SYNTHESIS OF HETEROCYCLIC COMPOUNDS IN THE PRESENCE OF TRANSITION METAL COMPLEXES (REVIEW)

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The most recent data on reactions involving the formation of heterocycles that take place in the presence of palladium, nickel, cobalt, and iron complexes are examined. The mechanisms of the reactions are discussed in the light of modern concepts of catalysis by metal complexes. The particular significance of metal complex catalysts for the synthesis of heterocycles with unique structures is demonstrated.

The last decade is characterized by increasing interest in organic syntheses involving the participation of transition metal complexes and, in particular, in the synthesis of heterocyclic compounds. In the present review two types of reactions of this sort are discussed. The first type, which is based on intramolecular cyclization reactions, is widely used in the synthesis of furan, pyran, pyrrole, pyridine, indole, and benzo- and dibenzofuran derivatives, as well as some flavones and alkaloids. The second type includes reactions involving heterocyclization with the participation of two or more molecules activated as a result of complexing with transition metals. Reactions involving the oligomerization of 1,3-dienes in the presence of oxygen-, nitrogen-, sulfur-, and silicon-containing compounds that are catalyzed by palladium and nickel complexes should primarily be classified as reactions of this type. This method has been used to obtain derivatives of tetrahydropyran, piperidine, and a number of heterocycles containing eight to 14 atoms in the ring.

Reactions of the first type are carried out with palladium and nickel halides, acetates, or acetylacetonates as the reagents. Nickel and platinum complexes with electron-donor ligands such as phosphines and nitriles, which have the ability to stabilize the catalytically active complexes and participate in the reduction of the metals to low-valence states, are very often used. Complexes of zero-valent metals of the $Pd(PR_3)_4$, $Ni(PR_3)_4$, and $Co_2(CO)_8$ type are rarely employed. The low-valence complexes are quite often generated in the reaction medium by the action of strong reducing agents ($NaBH_4$ and AlR_3) on the metal salts.

The application of complexes of low-valence palladium, nickel, cobalt, and iron, which are most often prepared in situ by reduction of the metal salts by means of organoaluminum or organomagnesium compounds in the presence of ligand activators, has been described for reactions of the second type. Previously prepared complexes such as $Fe_2(CO)_9$ are utilized in a number of cases.

It should be emphasized that the formation of σ and π complexes as catalytically active intermediates in processes involving the linear and cyclic oligomerization of dienes has been proved experimentally. These results are widely used in the literature in the postulation of the mechanisms of reactions to form heterocycles.

The schemes presented in this review include the most probable pathways of the reactions and are based on the modern concepts of catalysis by metal complexes.

Synthesis of Heterocycles by Intramolecular Cyclization

Oxygen-Containing Heterocycles. Unsaturated alcohols and acids are readily cyclized under the influence of palladium complexes to give five- and six-membered heterocycles. For example, β,γ- and γ,δ-unsaturated acids are converted to unsaturated lactones in moderate yields in the presence of Li_2PdCl_4 [1]. The reaction proceeds through π and σ complexes of palladium, as is apparent from the scheme for the formation of β-angelica lactone (I) from 3-pentenoic acid,

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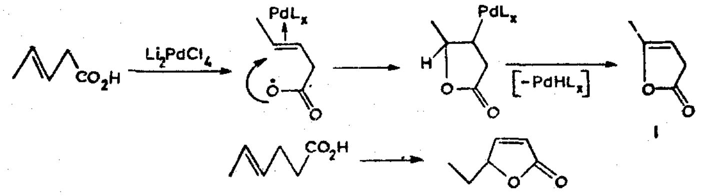
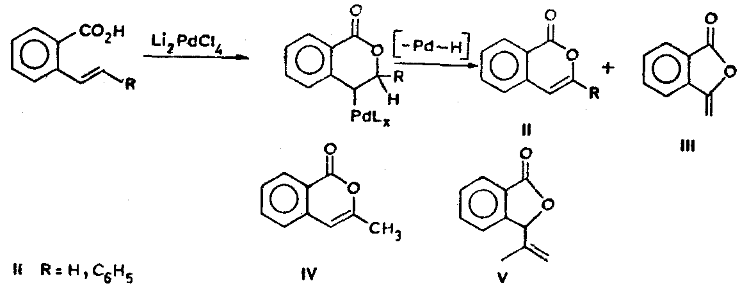


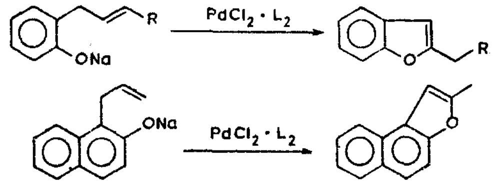
Isocoumarin II and phenylisocoumarin were synthesized in ~45% yields by dehydrocyclization of o-carboxystyrene and o-carboxystilbene by means of Li_2PdCl_4 [1]. The yields can be increased by using the $PdCl_2 \cdot 2CH_3CN$ complex as the catalyst. Of course, methylenephthalides III are formed along with isocoumarins in this case [2].

o-Allylbenzoic acids are converted to isocoumarins II and IV in 60-96% yields under the influence of $PdCl_2 \cdot 2CH_3CN$. o-Methallylbenzoic acid, which gives phthalide V, constitutes an exception to this.

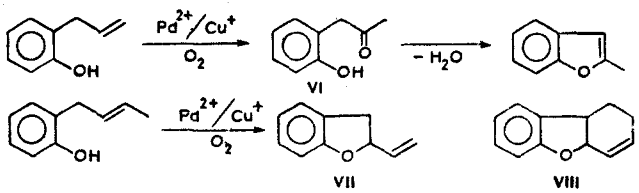


II R = H, C_6H_5 III IV V

Benzo- and naphthofuran derivatives were obtained in the presence of equimolar amounts of the $PdCl_2 \cdot 2C_6H_5CN$ complex. As in the case of synthesis of isocoumarins, base is added to the system to tie up the hydrogen chloride that is liberated. Although the yields do not exceed 50%, the reaction takes place under mild conditions (in benzene solution at room temperature) [3, 4]. A catalytic variant [4] constitutes a valuable improvement in this method.

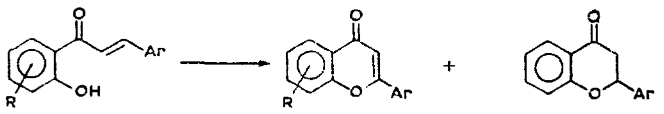


The oxidation of olefins with oxygen in the presence of a palladium—copper catalyst leads to aldehydes or ketones [5, 6]. The formation of benzofurans under these conditions probably proceeds through a step involving ketophenol VI. It is characteristic that o-(2-butenyl)phenol gives vinylcoumarin VII, while cyclohexenylphenol gives VIII [4].

