can be broken, e.g. in the hydrogenation of BC in the presence of Raney nickel, the 2,2'-diaminodiphenyl is formed (101).

The photochemical reaction of BC in acidic solvents gives the carbazole (134).

When BC was reduced with metallic sodium or with sodium biphenylenide in hexamethylphosphoramide, the radical anion of BC was formed (135).

Upon treatment of bromo- and dibromo-BC with $LiAlH_4$, Corbett and Holt [98] found, that the Br atom was removed from 1 and 4 positions, e.g.:

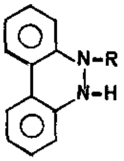


Such debromination of 1- and 4-bromo-BC is rather unexpected, $LiAlH_4$ in general not reducing aromatic halogenoderivatives.

5,6-Dihydro-BC

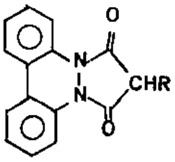
Numerous publications are dealing with 5,6-dihydro-BC. This compound is formed in the photoreduction of BC (136,137), in the polarographic reduction of BC (138), or in the reduction of BC with hydrogen in the presence of Pd/Al (139). Etienne and Piat (139) investigated reactions of 5,6-dihydro-BC:

a) 5,6-dihydro-BC is very reactive; with acid anhydrides mono- or diacylderivatives are formed:



R = -COMe, $-CO-CH_2-CH_2-COOH$

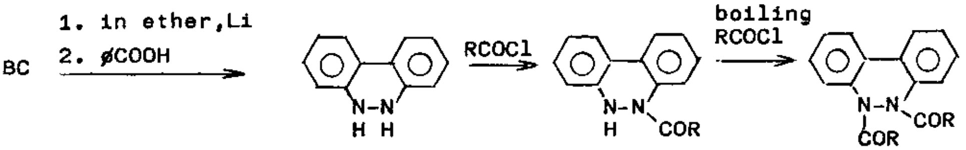
b) reaction of 5,6-dihydro-BC and ethyl malonate is a convenient route for the synthesis of compounds with a pharmaceutical activity. In this way there were obtained:



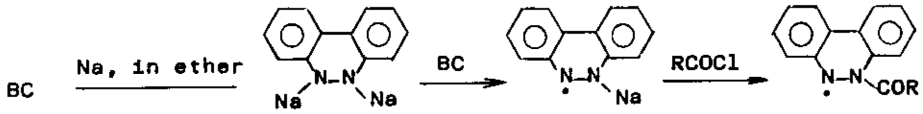
R = H, $n-C_4H_9$

c) 5,6-dihydro-BC upon treatment with Na gives a very reactive disodium derivative.

Acylation of 5,6-dihydro-BC to its mono- and diacylderivatives proceeds as seen below (140):



The 5,6-dihydrobenzo[c]cinnolinic radicals have been obtained in the reaction (140):

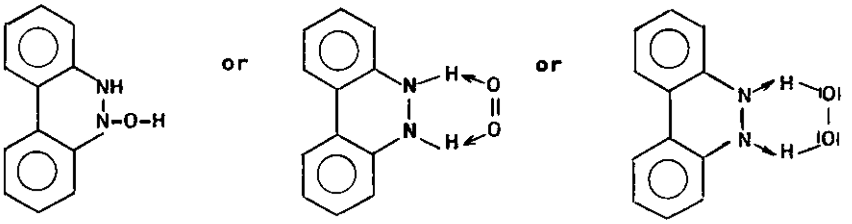


5,6-Dihydro-BC, when exposed on air, undergoes very easily an autoxidation to 5,6-dihydro-BC-peroxide. 5,6-Dihydro-BC-peroxide is a generator of H_2O_2, produced in a cyclic process (139):

$$R + H_2 = RH_2$$

$$RH_2 + O_2 = H_2O_2 + R$$

The 5,6-dihydro-BC-peroxide was isolated in spite of its unstability; the hypothesis of its structure is (139):



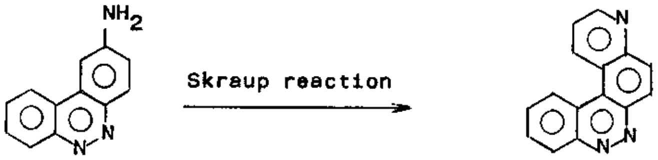
3. Substitution

Nitration of BC with a nitrating mixture yields 1-nitro- and 4-nitroderivatives. The reactivity sequence, resulting from the calculations made for the protonated form, is compatible with the experimental results, and is as follows: $1 > 4 > 3 > 2$. Numerous papers are dealing with nitration of BC (12 ,141-143). Nitration of BC-N-oxide is described (128, 141, 143). In the nitration of methyl-BC and their N-oxides there was observed the activating influence of methyl groups (143).

To reduce nitro-BC to amino-BC the reagents which do not affect the middle ring have to be used, i.e. $SnCl_2$ + HCl, Na hydrosulfite, hydrogen (low pressure) in the presence of Raney Ni or of Pt, sodium amalgam + alcohol (142). Reduction of nitro-BC and their N-oxides to amino-BC or to amino-BC-N-oxides is described in

(48, 128); reduction of nitromethyl-BC and their N-oxides - in (143). The Sandmeyer reaction of amino-BC (128, 129), as well as of their N-oxides (128, 144) was reported.

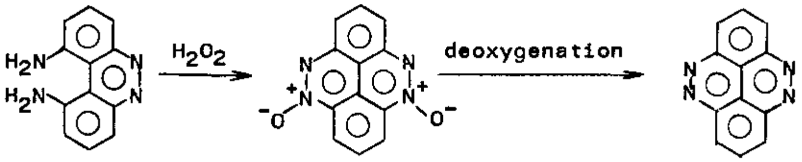
Śliwa and Szulc (38), subjecting 2-amino-BC to Skraup reaction obtained chino[5, 8c]cinnoline; the cyclization occurs in the position 1, and not 3, to give the angular product. This higher reactivity of the position 1 is compatible with the localization energy values, calculated by HMO method.



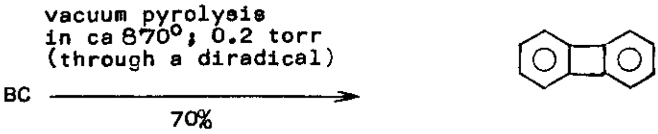
Corbett (145) brominated BC in the presence of Ag_2SO_4 and H_2SO_4 to obtain 4-bromo-BC. The chlorination of BC in the presence of $AlCl_3$ yielded octachloro-BC (146). Reaction of BC with Me_2NLi results in dimethylamination in the positions 4 and 7 (147).

Chloro-BC undergo nucleophilic substitution with sodium alcoxides to give alcoxyderivatives (148).

To BC system a new heterocyclic ring can be fused, e.g. from 1,10-diamino-BC there is formed tetraazapirene (149):

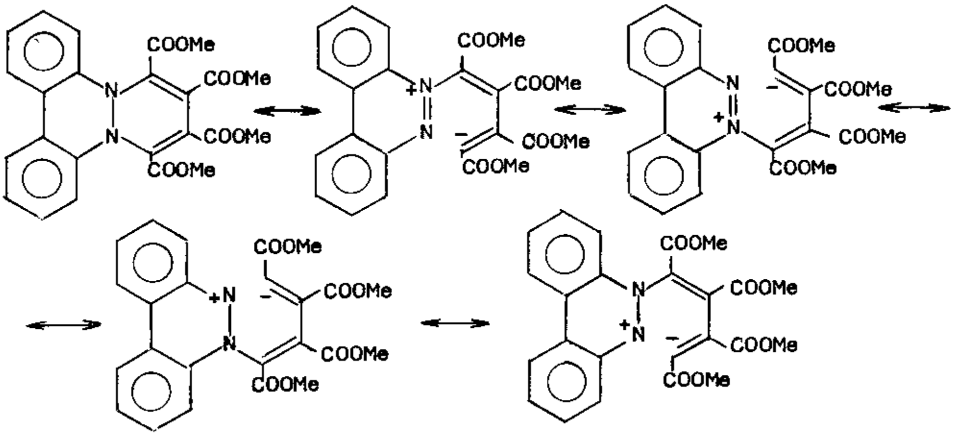


MacBride (146) synthesized biphenylene by thermal extrusion of molecular nitrogen from BC:



Similar reaction was carried out on octachloro-BC (146).

