Heterocycles Synthesis at Carbonylation of Acetylenic Compounds

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Abstract

The carbonylation of unsaturated hydrocarbons, alcohols, organic halides and other substrates catalyzed by transition metals, salts of transition metals and organometallic complexes is a wide used synthesis method of new carbonyl, carboxyl and alkoxy carbonyl containing compounds including creation or modificationt of heterocycles.

The data about synthesis of heterocycles at carbonylation of acetylenic compounds have been appeared at last 20 years and are demonstrated in our review.

Introduction of carbon monoxide in the catalytic reactions of acetylenic compounds permits to obtain in oneput process the diverse heterocycles, having carbonyl, carboxyl or alkoxycarbonyl substitutes or containing these fragments inside of heterocycles.

Introduction

The carbonylation of unsaturated hydrocarbons, alcohols, organic halides and other substrates catalyzed by transition metals, salts of transition metals and organometallic complexes is a wide used method of new carbonyl, carboxyl and alkoxycarbonyl containing compounds synthesis including creation or modification of heterocycles [1-8]. However the data about synthesis of heterocycles at carbonylation of acetylenic compounds in these books and reviews practically are absent because ones mainly have ap-

peared at last 25 years. These data are given in our review.

The synthesis of alkoxycarbonyl derivatives of dimethylenepyrrolidines

It is found by Chiusoli G.P. et al. that α,α-tetra-alkylsubstituted dipropargylamines react with carbon monoxide and alcohols or water in the presence of $PdCl_2$ – thiourea complex forming alkoxycarbonyl derivatives of dimethylenepyrrolidines (**1**, **2**) [9,10] (Scheme 1).
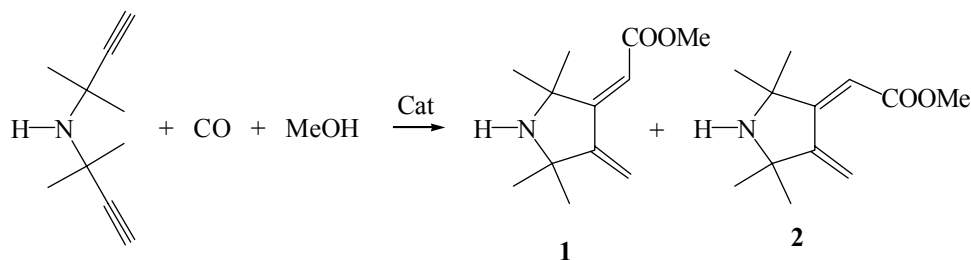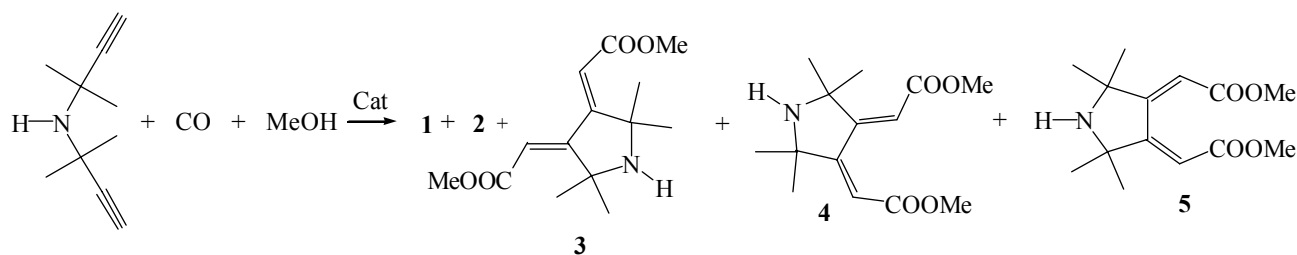

Scheme 1

On using of $PdCl_2$ as catalyst in the presence of oxygen apart from carbon monoxide ($CO/O_2 = 90:10$) in methanol dimethoxycarbonyl dimethylenepyrrolidines (**3** and **4**) mainly are forming besides of monomethoxycarbonyl derivatives **1** and **2**. Similar pic-

ture is at catalysis by Pd^0/C in the presence of KI and oxygen ($CO/O_2 = 94:6$). At that the third stereo isomer of methoxycarbonyl dimethylenepyrrolidine (**5**) is formed in a small amount [11] (Scheme 2).

Methoxycarbonylation of dipropargylmethyl-amine at catalysis by $PdCl_2$ – thiourea complex leads

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Scheme 2

to both mono- and dimethoxycarbonyldimethylene pyrrolidines forming but with smaller yields [11].

    At the oxidative alkoxycarbonylation of dipropargylamines and amides by mixture of CO/air at 4 bar pressure in the alcohole at Pd^0/C catalysis in the pres-

ence of KI the mixture of 3,4-bis(alkoxycarbonyl-methylene)pyrrolidines **6** has been obtained. An isomerization of those in the various conditions leads to the forming of pyrrols **7** and free pyrrolo-3,4-di-acetic acids **8** [12] (Scheme 3).
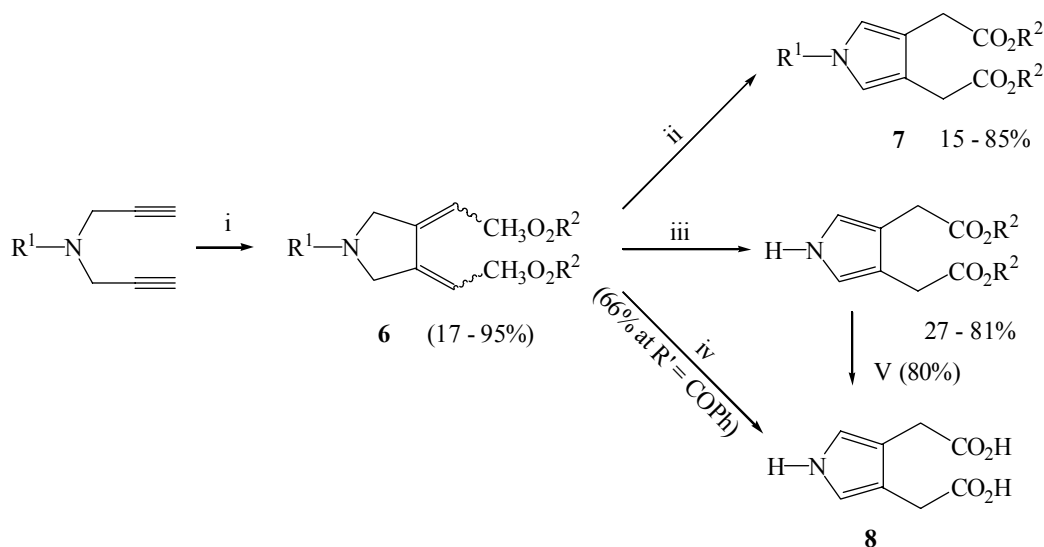
R^1 = alkyl, aryl, alkoxycarbonyl, tosyl; R^2 = alkyl
i: CO/air, R^2OH, Pd/C, KI;
ii: DMSO or MeCN/Et_3N, 25 – 70°C, 3 – 70 h.

iii: R^2OH, Et_3N, 25 – 80°C, 5 – 70 h.
iv: (1) $Ba(OH)_2/H_2O$, 100°C, 15 h. (2) H_2SO_4/H_2O.
v: (1) $NaOH/H_2O$, 100°C, 30-40 min. (2) H_2SO_4/H_2O, 0°C.

Scheme 3

The polycyclic heterocycles formation

    Chiusoli G.P. with co-workers have founded, that the polycyclic products **10-12** were formed at carbonylation of 1,6-diynes **9** in the presence of Pd^0 on charcoal [13] (Scheme 4).

    Reaction proceeds at the room temperature and atmospheric pressure of carbon monoxide. Polycyclic compounds **11** are formed at dimerization of cyclopentadienone **10**. When the reaction is carried out in a base – alcohol medium (at X = NH, NMe, R = alkyl) the cyclopentadienone **10** "is catched" by

alkoxyl group with the forming of corresponding alkoxycyclopentenones **12**. Application of various alkenes and alkynes as dienophiles, using for "catching" of cyclopentadienones **10**, allows to extend the number of obtaining heteropolycyclic compounds **13-15** (Scheme 5) [14].

    Palladium on charcoal (10%), complexes of $Pd°$ such as $Pd_2(dba)_3$ (dba – dibenzyledenacetone) or palladium salts lightly reducing in reaction conditions up to metallic Pd are used as catalysts. The using of alkynes as dienophiles leads to obtaining of products those are spontaneously aromatizated at the heating.

The better yields of polycyclic compounds **13** and **15** (up to 98%) are observed in reaction of alkenes and alkynes with terminal double and triple bonds. In the absence of CO in the same reaction conditions any reactions not proceed. But at the using of Ni and Co complexes as catalysts the cycloaromatization reaction of dialkynes **9** has proceeded [15].