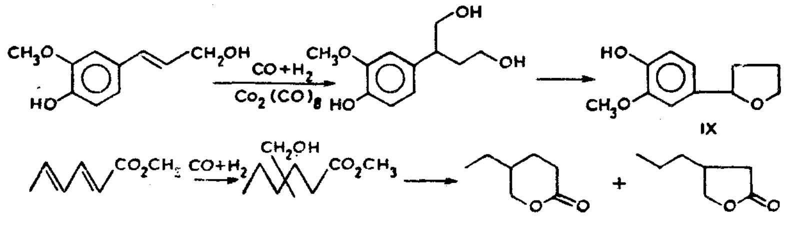


VI VII VIII

o-Hydroxychalcones are converted to mixtures of flavones and flavanones in high yields under the influence of $Pd(OAc)_2$ [7].



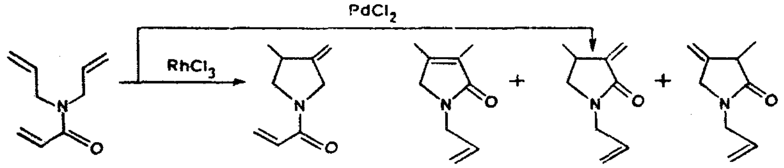
Tetrahydrofuran derivatives (for example, IX [8]) were obtained by hydroformylation of allyl alcohols in the presence of $Co_2(CO)_8$. Unsaturated acids are converted to lactones under the same conditions; thus X and XI were obtained from methyl sorbate [9]. Thus, this method is based on the cyclodehydration of the glycols or hydroxy acids that are formed during hydroformylation. Syntheses of this type with the use of carbon monoxide were described in [10-13] and will not be examined in this review.



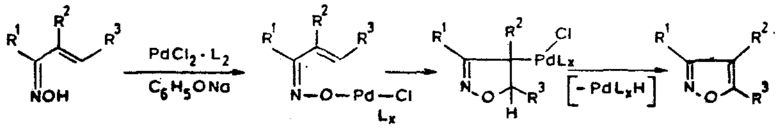
IX

X XI

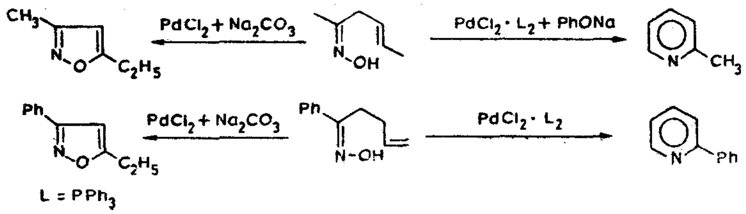
Nitrogen Heterocycles. Diallylacrylamide is cyclized under the influence of $PdCl_2$ to give a mixture of four substances with predominance of N-allylpyrrolidone derivatives [14, 15]. Rhodium chloride, on the other hand, gives an N-acryloylpyrrolidine derivative. It is not difficult to see that the reaction proceeds via a scheme involving dimerization of the olefins under the influence of palladium and rhodium compounds [16].



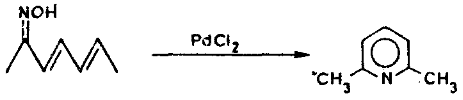
The dehydrocyclization of α,β-unsaturated ketoximes in the presence of palladium chloride, acetate, or acetylacetonate complexes with phosphines gives isoxazoles [17, 18].



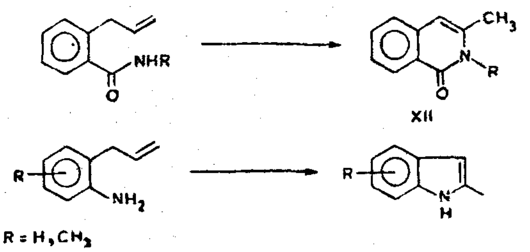
The result of cyclization of oximes of β,γ- and γ,δ-unsaturated ketones depends on the type of catalyst. Thus, pyridines of isoxazoles can be obtained from 2-oximino-4-hexene and phenyl 3-butenyl ketone oxime [18].



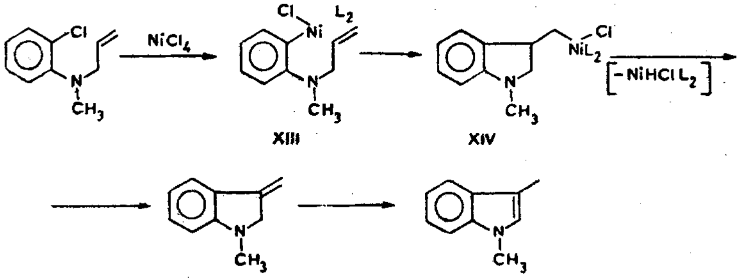
The mechanism of formation of pyridines is not at all clear. Hosokawa and co-workers [18], who assumed that the reaction includes a dehydrogenation step, accomplished the cyclization of 2-oximino-3,5-heptadiene and 2,6-lutidine.



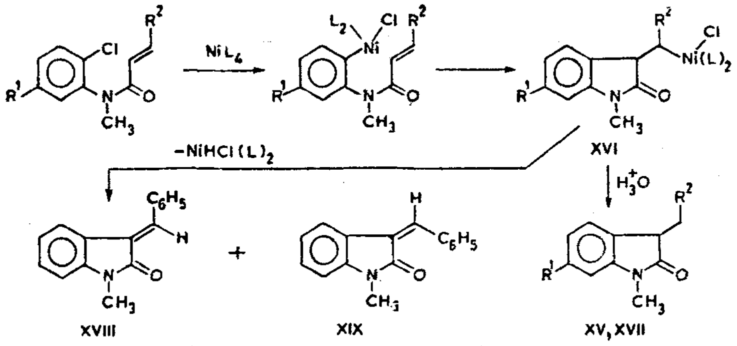
The dehydrocyclization of 2-allylbenzamides under the influence of the $PdCl_2—(CH_3CN)_2—NaH$ system is a convenient method for the synthesis of isoquinolone derivatives XII [2], while 2-allylanilines are converted to 2-methylindoles [19].