BC and its N-oxides undergo numerous cycloaddition reactions, e.g. BC gives with MeOOC-C≡C-COOMe the adduct (1:2), being probably a resonance hybrid of following structures (150):

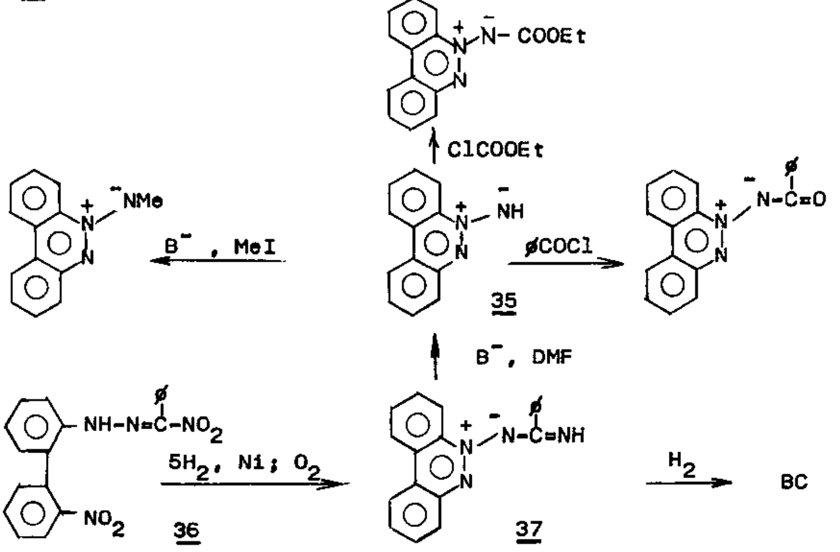


Similar adduct was obtained from 3,8-dimethyl-BC (151). The formation of the adduct of BC-N-oxide with $\mathrm{MeOOC{-}C{\equiv}C{-}COOMe}$ is described (152).

4. Ylides

It is not possible to discuss here all synthetic approaches to benzo[c]cinnolinium ylides, which have been published recently.

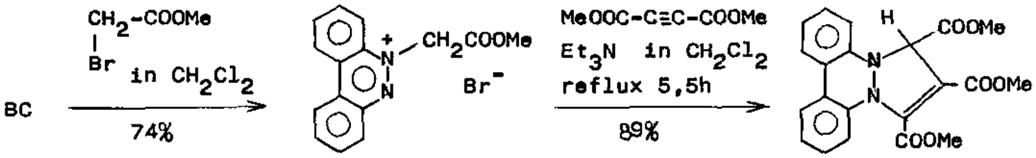
Ylide 35 was obtained by diazotisation of 2,2'-diaminodiphenyl (124,153), as well as from 36 by its reduction and subsequent oxidation, followed by treatment of the resulting product 37 with methanolic KOH in DMF (125). Ylide 35 can be easily ethoxycarbonylated (153), methylated (125) or benzoylated (124). The benzoyl derivative can be also obtained by hydrolysis of 37 (125). The hydrogenation of 37 affords BC in a high yield (125).



BC reacts with active methylene compounds such as $BrCH_2CO\phi$, $BrCH_2COOMe$, $BrCH_2COOEt$ to give the the benzo[c]cinnolinium bromides. These compounds subjected to dehydrobromination give ylides, which can be considered as extended dipoles. These upon treatment with various dipolarophiles (e.g. MeOOC-C≡C-COOMe, EtOOC-C≡C-COOEt, EtOOC-N=N-COOEt) undergo cycloaddition reactions.

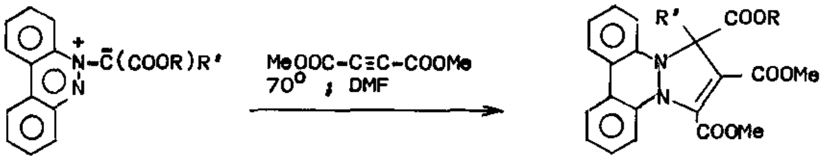
Cycloadditions involving extended dipolar systems offer the possibility of a simple route to medium ring heterocycles; the periselectivity observed in such processes being of practical as well as of theoretical interest (154). The syntheses of some ylides are described (124, 125, 153, 155).

An example of ylide formation and its 1,3-cycloaddition is the reaction (156):

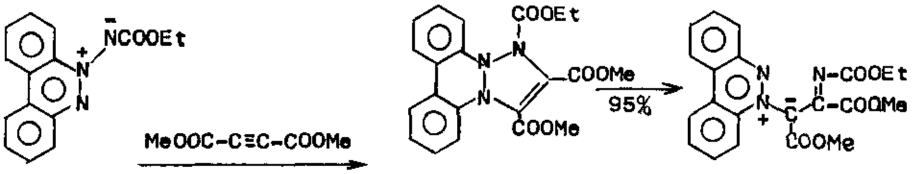


Similar reactions were reported (157).

Other reactions of ylides are given by Gait et al. (158):



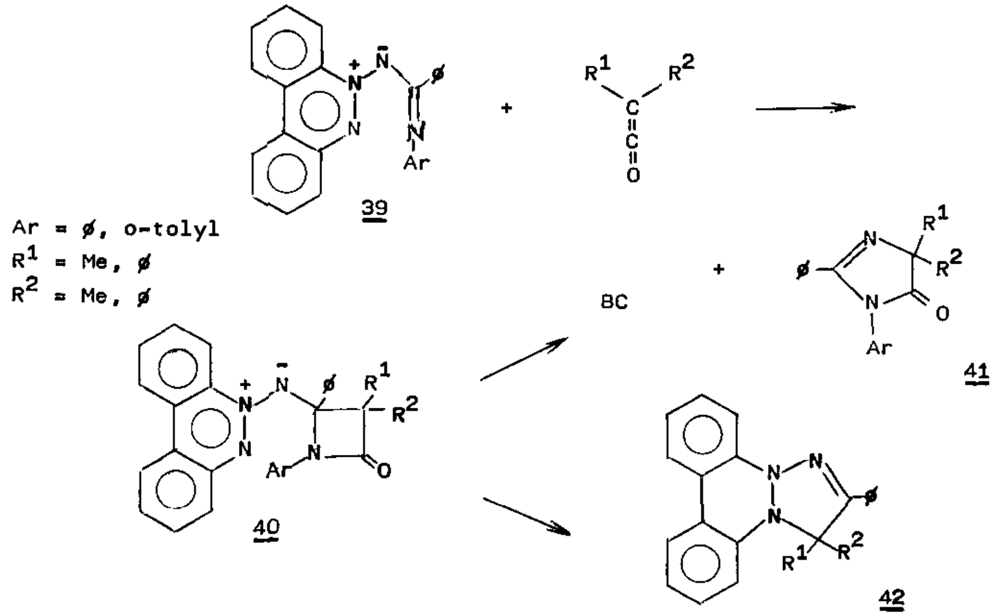
and by Challand et al. (159). In this case the first step gives rise to the triazole derivative, which undergoes a spontaneous electrocyclic ring opening to afford the azomethineimine <u>38</u>:



<u>38</u>

Similar reaction was carried out by Gait et al. (160).

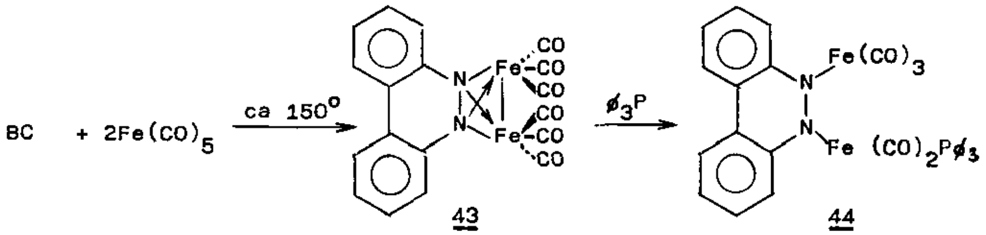
The iminoazimine ylides 39 give with ketones as dipolarophiles 2+2 cycloadducts, i.e. β-lactams 40, which on heating yield (depending on the ketene substituents) BC and 1,2,4,4-tetrasubstituted imidazole-5-ones 41, or triazoles 42 (154).



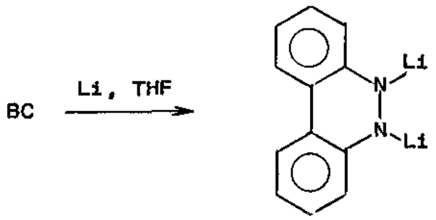
Ylides 39 undergo also a 1,5-dipolar cyclization, followed by retro-1,3-dipolar cycloaddition (161). Examples of ther cycloadditions are reported (162).

5. Metal complexes of BC

There are known numerous metal complexes of BC, e.g. with Fe, Co, Ni, Cu, Cd (163) and with Ag, Pd and Au (164). Kooti and Nixon (165) obtained pentacarbonyl-Cr, Mo and W complexes of a general formula: metal$(CO)_5$-BC. A large amount of papers is dealing with complexes of BC with $Fe(CO)_5$ (166). The complex 43 upon treatment with triphenylphosphine yields 44.



