SELECTIVE PALLADIUM-CATALYZED CARBON-CARBON FORMING REACTIONS AND THEIR APPLICATION IN NATURAL PRODUCT SYNTHESIS

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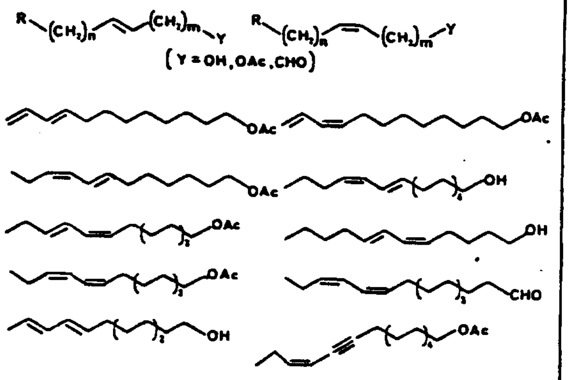
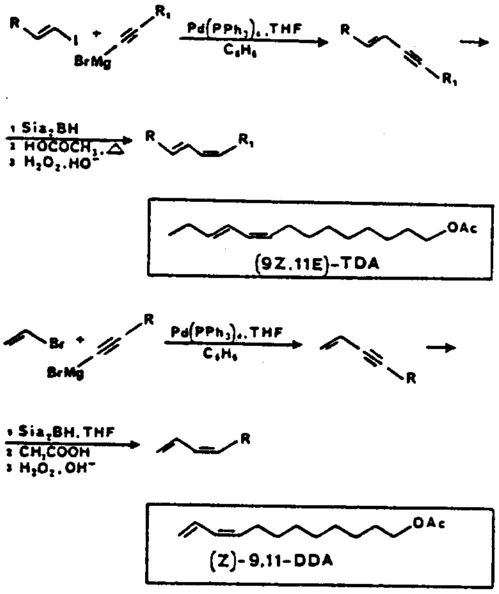
MONOUNSATURATED AND CONJUGATED POLYUNSATURATED SEX PHEROMONE COMPONENTS OF LEPIDOPTERA



(Y = OH, OAc, CHO)

SYNTHESIS OF CONJUGATED DIENIC INSECT SEX PHEROMONES



Tetrahedron (1981) ; Synthesis (1981)

H.P.Dang, G.Linstrumelle (1978)

SYNTHESES BY PALLADIUM-CATALYZED REACTIONS

- Terminal 3-yn-1-enes
- Symmetrically or unsymmetrically substituted diaryl or diheteroaryl acetylenes
- Symmetrically disubstituted 1,3-diynes
- 3-Alkyl-4-(1-alkynyl)-hexa-1,5-diyn-3-enes
- Functionalized π-excessive heteropolyaromatic compounds
- Functionalized conjugated internal (E)-enynes[a,b]
- Functionalized terminal (Z)- and (E)-1,3-dienes[a]
- (Z)- or (E)-1-ethoxycarbonyl-3-yn-1-enes[a]
- (Z)- and (E)-alkenes and 1,ω-dienes[a]
- (E)-alkenes and (E)-1,ω-dienes[b]
- (E)-1,5-diyn-3-enes[b]
- (E)-1-bromo-3-yn-1-enes[b]

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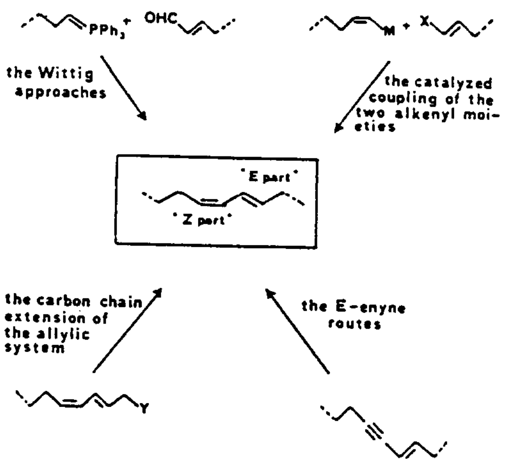
a) stereospecific synthesis

b) stereoselective synthesis

SOME APPROACHES TO THE SYNTHESIS OF CONJUGATED (E,Z) OR (Z,E) DIENIC SEX PHEROMONE COMPONENTS



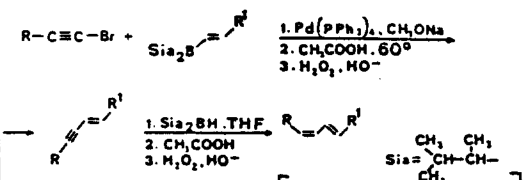
the Wittig approaches

the catalyzed coupling of the two alkenyl moieties

the carbon chain extension of the allylic system

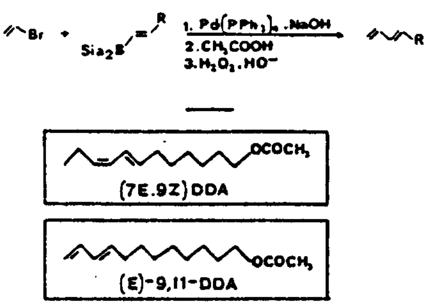
the E-enyne routes

SCHEME 1

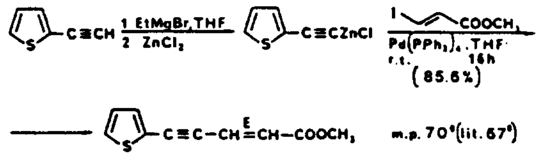


[A. Suzuki (1979); R. Rossi (1981)]