The application of nickel complexes opens up interesting possibilities. Thus 2-chloro-N-methyl-N-allylaniline is cyclized to 3-methylindole under the influence of a stoichiometric amount of $Ni[P(C_6H_5)_3]_4$ [20]. The complex is readily obtained by reduction of nickel acetylacetonate in the presence of 4 moles of triphenylphosphine by the action of $(C_2H_5)_2AlOC_2H_5$ [21] or $(C_2H_5)_3Al$. The formation of the indole proceeds through a step involving σ complex XIII. The next step is intramolecular carbometallation, which leads to XIV. The process concludes with splitting out of a hydride complex of nickel and migration of the double bond. According to [22], the yields of indoles increase if oxygen is fed into the reaction mixture; triphenylphosphine is converted to the oxide in this case. The cyclization of chloro-N-allyl-N-methylaniline also takes place under the influence of Grignard reagents in the presence of catalytic amounts of the $NiCl_2[P(C_6H_5)_3]_2$ complex [22]. The role of the Grignard reagent reduces to reduction of the nickel to the catalytically active low-valence form.



Primarily oxindoles (for example, XV [22]) are formed if 2-chloro-N-methylanilides of α,β-unsaturated acids are used for cyclization under the influence of $Ni[P(CH_6H_5)_3]_4$. It is apparent that the reaction stops at the intramolecular carbometallation step with the formation of stable (under the reaction conditions) σ complexes of nickel of the XVI type. Hydrolysis of the σ complexes gives reaction products XV. In a number of cases the reaction can be directed to favor splitting out of nickel hydrides. For example, cinnamic acid 2-chloro-N-methylanilide undergoes cyclization to give a mixture of saturated (XVII) and unsaturated (XVIII and XIX) compounds. The latter predominate when dimethylformamide (DMF) is used as the solvent. In toluene the yield of oxindole XVII is twice the yields of XVIII and XIX.

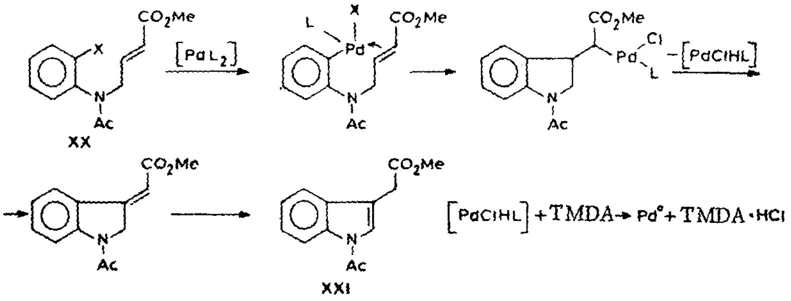


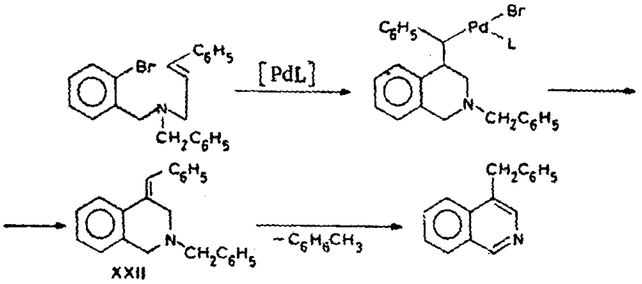
XV $R^1 = H, OCH_3$; $R^2 = CO_2CH_3, CN$; XVII $R^1 = H$, $R^2 = C_6H_5$

Acrylic acid 2-chloro-N-methylanilide undergoes less selective cyclization to give 1-methyl-2-quinolone along with the expected oxindole.

The use of phosphine complexes of palladium makes it possible to realize a catalytic variant of the indole cyclization. According to [23], 2-haloacetanilide derivatives of the XX type are converted to indoles XXI in 8-43% yields under the influence of the $Fd(OAc)_2$—

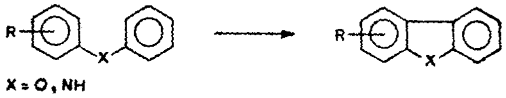
$P(C_6H_5)_3$ catalytic system in the presence of tetramethylethylenediamine (TMDA). 2-Bromo-N-benzyl-N-cinnamylbenzylamine is cyclized to 4-benzylisoquinoline in the presence of the same catalytic system. Benzylidene derivative XXII is simultaneously formed.



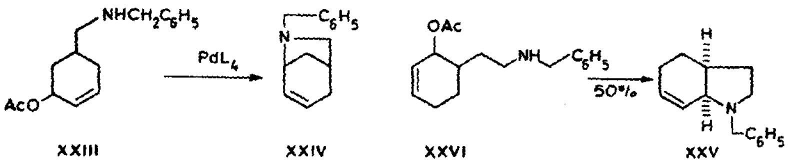


Palladium-containing catalysts have displayed high activity in the oxidative coupling of aromatic compounds. For example, palladium acetylacetonate in the presence of triphenyl phosphite converts diphenyl ether to dibenzofuran [24]. The reaction is carried out under pressure with a mixture of oxygen and nitrogen, and the amount of catalyst used is 3-5% of the amount of the substrate.

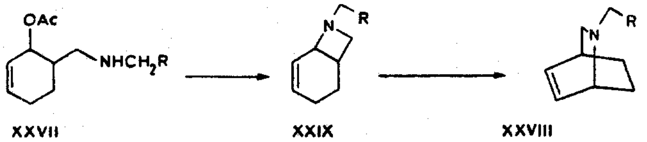
The stoichiometric coupling of diphenyl ether and diphenylamine derivatives proceeds extremely smoothly [25]. As a rule, the yields of monosubstituted dibenzofurans and carbazoles are no lower than 65%. Palladium acetate was used as the catalyst; the reaction is best carried out in acetic acid solution.

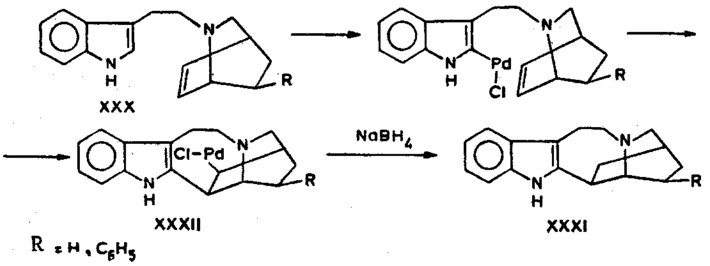


Cyclization catalyzed by palladium complexes has been successfully used in the synthesis of alkaloids and alkaloidlike structures [26, 27]. Thus amine XXIII is converted to 6-azabicyclo[3.2.1]-3-octene XXIV in 67% yield under the influence of catalytic amounts of $Pd[P(C_6H_5)_3]_4$ in the presence of triethylamine. Hexahydroindole XXV was synthesized by cyclization of amine XXVI under the influence of the same catalyst.