The methoxycarbonylation of N,N-dipropar-gylarylamines

We have shown, that at oxidative methoxy-carbonylation of N,N-dipropargylarylamines by carbon monoxide in methanol at $PdCl_2$ catalysis in the presence of $CuCl_2$ and AcONa cyclic compounds – dimethyl-1-aryl-5-methoxycarbonylmethylene-1,2,5,6-tetrahydropyridine-3,4-dicarboxylates **17** are formed besides of alicyclic diesters of aminodicarboxylic acids **16** (Scheme 6) [16,17].
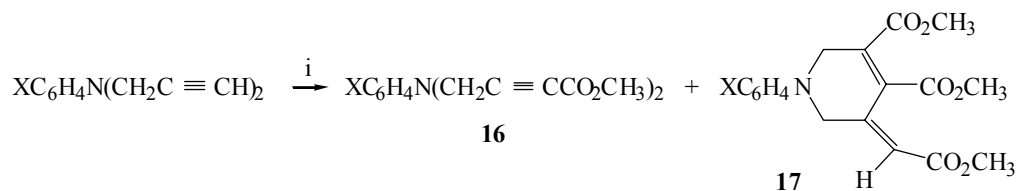

X = NH, O; R = H, Alk
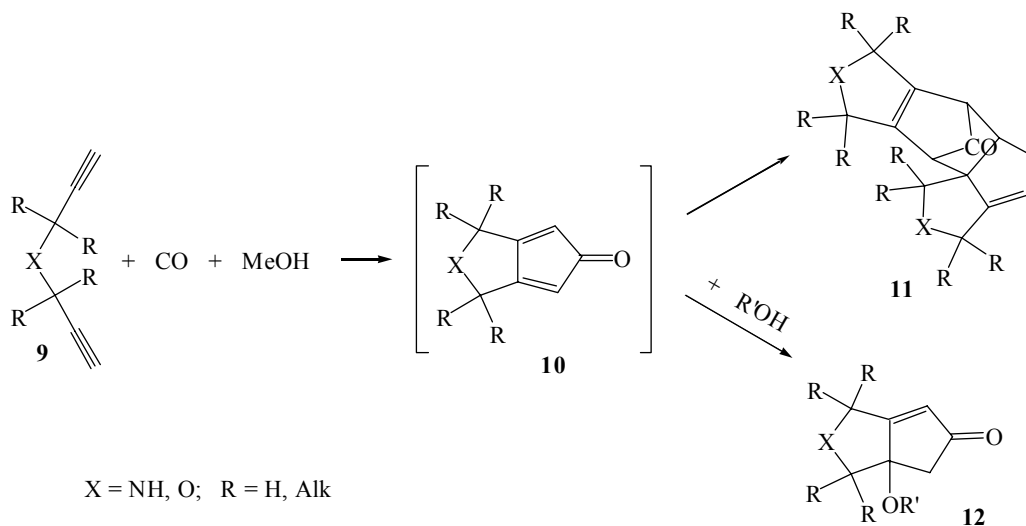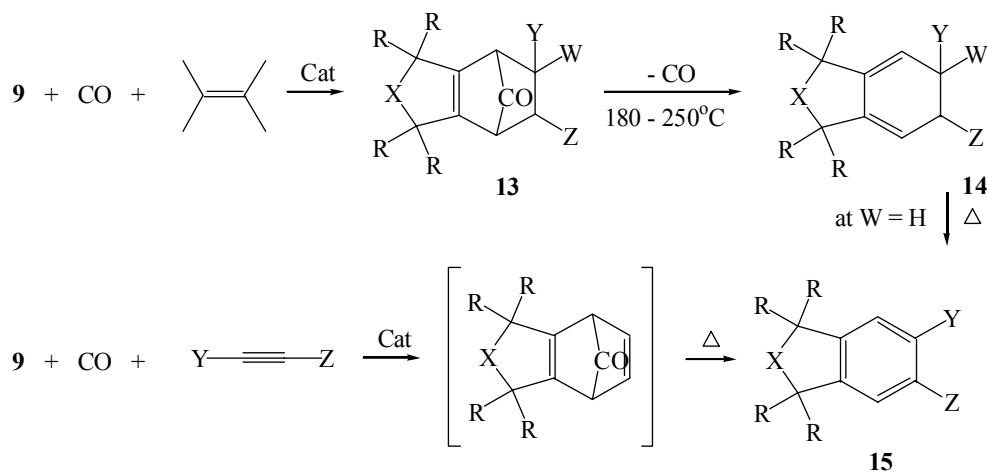
Scheme 4

X = NH, NCO$_2$Me, NCOPh, O; Y = Ph, CO$_2$Me, H,CN, CH=CH$_2$; Z = H, Me, CO$_2$Me; W = H, Me, CO$_2$Me

Scheme 5

i   CO, MeOH, 10% (mol) PdCl$_2$, 4 equiv. CuCl$_2$, 1 equiv. AcONa на 1 equiv. from amine
17   X = H (11%), p-Cl (36%), m-Cl (40%), m-Br (47%), o-Cl (24%), o-Br (45%)

Scheme 6

The forming of cyclic aminotriesters **17** takes place by additive methoxycarbonylation of one from arylaminodiesters **16** triple bonds followed by cyclization. Observing depence for cyclic **17** and alicyclic arylaminoesters **16** forming from electron nature and position of substituent X (at X = p-CH$_3$, p-OCH$_3$ and p-Br cyclic compound **17** yet unforms) in aryl ring apparently is caused by stability of intermediate complexes of aminodiesters **16** with catalyst PdCl$_2$ [17].

High stereoselective cyclization/carbonylation of propargylallylamines

Oppolzer W. et al. have shown that catalyzed by nickel and palladium complexes high stereoselective cyclization/carbonylation reaction of propargylallylamines **18 a, b** furnishs mono- **19** and bicyclic **20**, **21** derivatives of pyrrolidines (Scheme 7) depending on used catalyst and reaction conditions [18,19] (in the Table 1).
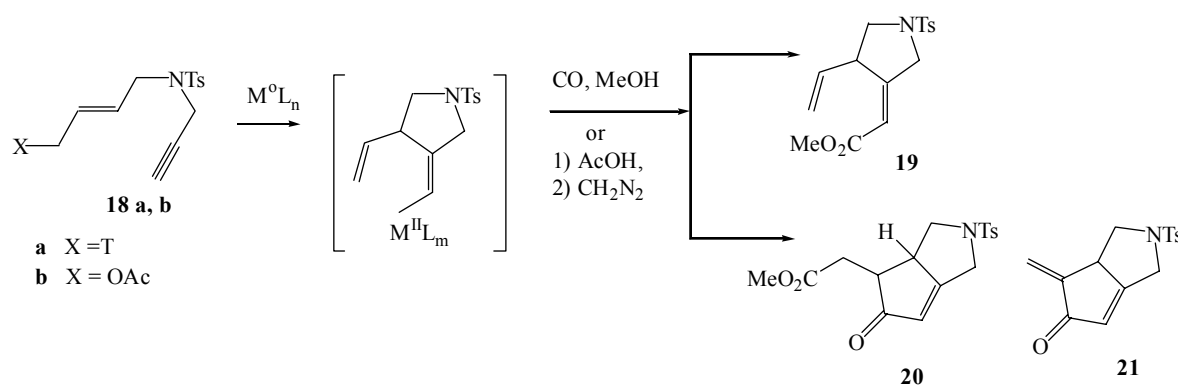
Table 1

Nickel (0) and palladium (0) catalyzed cyclization/carbonylation of amines **18 a, b**

N	18	Catalyst	Reaction conditions	Products yields, %		
			(time, h)	**19**	**20**	**21**
1	a	Ni(CO)$_3$PPh$_3$	A (20)	69	-	-
2	a	Ni(COD)$_2$/dppb	A (12)	23	57	-
3	b	Pd(dba)$_2$/PPh$_3$	B (2)	13	50	16

a. A: 25 mol % Ni(0), THF / MeOH 4:1, CO (1 atm) room temp.

B: 10 mol % Pd(0), HOAc, CO (1 atm), 45°C.

Scheme 7

Synthesis of indoles and benzofurans

Palladium chloride catalyzed carbonylation of o-hexynyl anilines **22** and phenols **24** gives the methyl-2-butylindole-3-carboxylate **23** and methyl-2-butylbenzofuran-3-carboxylate **25** correspondingly [20] (Scheme 8).

The mechanism of process includes the formation of intermediate bicyclic Pd complex, carbonylating by CO into acylpalladium complex, giving in reaction with methanol the final product and Pd^0 species. Catalyst regeneration happens in result of Pd^0 into Pd^{2+} oxidation with participation of CuCl$_2$ [20].