SCHEME 2

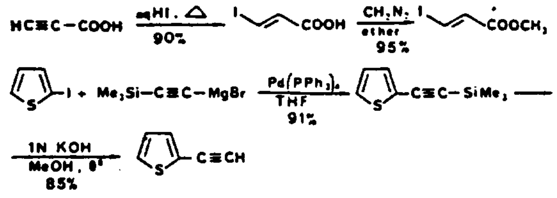


SYNTHESIS OF METHYL (E)-5-(2-THIENYL)-2-PENTEN-4-YNOATE FROM METHYL (E)-3-IODO-ACRYLATE

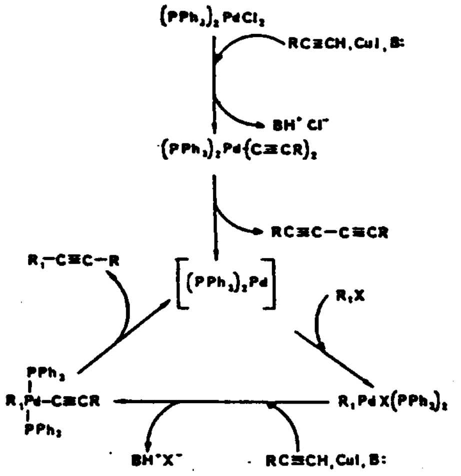


[λ_{max} (ε)(THF): 335(24360), 325(25860), 265 nm(11540)
M.S. 192 (M^+), 177, 161, 133, 121, 89, 74, 63, 45.]

This compound was isolated from *Anthemis fuscata* Brot.

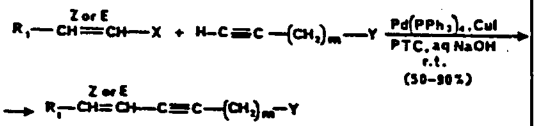


CATALYTIC CYCLE FOR THE Pd–Cu CATALYZED REACTION OF 1-ALKYNES WITH ALKENYL OR ARYL HALIDES



K. Sonagashira, 1975 : B = Et_2NH, Et_3N in C_6H_6
R. Rossi, 1982 : B = aq NaOH + PTC

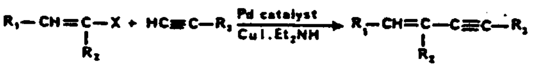
STEREOSPECIFIC SYNTHESIS OF 1,3-ENYNES BY Pd–Cu CATALYZED REACTION OF 1-ALKYNES WITH (Z)- OR (E)-1-HALO-1-ALKENES



$$R_1{-}\overset{Z\ \text{or}\ E}{CH{=}CH}{-}X + H{-}C{\equiv}C{-}(CH_2)_m{-}Y \xrightarrow[\substack{PTC,\ aq\ NaOH\\ r.t.\\ (50-90\%)}]{Pd(PPh_3)_4,\ CuI} R_1{-}\overset{Z\ \text{or}\ E}{CH{=}CH}{-}C{\equiv}C{-}(CH_2)_m{-}Y$$

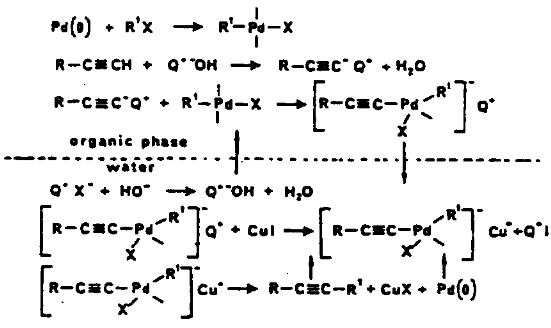
[X = I, Br ; Y = H, OH, $CH(OEt)_2$; m = 1—10]

Tetrahedron (1982)(1983)



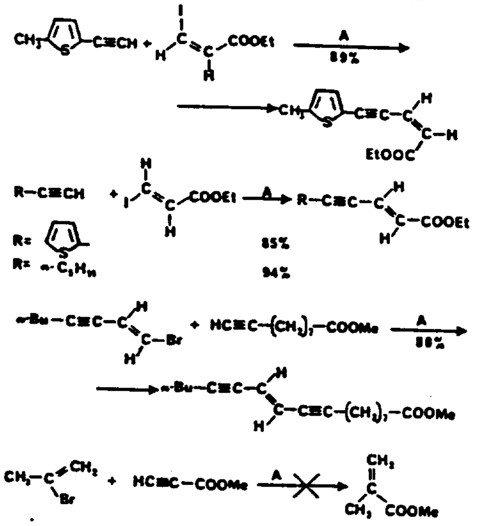
$$R_1{-}CH{=}\underset{\substack{|\\ R_2}}{C}{-}X + HC{\equiv}C{-}R_3 \xrightarrow[CuI,\ Et_2NH]{Pd\ catalyst} R_1{-}CH{=}\underset{\substack{|\\ R_2}}{C}{-}C{\equiv}C{-}R_3$$

K. Sonagashira (1975)



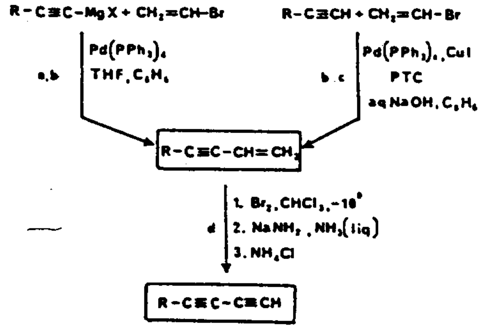
Pheromone	**Insect**
 (3Z,5E)–TDDA	Prionoxystus robiniae
 (3Z,5Z)–TDD acid	Attagenus elongatulus
 (Z)–9,11–DDA	Diparopsis castanea
 (5Z,7E)–DDol	Malacosoma disstria
 (Z)–13–HDDenynylA	Thaumetopoea pityocampa
 (7E,9Z)–DDA	Lobesia botrana
 (E)–9,11–DDA	D. castanea

SYNTHESIS OF 1,3-ENYNES CONTAINING ALKOXY CARBONYL GROUPS BY AN IMPROVED SONAGASHIRA'S PROCEDURE



A = Pd(PPh$_3$)$_4$, CuI; Et$_3$N, C$_6$H$_6$; room temp.