Amines of the XXVII type are very readily cyclized to quinuclidine derivatives XXVIII. The reaction proceeds through a step involving isomerization of the initially formed azetidine XXIX under the influence of a palladium catalyst. Quinuclidines XXX, which contain indole substituents, have been used for the synthesis of the alkaloid ibogamine XXXI and its de-ethylated derivative. The synthesis concludes with α-lithiation of the indole ring, treatment with mercuric chloride, and transmetallation of the organomercury compound by the action of the $PdCl_2(CH_3CN)_2$ complex and reduction of the σ complex of palladium (XXXII) with sodium borohydride. The alkaloids were obtained in 30-40% yields [26, 27].

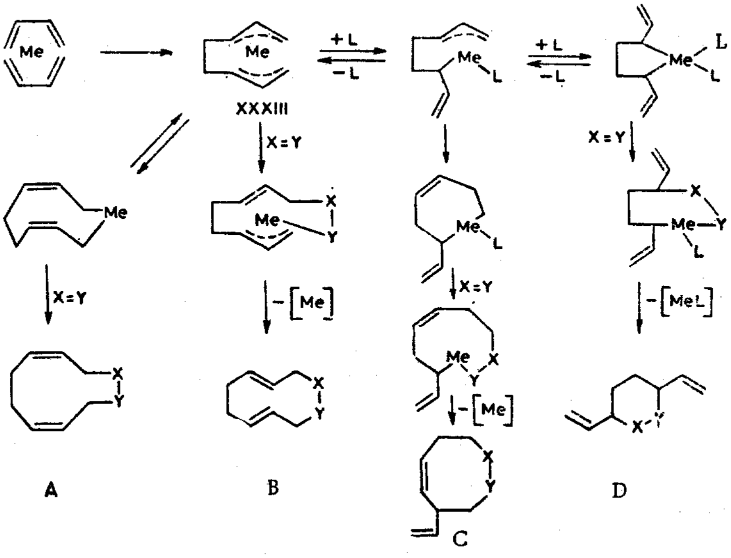


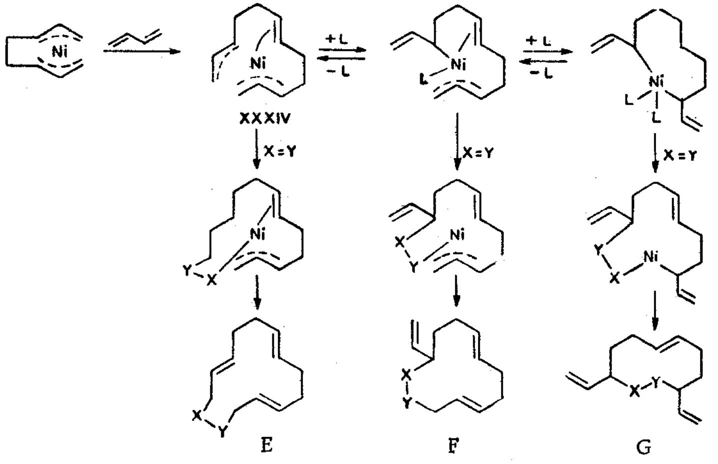


Syntheses of nitrogen heterocycles from primary and secondary amines or amides and carbon monoxide in the presence of metal carbonyls were described in earlier reviews [10-13] and will not be examined.

Synthesis of Heterocycles by Coupling of Several Activated Molecules

Cyclooligomerization Reactions of 1,3-Dienes. It is known [28-30] that reactive σ- and π-allyl complexes are formed by the action of various reducing agents on transition metal compounds in the presence of 1,3-dienes; for example, complexes that contain two fragments of diene XXXIII are most typical for palladium, while nickel may also give complexes XXXIV. Depending on the steric situation, which changes as a result of penetration of the coordination sphere of the metal by the ligands, the indicated complexes may be converted to the σ-isomeric

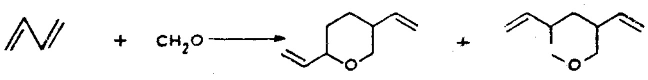




forms. The above-indicated possible schemes for the formation of heterocycles can be imagined if a molecule that has a reactive fragment with an X=Y bond (for example, aldehydes, ketones, imines, etc.) enters the coordination sphere.

We will subsequently show that, of the indicated pathways, Schemes C-E have been realized up until now.

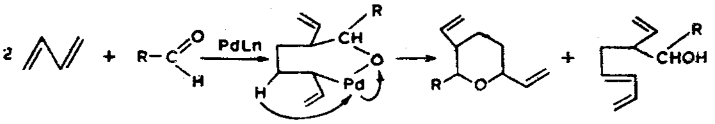
The possibility of the preparation of tetrahydropyran derivatives was demonstrated for the first time in [31]. Two compounds, to which structures XXXV and XXXVI were assigned, were obtained when butadiene was heated with aqueous formaldehyde in the presence of $Pd[P(C_6H_5)_3]_4$.



XXXV XXXVI

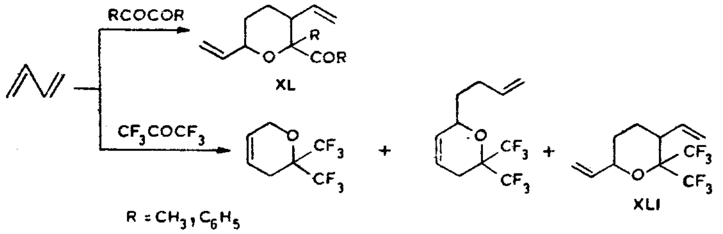
However, the formation of 3,5-disubstituted isomer XXXVI was not confirmed in any of the subsequent publications. For example, the preparation of only 2,5-divinyltetrahydropyran in the presence of the $Pd(acac)_2$–$P(C_6H_5)_3$ catalyst was reported [32, 33].

According to [34, 35], aliphatic and aromatic aldehydes, as well as some ketones, react with butadiene. Aldehydes are given mixtures of stereoisomers of 3,6-divinyltetrahydropyrans XXXVII and octatriene alcohols XXXVIII, which are formed as a result of hydride transfer in complex XXXIX. As a rule, the yields of the tetrahydropyrans are quite high.



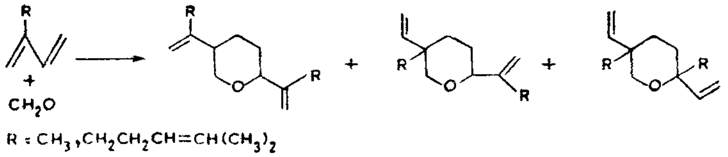
XXXIX XXXVII XXXVIII

Diacetyl and benzil give compounds of the XL type, whereas a mixture of products containing the desired product (XLI) in extremely low yield was obtained from hexafluoroacetone.