Lately the sphere of reaction application has extended and the series of 2-substituted 3-methoxycarbonylindoles and benzofurans **26** has been obtained. Only lactams **27** have formed from 2-alkynylformanilides in these conditions [21] (Scheme 9).
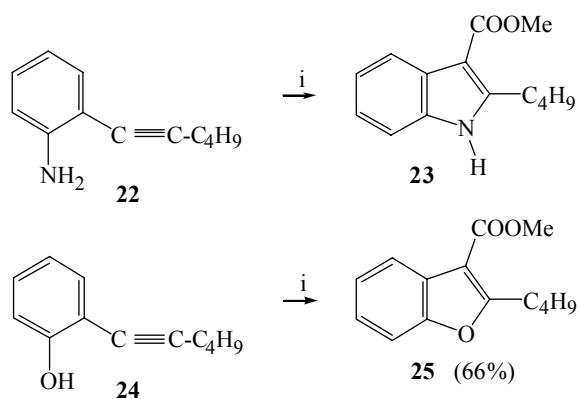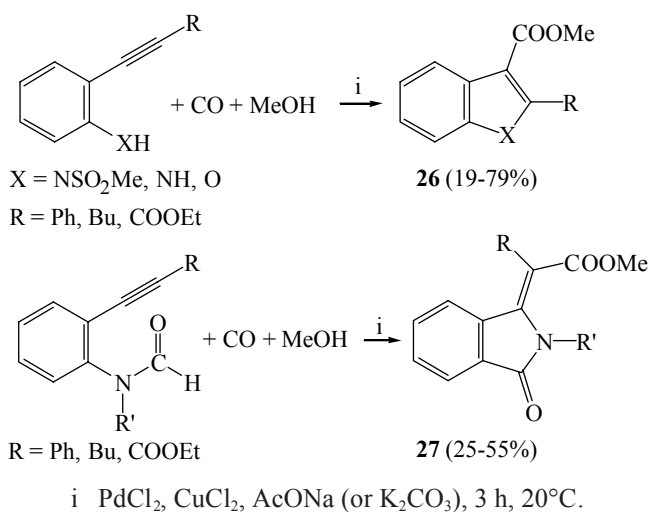

i   CO, MeOH, NaOH, PdCl$_2$, CuCl$_2$

Scheme 8

The palladium-catalyzed reaction of readily accessible 2-alkynyltrifluoroacetanilides with aryl halides and vinyl triflates under a carbon monoxide atmosphere (1 or 7 atm) in the presence of potassium carbonate produces 2-substituted-3-acyl indoles in fair to good yield. The acidity of the nitrogen-hydrogen bond proved to be primary importance for the success of the reaction. The methodology has been applied to the synthesis of pravadole **30**, a drug that shows analgesic activity against postoperative pain in man. Pravadole **30** was prepared from acylindole **29**, wich was obtained by palladium-catalyzed carbony-
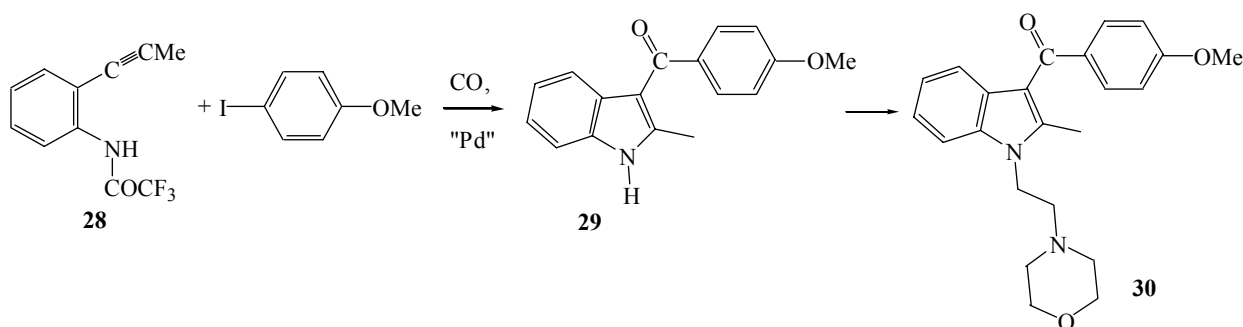
lative cyclizaton of alkynyltrifluoracetanilide **28** with p-iodanisole [22] (Scheme 10).
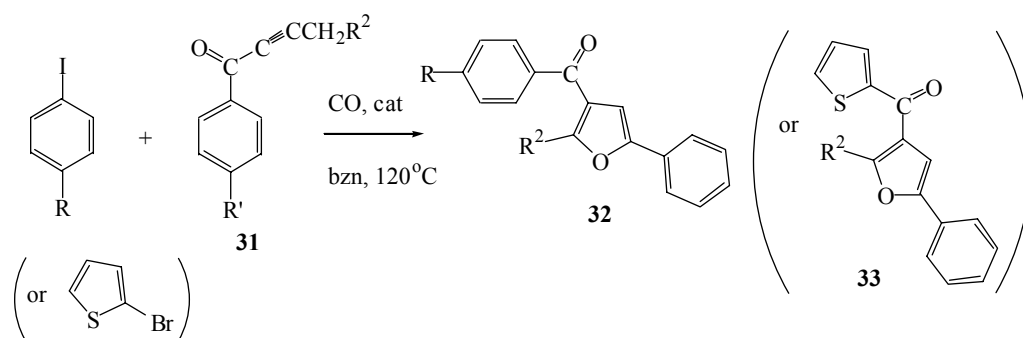
Synthesis of substituted furans

2-R^2-3-(4-R-benzoyl)-5-(4-R'-phenyl)furans **32** are synthesized by palladium-catalyzed cross-carbonylation of aryl iodides and 1-aryl-2-alkynyl-1-ones **31** with CO in benzene in the presence of PdCl$_2$(PPh$_3$)$_2$ at 120°C (Scheme 11). Analogously 2-R^2-3-thienoyl-5-phenyl furans **33** were obtained from 2-bromothiophene and arylalkynylketones **31** [23].

X = NSO$_2$Me, NH, O
R = Ph, Bu, COOEt

26 (19-79%)

R = Ph, Bu, COOEt

27 (25-55%)

i PdCl$_2$, CuCl$_2$, AcONa (or K$_2$CO$_3$), 3 h, 20°C.

Scheme 9

28

29
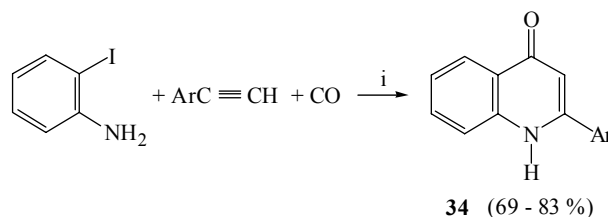
30

Scheme 10

31

32

33

Scheme 11

Synthesis of 2-aryl-4-quinolones

Carbonylation of o-iodoaniline and terminal aryl-acetylenes in the presence of palladium complexes leads to 2-aryl-4-quinolones **34** [24] (Scheme 12).

The alteration of pressure, amines, solvents and catalysts allows to find the best conditions those are given at the Scheme 12. The best catalyst is PdCl$_2$ (dppf) complex (dppf is 1,1'-bis(diphenylphosphino)ferrocene.

Synthesis of aurone or chromones

Carbonylation of o-iodophenol in the presence of phenyl acetylene, potassium acetate and Pd(PPh$_3$)$_4$ in anisole at 1 atm CO leads to aurone **35** formation (Scheme 13) [25].

Reaction carrying out in the secondary amine (the best one – is Et$_2$NH) at 20 atm CO and catalysis by 2 mol % PdCl$_2$(dppf) leads to flavone **36** (scheme 13) [26]. Selective formation of aurone or flavone at carbonylation of o-iodophenole and phenylacetylene depends on reaction conditions (temperature, CO pressure) and used bases. The influence of the nature of a solvent, amine, catalyst, carbon monoxide pressure, and temperature on the yield of the flavone was studied [26,27].

Palladium – catalysed coupling of o-iodophenols proceeds either with aryl or heteroaryl halides and alkylacetylenes giving the corresponding 2-substituted chromones **37** in good yields (scheme 13) [27].

Synthesis of (E)- and (Z)-substituted methylene-3,4-dihydro-2H-1-benzopyranes
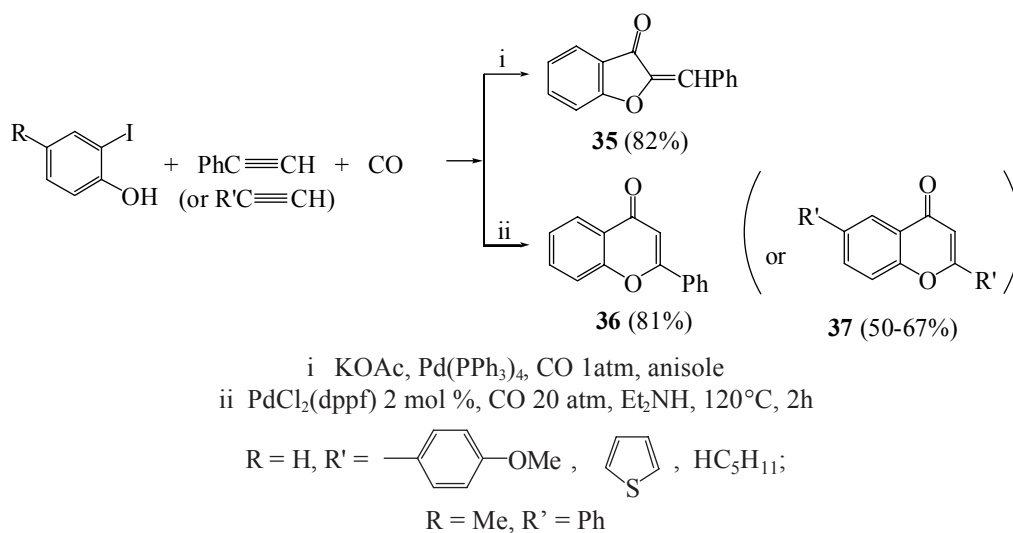
A stereocontrolled synthetic approach to (E)- and