BC undergoes the reaction with $Fe_2(CO)_9$ to give complexes of a formula $Fe_2(CO)_7$-BC (167). BC forms also the adducts with Li and Na (168), e.g.:



c) Properties

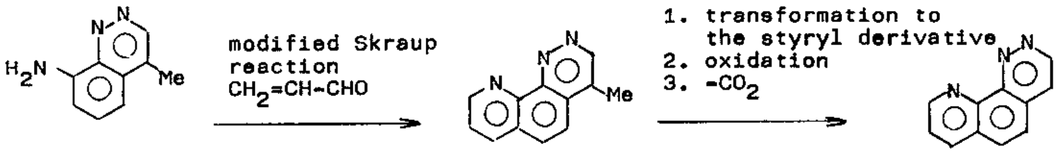
The data concerning the crystalline structure of BC and its di-N-oxide are reported in (169). The dipole moment measurements of BC and its N-oxide are described (170). The calculation of the electronic structure of BC showed the highest electron density in 1,10 and 2,9, and the lowest one - in 4,7 positions (171,172). There were reported the ionization constants of BC (114) and its prototropic equilibrium constants (173). Radiationless processes of BC (174) and polarographic reduction of BC and of its N-oxides (175) have been described. UV spectrum of BC consists of four absorption bands; as compared with phenanthrene it shows the bathochromic shift of p and α bands, and the increase of the α band intensity (98, 106, 176). UV spectra of substituted (Me, Br, Cl, NH_2, NO_2) BC and their N-oxide have been investigated (98,106, 143). UV spectrum of 5,6-dihydro-BC (137) and electronic spectra of radical anion of BC and its ESR spectra (135) have been described.
There were studied fluorescence spectra of BC (177) and its ^{1}H NMR spectra (178). IR spectrum of BC-di-N-oxide (179) and mass spectra of substituted BC (180) have been reported.
Biological activities of BC derivatives include anticancerogenic (123,139,181), and fungicidal action (96). BC or its mono- or di-N-oxides, as well as their derivatives, e.g. 3,8-bis-trifluoromethylated are stabilizers for dielectrics (182). BC, owing to its redox properties can be used as a starting material for H_2O_2 production (139). Some BC derivatives can be applied as dyes (122,172). Certain metal complexes of BC are used as gasoline combustion catalysts or as polymerization initiators of styrene (166).

4. TRIAZAPHENANTHRENES

a) Syntheses

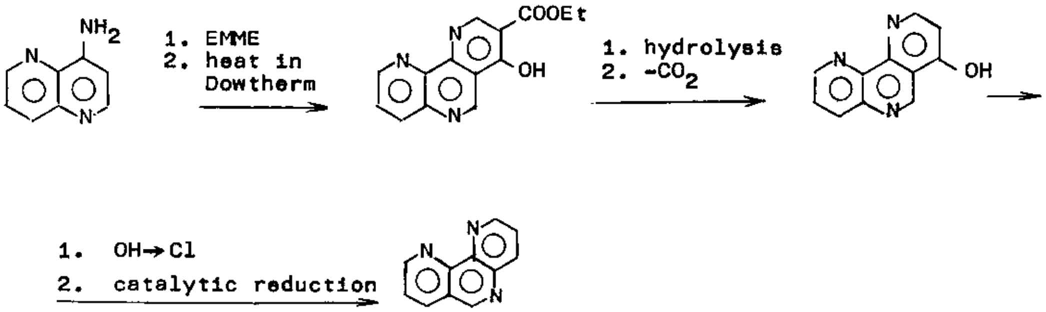
In order to obtain chelating agents there was carried out the synthesis of triazaphenanthrenes (TAP) with two N atoms in 1 and 10 positions, and the third N atom in 2,3,4 or 5 position.

The synthesis of 1,2,10-TAP was accomplished in the following manner: 8-amino-4-methyl-cinnoline was converted to 4-methyl-1,2,10-TAP by a modified Skraup reaction involving acrolein. The methyl group then was removed by conversion to the styryl derivative, oxidation to the acid and decarboxylation (183):

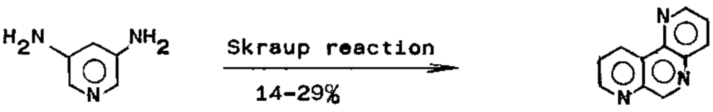


In a similar way the amino derivatives of quinazoline and quinoxaline were converted into 1,3,10- and 1,4,10-TAP (183).

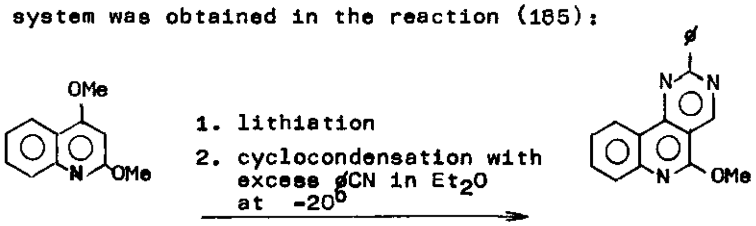
For the synthesis of 1,5,10-TAP, the reaction of 4-amino-1,5-naphthyridine with ethyl ethoxymethylenemalonate (EMME) has been applied. The Skraup reaction on this compound did not take place (183).



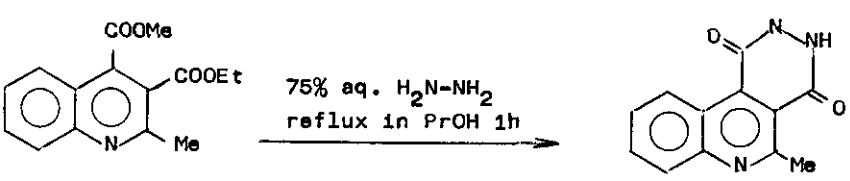
The Skraup reaction of 3,5-diaminopyridine, resulting in 1,5,7-TAP, was accomplished by Czuba (184):



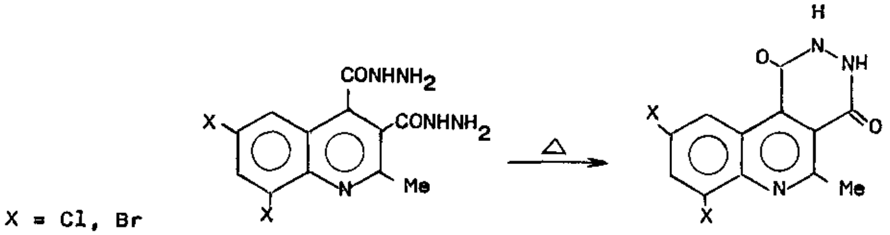
The 1,3,6-TAP system was obtained in the reaction (185):



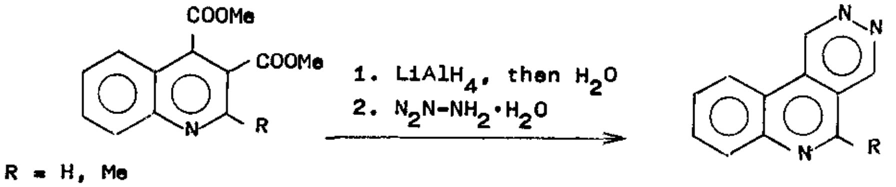
and the 2,3,6-TAP system - in the reaction (186):



The substituted 5-methyl-2,3-dihydro-2,3,6-TAP-1,4-diones were synthesized on heating dihydrazide of the substituted 2-methyl-quinoline-3,4-dicarboxylic acid (187):

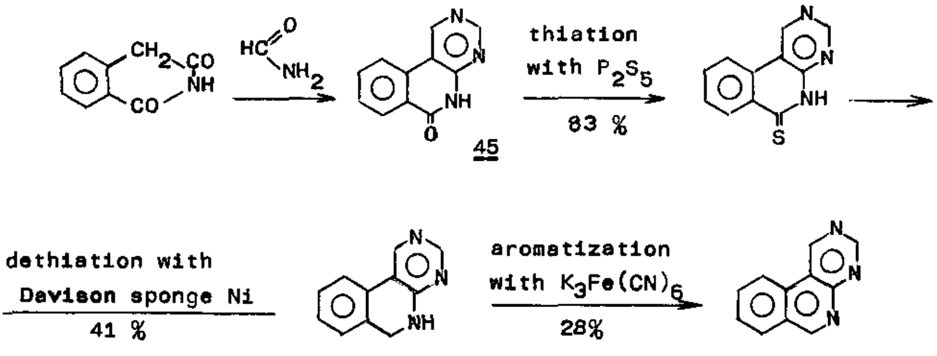


In order to obtain 2,3,6-TAP Godard et al. (188) carried out the following reaction:

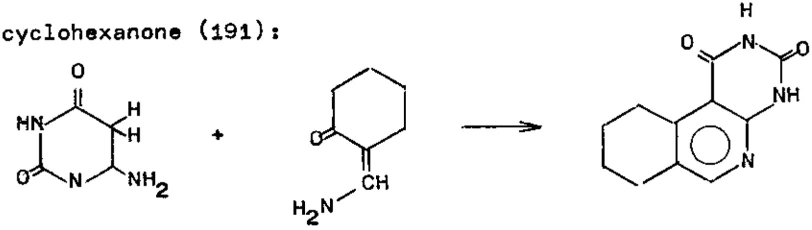


An extensive literature is concerning the synthesis of 5-aza-analogues of 2,4--DAP as potential antitumor agents and antifolates.