PREPARATION OF 3-YN-1-ENES AND TERMINAL CONJUGATED DIYNES BY PALLADIUM-CATALYZED ALKYNYLATION REACTIONS



(R=alkyl, heteroaryl)

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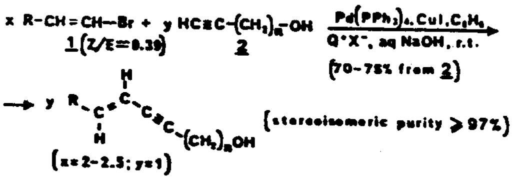
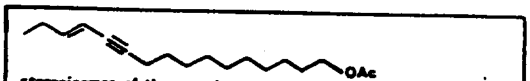
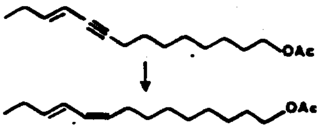
a) Rossi et al., Synthesis, 359 (1981)
b) Rossi, Carpita, Lezzi, Tetrahedron, 40, 2773 (1984)
c) Rossi et al., ibidem, 38, 631 (1982)
d) Negishi et al., J. Org. Chem. 49, 2629 (1984)

PALLADIUM-CATALYZED DIASTEREOSELECTIVE SYNTHESIS OF INTERNAL CONJUGATED (E)-ENYNES





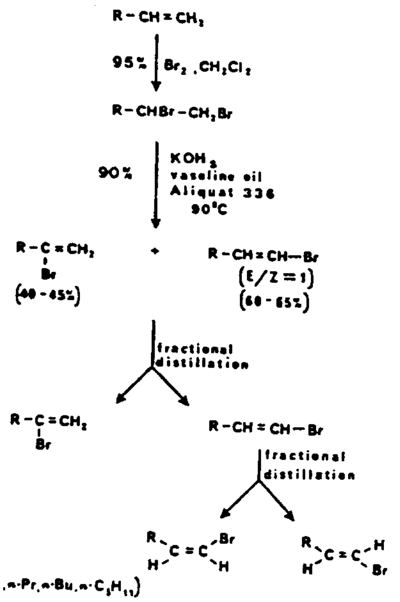
stereoisomer of the sex pheromone of Thaumetopea pityocampa



main sex pheromone component of Spodoptera litteralis

(Rossi, Carpita, Piccardi, 1983)

PREPARATION OF 1-BROMO-1-ALKENES

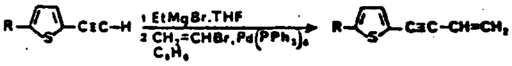


(R = Me, Et, n-Pr, n-Bu, n-C$_5$H$_{11}$)

(Rossi, Carpita, Piccardi, 1983)

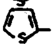
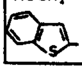
SYNTHESIS OF NATURALLY-OCCURRING ACETYLENIC THIOPHENS AND RELATED COMPOUNDS

a)



R= 2-thienyl 93% yield
R= phenyl 90%

b) $R^1-C\equiv CH + R^2-X \xrightarrow[Q^+X^-,\ 2.5N\ NaOH,\ r.t.]{Pd(PPh_3)_4,\ CuI,\ C_6H_6} R^1-C\equiv C-R^2$ (54–99%)

R^1	R^2	X
		I
$HO-(CH_2)_n-$		I
	$CH_2=CH-$	Br
	$CH_2=CH-$	Br
$HOCH_2-$		I
$(C_2H_5O)_2CH-$		I
$HOCH_2-$		Br
$HOCH_2-$		Br
	$HO-(CH_2)_2-$	I

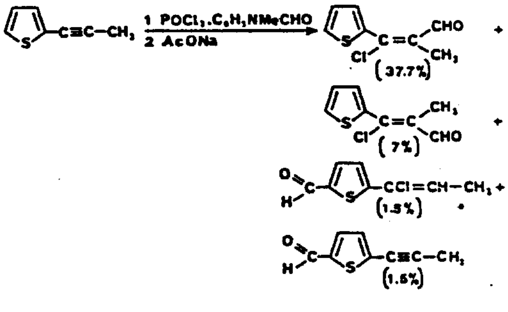
Tetrahedron, 40, 2773 (1984).

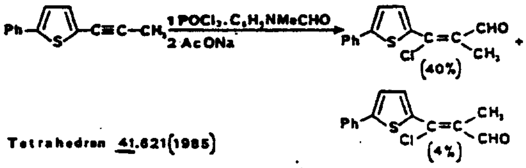
NATURALLY-OCCURRING ACETYLENIC COMPOUNDS AND DERIVATIVES

$HC\equiv C-CH_3 + Het-I \xrightarrow[Q^+X^-,\ 2.5N\ NaOH]{Pd(PPh_3)_4,\ CuI,\ C_6H_6} Het-C\equiv C-CH_3$

Het =  (93%)

Het =  (80%)





Tetrahedron 41, 621 (1985)

CHEMOSELECTIVITY OF THE PALLADIUM CATALYZED ARYLATION OF 1,ω-ALKYNOLS

$Ar-X + HC\equiv C-(CH_2)_n-OH \xrightarrow[PTC,\ aq\ NaOH,\ r.t.]{Pd(PPh_3)_4,\ CuI} Ar-C\equiv C-(CH_2)_nOH$

(X=Br; I)

54–98%

Significant Pd-assisted transfer hydrogenation of aryl halides is not observed.

$Ar-Br + R-CH_2OH \xrightarrow[Aliquat-336,\ 70^\circ]{aq\ NaOH,\ PdCl_2(PPh_3)_2} ArH + R-CHO$

[Zoran and Sasson, J. Mol. Catal., 27, 349 (1984)]

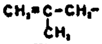
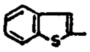
BIOLOGICAL PROPERTIES OF SOME THIOPHENE DERIVATIVES

- Phototoxicity against microorganisms (e.g. *Saccharomyces cerevisiae*, *Bacillus subtilis*, *Escherichia coli*, *Candida albicans*, *Streptococcus faecalis*, *S. albus*).
- Photo-enhanced activity against fungi, insect larvae and eggs, nematodes, human erythocites.
- Herbicidal properties.
- Seed-germination inhibitors.

Photobiocidal thiophenes have great ecological importance as protective chemicals in nature.

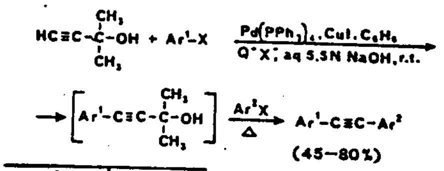
Palladium-catalyzed synthesis of thiophene acetylenic derivatives (1) by coupling of 1-alkynyltrimethylsilanes (5) with organic halides (2).