i Et$_2$NH, "Pd" cat, 120°C, 20 atm, 1 h.
Ar = Ph, C$_6$H$_6$OMe

Scheme 12

(Z)-substituted methylene-3,4-dihydro-2H-1-benzo-pyrans **39 a-c** is developed from o-iodoalkynes **38 a, b** using as a key palladium-catalyzed intramolecular cyclic carbopalladation of iodoalkynes **38** followed by carbonylation or a hydride ion capture process (Scheme 14) [28].
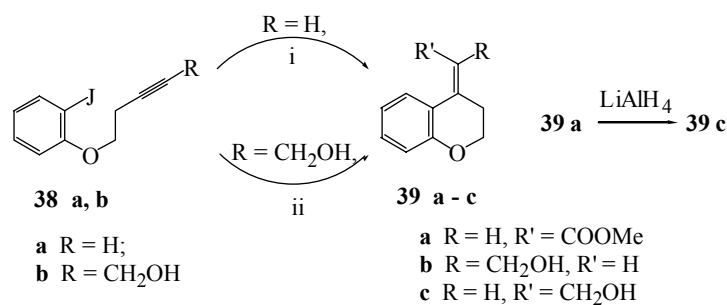
The influence of various solvents, catalysts and additives on the yields of benzopyrans **39** was studied. The best reaction conditions were (i) for obtaining benzopyran **39a** (79% yield) and (ii) for benzopyran **39b** (79% yield).

Facile stereoselective synthesis of oxathiolanes

The stereoselective interaction of alkynols **40** with elemental sylfur, carbon monoxide and triethyl amine gives the salts **41**, those are cyclized into 4-alkylidene-2-oxo-1,3-oxathiolanes **42** in the presence of catalytic amounts of catalyst (scheme 15). CuJ shows the best activity among studied catalysts (CuCl, CuCl$_2$, CuBr, CuBr$_2$, CuI, CuSO$_4$, FeCl$_2$·4H$_2$O, FeCl$_3$, CoCl$_2$, CoBr$_2$, CoI$_2$, NiCl$_2$, ZnCl$_2$, ZnBr$_2$, ZnI$_2$, PdCl$_2$) [29].

i KOAc, Pd(PPh$_3$)$_4$, CO 1atm, anisole
ii PdCl$_2$(dppf) 2 mol %, CO 20 atm, Et$_2$NH, 120°C, 2h

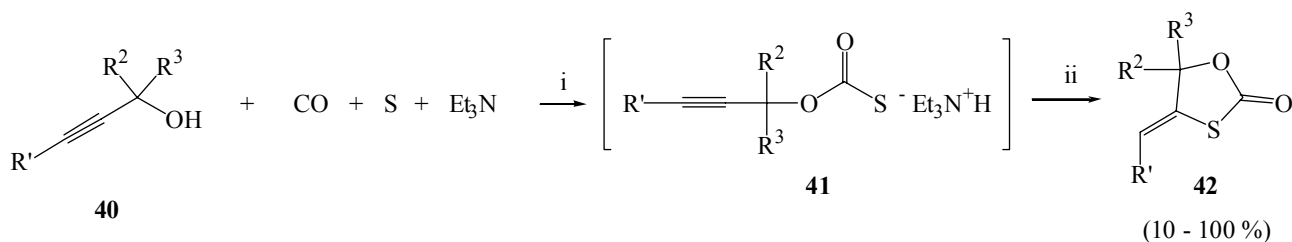R = H, R' = —⟨ ⟩—OMe , ⟨S⟩ , HC$_5$H$_{11}$;

R = Me, R' = Ph

Scheme 13

i Pd(PPh₃)₄ (10%), CO (1 atm), Et₃N (4 equiv.), AgOAc (3 equiv.) in MeOH – DMF – H₂O (1:1:0.2) at 100°C.
ii HCOONa (2 equiv.), Bu₄NCl (2 equiv.), Pd(OAc)₂ (10%), PPh₃ (20%) in DMF at 80°C.

Scheme 14

i THF, 30 atm, 80°C, 4 h, ii CuI, r.t., 18 h, R', R², R³ = H, Me, Et, CH₂OH, Ph

Scheme 15

Formation of unsaturated lactams

α-Methylene-β-lactams **43** are formed at carbonylation of α,α-disubstituted propargylalkylamines, then γ-lactams **44** are formed from unsubstituted or acylated amines [30] (Scheme 16).

The same authors have shown for the first time that on simaltaneously interaction of the propargylalkylamines with a carbon monoxide and a carbon dioxide catalyzed by PdI₂ or Pd⁰/C in the presence of KI consistent carboxylation and alkoxycarbonylation reactions proceed leading to Z- and E-[(alkoxycarbonyl)methylene]oxazolidin-2-ones **45 a** and **45 b** [31,32] (Scheme 17).

In the absence of carbon monoxide only oxazolidinone **46** has been formed (Scheme 18).

α-Methylene-γ-butyrolactones synthesis

Interest in the synthesis methods of α-methylene-γ-butyrolactones is supported owing to high biological activity and the wide spectrum of physiological action of natural products, containing α-methylenelactonic unit [33, 34]. For example, elephantopin, euparotin acetate and vernolepin show antitumore activity [33], as a natural sesquiterpene lactone phantomolin shows cytotoxic activity [34].

Among other synthetic methods for such structural inits catalytic cyclocarbonylation of acetylene alcohols at first had not great importance, because of it gave low yields of α-methylene-γ-butyrolactone **47** by reaction of 3-butyn-1-ol with stoichiometric amount of nickel tetracarbonyl [35] (Scheme 19).
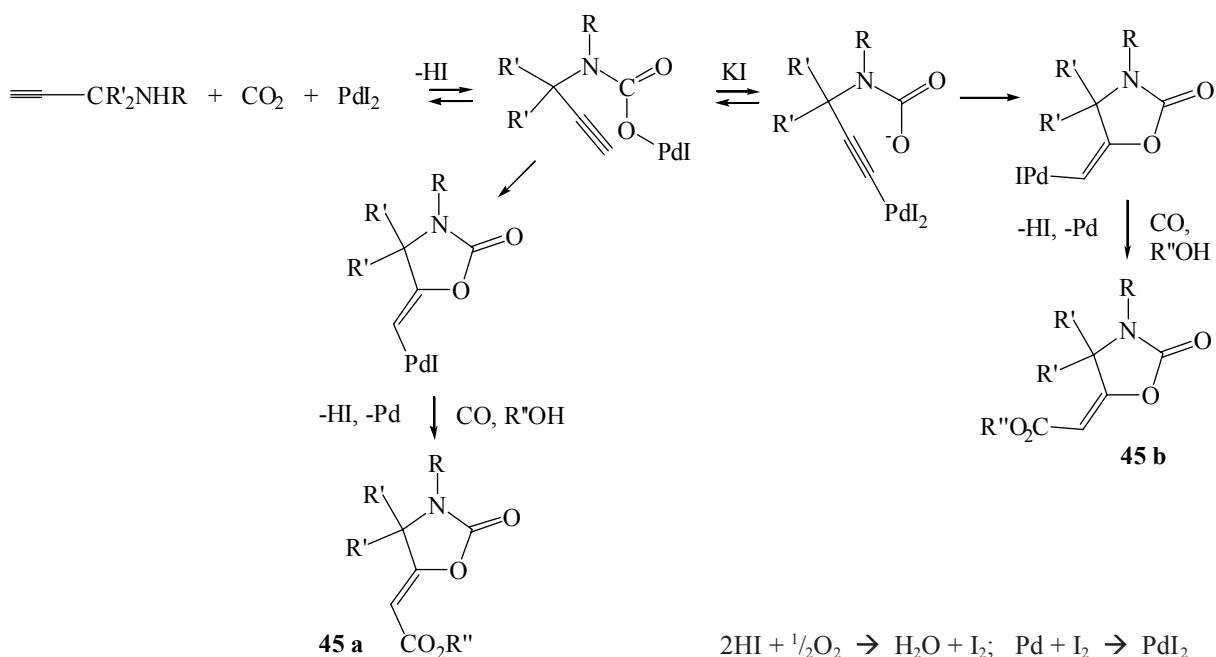
Norton J.R., Murray T.F. et al. have given a general method of α-methylenelactones **48** synthesis in mild conditions, that has been in cyclocarbonylation of ethynyl alcohols at organopalladium complexes catalysis [36,37] (Scheme 20).
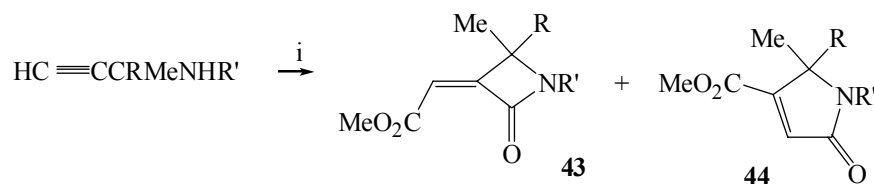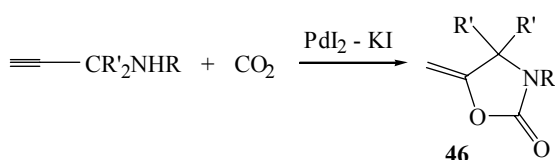

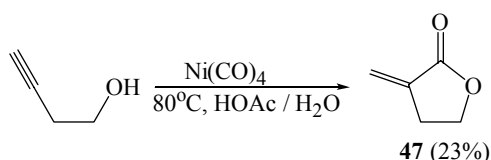R = Me, Et; R' = COPh, Alk, H, COAlk
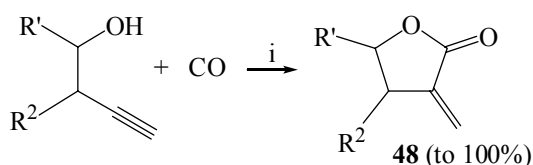i CO/air, Pd⁰/C, KI, MeOH

Scheme 16

Scheme 17

Scheme 18

Scheme 19

R^1, R^2 = H, (CH$_2$)$_2$Br, (CH$_2$)$_2$CH=CH$_2$, (CH$_2$)$_3$, (CH$_2$)$_4$, (CH$_2$)$_5$
i PdCl$_2$ (0.07 equiv.), SnCl$_2$ (0.07 equiv.), PPh$_3$ (or PBu$_3$) (0.14 equiv.),
CO (to 7.8 atm.), MeCN, 65-75°C.