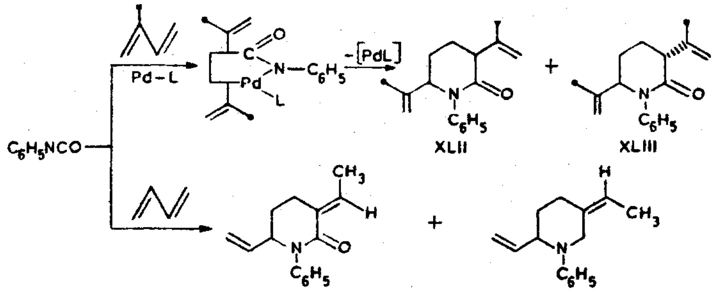


Isoprene and myrcene also react with formaldehyde to give complex mixtures of structural isomers and stereoisomers [33]. These products and their derivatives are patented as aromatic principles and selective solvents [36-38].

Piperidine derivatives were obtained by the reaction of 1,3-dienes with compounds that contain a C=N bond. Thus, phenyl isocyanate reacts with isoprene under the influence of a bis(triphenylphosphine)–maleic anhydride–palladium catalyst to give XLII and XLIII; XLIV and

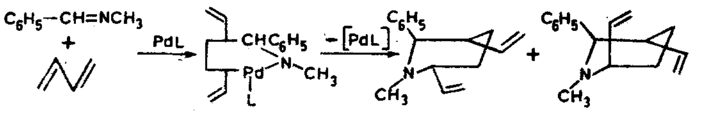


XLV were obtained from butadiene [39]. Benzylidene-methylamine and butadiene react in the presence of the $Pd(NO_3)_2$–$P(C_6H_5)_3$ system to give four stereoisomeric 1-methyl-2-phenyl-3,6-divinylpiperidines in up to 91% overall yield. The two thermodynamically most stable XLVI and XLVII isomers are obtained when the mixture is heated [40].



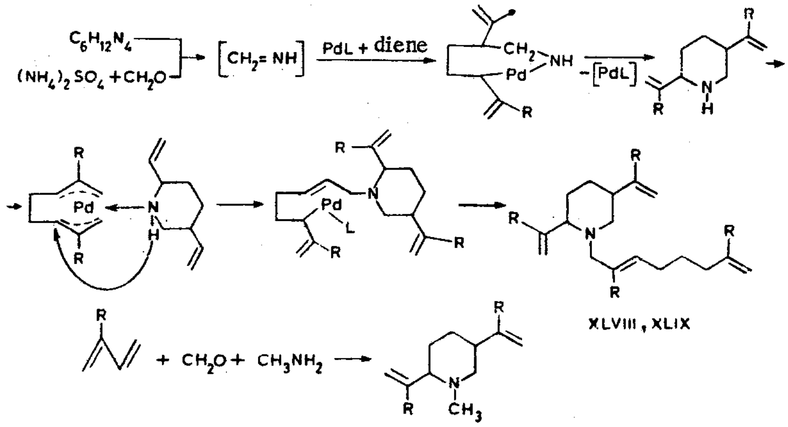
XLII XLIII

XLIV XLV



XLVI XLVII

Scheme D is the basis of the synthesis of 1,2,5-trisubstituted piperidines [41-43]. Butadiene reacts with an aqueous solution of urotropin, which is a source of methyleneimine, under the influence of the $Pd(acac)_2$—$P(C_6H_5)_3$—$Al(C_2H_5)_3$ catalytic system to give XLVIII. The reaction also takes place between butadiene and formalin in the presence of $(NH_4)_2SO_4$. It is characteristic that NH_4Cl directs the reaction to favor the formation of 2,5-divinyltetrahydropyran and tri(2,7-octadienyl)amine, whereas ammonium phosphates deactivate the catalyst.



XLVIII, XLIX

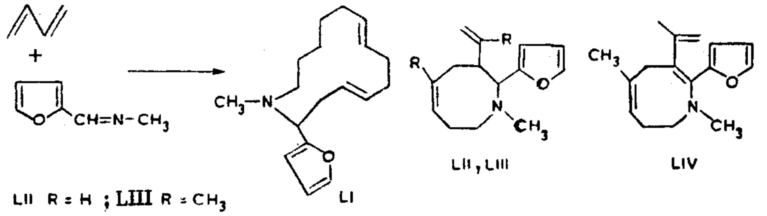
L

XLVIII R = H ; XLIX R = CH_3; L R = H,CH_3

Isoprene gives piperidine XLIX. The reaction cannot be stopped at the step involving the formation of 2,5-divinylpiperidine, since the latter reacts immediately with the bis(π-allyl) complex of palladium.

Piperidines L are formed if butadiene or isoprene are subjected to reaction with methylamine and formaline in aqueous solution.

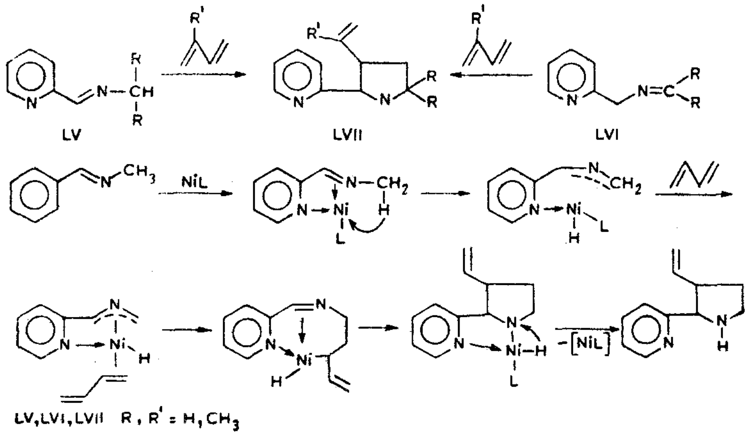
The structure of the aldimine and the type of catalyst have a very strong effect on the formation of the intermediate, and this ultimately affects the structures of the reaction products. Thus the possibility of the realization of Schemes C and E was demonstrated on passing to furfuralmethylamine. Butadiene reacts with the imine under the influence of the Ni(acac)—$Al(C_2H_5)_3$—$P(C_6H_5)_3$ catalytic system to give 2:1 and 3:1 adducts LI and LII, whereas two eight-membered heterorings (LIII and LIV) were obtained with isoprene [44].