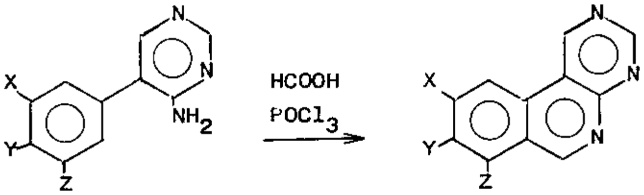
The 2,4,5-TAP system can be easily obtained in the reaction of homophthalimide with formamide, resulting in 45 (189), this compound is subjected to the thiation, followed by dethiation and aromatization (190):



2,4,5-TAP system can be also synthesized by reacting 4-aminouracil with 2-aminomethylenecyclohexanone (191):



Koyama et al. (192) obtained 2,4,5-TAP and its derivatives on heating 4-amino-5-arylpyrimidines with excess HCOOH and $POCl_3$:

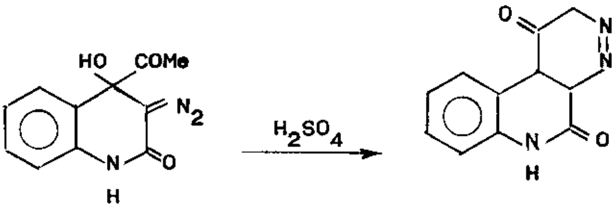


e.g.
X = Me, Y = Z = H
X = Z = OMe, Y = H

In another method of synthesis of disubstituted 2,4,5-TAP, the amino group of 4-amino-5-arylpyrimidine was acetylated and the resulting acyl derivative subjected to Bischler-Napieralski cyclization with PPA (193).

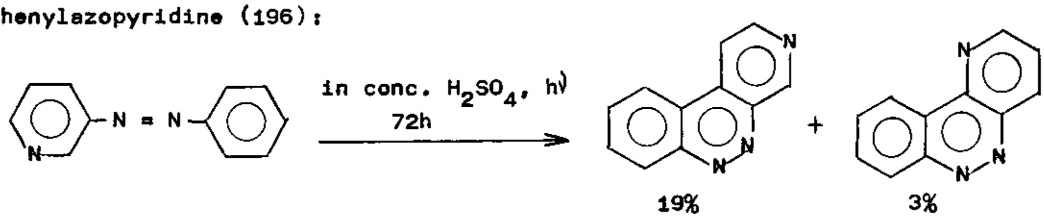
Lalezari and Sadeghi-Milani (194), starting with quinoline-3,4-dicarboxylic acids synthesized 2,4,6-TAP system and incorporated it into a steroidal structure. Obtained polyazasteroids are potential pharmacological agents.

To synthesize the 3,4,6-TAP system, there was performed an acid catalyzed decomposition of 46 ; here an interesting ring closure took place (195).

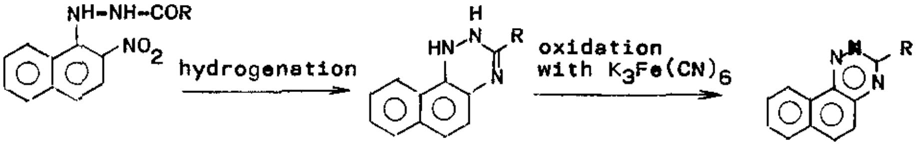


46

Isomeric 3,5,6- and 1,5,6-TAP were obtained by photochemical cyclization of 3-phenylazopyridine (196):



Berényi et al. (197) accomplished the hydrogenation of 47, followed by aromatization of 3-substituted 1,2-dihydro-1,2,4-TAP, resulting in 3-substituted 1,2,4-TAP:



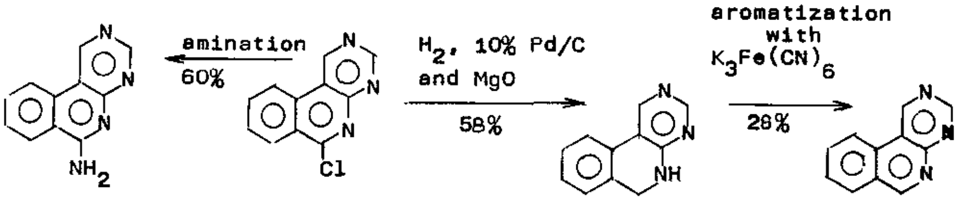
47

b) Reactivity

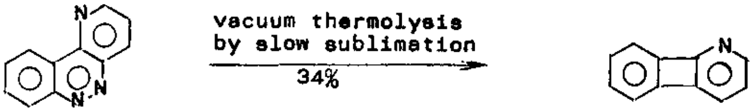
The derivatives of 1,2,10-TAP have been shown to have certain advantages over 1,10-phenanthroline as chelating agents, this fact being due to the third N atom in the 2 position (198).

1,5,7-TAP was oxidized with chromic acid to 1,5,7-TAP-6-[5H]-one (184). 4-Methyl-2,3-dihydro-2,3,6-TAP-1,4-dione upon treatment with halogenophosphides or diazomethane gives dihalogeno- or dimethoxyderivatives (186).

Amination and hydrogenation of 6-chloro-2,4,5-TAP proceeds as follows (190):



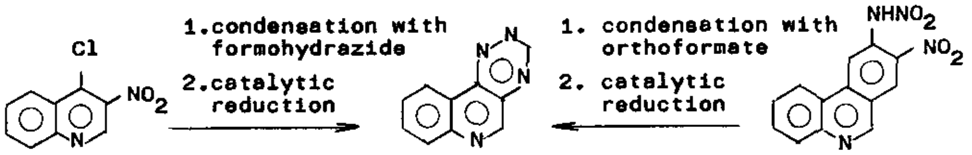
Barton and Walker (196) investigated vacuum thermolysis of 1,5,6- and 3,5,6-TAP, resulting in azabisphenylenes.



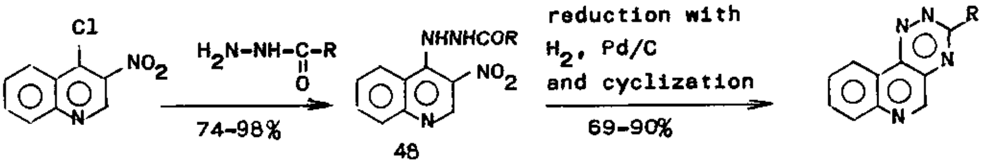
5. TETRAAZAPHENANTHRENES

a) Syntheses

1,2,4,6-tetraazaphenanthrene (FAP) was obtained by two routes (199):

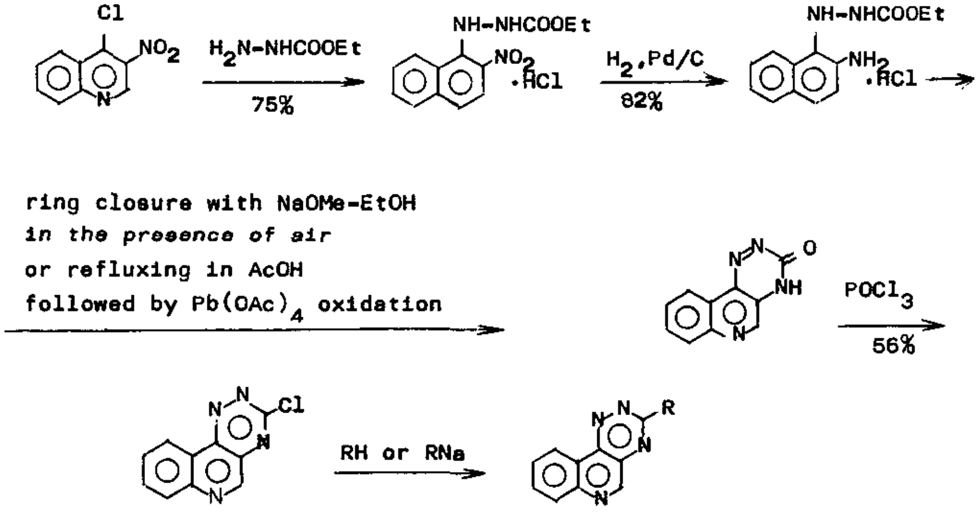


Berényi et al. (200) synthesized 3-substituted 1,2,4,6-FAP by reacting 3-nitro-4-chloroquinolines with acid hydrazides, and subjecting resulting 48 to reduction, followed by cyclization:



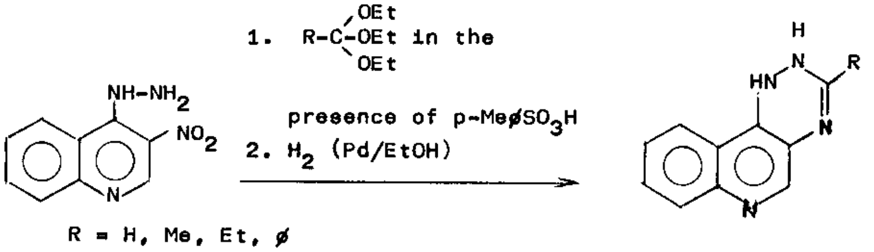
R = alkyl, ø etc.

