Tetrahedron Letters,Vol.27,No.22,pp 2529-2532,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

DIASTEREOSELECTIVE SYNTHESIS OF (E)-ALKENES AND (E)-1,ω-DIENES STARTING FROM DIASTEREOISOMERIC MIXTURES OF 1-BROMO-1-ALKENES : NEW SYNTHESES OF MONOUNSATURATED OR BRIDGED RING-KETAL NATURALLY OCCURRING SUBSTANCES.

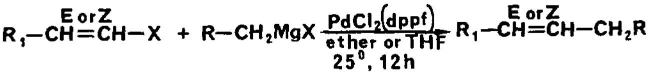
Renzo Rossi and Adriano Carpita

Dipartimento di Chimica e Chimica Industriale-Università di Pisa- via
Risorgimento 35 - 56100 PISA -ITALY

Summary: The $PdCl_2$*(dppf)-catalyzed cross-coupling reaction between diastereoisomeric mixtures of 1-bromo-1-alkenes which contain n equiv. of (E)-stereoisomers and n equiv. of Grignard reagents allows to obtain (E)-alkenes or (E)-1,ω-dienes having 95.5-99% stereoisomeric purity in satisfactory yields.Such compounds are useful precursors to several naturally occurring substances.*

The cross-coupling of alkenyl halides with primary alkyl Grignard reagents which possess β-hydrogen atoms can be efficiently performed using dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium, [$PdCl_2$(dppf)], as catalyst.[1,2]

Recently we employed this catalyzed cross-coupling reaction to prepare,stereospecifically and in satisfactory yields,starting from (Z)-1-bromo- and (E)-1-iodo-1-alkenes,(Z)- and (E)-alkenes,respectively[3],some of which are precursors to naturally occurring substances.

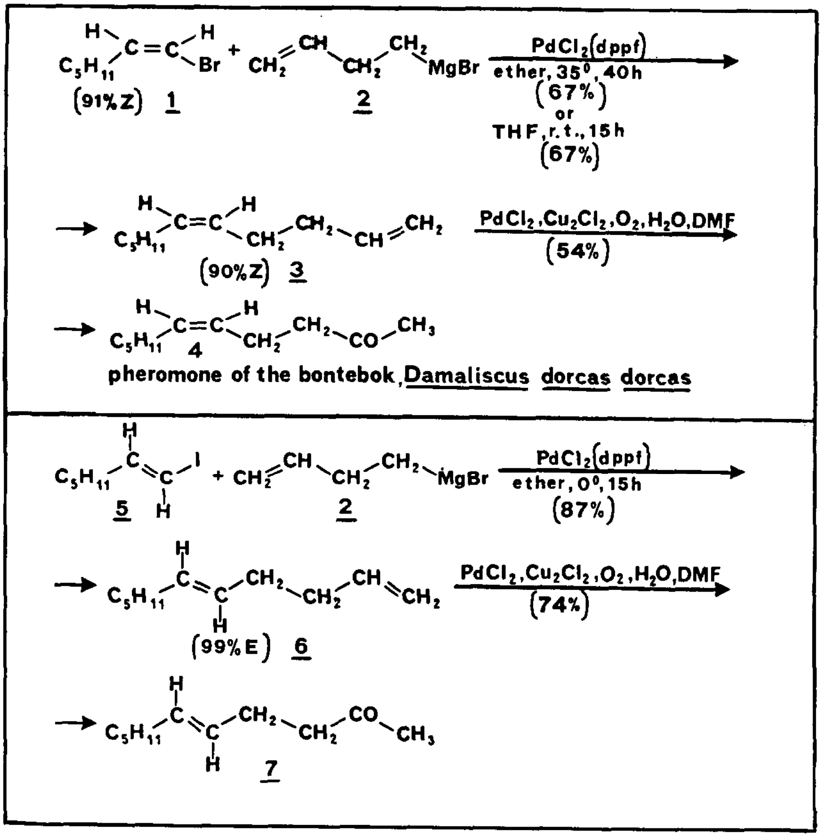


$$R_1-\overset{E\,or\,Z}{CH=CH}-X + R-CH_2MgX \xrightarrow[\substack{\text{ether or THF}\\ 25^\circ,\ 12h}]{PdCl_2(dppf)} R_1-\overset{E\,or\,Z}{CH=CH}-CH_2R$$

Thus,(Z)-and (E)-1,5-undecadiene,(3) and (6),were obtained in 67% and 87% yields,respectively[4].These dienes were then easily transformed into (Z)-5-undecen-2-one (4) and its (E)-stereoisomer,(7),respectively (Scheme).Compound 4 is the principal volatile component of the pedal gland exudate of the bontebok,*Damaliscus dorcas dorcas*.[5,6]

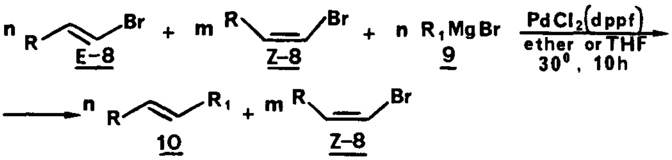
During our studies on this palladium-catalyzed coupling reaction we also observed that the reactivity of (E)-1-bromo-1-alkenes was higher than that of the corresponding (Z)-stereoisomers.[7]Thus,it appeared interesting to attempt a stereoselective synthesis of (E)-alkenes or (E)-1,ω-dienes by coupling easily available diastereoisomeric mixtures of 1-bromo-1-alkenes[8] with molarly deficient Grignard reagents.