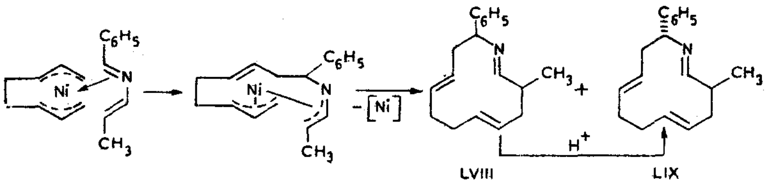
LII, LIII LIV LI

LII R = H ; LIII R = CH_3

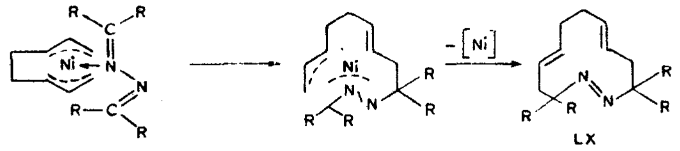
When imines of the pyridine series (LV and LVI) are subjected to reaction with dienes, [3 + 2] cycloaddition to give nornicotine derivatives LVII occurs in the presence of a nickel–phosphine catalyst. In the scheme presented below, one's attention is directed to the formation of complexes with 2-aza-π-allyl ligands [45].



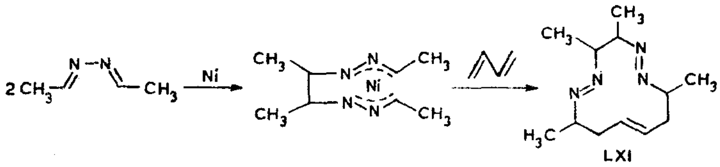
N-Alkenylaldimines behave like azabutadienes in that they react with two molecules of butadiene to give 1-aza-1,5,9-cyclododecatriene derivatives (for example, LVIII and LIX) [46]. Under the influence of acids cis isomer LVIII is isomerized to trans isomer LIV.



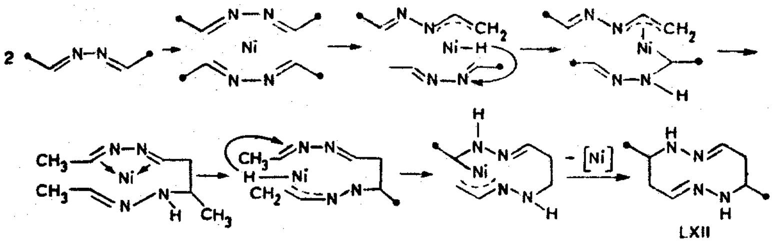
Butadiene reacts with various azines under the influence of the $Ni(acac)_2$–$(C_2H_5)_2AlOC_2H_5$–$P(C_6H_5)_3$ catalytic system via a similar scheme. The reaction products are 1,2-diaza-1,5,9-cyclododecatrienes LX [47]. The yields of these interesting compounds are remarkably high (up to 93%), and this indicates the high reactivities of azines [47].



A detailed study of the reaction of butadiene with acetaldazine made it possible to establish the formation of not only stereoisomeric 2 + 1 adducts of the LX type but also 1,2,5,6-tetraaza-1,5,9-cyclododecatriene LXI [48].

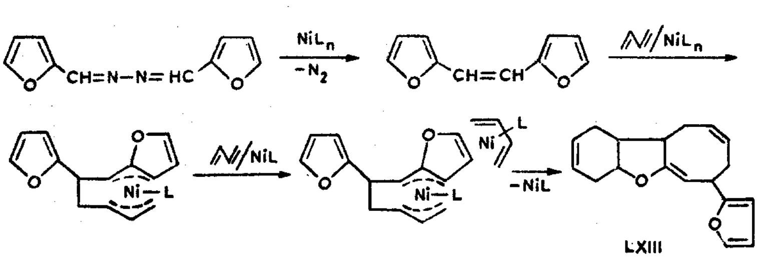


It is interesting to note that acetaldazine itself is dimerized on the $Ni(acac)_2$–$P(o\text{-}C_6H_5C_6H_4O)_3$–$(C_2H_5)_2AlOC_2H_5$ catalyst to give tetraazacyclodecadiene LXII, the mechanism of the formation of which is not discussed in [48]. One may assume the following scheme for cyclodimerization, which includes a step involving intermolecular hydride transfer.



LXII

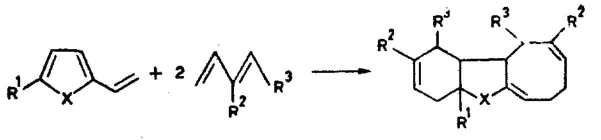
Furfuraldazine displayed an interesting feature: it decomposes with nitrogen evolution even under mild conditions under the influence of a nickel—phosphine catalyst. Butadiene subsequently adds to the resulting difurylethylene molecule to give LXIII.



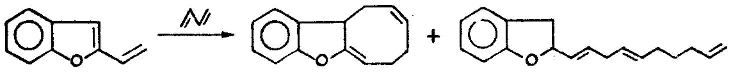
LXIII

This reaction pathway is not surprising, since it was recently shown that 2-vinylfuran and vinyl-α-methylfuran add two molecules of butadiene in the presence of a nickel—phosphine catalyst to give 10-oxatricyclo[9.4.0.$0^{2,9}$]-4,8,13-pentadecatrienes LXIV; isoprene, piperylene, and 3-methyl-1,3,6-heptatriene also undergo this reaction [49-52]. A linear copolymer (LXV) and only traces of a cyclic product (LXVI) were obtained from 2-vinylbenzofuran [49].

The same scheme was the basis of the synthesis of 10-thia- and 10-azatricyclo[9.4.0.$0^{2,9}$]-4,8,13-pentadecatrienes LXVII from 2-vinylthiophene and 1-methyl-2-vinylpyrrole [53, 54]. In experiments with d_6-butadiene it was established [51] that the indicated reactions take place without hydride transfer by coupling of the activated molecules.