Similar compounds, substituted in the 3 position by Cl, NH_2, OMe and other groups were synthesized upon treatment of 3-nitro-4-chloroquinoline with $H_2N-NH-COOEt$; the subsequent reduction and cyclization led to the 1,2,4,6-FAP system (201):

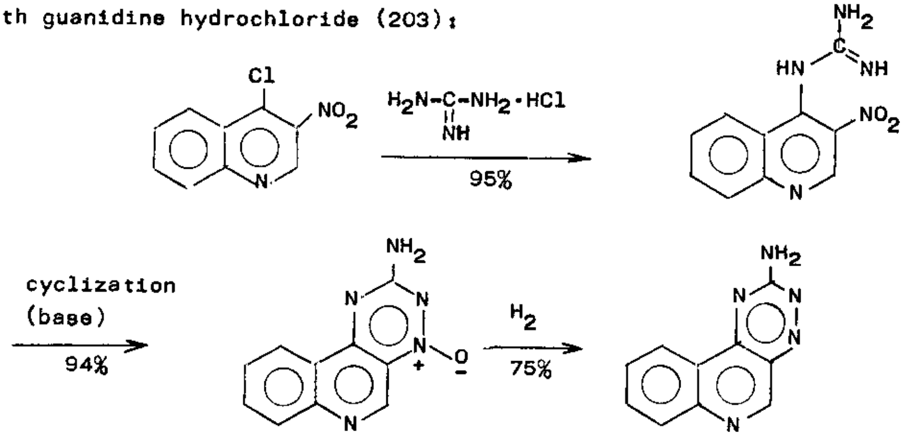


R = Cl, NH_2, OMe

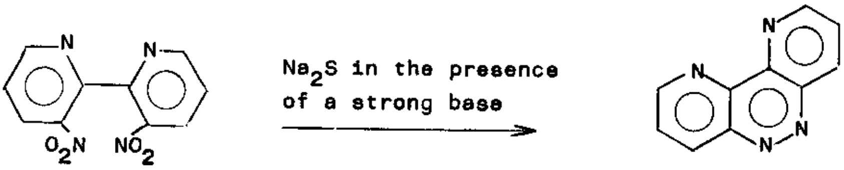
3-Nitro-4-hydrazinoquinoline reacts with orthoesters to give 3-alkyl-1,2-dihydro-1,2,4,6-FAP (202):



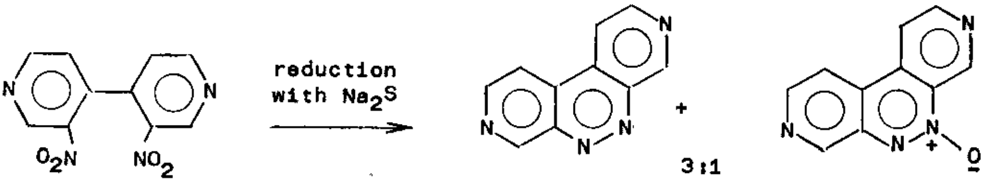
The 1,3,4,6-FAP system was obtained in the reaction of 3-nitro-4-chloroquinoline with guanidine hydrochloride (203);



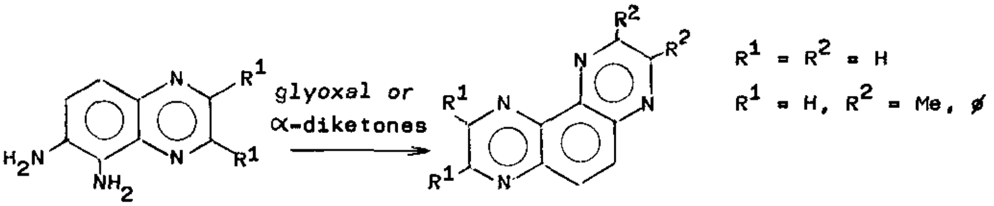
Reduction of 3,3'-dinitro-2,2'-dipyridyl yields 1,5,6,10-FAP (204)



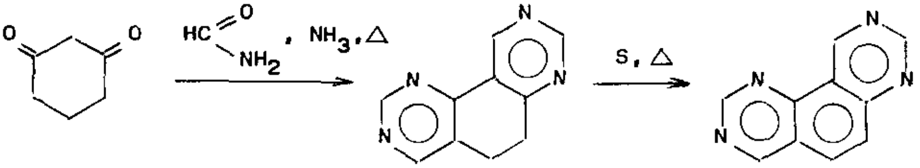
and reduction of 3,3'-dinitro-4,4'-dipyridyl affords a mixture of 3,5,6,8-FAP and its 5-N-oxide; this can be deoxygenated with Fe (205).



Condensation of substituted 5,6-diaminoquinoxaline with α-dicarbonyl compounds afforded 1,4,7,10-FAP and its derivatives (183, 206);

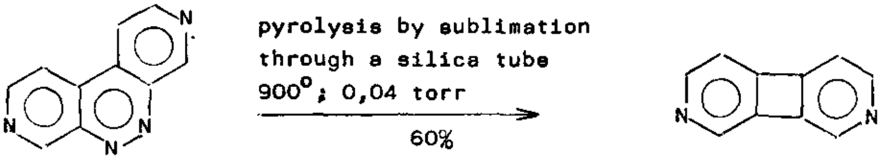


Koyama et al. (207) condensed cyclohexane-1,3-dione with formamide and dehydrogenated the resulting dihydrocompound to obtain 2,4,8,10-FAP:



b) Reactivity

Thermal extrusion of N atom from aromatic systems has recently proved to be a useful synthetic route to diazabiphenylenes (205):



c) Properties

There were investigated ^1H NMR spectra of 1,4,7,10-FAP and their derivatives (206), as well as ^1H NMR and IR spectra of 2,4,8,10-FAP (207).

1,2,4,6-FAP and its 3-substituted derivatives have antiinflammatory, antimicrobial (199,200) and antifungal activities (201). 1,2-Dihydro-1,2,4,6-FAP or 3-substituted 1,2-dihydro-1,2,4,6-FAP (free or in the form of salts) possess antimicrobial properties (200,202). 1,5,6,10-FAP has an antiinflammatory activity (204).

REFERENCES

1. J.Młochowski and W.Śliwa, *Wiad.Chem.*, 1972, **26**, 603
2. W.Śliwa and J.Młochowski, *Wiad.Chem.*, 1972, **26**, 823
3. J.Młochowski, W.Śliwa and L.Achremowicz, *Roczn.Chem.*, 1974, **48**, 787
4. Y.Hamada and I.Takeuchi, *Chem.Pharm.Bull.*, 1971, **19**, 1857
5. Y.Hamada, I.Takeuchi and H.Hirota, *Chem.Pharm.Bull.*, 1974, **22**, 485
6. Y.Kobayashi, I.Kumadaki and K.Morinaga, *Chem.Pharm.Bull.*, 1969, **17**, 1511
7. M.Jastrzębska-Glapa and J.Młochowski, *Roczn.Chem.*, 1976, **50**, 987.
8. M.Jastrzębska-Glapa, J.Młochowski and W.Śliwa, *J.Prakt.Chem.*, 1977,**319**, 883
9. H.H.Perkampus and G.Kassebeer, *Ann.*, 1966, **696**, 1
10. H.H.Perkampus and B.Behjati, *J.Het.Chem.*, 1974, **11**, 511
11. I.Ninomiya, T.Kiguchi, S.Yamaguchi and T.Naito, *C.J.S.Perkin I*,1976, 1861
12. I.Ninomiya, Japan Kokai 1974, 7.461.198, 7.461.199, *Chem.Abstr.*, 1975, **82**, 43389g,75665t
13. K.Itoh and Y.Kanaoka, *Chem.Pharm.Bull.*, 1974, **22**, 1431
14. S.V.Kessar, M.Singh, P.Jit, G.Singh and A.K.Lumb, *Tetr.Lett.*, 1971, 471
15. S.V.Kessar and G.S.Joshi, *Tetr.*, 1973, **29**, 419
16. M.A.Akhtar and J.A.D.Jeffreys, *Tetr.Lett.*, 1970, 3329
17. S.V.Kessar, V.P.Gupta, P.S.Pahva and P.Singh, *Tetr.Lett.*, 1976, 3207
18. A.Godard, D.Brunet, G.Queguiner and P.Pastour, *C.R.Acad.Sc.Paris,* 1977, **284C**, 459
19. Sterling Drug Inc., Brit. 1969, 1147,760, *Chem.Abstr.*, 1969, **71**, 49967a
20. M.Pesson, P.de Lajudie, M.Antoine, Ph.Girard and M^{me} S. Chabassier, *C.R.Acad.Sc.Paris,* 1975, **280C**, 1385; M.Pesson, Fr.Demande, 1975, 2.258.855, *Chem.Abstr.*, 1976, **84**, 121 801e
21. F.Michajliszyn, E.M.Braude and A.F.Bekhli, *Chim.Gieterocykl.Soedin.*, 1975, **12**, 1660
22. H.Ott and R.Suess, Ger.Offen. 1975, 2.503.156, *Chem.Abstr.*, 1976, **83**, 193279t
23. H.C.Longuet-Higgins and C.A.Coulson, *J.Chem.Soc.*, 1949, 971; H.H.Perkampus, J.V.Knop, A.Knop and G.Kassebeer, *Z.Naturforsch.*, 1967, **22a**, 1419; B.Tinland, *Tetr.* 1969, **25**, 583.
24. J.Młochowski, *Prace Nauk.Inst.Ch.Org.i Fiz.Pol.Wrocł.*, Ser.Studia i Mat., Wrocław, Poland 1975, 9/6