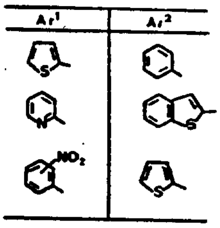
$$\underset{\underline{5}}{(CH_3)_3Si-C\equiv C-R_2} + \underset{\underline{2}}{R_1-J} \xrightarrow[BnEt_3N^+Cl^-,\ aq\ 2.5N\ NaOH]{(PPh_3)_4Pd,\ CuI,\ C_6H_6,\ 40^{b}} \underset{\underline{1}}{R_1-C\equiv C-R_2}$$

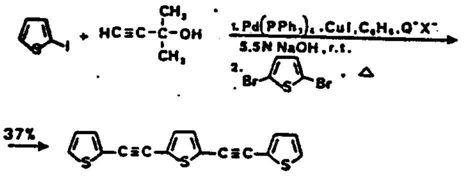
Organic halide (2)	R_1	1-Alkynyltrimethylsilane (5)	R_2	Reaction time (h)	(5)/(2) molar ratio	Product (1)	Isolated yield %
2a		5c		40	1	1n	68
2a		5d	 $CH_2=C(CH_3)-CH_2-$	36	1.1	1o	60
2f		5c		40	1.2	1p	65

(Rossi, Carpita, Lezzi, 1984)

ONE-POT PALLADIUM-CATALYZED SYNTHESIS OF DIARYLALKYNES





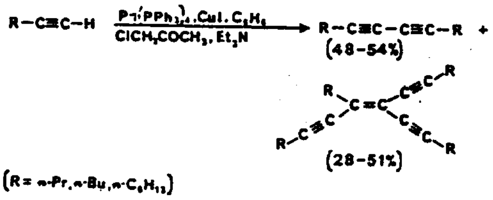


Synthesis, 1984

A PALLADIUM-PROMOTED ROUTE TO 3-ALKYL-4-(1-ALKYNYL)-HEXA-1,5-DIYN-3-ENES AND/OR 1,3-DIYNES

$$R{-}C{\equiv}C{-}H \xrightarrow[\substack{ClCH_2COCH_3\ (1\ equiv)\\ Et_3N\ (2\ equiv)}]{Pd(PPh_3)_4,\ CuI,\ C_6H_6} R{-}C{\equiv}C{-}C{\equiv}C{-}R$$

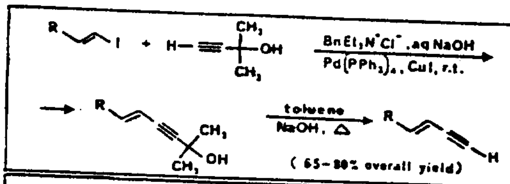
R	yield %
2-thienyl	87
phenyl	94
t-butyl	98

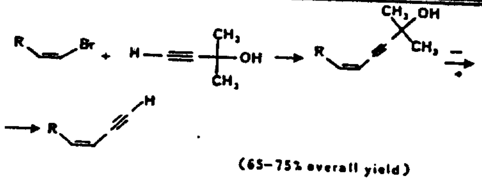


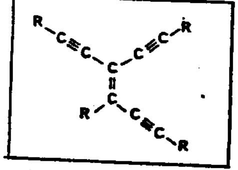
($R = n\text{-}Pr, n\text{-}Bu, n\text{-}C_6H_{13}$)

Tetrahedron Lett., 26, 523 (1985)
ESOC IV

STEREOSPECIFIC SYNTHESIS OF 3-EN-1-YNES BY Pd-CATALYZED REACTION OF 1-HALO-1-ALKENES WITH 2-METHYL-3-BUTYN-2-OL

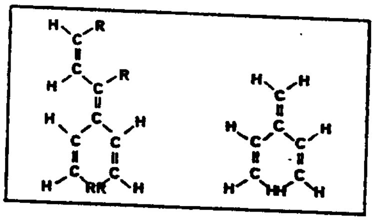






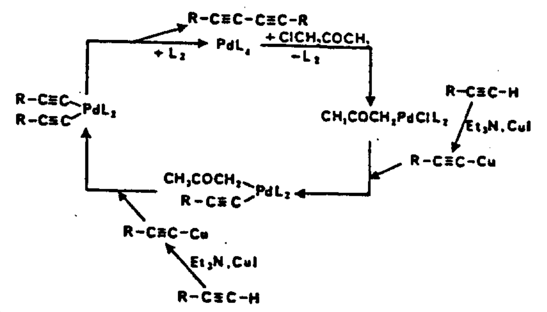
These compounds are characterized by a previously undescribed chromophore system ($R = C_6H_{13}$: $\lambda_{max}(\varepsilon)$ 303 (2370), 292 (24900), 285 (23350), 275 (16500), 250 (5970), 236 (6600), 227 nm (6700).).

They are precursors to some dendralenes, a group of cross-conjugated polyolefins derived from 3-methylene-1,4-pentadiene.



These substances are novel substrates for addition and rearrangement reactions, and model compounds for spectroscopic studies.

INTERPETATION



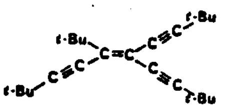
<u>Results consistent with the hypothesis that aliphatic 1,3-diynes represent intermediates in the formation of entriynes</u>:

$$n\text{-}Pr{-}C{\equiv}CH + t\text{-}Bu{-}C{\equiv}CH \xrightarrow[Et_3N,\ CH_3COCH_2Cl]{Pd(PPh_3)_4,\ CuI}$$

10 of the 19 expected products were obtained. Three of these compounds were:

$n\text{-}Pr{-}C{\equiv}C{-}C{\equiv}C{-}n\text{-}Pr$, $t\text{-}Bu{-}C{\equiv}C{-}C{\equiv}C{-}t\text{-}Bu$, $t\text{-}Bu{-}C{\equiv}C{-}C{\equiv}C{-}n\text{-}Pr$