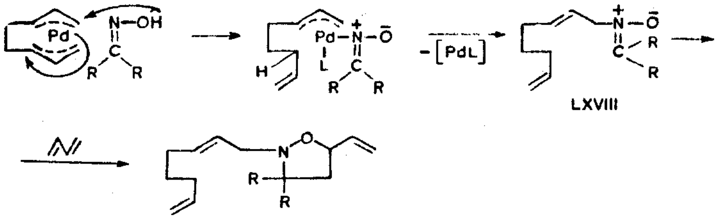
LXIV, LXVII



LXVI LXV

LXIV X = O; LXVII X = S, N—CH_3

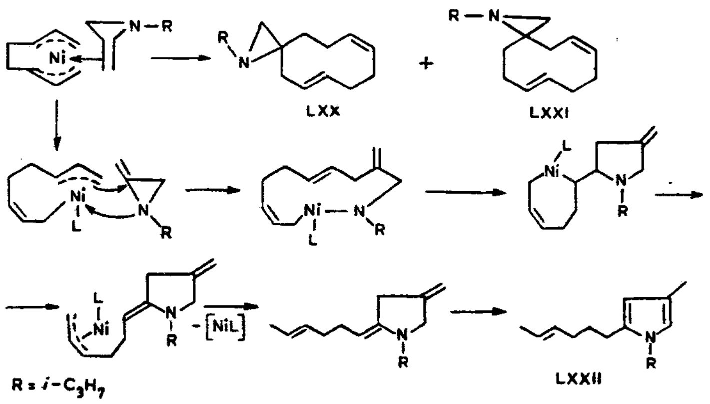
With respect to the problem of diazabutadienes it must be emphasized that glyoxal bis(N, N-dimethylhydrazone) does not form heterocycles [48]. Oximes react with butadiene in the presence of the $Pd(NO_3)_2$—$P(C_6H_5)_3$ system to give initially nitrones LXVIII, which subsequently add to the diene molecule to give isooxazolidines LXIX [55]. The reaction takes place with hydride transfer.



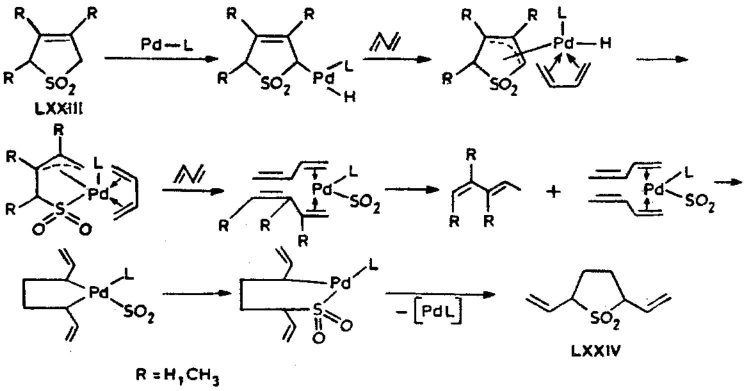
LXVIII

LXIX

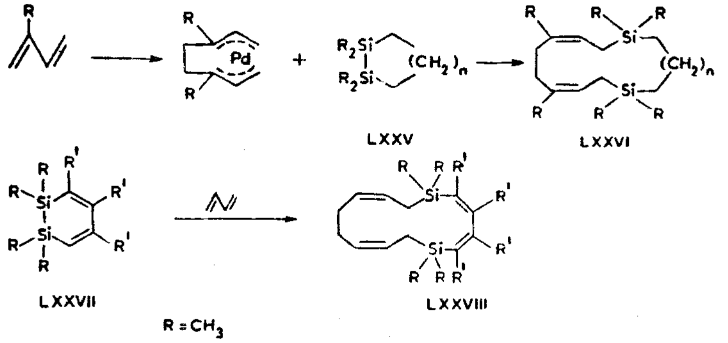
An original method for the synthesis of pyrrole derivatives involves the cyclooligomerization of butadiene. According to [56, 57], butadiene reacts with 1-isopropylmethyleneaziridine under the influence of nickel—phosphine catalysts to give, in addition to products of addition to the double bond (LXX and LXXI), pyrrole LXXII, the formation of which is explained by the scheme:



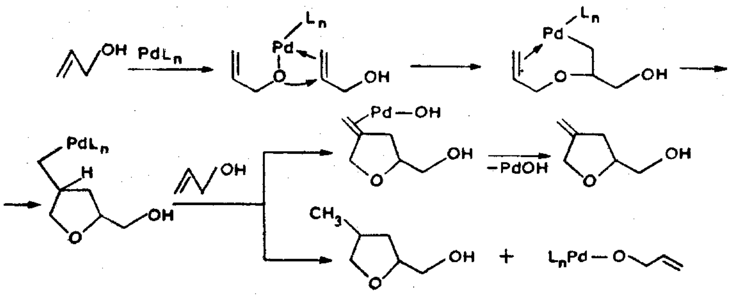
A new approach to the synthesis of sulfolane derivatives is the reaction of 3-sulfolenes with butadiene and isoprene catalyzed by palladium–phosphine complexes [58-60]. For example, 3-sulfolenes LXXIII are converted to cis- and trans-2,5-divinylsulfolanes LXXIV under the influence of butadiene.



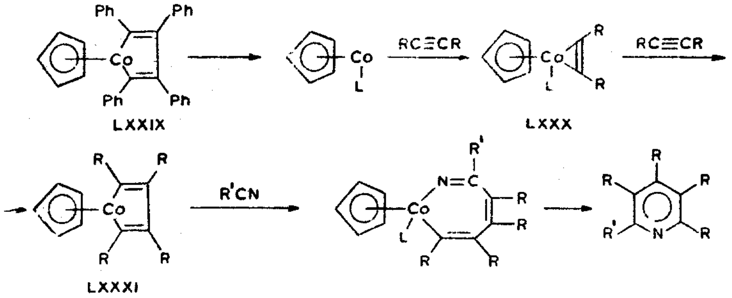
Macrocyclic silicon-containing heterocycles are formed in high yields from dienes and disilacyclanes under the influence of $PdCl_2 \cdot [P(C_6H_5)_3]_2$. Thus, LXXVII and LXXVIII, respectively, were obtained from LXXV and LXXVI [61].



Other Syntheses Based on the Catalytic Activation of Unsaturated Compounds. Allyl alcohol reacts with $PdCl_2$ to give a mixture of 4-methyl- and 4-methylenetetrahydrofurfuryl alcohols [62].

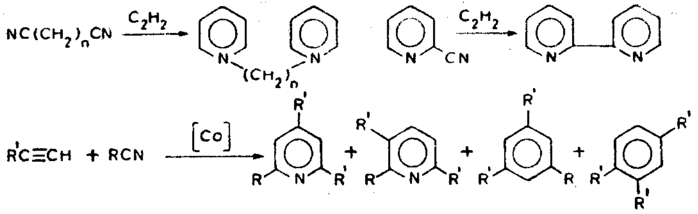


The synthesis of pyridines from acetylenes and nitriles is interesting. The LXXIX complex, the role of which consists in its ability to undergo conversion to intermediate complexes LXXX and LXXXI under the influence of acetylenes, must be used as the catalyst [63]. Intermediate complexes LXXX and LXXXI readily react with nitriles to give pyridines.