Scheme 20

Comparative study of the ability of the various catalytic systems to cyclocarbonylate of acyclic and cyclic alcohols has shown that system PdCl$_2$, anhydrous SnCl$_2$ and 2 equiv. of tertiary phosphine in acetonitrile is the best one. At that not only α-methylene γ-lactones, but δ-lactones of various structure in cis- and trans-fused rings can be made with rather high yields, if the substrate concentration is kept sufficiently low (0.1-1M), to direct the reaction into intramolecular cyclization way. Study of cyclocarbonylation mechanism shows at first carboalkoxy intermediate species is formed from Pd(II), CO and acetylene alcohol, followed by intramolecular cis addition to the triple bond [37,38] (Scheme 21).

Competitive intermolecular insertion of the triple bond in another substrate can occur, leading to obtaining of dimeric and, eventually, polymeric products. Cleavage of the vinyl-palladium bond by the proton generated in the first reaction removes the product and regenerates the initial Pd(II) complex. In the course of mechanism studies the authors design a much more efficient Pd(II) catalyst system with SnCl$_2$ as a cocatalyst, that of role is in labilizing of palladium coordination sphere. As at use of PdI$_2$/Bu$_3$P/MeCN catalyst system the rate-determining step evidently being the uptake of CO by Pd, then for second catalyst system case (PdCl$_2$/2Ph$_3$P/SnCl$_2$/MeCN) the rate- determining step is coordination of the substrate, followed by
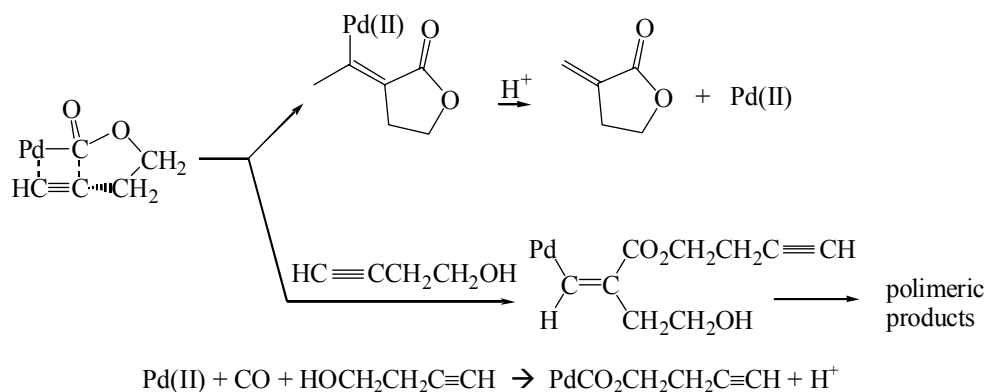
Scheme 21

rapid uptake of CO and completion of the cyclocar-   bonylation reaction [38] (Scheme 22).
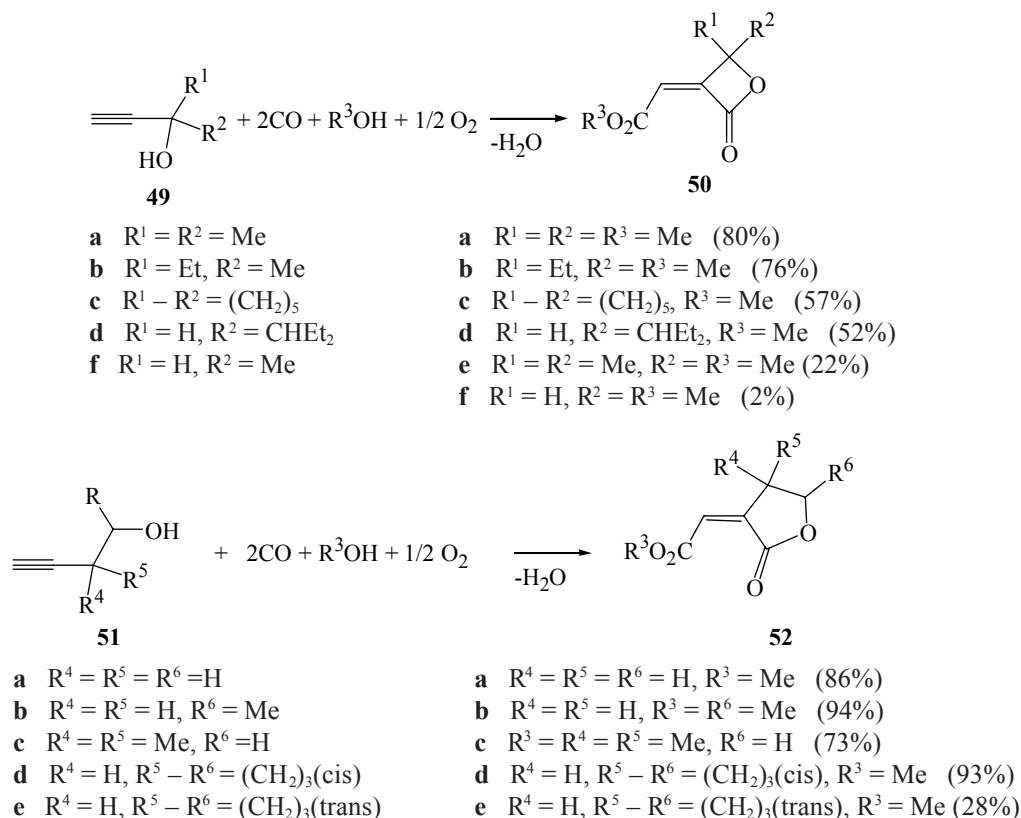