25. J.Młochowski and Z.Skrowaczewska, Roczn.Chem., 1973, 47, 2255

26. J.Młochowski, Roczn.Chem., 1974, 48, 2145

27. W.Śliwa, Pol.J.Chem., 1978, 52, 271

28. J.Młochowski, Roczn.Chem., 1977, 51, 665

29. W.Śliwa and M.Jastrzębska-Glapa, Sixth Symp. on Chemistry of Het.Compounds, Brno 1978, p.152

30. K.Kloc, J.Młochowski and Z.Szulc, J.Prakt.Chem., 1977, 319, 959; J.Młochowski and Z.Szulc, Wiad.Chem., 1977, 31, 665; J.Młochowski, W.Śliwa, Z.Skrowaczewska and Z.Szulc, Sixth Intern.Congr. on Het.Chemistry, Tehran, Iran 1977, p.157; J.F.Eckhard and L.A.Summers, Aust.J.Chem., 1973, 26, 2727

31. J.Młochowski and K.Kloc, Roczn.Chem., 1973, 47, 727

32. W.Śliwa and J.Młochowski, Roczn.Chem., 1976, 50, 695

33. Y.Hamada and I.Takeuchi, Chem.Pharm.Bull., 1976, 24, 2769

34. K.Kloc and J.Młochowski, Roczn.Chem., 1975, 49, 1621

35. Y.Kobayashi, I.Kumadaki and H.Sato, J.Org.Chem., 1972, 37, 3588

36. M.Jastrzębska-Glapa, J.Młochowski and W.Śliwa, Pol.J.Chem., in press

37. M.Jastrzębska-Glapa, J.Młochowski and W.Śliwa, Meeting of Pol.Chem.Soc., Łódź, Poland 1978, A, 2/60

38. W.Śliwa and Z.Szulc, J.Prakt.Chem., 1977, 319, 362

39. W.Weissenfels, E.Lippmann and J.Punkt., Z.Chem., in press

40. A.Sucharda-Sobczyk, L.Sobczyk, J.Młochowski and A.Koll, Roczn.Chem., 1974, 48, 1265; H.H.Perkampus, P.Mueller and J.V.Knop, Z.Naturforsch., 1971, 26B, 83

41. A.Grabowska and B.Pakula, Proc.Int.Conf.Lumin., 1966, 1, 368 ; A.Grabowska, B.Pakula and J.Pančir, Photochem. Photobiol., 1969, 10, 415

42. H.Basara, Z.Ruziewicz and H.Zawadzka, J.Lumin., 1978, 17, 283

43. H.H.Perkampus and W.Rother, Spectrochim.Acta, 1974, 30A, 597; D.Smith, P.T.Taylor, J.Vause and W.S.Waring, Chem.Comm., 1978, 369

44. Th.Bluhm, A.Bluhm, B.Behjati and J.V.Knop, Ber.Buns.Phys.Chem., 1978, 82, 624

45. H.H.Perkampus, Z.Naturforsch., 1960, 22a, 1430; J.Kuthan and V.Škala, Z.Chem., 1966, 6, 422

46. M.Jastrzębska-Glapa and J.Młochowski, Meeting of Pol.Chem.Soc., Warszawa 1976, B/250

47. J.Młochowski and W.Śliwa, Roczn.Chem., 1974, 48, 1469

48. W.Śliwa, Prace Nauk.Inst.Ch.Org. i Fiz.Pol.Wrocł., Ser.Studia i Mat., Wrocław, Poland 1978, 13/8

49. A.Chodkowska and Z.R.Grabowski, Chem.Phys.Lett., 1974, 24,11 ; A.Chodkowska, Pr.Wydz.Mat.Fiz.Chem.Uniw., Ser.Fiz., Poznań, Poland 1975, 19, 165

50. N.S.Hush, A.S.Cheung and P.R.Hilton, J.Electr.Spectr.Relat.Phenom., 1975, 7, 385

51. H.Budzikiewicz, V.Kramer and H.H.Perkampus, Z.Naturforsch., 1970, 25B, 178 ; W.Paudler and T.Kress, J.Org.Chem., 1967, 32, 2616

52. S.Kato, J.Nakaya and E.Imoto, Rev.Polarogr., 1971, 17, 1

53. G.P.Bean, J.Chem.Soc.B, 1971, 2339; M.Berndt and W.Woźnicki, Acta Phys.Polon., 1973, 43A, 101

54. K.G.Gupta, S.V.Kessar and B.Singh, Microbiol., 1970, 19, 1017

55. M.Tuszkiewicz, E.Pleszczyńska, J.Młochowski and Z.Skrowaczewska, Med.Dośw.Mikrobiol., 1975, 27, 11

56. Ch.M.Hall, J.B.Wright, H.G.Johnson and A.J.Taylor, J.Med.Chem., 1977, 20, 1337

57. W.Rittersdorf, H.Rey, W.Guthlein and P.Rieckmann, Ger. 2.235.152, 1974, Chem.Abstr., 1974, 80, 142 769h

58. F.M.Plakogiannis, Pharm.Acta Helv., 1975, 50, 116

59. J.Młochowski and W.Śliwa, Roczn.Chem., 1971, 45,803

60. W.Oettmeier and R.Grewe, Z.Naturforsch., 1974, 29C, 545

61. L.P.Bush, H.Burton and J.A.Boiling, J.Agric.Food Chem., 1976, 24, 869

62. W.Jahn, Neunyn-Schmiedberg's Arch.Pharmacol., 1972, 272, 182

63. K.Hori, T.Hashimoto and M.Nozaki, J.Biochem.,Tokyo, 1973, 74, 375

64. W.D.Munslow and Th.J.Delia, J.Het.Chem., 1976, 13, 675

65. H.H.Perkampus and Th.Bluhm, Tetr., 1972, 28, 2099

66. C.E.Loader and C.J.Timmons, J.Chem.Soc.C , 1967, 1343

67. A.Rosovsky and E.J.Modest, J.Org.Chem., 1966,31, 2607

68. W.Dymek and D.Sybistowicz, Roczn.Chem., 1962, 36, 1639; 1963, 37, 547

69. R.Gompper, H.E.Noppel and H.Schaefer, Angew.Chem., 1963, 75, 918

70. A.Rosovsky, K.Chen, M.Nadel,N.Papathanasopoulos and E.J.Modest, J.Het.Chem., 1972, 9, 275

71. A.Rosovsky and E.Modest, J.Het.Chem., 1966, 3, 387

72. K.Sengupta, S.Chatterjee, H.K.Protopapa and E.J.Modest, J.Org.Chem., 1972, 37, 1323

73. T.Koyama, T.Hirota, F.Yagi, S.Ohmori and M.Yamato, Chem.Pharm.Bull., 1975, 23, 3151

74. E.C.Taylor and Y.Shvo, J.Org.Chem., 1968, 33, 1719

75. E.C.Taylor, A.McKillop, Y.Shvo and G.H.Hawks, Tetr., 1967, 23, 2081

76. V.F.Sedova, L.D.Dikanskaya and V.P.Mamaev, Izv.Sibirsk.Otdel.Akad.Nauk SSSR, Ser.Khim.Nauk, 1966, 98; Chem.Abstr., 1966, 65, 13 701e

77. V.P.Mamaev and V.F.Sedova, Biol.Act.Sojedin.Akad.Nauk SSR, 1965, 32; Chem. Abstr., 1968, 63, 18082a

78. W.Ziegenbein and W.Franke, Angew.Chem., 1959, 71, 628

79. W.Dymek and D.Sybistowicz, Monatsh.Chem., 1965, 96, 542; J.Goerdeler and D.Weber, Chem.Ber., 1968, 101, 3475

80. U.K.Pandit, F.A.van der Vlugt and A.C.van Dalen, Tetr.Lett., 1969, 42, 3693

81. G.Henseke and W.Lemke, Chem.Ber., 1958, 91, 101

82. E.Hayashi and H.Saito, Yakugaku Zasshi, 1966, 86, 687 ; Chem.Abstr., 1966, 65, 16 970c,e

83. E.C.Taylor and J.V.Berrier, Heterocycles, 1977, 6, 449

84. J.Kobe, A.Krbavcic, B.Stanownik and M.Tišler, Croat.Chem.Acta, 1969, 41, 245

85. A.Rosovsky, N.Papathanasopoulos , E.Modest, J.Het.Chem., 1972, 9, 1235,1449

86. V.P.Mamaev and V.F.Sedova, Chim.Gieterocykl.Sojed., 1965, 608, 787

87. J.Faust, J.Prakt.Chem., 1977, 319, 65

88. H.Bredereck, F.Effenberger and G.Simchen, Chem.Ber., 1965, 98, 1087

89. G.B.Bennett, J.Het.Chem., 1978, 15, 671

90. J.K.Landquist, J.Chem.Soc., 1953, 2816

91. F.Dörr, H.Gropper, Angew.Chem., 1962, 74, 354

92. D.Rehm, Z.Naturforsch., 1970, 25A, 1442

93. R.B.Brundrett, D.V.Roswell and E.H.White, J.Am.Chem.Soc., 1972, 94, 7536; E.H.White and R.B.Brundrett, Chemiluminescence Biol., Pap.Int.Conf. 1972, 231, Chem.Abstr., 1973, 79, 65361a