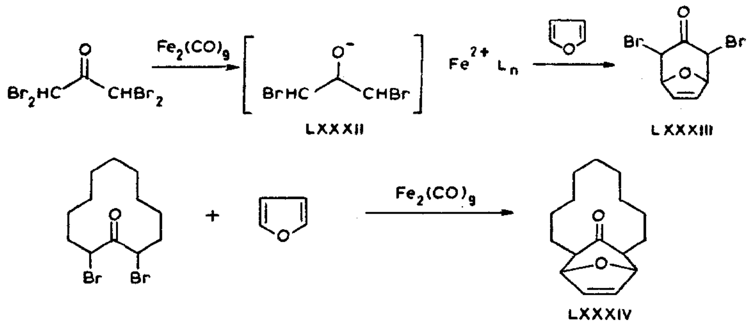
Instead of the difficult-to-prepare LXXIX complex, it is more convenient to use complexes that are formed in the reduction of Co^{2+} salts by means of $NaBH_4$, lithium and magnesium metals, and organoaluminum compounds [64].

Mixtures of pyridines are formed in high yields when monosubstituted acetylenes are used. α,ω-Dipyridylalkanes are obtained from α,ω-dinitriles, while dipyridyls are obtained from cyanopyridines [65]. The yields in the case of catalysis by means of $C_5H_5Co(C_8H_{12})$ are very high. A review of the synthesis of pyridines from nitriles and acetylenes has been published [66].



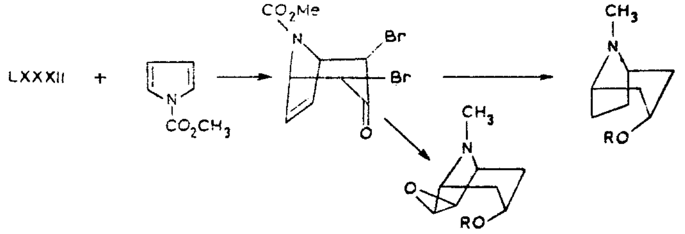
The industrial synthesis of α-picoline and 2-methyl-5-ethylpyridine from ethylene and ammonia under 30-100 atm pressure at 100-300°C, which is based on the use of the catalytic activity of a palladium-copper couple, has recently been worked out [67].

An elegant approach to the synthesis of oxygen- and nitrogen-containing heterocycles was proposed in [68, 69]. According to [70], α,α'-dibromo- and α,α,α',α'-tetrabromo ketones react with $Fe_2(CO)_9$ to give divalent iron complexes of the LXXXII type, which react readily

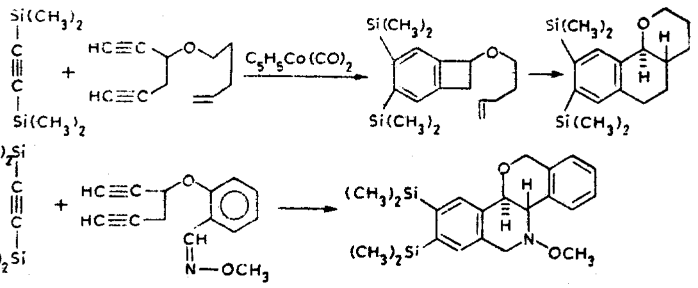


with activated double bonds, as well as with conjugated systems. For example, tetrabromoacetone was used for the synthesis of oxabicyclic system LXXXIII from furan, while dibromocyclododecanone was used to obtain oxatricyclane LXXXIV [69, 70].

The elegant synthesis of alkaloids of the tropane series was accomplished on the basis of tetrabromoacetone and 1-carboxymethylpyrrole [71].



In concluding this review we must point out an extremely remarkable method for the synthesis of heterocycles with complex structure that is based on the simultaneous use of the coupling of activated fragments and intramolecular cyclization. Bis(trimethylsilyl)acetylene serves as one of the reagents. The cyclized substrate has two ethynyl groups and a double bond. The reaction is catalyzed by means of cyclopentadienylcobalt dicarbonyl. The benzocyclobutene system is formed in the first step and subsequently undergoes intramolecular cyclization [72].



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2-AMINO-3-(BENZIMIDAZOL-2-YL)BENZO[b]FURANS

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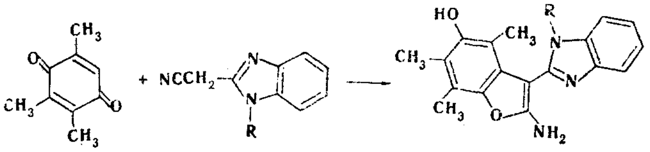
UDC 547.728.1'785.5

The corresponding 2-amino-3-(benzimidazol-2-yl)benzo[b]furans were obtained by reaction of 2,3,5-trimethyl-1,4-benzoquinone with 2-cyanomethylbenzimidazoles. It is shown that new benzo[b]furo[2',3':4,5]pyrimido[1,6-a]benzimidazole polynuclear heterocyclic systems (bases and quaternary salts) are formed in the reaction of these products with acylating agents.

We have previously shown that the corresponding 2-amino-3-(benzimidazol-2-yl)benzo[b]furan is formed in the reaction of 2-methyl-5-isopropyl-1,4-benzoquinone with 2-cyanomethylbenzimidazole (IIa) [1]. During a study of the general character of this reaction we found that 2,3,5-trimethyl-1,4-benzoquinone (I) reacts similarly with nitrile IIa to give 2-amino-3-(benzimidazol-2-yl)-5-hydroxy-4,6,7-trimethylbenzo[b]furan (IIIa). It is interesting that the compound forms a monosolvate with dimethylformamide (DMF), in which form it was also isolated from the reaction mixture. This is confirmed by the results of elementary analysis and the PMR spectrum, in which signals of the exchanged protons of amino and hydroxy groups at 6.85 ppm, signals of five methyl groups at 2.18-2.87 ppm, a multiplet of aromatic protons of the benzimidazole ring (7.27 ppm), and a singlet of the CH proton of DMF at 7.89 ppm are observed. A band of a keto group at 1658 cm^{-1} is present in the IR spectrum of IIIa. The complex does not decompose when it is recrystallized or heated in vacuo, and derivatives of the previously described [1] benzo[b]furo[2',3':4,5]pyrimido[1,6-a]benzimidazole system (IV) (Table 1) are formed and decomposition of the solvate is observed only when it is treated with acylating agents (acid anhydrides and chlorides and ortho esters).



I IIa,b IIIa,b

II, IIIa R=H; b R=CH_3

Benzoquinone I also reacts with 1-methyl-2-cyanomethylbenzimidazole (IIb) to give N-methyl derivative IIIb. The properties of IIIb differ from those of unsubstituted analog IIIa. In particular, acetic anhydride acylates only the amino and hydroxy groups of IIIb to give the corresponding V. Whereas the IR spectrum of IVb does not contain absorption above

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