here L = PPh$_3$
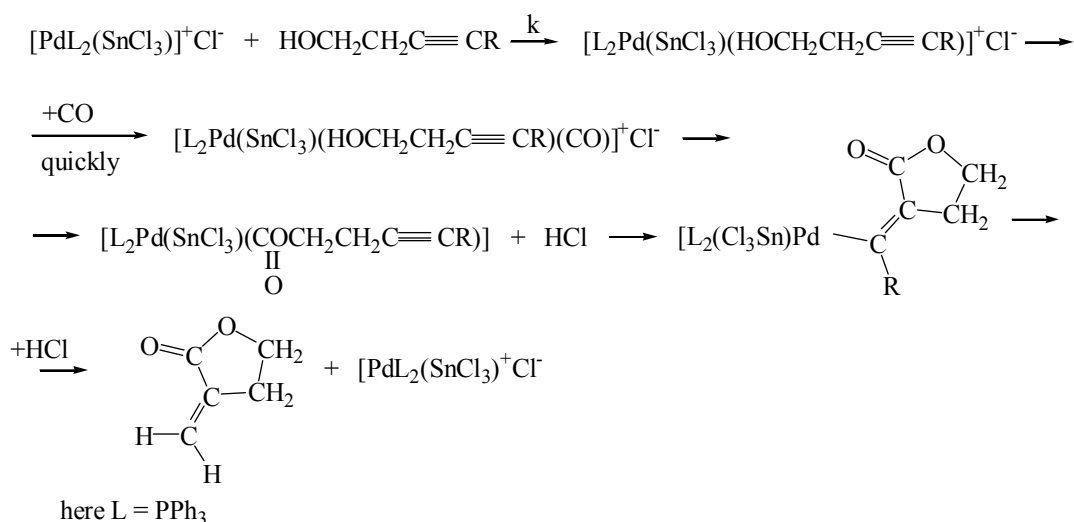
Scheme 22

Stereoselective synthesis of (Z)-α-(alkoxy-carbonyl) methylene β- and γ-lactones

(Z)-α-(Alkoxycarbonyl)methylene β- **50** and γ-lactones **52** can be obtained in fair to excellent yields and witn high catalytic efficiencies by PdI$_2$/KI cata-lyzed oxidative dialkoxycarbonylation of propynyl alcohols (α,α-dyalkyl substituted, or α-monoalkyl substituted) with a sufficiently bulky alkyl group **49** and but-3-yn-1-ols **51**, respectively. Reactions are carried out in alcoholic media under mild conditions (70-80°C and 20 atm of a 3:1 mixture of carbon mono-xide and air) (Scheme 23) [39,40]. Possible reaction pathways are discussed.
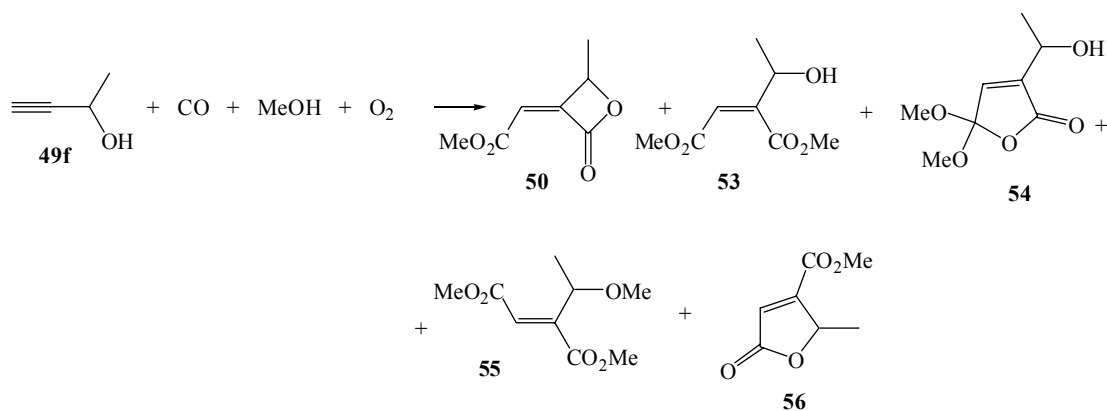
The presence of alkyl substituents α to the triple bond is essential in order to achieve good selectivi-

ties for β-lactones **50**. Yields of β-lactones deriving from α-monoalkylsubstituted propynyl alcohols are very low if the alkyl group is not sterically demand-ing. Thus, but-3-yn-2-ol **49f** yielded only 2% of the corresponding β-lactone **50f** at 80% conwersion. Maleic diester **53** (50%), its cyclic tautomer **54** (9%), the fumaric derivative **55** (12%) and γ-lactone **56** (6%) accounted for the converted substrate (Scheme 24).

In contrast to the propynyl alcohols, substitution α to the triple bond of but-3-yn-1-ols **51** is not nec-essary in order to direct the carbonylation process towards ring closure to give γ-lactones selectively. But-3-yn-1-ol **51**, pent-4-yn-2-ol **51b** and cis-2-ethy-nylcyclopentan-1-ol **51d** were, in fact, converted into their corresponding γ-lactones **52a**, **52b** and **52d** in

$$\text{49} + 2CO + R^3OH + 1/2\,O_2 \xrightarrow[-H_2O]{} \text{50}$$

49

a $R^1 = R^2 = Me$
b $R^1 = Et$, $R^2 = Me$
c $R^1 - R^2 = (CH_2)_5$
d $R^1 = H$, $R^2 = CHEt_2$
f $R^1 = H$, $R^2 = Me$

50

a $R^1 = R^2 = R^3 = Me$ (80%)
b $R^1 = Et$, $R^2 = R^3 = Me$ (76%)
c $R^1 - R^2 = (CH_2)_5$, $R^3 = Me$ (57%)
d $R^1 = H$, $R^2 = CHEt_2$, $R^3 = Me$ (52%)
e $R^1 = R^2 = Me$, $R^2 = R^3 = Me$ (22%)
f $R^1 = H$, $R^2 = R^3 = Me$ (2%)

$$\text{51} + 2CO + R^3OH + 1/2\,O_2 \xrightarrow[-H_2O]{} \text{52}$$

51

a $R^4 = R^5 = R^6 = H$
b $R^4 = R^5 = H$, $R^6 = Me$
c $R^4 = R^5 = Me$, $R^6 = H$
d $R^4 = H$, $R^5 - R^6 = (CH_2)_3(cis)$
e $R^4 = H$, $R^5 - R^6 = (CH_2)_3(trans)$

52

a $R^4 = R^5 = R^6 = H$, $R^3 = Me$ (86%)
b $R^4 = R^5 = H$, $R^3 = R^6 = Me$ (94%)
c $R^3 = R^4 = R^5 = Me$, $R^6 = H$ (73%)
d $R^4 = H$, $R^5 - R^6 = (CH_2)_3(cis)$, $R^3 = Me$ (93%)
e $R^4 = H$, $R^5 - R^6 = (CH_2)_3(trans)$, $R^3 = Me$ (28%)

Scheme 23

$$\text{49f} + CO + MeOH + O_2 \longrightarrow \text{50} + \text{53} + \text{54} + \text{55} + \text{56}$$
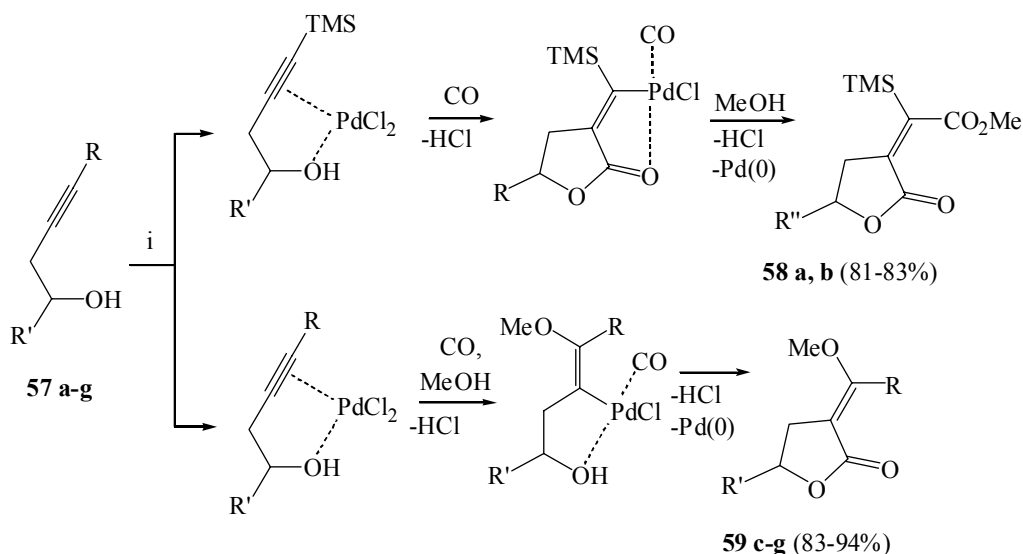
Scheme 24

excellent yields. Where there was dialkyl substitution α to the triple bond as in **51c**, the reaction was slower, and the product yield of the γ-lactone **52** lower. When cyclization is disfavoured by molecular geometry, as in the case of trans-2-ethynylcyclopentan-1-ol **51**, product distribution changes in favour of maleate, the γ-lactone **52e** being obtained as by–product [39].

Palladium (II)-catalized dicarbonylation of 4-(trimethylsilyl)-3-butyn-1-ols **57a** and **57b** in the presence of propylene oxide and ethyl orthoacetate in methanole-dichloromethane under carbon monox-

ide at atmospheric pressure afforded cis-dicarbonylated α-methylene-γ-butyrolactones **58 a, b** respectively. 4-Alkyl- and 4-aryl-3-butyn-1-ols **57 c-g**, on the other hand, undergo trans alkoxycarbonylation across the triple bond and selectively furnish E-tetrasubstituted α-methylene-γ-butyrolactones **59 c-g** (Scheme 25) [41].

Formation of α-(triorganosilyl)methylene β-, γ-, and δ-lactones

Cyclocarbonylation of acetylenic alcohols **60, 63,**
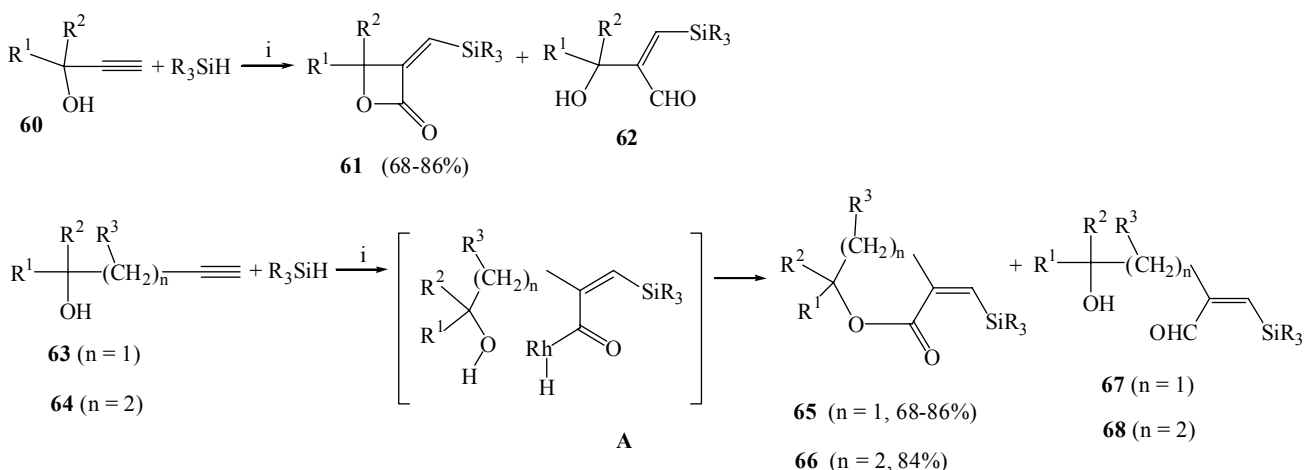
Scheme 25

a R = TMS (trimethylsilyl), R' = H; b R = TMS, R' = Me; c R = Me, R' = H;
d R = Et, R' = H; e R = Et, R' = Me; f R = t-Bu, R' = Me; g R = Ph, R' = Me;
i CO (1 atm), PdCl$_2$ (0.01 – 0.1 equiv.), CuCl$_2$ (3 equiv.), propylene oxide (5 equiv.),
MeC(OEt)$_3$ (0.4 equiv.), MeOH, room temp.