94. N.W.Kalenda and D.J.Beavers, Def.Publ.US Pat.Off. 794.405, 1969, Chem.Abstr., 1969, 71, 17524n, Fr.Demande 2.029.439, 1970, Chem.Abstr., 1971, 75, 28253g

95. R.F.Stamm, J.S.Brinen, E.H.Tennant and W.Halverson, US 3.968.051, 1976, Chem.Abstr., 1977, 86, 17557k

96. L.J.Weaver, US 3.012.909, 1959, Chem.Abstr., 1962, 56, 8726e

97. V.Kornblum and D.L.Kendall , J.Am.Chem.Soc., 1952, 74, 5782; A.Etienne, A.Le Berre and E.Louvet, Fr. 1.405.863,1965, Chem.Abstr., 1965, 63, 14 879d

98. J.F.Corbett and P.F.Holt, J.Chem.Soc., 1961, 5029

99. H.Stetter and M.Schwarz, Chem.Ber., 1957, 90, 1349; E.Kmiecik, J.Org.Chem. 1965, 30, 2014, US 3.417.088, 1968, Chem.Abstr., 1969, 70, 57 873m

100. R.E.Moore and A.Furst, J.Org.Chem., 1958, 23, 1504; P.M.G.Bavin, Can.J.Chem., 1958, 36, 238

101. J.Radell, L.Spialter and J.Hollander, J.Org.Chem., 1956, 21, 1051

102. V.Kalyanaraman and M.V.George, J.Org.Chem., 1973, 38, 507

103. J.F.Corbett and P.F.Holt, J.Chem.Soc., 1961, 3695

104. J.I.G.Cadogan and M.Cameron-Wood, Proc.Chem.Soc., 1962, 361; J.F.Corbett, Chem.Comm., 1968, 1257

105. G.M.Badger and W.F.H.Sasse, J.Chem.Soc.1957, 4

106. J.H.Corbett and P.F.Holt, A.N.Hughes and Mrs.M.Vickery,J.Chem.Soc., 1962, 1812

107. F.E.Kempter and R.N.Castle, J.Het.Chem., 1969, 6, 523

108. C.Angelini, Ann.Chim.Rome, 1957, 47, 879, C.W.Muth, N.Abraham, M.L.Linfield, R.B.Worting and A.E.Pacovsky, J.Org.Chem., 1960, 25, 736

109. J.W.Barton and J.F.Thomas, J.Chem.Soc., 1964, 1265

110. P.F.Holt, B.I.Hopson-Hill and C.J.McNae, J.Chem.Soc., 1961, 1404; F.Johnson, US 3.087.929, 1963, Chem.Abstr., 1963, 59, 11 530e; S.F.Gait, M.E.Peek, C.W.Rees and R.C.Storr. J.C.S.Perkin I, 1974, 1248

111. L.A.Neiman, V.I.Maimind and M.M.Shemyakin, Izv.Akad.Nauk SSSR, Ser.Khim., 1964, 7, 1357, Chem.Abstr., 1964, 61, 11 991c; J.S.Swenton, T.J.Ikelar and B.H.J.Williams, J.Am.Chem.Soc., 1970, 92, 3103; A.Yabe and K.Honda, Bull.Chem.Soc.Jap., 1976, 49, 2495

112. Y.Kobayashi, I.Kumadaki, Y.Hanzawa and M.Mimura, Chem.Pharm.Bull., 1975, 23, 636

113. J.Mayfield, J.Aust.Chem.Soc., 1966, 19, 1445

114. G.E.Lewis, J.Org.Chem. 1960, 25, 2193

115. M.Dewar and G.E.Lewis, J.Aust.Chem.Soc., 1963, 6, 16; C.P.R.Joshua and V.N.R.Pillai, Tetr.Lett., 1973, 3559

116. G.M.Badger, R.J.Drewer and G.E.Lewis, Aust.J.Chem., 1963, 16, 1042

117. G.E.Lewis, Tetr.Lett., 1960, 12

118. G.E.Lewis and R.J.Mayfield, Aust.J.Chem., 1966, 19, 1445

119. C.P.R.Joshua and V.N.R.Pillai, Tetr.Lett., 1972, 2493, Tetr. 1974, 30,3333

120. G.M.Badger, R.J.Drewer and G.E.Lewis, *Aust.J.Chem.*, 1964, **17**, 1036

121. D.Jerchel and H.Fischer, *Chem.Ber.*, 1955, **88** , 1595

122. E.Waldau and R.Pütter, *Angew.Chem.*, 1972, **84**, 822, Ger. Offen. 2.118.491, 1972, *Chem.Abstr.*, 1973, **78** , 43 501s

123. M.J.S.Dewar and W.H.Poesche, *J.Chem.Soc.*, 1963, 2201

124. F.S.Gait, C.W.Rees and R.C.Storr, *Chem.Comm.*, 1971, 1545

125. F.A.Neugebauer and F.Fischer, *Chem.Ber.*, 1973, **106**, 1589

126. H.Nagasawa, *Tetr.Lett.*, 1966, 2898

127. I.Suzuki, M.Nakadate, T.Nakashima and N.Nagasawa, *Tetr.Lett.*, 1966, (25), 2899

128. J.W.Barton and M.A.Cockett, *J.Chem.Soc.*, 1962, 2454

129. P.F.Holt and R.Oakland, *J.Chem.Soc. (C)* , 1966, 1306

130. N.F.Tyupalo, Y.A.Yakobi, A.A.Stepanyan, L.F.Budennaya and A.Z.Kozorezov, *Ukr.Chim.Zhurn.*, 1976, **42**, 394, *Chem.Abstr.*, 1976, **85**, 46 577b

131. A.E.Blood and C.R.Noller, *J.Org.Chem.*, 1957, **22**, 711; J.I.Cadogan, M.Cameron-Wood, R.K.Mackie and R.J.G.Searle, *J.Chem.Soc.*, 1965, 4831

132. R.Tanikaga, *Bull.Chem.Soc.Japan*, 1968 , **41**, 1664

133. H.Teuber and D.Cornelius, *Chem.Ber.*, 1965, **98**, 2111

134. H.Inoue and Y.Matsuka, *Chem.Lett.*, 1972, 713

135. J.Chaudhuri, S.Kume, J.Jagur-Grodziński and M.Szwarc, *J.Am.Chem.Soc.*, 1968 , **90**, 6421

136. S.G.Cohen and G.A.Davis, *J.Chem.Soc. (D)*, 1971, 675

137. H.Inoue and M.Matsumoto, *Nippon Kagaku Kaishi*, 1974, 203, *Chem.Abstr.*, 1974, **80**, 119 725p

138. H.Lund, *Acta Chem.Scand.*, 1967, **21**, 2525; A.Millefiori, *Acta Chem.Roma*, 1969, **15**, 68

139. A.Etienne and R.Piat, *Bull.Soc.Chim.France*, 1962, 292

140. G.Wittig and A.Schuhmacher, *Chem.Ber.*, 1955, **88** , 234

141. J.C.Arcos, M.Arcos and J.A.Miller, *J.Org.Chem.* 1956, **21**, 651

142. W.T.Smith Jr., P.R.Ruby, *J.Am.Chem.Soc.*, 1954, **76**, 5807

143. J.Corbett, P.F.Holt and Mrs.M.L.Vickery, *J.Chem.Soc.*, 1962, 4384, 4860; M.Ohta, Japan Kokai 75. 100.067, 1975; *Chem.Abstr.*, 1976, **84**, 44 108e

144. J.W.Barton and J.F.Thomas, *J.Chem.Soc.*, 1964, 1265

145. J.F.Corbett, *J.Chem.Soc. (C)* , 1967, 1638

146. J.A.H.MacBride, *Chem.Comm.*, 1972, 1219

147. G.E.Lewis, R.H.Prager and R.H.M.Ross, *Aust.J.Chem.*, 1975, **28** , 2459

148. G.Lewis and C.Rees, *J.Aust.Chem.Soc.*, 1968, **21**, 1097; 1970, **23**, 619

149. P.F.Holt, *J.Aust.Chem.Soc.*, 1960, **13**, 3216

150. A.N.Hughes and T.Monkoltananont, *Chem.and Ind.*, 1967, 662

151. P.J.Abbott, R.M.Acheson, M.W.Foxton, N.R.Raulins and G.E.Robinson, *J.C.S.Perkin I* , 1972, 2182

152. S.R.Challand, C.W.Rees and R.C.Storr, *Chem.Comm.*, 1973, 837

153. S.F.Gait, M.E.Peak, C.W.Rees and R.C.Storr, *J.C.S.Perkin I* , 1975, 19

154. J.J.Barr and R.C.Storr, *Chem.Comm.*, 1975, 788

155. W.Śliwa, *Wiad Chem.*,1971, **25**, 1, 201; M.Dorneanu, *An.Stiin.Uniw. "Al. J.Cuza"*, Iasi Sect., 1973, 1c, **19**, 223