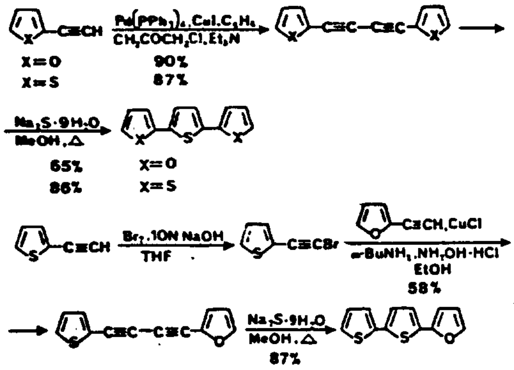
The other 7 compounds had mass spectra consistent with 3-alkyl-4-(1-alkynyl)-hexa-1,5-diyn-3-enes containing either n-Pr or t-Bu moieties. These compounds did not include



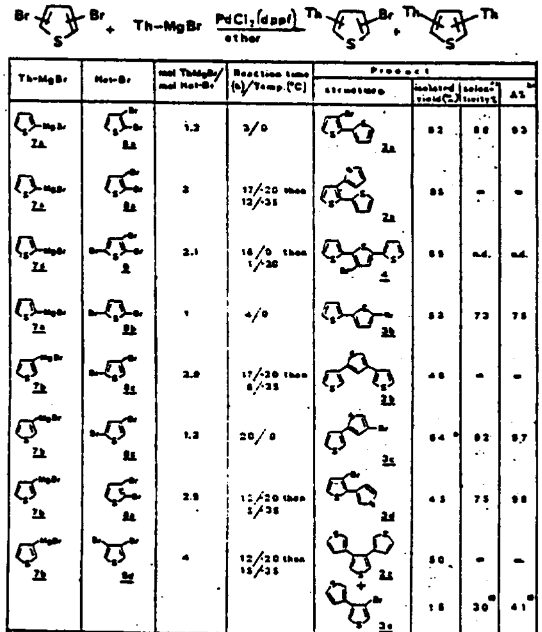
SYNTHESIS OF π-EXCESSIVE HETEROPOLYAROMATIC COMPOUNDS

X=Y=Z=S
X=Y=S , Z=O
X=Z=S , Y=O
X=Z=O , Y=S

X=Y=S
X=O , Y=S
X=S , Y=O



Tetrahedron 41,1919(1985)
ESOC IV



Th-MgBr	Het-Br	mol ThMgBr/ mol Het-Br	Reaction time (h)/Temp.(°C)	Product structure	isolated yield(%)	selectivity%[a]	A%[b]
7a	8a	1.2	3/0	3a	82	88	93
7a	8a	2	17/-20 then 12/-35	2a	85	–	–
7a	9	2.1	16/0 then 1/-20	4	81	n.d.	n.d.
7a	9b	1	4/0	3b	83	73	78
7b	9c	2.0	17/-20 then 8/-35	2b	46	–	–
7b	8c	1.3	20/0	3c	64	82	87
7b	8d	2.5	12/-20 then 2/-35	3d	43	75	98
7b	9d	4	12/-20 then 15/-35	2c	50	–	–
				3e	18	30[c]	41[c]

a) Selectivity % = [illegible]

b) A% = [illegible]

c) [illegible]

Gazz.Chim.Ital.1985
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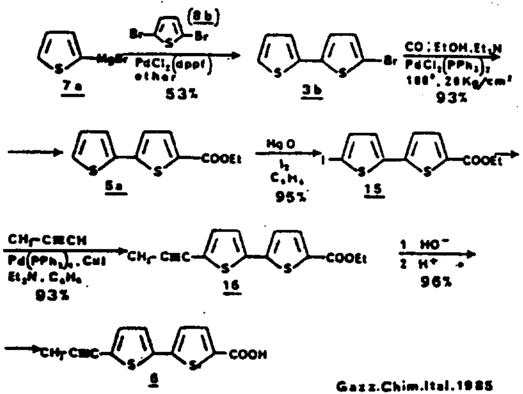
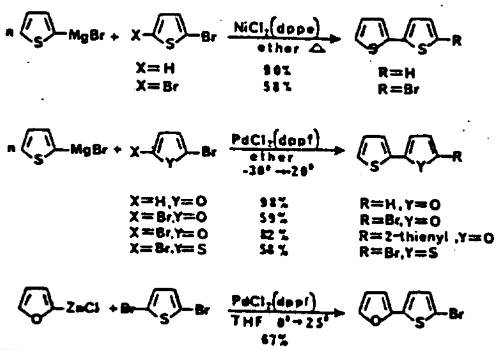
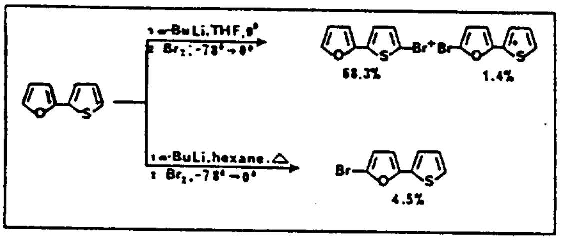
SYNTHESIS OF ARCTIC ACID



Gazz.Chim.Ital.1985

HETEROARYLATION OF HETEROARENE DIHALIDES



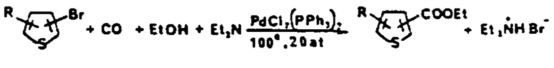


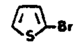
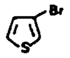
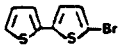
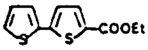
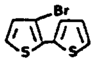
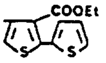
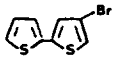
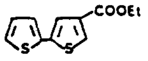
dppe = $Ph_2PCH_2CH_2PPh_2$

dppf =

Tetrahedron,41,1919(1985)

ETHOXYCARBONYLATION OF SOME THIENYL BROMIDES



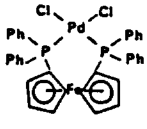
Heteroaryl bromide	Catalyst (mole%)	Reaction time (h)	Product	Isolated yield (%)
	1.2	20		96
	1.2	21		55
	3.0	10		93
	2.0	15		48
	3.0	22		87