64 gives α-(triorganosilul)methylene β- **61**, γ- **65**, and δ- **66** lactones with the assistance of an appropriate base and Rh$_4$(CO)$_{12}$. Lactone formation depends on both steric and electronic has factors. In fact, the ratio of β-lactone **61** to 3-silylpropenal **62** was remarkably affected by the silane and base employed in the carbonylation of acetylenic alcohols **60**. Improvement of the selectivity for β-lactone was attained by the use of either a bulkier silane, as t-BuMe$_2$SiH, or stronger base, such as 1,8-diazabicyclo [5.4.0] undec-7-ene (DBU) [42] (Scheme 26). Carbonylation of **60** without of base, however, results in the formation of **62** selectively.

γ-Lactone **65** is derived from homopropargyl type alcohols **63** by a similar operation even more easily than **61** already with employment of Me$_2$PhSiH and Et$_3$N. This operation is also applicable to the synthesis of six-membered α-silylmethylene lactones **66**, although a combined use of t-BuMe$_2$SiH and Et$_3$N is required for the selective formation of δ-lactone **66**.

R^1, R^2 = H, Me, (CH$_2$)$_4$, (CH$_2$)$_5$, (CH$_2$)$_6$; R = Me, Ph, t-Bu, Et, i-Pr,
i CO (15-40 kg/sm^2), base (1 equiv. Et$_3$N, 0.1 equiv. DBU or
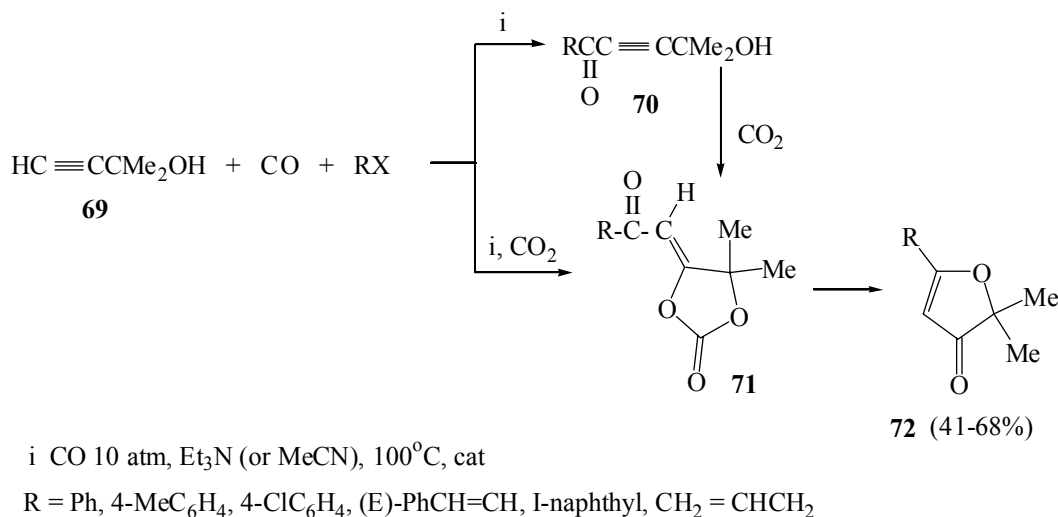DABCO – 1,4-diazabicyclo[2,2,2]octane, Rh$_4$(CO)$_{12}$ (0.001 equiv.) at 100°C in benzene.

Scheme 26

Intermediate **A** may be proposed as the common intermediate to give lactone and propenal derivatives.

Synthesis of 3(2H)-furanones

At catalysis of transition metals triphenylphosphyn complexes (Fe, Co, Ni, Ru, Rh, Pt, the best $PdCl_2(PPh_3)_2$) 3(2H)-furanones **72** are formed from 1,1-dimethylprop-2-ynol **69**, carbon monoxide and RX in the carbon dioxide atmosphere. Reaction mechanism includes intermediate producing of acetylenic ketone **70**, followed by the forming of the cyclic carbonate **71** from ketone and CO_2, that of decarboxylates quantitatively into furanone **72** [43] (Scheme 27). It was not possible to cyclize I-methylprop-2-ynol or prop-2-ynol by similar manner.

i CO 10 atm, Et₃N (or MeCN), 100°C, cat

R = Ph, 4-MeC₆H₄, 4-ClC₆H₄, (E)-PhCH=CH, I-naphthyl, CH₂ = CHCH₂
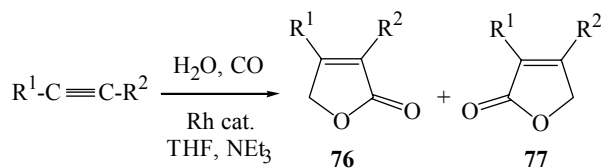
Scheme 27

Selective synthesis of furan-2(5H)-ones

The rhodium catalysed carbonylation of acetylenes in alcohols giving 5-alkoxyfuran-2-(5H)-ones in satisfactory yields has been reported [44,45].
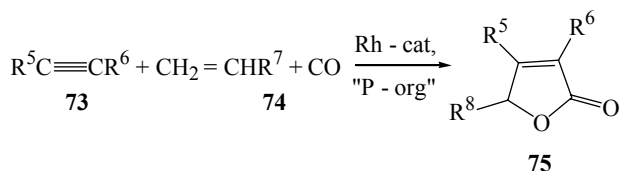
The reaction of acetylene gomologs **73** and alkenes **74** with CO in the presence of Rh-cat and organophosphoric compounds [PR'R²R³,P(OR')(OR²) OR³ or R¹R²P(CH₂)PR³R⁴, for R¹ – R⁴ = H, alkyl, n = 1-4] gives lactones **75** with high yield (Scheme 28) [46].

The general method of selective synthesis of fu- ran-2(5H)-ones **76** and **77** from acetylenes has been proposed, being in elaboration of lasts by water gas and carbon monoxide (100 atm) in THF containing triethylamine at 100°C in the presence of rhodium carbonyl cluster catalyst [47,48] (Scheme 29).
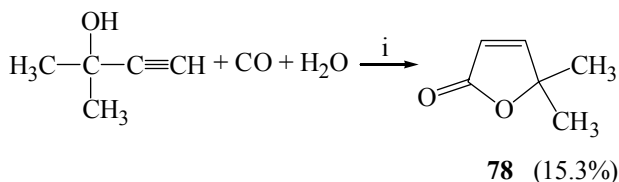

Scheme 29

The isomer ratio of the formed furanones **76** and **77** depends on electronic and steric nature of the substituents. As catalysts, rhodium carbonyl clusters such as $Rh_4(CO)_{12}$ and $Rh_6(CO)_{16}$ are the best among the tested transition metal complexes. Ruthenium carbonyls showed a very low activity, but cobalt and iron carbonyls were almost inactive for the present rection. The presence of amines such as diethylamine or triethylamine is essential for the selective synthe-

R⁵, R⁶ = H, Alkyl, Aryl, Silyl, Alkoxycarbonyl, Acyl
R⁷ = H, Hal, Alkyl, Alkoxycarbonyl, CN, Acyl
R⁸ = CH₂CH₂R⁷ or CHMeR⁷

Sheme 28

sis of furanones. The absence of amines resulted in a marked decrease in both catalytic activity and product selectivity.

Carbonylation of 2-methylbut-3-yn-2-ol catalyzed by $Co_2(CO)_8$ in benzene proceeds with low yield, but 100% selectivily giving 5,5-dimethylfuran-2(5H)-one **78** (Scheme 30) [49].

78 (15.3%)
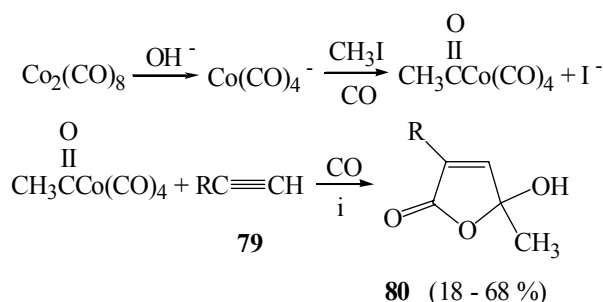
i 150°C, 100 atm, $Co_2(CO)_8$ (5 mol %) benzene.