156. D.G.Farnum, R.J.Alaimo and J.M.Dunston, *J.Org.Chem.*, 1967, **32**, 1130

157. E.Carp, M.Dorneanu and I.Zugravescu, *Rev.Roum.Chim.*, 1976, **21**, 1203; *Chem.Abstr.*, 1977, **86**, 16 626v; *An.Stiin.Uniw. "Al.J.Cuza"* Iasi Sect., 1c, 1974, **20**, 35

158. F.Gait, M.J.Rance, C.W.Rees and R.C.Storr, *Chem.Comm.*, 1972, 806

159. S.R.Challand, S.F.Gait, M.J.Rance, C.W.Rees and R.C.Storr, *J.C.S.Perkin I*, 1975, 26

160. S.F.Gait, M.J.Rance, C.W.Rees and R.C.Storr, *Chem.Comm.*, 1972, 688

161. J.J.Barr, R.C.Storr and J.A.Rinmer, *Chem.Comm.*, 1974, 657

162. E.Carp, M.Dorneanu and I.Zugravescu, *Rev.Roum.Chim.*, 1974, **19**, 1507; *Chem.Abstr.*, 1975, **82**, 72 912q; M.J.Rance, C.W.Rees, P.Spagnolo and R.C.Storr, *Chem.Comm.*, 1974, 658

163. J.R.Allan, G.A.Barnes and H.D.Brown, *J.Inorg.Nuclear Chem.*, 1971, **33**,3765

164. J.J.Porter, J.L.Murray and K.B.Takvorian, *J.Het.Chem.*, 1973, **10**, 43; H.Hüttel and A.Konietzny, *Chem.Ber.*, 1973, **106**, 2098

165. M.Kooti, J.F.Nixon, *J.Organomet.Chem.*, 1974, **76C**, 29

166. R.P.Bennett , US 3.830.807 , 1974; US, 3.869.453 , 1975; *Chem.Abstr.*, 1975, **82**, 43 602h; **83**, 59053m

167. M.Herberhold and K.Leonhard, *J.Organomet.Chem.*, 1974, **78** ,253

168. G.Wittig, M.A.Jesaitis and M.Glos, *Ann.*, 1952, **577**, 1

169. R.Hulme, *Chem.Ind.*, 1962, 42; H.van der Meer, *Acta Crystallogr.*, 1972, **B28** , 367

170. R.S.Armstrong and R.J.W. Le Fevre, *Aust.J.Chem.*, 1966, **19**, 29, D.N.Reilingh de Vries and R.P.H.Rettechnick,*J.Chem.Phys.*, 1971,**54**,2723

171. M.J.S.Dewar and P.Maitlis, J.Chem.Soc., 1957, 2521

172. J.Sühnel and J.Fabian, Z.Chem., 1974, 14, 275

173. R.E.Ballard and J.W.Edwards, Spectrochim.Acta, 1964, 20, 1275

174. M.A.El-Sayed, J.Chem.Phys., 1963, 38, 2834; H.Rau, Ber.Buns.Phys.Chem., 1968 , 72, 408; H.Dewey and S.G.Hadley, Chem.Phys.Lett., 1971, 12,57; C.T.Lin and J.A.Stikeleather, Chem.Phys.Lett., 1976, 38 , 561

175. T.R.Emerson and C.W.Rees, J.Chem.Soc., 1962,1923; S.Millefiori, Ann.Chim. Rome, 1969, 59, 15

176. G.M.Badger, R.S.Pearce and R.Pettit, J.Chem.Soc., 1951, 3199; G.M.Badger and I.S.Walker, J.Chem.Soc., 1956, 122; J.R.Honner, P.R.Nolt and B.K.Selinger, Aust.J.Chem., 1974,27, 1613

177. H.Baba and Ch.Mugiya, Bull.Chem.Soc.Jap., 1970, 43, 13; D.N.Reilingh de Vries, R.P.H.Rettschnick and G.J.Hoytink, J.Chem.Phys., 1971,54,2722; H.Rau and H.Biele, Ber.Buns.Phys.Chem. 1973,77,281; K.J.Mainusch, P.Pollmann and H.Stegemeyer, Z.Naturforsch., 1973, 28A, 1476; H.Basara and Z.Ruziewicz, J.Lumin., 1973,6,212

178. F.Dörr, G.Hohlneicher and S.Schneider, Ber.Buns., 1966,70, 803

179. W,Lüttke, Z.Elektrochem., 1957,61,976

180. J.H.Bowie, G.E.Lewis and J.A.Reiss, Aust.J.Chem., 1968 , 21,1233

181. F.E.King and T.J.King, J.Chem.Soc., 1945, 824; R.S.Braithwaite and P.F. Holt, J.Chem.Soc., 1959, 3025

182. S.D.Ross, J.Kuntz, US 2.734.035, 1956; Chem.Abstr., 1956, 50, 8945f

183. F.H.Case and J.A.Brennan, J.Am.Chem.Soc., 1959, 81,6297

184. W.Czuba, Roczn.Chem., 1967, 41, 289

185. A.C.Ranade, R.S.Mali, R.M.Gidwani and H.R.Deshpande, Chem.Ind., 1977, 310

186. D.Kreysing, G.Kempter and H.H.Stroh, Z.Chem., 1969,9,230

187. W.Ried and P.Weidemann, Chem.Ber.,1971, 104, 3341

188. A.Godard, G.Queguiner and P.Pastour, C.R.Acad.Sc.Paris, 1975,281C, 941

189. G.Bellomonte, G.Caronna and S.Palazzo, Gazz.Chim.Ital., 1966,96,1108

190. A.Rosovsky and N.Papathanasopoulos, J.Het.Chem., 1974, 11, 1081

191. H.Junek and I.Wrtilek, Monatsh.f.Chem., 1970, 101, 1130

192. T.Koyama, T.Hirota, Y.Shinoara, S.Fukuoka, M.Yamato and S.Ohmori, Chem.Pharm.Bull., 1975,23,494

193. T.Koyama, T.Hirota, M.Yamato and N.Ohta, *Yakugaku Zasshi*, 1973,**93**,330; *Chem.Abstr.*, 1973,**78** ,159 543m

194. I.Lalezari and S.Sadeghi-Milani,Sixth Intern,Congr.of Het.Chemistry, Tehran, Iran 1977, PI/B, 113

195. G.J.B.Cajipe, G.Landen, B.Semler and H.W.Moore, *J.Org.Chem.*, 1975, **40**, 3874

196. J.W.Barton and R.B.Walker, *Tetr.Lett.*, 1975,(8),569

197. Mrs.D.Berényi, P.Benkó and L.Pallos, *Magy.Kem.Foly*, 1976, **82**, 180; *Chem.Abstr.*, 1976, **85**, 78090d

198. S.Irving and R.Williams, *Analyst*, 1952,**77**, 813

199. G.Zólyomi and E.Berényi, *Chem.Ber.*, 1976,**109**,2338

200. E.Berényi, L.Pallos, L.Petocz, P.Benkó, P.Gorog, Z.Budai and E.Kiszelly, Ger.Offen. 2.322.486, 1973; *Chem.Abstr.*, 1974, **80**,27 304r; *Acta Chim. Acad.Sci.Hung.* 1976, **90**, 399; *Chem.Abstr.*, 1977,**86**, 139 998a

201. G.C.Wright, J.E.Gray and C.N.Yu, Ger.Offen. 2.216.241,1972; *Chem.Abstr.*, 1973, **78** , 16 238e; *J.Med.Chem.*,1974,**17**,244

202. E.Gy.T.Gyogyszervegyeszeti Gyar, Brit. 1.382.781, 1975; *Chem.Abstr.*, 1975, **83**, 43 386m

203. E.Berényi, P.Benkó and L.Pallos, *Acta Chim.Acad.Sci.Hung.*, 1976,**90**,395; *Chem.Abstr.*, 1977, **86**, 139 997z

204. A.Etienne and G.Izoret, Fr. 1.369.401, 1964; *Chem.Abstr.*, 1965,**62**,570g

205. J.A.H.MacBride, *Chem.Comm.*, 1974,359

206. R.Nasielski-Hinkens, M.Benedek-Vamos, Y.Hautain and J.Nasielski, *J.C.S. Perkin I*, 1975,1229; *Bull.Soc.Chim.Belg.*, 1976, **85**, 781

207. T.Koyama, S.Fukuoka, T.Hirota, J.Maeyama, S.Ohmori and M.Yamato, *Chem. Pharm.Bull.*, 1976,**24**,591

Received, 11st January, 1979