Gazz.Chim.Ital. 1985
ESOC I

STEREOSPECIFIC SYNTHESIS OF (Z)- AND (E)-DISUBSTITUTED ALKENES

$$\overset{Z\ or\ E}{R-CH=CH-X} + R_1-MgX \xrightarrow[\text{ether or THF}\ 0°-35°]{PdCl_2(dppf)} \overset{Z\ or\ E}{R-CH=CH-R_1}$$

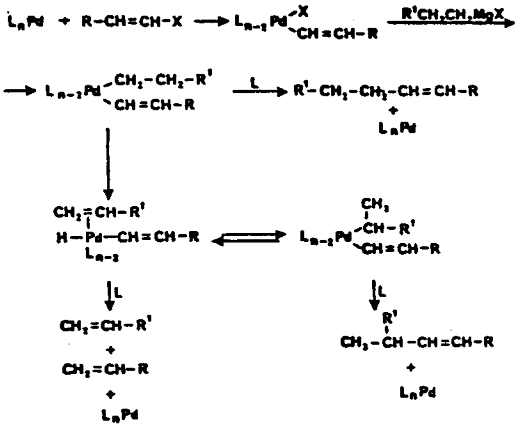
Carpita,Lezzi,Rossi (1985)



[Hayashi et al. J. Am.Chem.Soc.106,158(1984)]

This complex promotes the stereospecific cross-coupling reaction more efficiently than $Pd(PPh_3)_4$.
Isomerization and/or reduction of the alkyl Grignard reagent or homocoupling of the alkenyl halide are minimized.
These side-reactions occur more easily in THF than in ether.

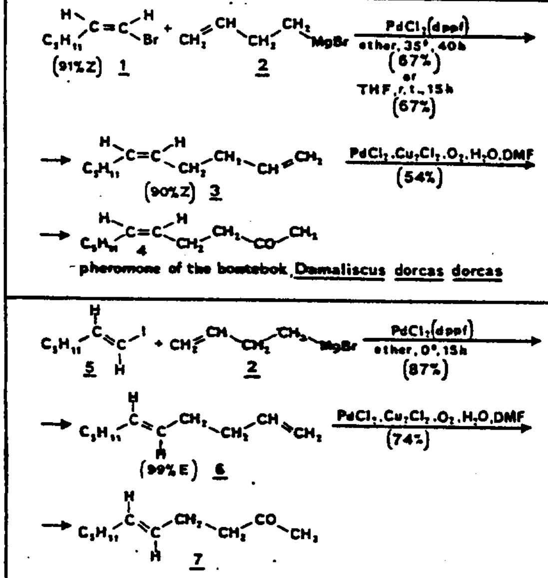
PALLADIUM-CATALYZED COUPLING REACTIONS BETWEEN ALKYLMAGNESIUM HALIDES AND 1-ALKENYL HALIDES



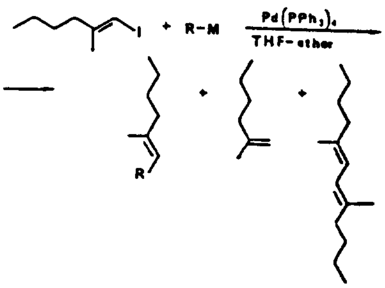
The Pd complex with the dppf ligand is capable of making the reductive elimination of the coupling product much faster than the β-elimination.

dppf =

SCHEME



pheromone of the bontebok, Damaliscus dorcas dorcas

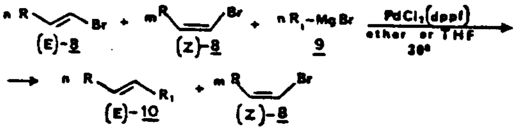


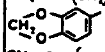
RM	yield %		
n-BuMgBr	25	51	8
n-BuZnCl	72	2	8
MgBr	21	37	11
ZnCl	81	trace	8

[E.Negishi et al., J. Am.Chem.Soc. 102, 3298(1980)]

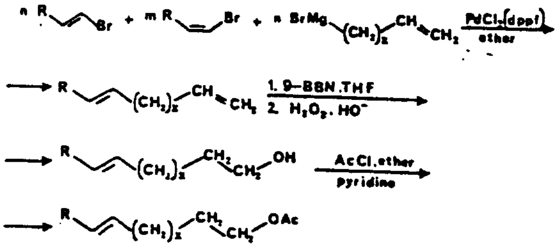
DIASTEREOSELECTIVE Pd-CATALYZED COUPLING REACTION BETWEEN GRIGNARD REAGENTS AND STEREOISOMERIC MIXTURES OF 1-BROMO-1-ALKENES:

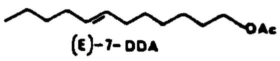
Synthesis of (E)-alkenes and (E)-1,ω-dienes.



Reagents				Product : (E)-10		
(E)/(Z)-8		9	8/9 molar ratio	stereoisomeric purity %	yield %	compound
R	E/Z	R₁				
Et	66/34	$CH_3-(CH_2)_2-$	1.49	98.3	61	10a
Et	62.5/37.5	$CH_2=CH-(CH_2)_4-$	1.61	98.0	79.5	10b
Me	27/73		3.54	95.5	65	10c
n-Bu	60.6/39.4	$CH_2=CH-(CH_2)_4-$	1.66	98.5	67	10d
Et	61.5/38.5	$CH_2=CH-(CH_2)_3-$	1.58	>99	57	10e

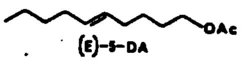
STEREOSELECTIVE SYNTHESIS OF (E)-ω-ALKEN-1-OLS AND/OR ACETATES WICH ARE INSECT SEX PHEROMONE COMPONENTS