Scheme 30

Synthesis of but-2-enolide

Alkynes **79** react smoothly with CO and CH_3J in a liquid-liquid two-phase system to yield regioselectivly the corresponding but-2-enolide **80**, most probably via the intermediate formation of acylcobalt complex (Scheme 31) [50,51].
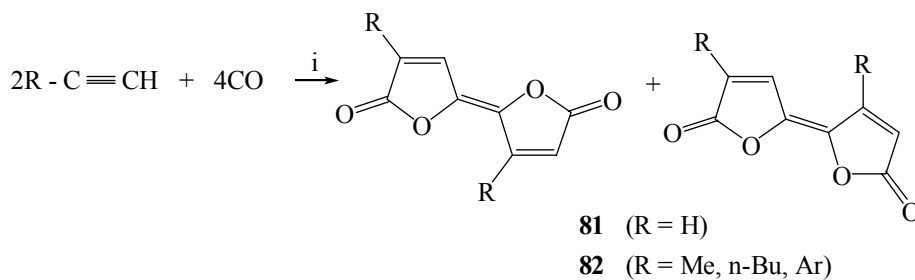

79

80 (18 - 68 %)

R = Ph, $(CH_2)_5CH$, 17-testosteronyl
i 5N NaOH/benzene, CTAB (Cetyltrimethylammonium bromide), room temp, 1 atm.

Scheme 31

When benzylbromide was used, no but-2-enolide

was formed, due to the fast hydrolysis of the acyl-cobalt intermediate prior to the alkyne complexation. Thus phenylacetic acid was the only product obtained. This inconvenience was circumvented by performing the reaction in the abcence of water in a solid-liquid system using a new kind of chelating agent, $N[(CH_2)_2O(CH_2)_2OCH_3]_3$ (TDA), wich has the same properties as a crown ether but without the toxicity and the work-up difficulties encountered with the macrocyclic catalysts [52] (Scheme 32).

40 %
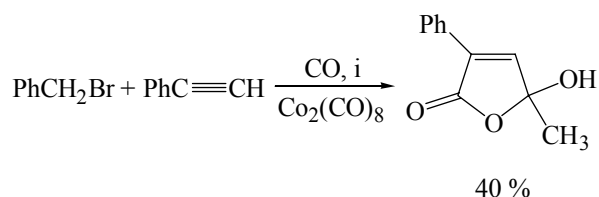
i $Co_2(CO)_8$ (30 mol %), NaOH, TDA (6 mol %), toluene, 60°C, 12 h, CO 1atm.

Scheme 32

### (E)-and (Z)-2,2-bifurylidene-5,5'-diones

Two groups independently announced the discovery of a catalytic reaction between CO and certain simple alkynes [53-56] (acetylene [53,54,56], propyne [53,55], hex-1-yne and some arylacetylenes [53]) that produces (E)- and (Z)- 2,2'-bifurylidene-5,5'-diones **81**, **82** (or bifurandiones [53], octatriene-diolides [54-56], 5-(oxofuran-2(5H)-ylidene)furan-2(5H)-ones according previous and systematic nomenclature) (Scheme 33).

The catalyst is $[CO_2(CO)_8]$, and the reaction has been run at temperatures around 100°C and CO pressures of 100-300 and up to 1000 bar. Polar aprotic solvents as MeCN, $MeNO_2$, acetone, N,N,N',N'-tetramethylurea, esters and ethers appear to be most suitable. The yields in acetone as the solvent have been improved by adding phosphines or phosphates [57]. In 1975, it was shown that Co complexes are

81 (R = H)
82 (R = Me, n-Bu, Ar)

i $Co_2(CO)_8$, 90-120°C, 100-300 bar

Scheme 33

intermediates in the catalytic reactions that leads to the bifurylidenediones [58,59]. In the course of the reinvestigation of this [Co₂(CO)₈]-catalized reaction between propyne and CO in acetone at 110°C and 170 bar five major products are produced: (E)-3,4'-dimethyl-2,2-bifurylidene-5,5-dione **83**, 3,5,8-tri-methylcoumarin **84**, 3a,7a-dihydro-2,4,7,7a-tetra-

methyl-1H-inden-1-one **85**, 2,6-dimethyl-5H-furo[3,2-b]pyran-5-one **86**, and 2,7-dimethyl-5H-furo[3,2-b]pyran-5-one **87** [60] (Scheme 34), and it has found that products distribution is strongly affected by CO pressure and propyne concentration. The structures of **85**, **86** and **88** were established by X-ray diffraction [60].
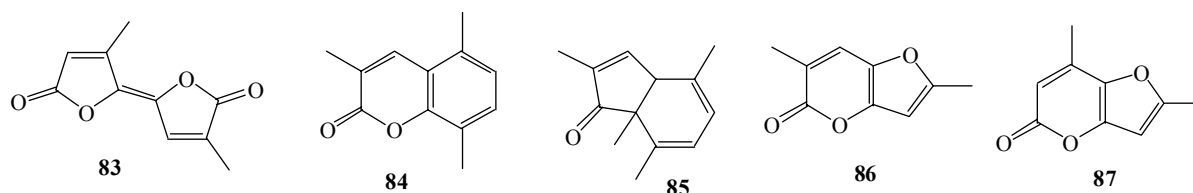
Scheme 34

γ-Butyrolactones synthesis

Alkynes **88 a-e** react with methyl iodide, bromo-pentacarbonylmanganese (or dimanganese decacar-bonyl), and carbon monoxide, under phase-transfer catalysis conditions, to give 2,4-disubstituted γ-buty-rolactones **89 a-e**. The reaction conditions are mild [35°C (1 atm)], and the process is a regiospecific one (Scheme 35) [61].
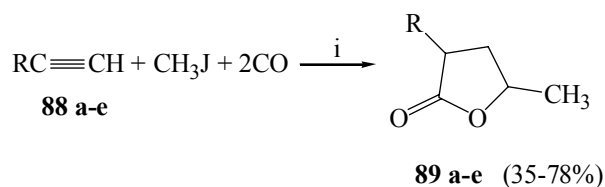

a R = Ph, b R = (CH₂)₂Ph, c R = n-Bu, d R = n-Hex, e R = p-CH₃C₆H₄
i Mn(CO)₅Br (1 equiv.), 5N NaOH, [PhCH₂NEt₃]⁺Cl⁻, CH₂Cl₂, 35°C, 1 atm CO

Scheme 35

## Anhydrides synthesis

The carbonylation of propargyl alcohol in ben-zene gives only resinous substances, but substituted propargyl alcohols such as 1-pentyn-3-ol **90a**, 2-methyl-3-butyn-2-ol **90b** and 1-ethynyl-cyclohexanol **90c** give substituted itaconic acid anhydrides selec-tively. The products are anhydrides of propylidene-succinic acid **88** (19%), teraconic acid **89** (42%) and cyclohexylidenesuccinic acid **90** (45%) (Scheme 36) [61].
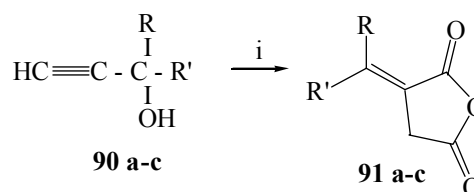
a R = H, R' = Et;
b R = R' = Me;
**c** R - R' = (CH₂)₅
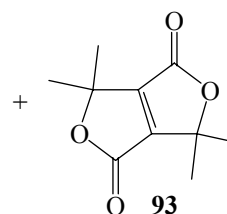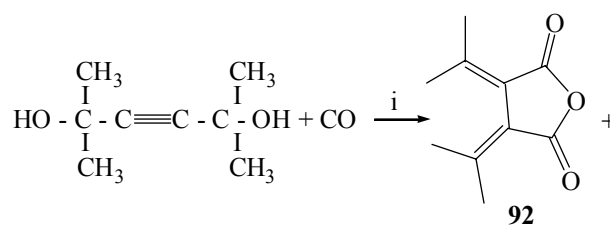
i PdCl₂ (10-20%), benzene, CO (100 atm), 100°C.

Scheme 36

The carbonylation of 2,5-dimethyl-3-hexyn-2,5-diol in benzene proceeds smoothly to give the anhy-dride of diisopropylidenesuccinic acid **92** (49%), as a main product accompanied by bis(1-hydroxy-1-methylethyl)furanic acid dilactone **93** (14%) (Scheme 36) [62].

The reaction of alkynes **94** with CO/O₂ in diox-

ane gives anhydrides **95** (Scheme 37) [63].

$$RC \equiv CH + CO + O_2 \xrightarrow{i}$$

94

95 (13-63%)
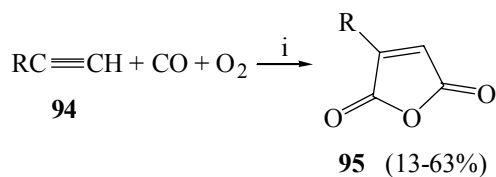
R = Ph; 4-MeC₆H₄; 4-ClC₆H₄; t-Bu, Hex, C₅H₄CH(OH)

i   Pd(OAc)₂/HQCl/NPMoV; MeSO₃H, 25°C, 15h.

Scheme 37

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