(E)-7-DDA

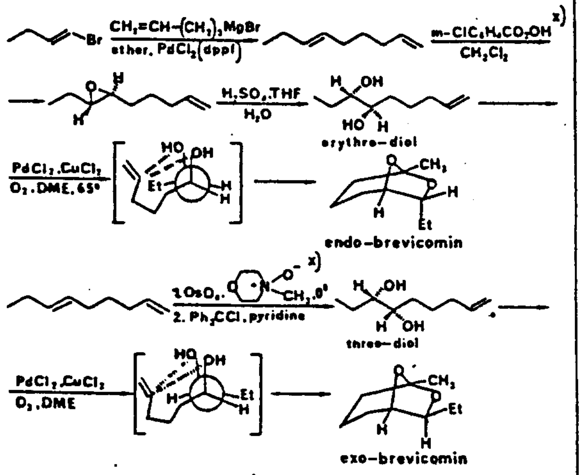
Argyroploce leucotreta



(E)-5-DA

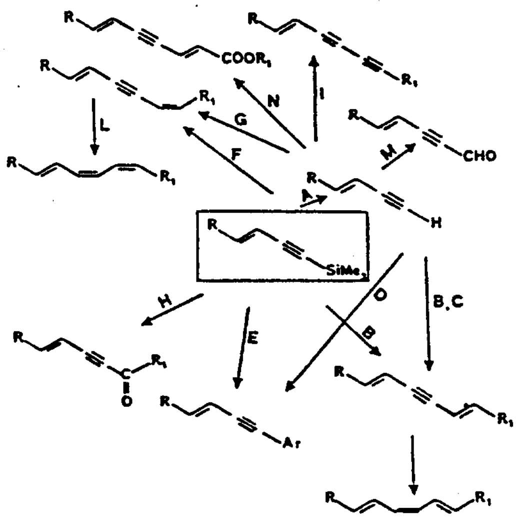
Anarsia lineatella

FORMAL SYNTHESIS OF BRIDGED RING-KETAL PHEROMONES :(±)-ENDO-BREVICOMIN AND (±)-EXO-BREVICOMIN

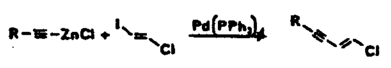


x)R.Grigg et al. (J.Chem.Soc.Perkin Trans. I, 1643(1984)) used a 80:20 mixture of (E)- and (Z)-1,6-nonadiene.

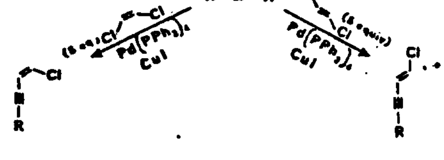
SOME POSSIBLE APPLICATIONS



A) KOH,CH_3OH ,or KF $2H_2O$.DMF ;B) R_1–CH $\overset{E}{=}$ CH–X ,Pd(0),CuI,Et_3N,C_6H_6; C) R_1–CH $\overset{E}{=}$ CH–X, Pd(0),CuI,PTC,$NaOH_{aq}$; D) ArX,Pd(0),CuI,Et_3N,C_6H_6; E) ArX,Pd(0),CuI,PTC,$NaOH_{aq}$, △ ; F) R_1–CH $\overset{Z}{=}$ CH–X ,Pd(0),CuI,PTC,$NaOH_{aq}$, △ ; G) R_1–CH $\overset{Z}{=}$ CH–X,Pd(0),CuI, Et_3N,C_6H_6 ; H) R_1–COCl,$TiCl_4$,CH_2Cl_2,-78°; I) R_1–C≡C–Br,CuCl,NH_2OH HCl,n-$BuNH_2$, EtOH ; L) Sia_2BH,THF,then AcOH,△,then H_2O_2,HO^-; L) EtMgBr,THF,then Me_2N–CHO ; N) I– CH $\overset{E}{=}$ CH–$COOR_1$,Pd(0),CuI,Et_3N,C_6H_6.

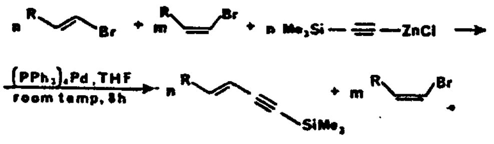


Negishi et al. 1983



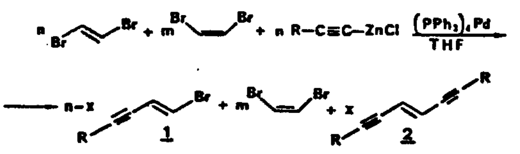
Ratovelomanana and Linstrumelle,1981

DIASTEREOSELECTIVE SYNTHESIS OF (E)-1-TRIMETHYLSILYL-3-EN-1-YNES



stereoisomeric purity ≥ 97.5%

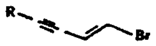
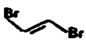
DIASTEREOSELECTIVE SYNTHESIS OF (E)-1-BROMO-3-YN-1-ENES



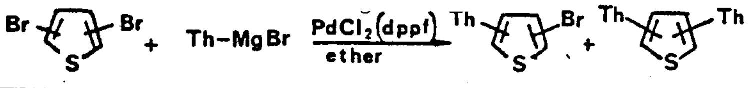
COMPOUND	ISOLATED YIELD (%) 1	ISOLATED YIELD (%) 2
R = n-C_4H_9	31.5	17
R = n-C_5H_{11}	42.1	18.6

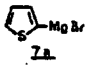
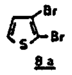
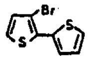
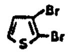
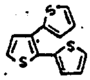
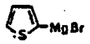
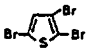
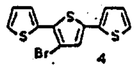
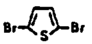
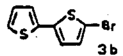
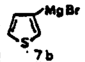
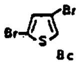
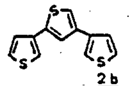
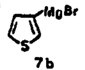
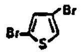
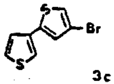
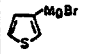
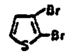
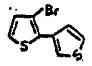
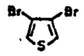
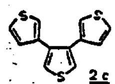
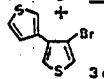
The reaction mixtures also contained small amounts of 1,3-diynes R-C≡C-C≡C-R.

REACTIVITY OF SOME BROMINATED SPECIES

The very high degree of diastereoselectivity of these Pd-catalyzed mono- and dialkynylation reactions indicates clearly that the reactivity of  is higher than that of  and that one of  is higher than that of . Moreover,  is more reactive than .

Possible explanation: (E)- and (Z)-1,2-dibromoethylene presumably exhibit different reactivity toward $(PPh_3)_4Pd$. In short, (E)-1,2-dibromoethylene probably undergoes the oxidative addition more easily than the corresponding (Z)-stereoisomer.



Th-MgBr	Het-Br	mol ThMgBr/ mol Het-Br	Reaction time (h)/Temp.(°C)	Product			
				structure	isolated yield(%)	selectivity%[a)]	A%[b)]
 7a	 8a	1.2	3/0	 3a	82	88	93
 7a	 8a	3	17/20 then 12/35	 2a	85	–	–
 7a	 9	2.1	16/0 then 1/20	 4	89	n.d.	n.d.
 7a	 8b	1	4/0	 3b	53	73	75
 7b	 8c	2.0	17/20 then 6/35	 2b	48	–	–
 7b	 8c	1.3	20/0	 3c	64	92	97
 7b	 8a	2.9	12/20 then 5/35	 3d	45	75	98
 7b	 8d	4	12/20 then 15/35	 2c +	50	–	–
				 3e	16	30[c)]	41[c)]

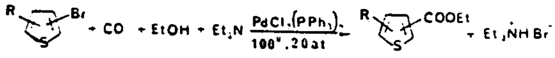
a) Selectivity % = [bromobithienyl]/[reacted thienyl dibromide] x 100. These values, based on GLC data, are referred to final concentrations of the considered compounds.

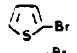
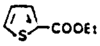
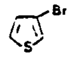
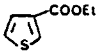
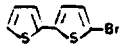
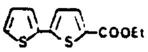
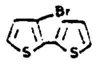
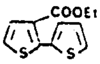
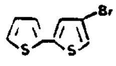
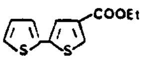
b) A% = [bromobithienyl]/{[bromobithienyl]+[diheteroarylated product]} x 100.

c) The selectivity after 1 hr at room temperature and 1 h at reflux was 57 %. The corresponding value of A was 81 %.

Gazz.Chim.Ital.1985
ESOC IV

ETHOXYCARBONYLATION OF SOME THIENYL BROMIDES



Heteroaryl bromide	Catalyst (mole%)	Reaction time (h)	Product	Isolated yield (%)
	1.2	20		96
	1.2	21		55
	3.0	10		93
	2.0	15		48
	3.0	22		87

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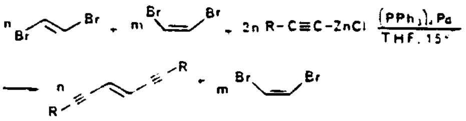
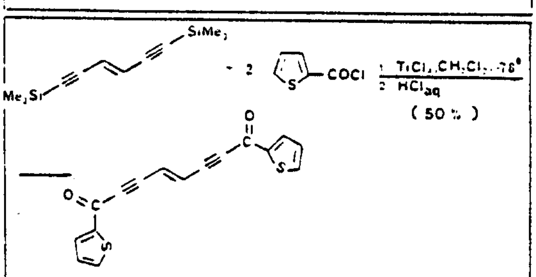
ESOC IV

DIASTEREOSELECTIVE COUPLING REACTION BETWEEN (E)/(Z)-1,2-DIBROMOETHYLENE AND 1-ALKYNYLZINC CHLORIDES: Synthesis of (E)-1,5-diyn-3-enes.

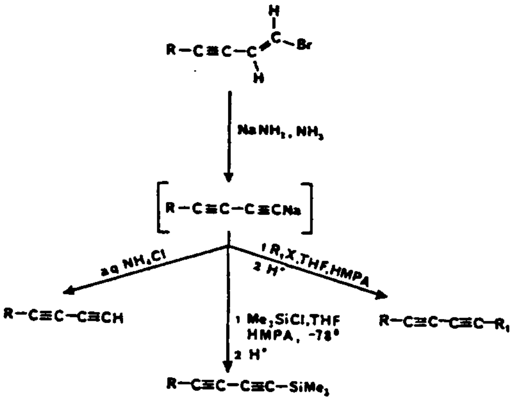


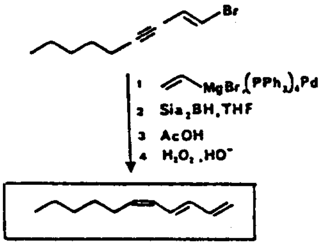
COMPOUND	YIELD (%)
R = n-C_4H_9	84.3
R = n-C_5H_{11}	99
R = C_6H_5	82.6
R = $Si(CH_3)_3$	87

Stereoisomeric purity: 100%

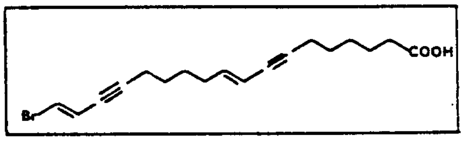


CONVERSION OF (E)-1-BROMO-3-YN-1-ENES INTO CONJUGATED DIYNES

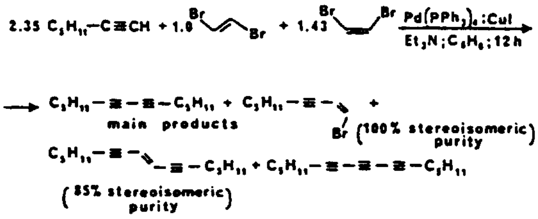


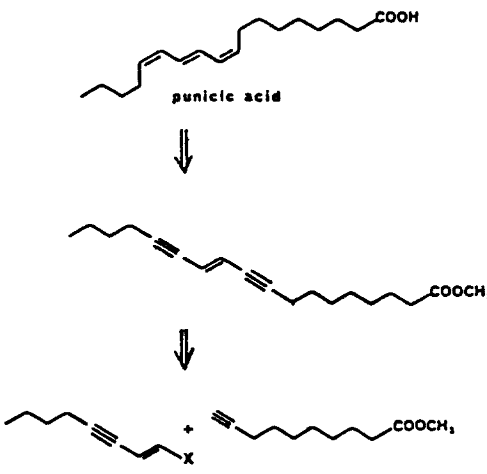


Compound isolated from the essential oil of _Galbanum_ (Y-R. Naves, 1967) and the Hawaiian seaweed _Dictyopteris_ (R.E.Moore, 1974)



Compound isolated from the marine sponge _Xetospongia testudinaria_ (R.J.Quinn, D.J.Tucker, 1985)





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