SCHEME



pheromone of the bontebok, *Damaliscus dorcas dorcas*

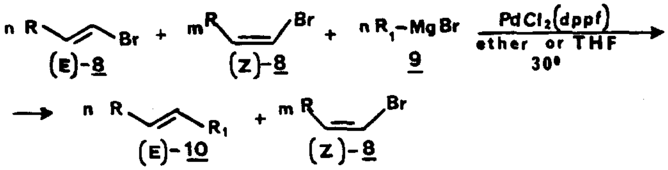
As expected, it was found that when a diastereoisomeric mixture of a 1-bromo-1-alkene which contained n equiv. of the (E)-stereoisomer was reacted at 30° with n equiv. of a Grignard reagent in ether or THF solution, in the presence of 2 mol% of $PdCl_2$(dppf), the reaction mixture contained the desired (E)-alkene having 95.5-98.5% stereoisomeric purity.[9] The isolated yield of the reaction was also satisfactory (61÷79.5%).

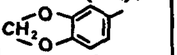


The high diastereoselectivity of the reaction was also confirmed by the (E)/(Z) ratio of the unreacted 1-bromo-1-alkene which was present in the final reaction mixture. The results obtained for some diastereoselective coupling reactions affording (E)-alkenes or (E)-1,ω-dienes are summarized in Table.

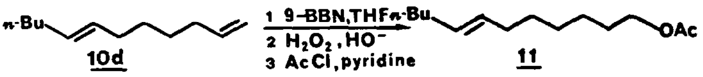
TABLE

Palladium catalyzed reaction between Grignard reagents and diastereoisomeric mixtures of 1-bromo-1-alkenes.



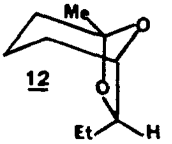
Reagents				Product : (E)-10		
(E)/(Z)-8		9	8/9 molar ratio	stereoisomeric purity %	yield %	compound
R	E/Z	R₁				
Et	66/34	$CH_3-(CH_2)_2-$	1.49	98.3	61	10a
Et	62.5/37.5	$CH_2=CH-(CH_2)_4-$	1.61	98.0	79.5	10b
Me	27/73		3.54	95.5	65	10c
n-Bu	60.6/39.4	$CH_2=CH-(CH_2)_4-$	1.66	98.5	67	10d
Et	61.5/38.5	$CH_2=CH-(CH_2)_3-$	1.58	99.0	57	10e

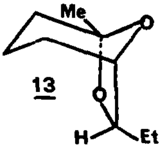
It must be noted that this method offers a convenient access to some natural products of predictable stereochemistry. Thus, isosafrol (10c), a naturally occurring phenyl-propanoid, was directly prepared in 95.5% stereoisomeric purity starting from a diastereoisomeric mixture of 1-bromo-1-propene which contained only 27% of the (E)-stereoisomer[10] (Table). On the other hand, treatment of (E)-1,7-dodecadiene (10d) with an equimolar amount of a THF solution of 9-BBN, followed by oxidation with H_2O_2 in NaOH and acetylation of the so obtained alcohol, afforded a 75% yield of (E)-7-dodecen-1-yl acetate (11), which is a pheromone component of *Argyroploce leucotreta*.[11]



Obviously, this procedure could be employed to prepare several other monounsaturated insect pheromone components, starting from the corresponding (E)-1,ω-dienes.

Finally, it is worthy of mention that (E)-1,6-nonadiene (10e) represents a suitable precursor either to (±)-endo-brevicomin (12) or (±)-exo-brevicomin (13)^{12}.Compound 12 enhances the aggregation of female and male beetles of the scolytid beetle *Dryocotes autographus*^{13} and compound 13 is an active component of the pheromone of the western pine beetle,*Dendroctonus brevicomis*^{14}.


12


13

ACKNOWLEDGMENTS:This work was supported by the Ministero della Pubblica Istruzione (Rome) and by the National Research Council of Italy (CNR),Special Grant I.P.R.A.-Sub-project 1 - Paper N **811**.

REFERENCES AND NOTES

1 T.Hayashi,M.Konishi,Y.Kobori,M.Kumada,T.Higuchi,K.Hirotsu,J.Am.Chem.Soc.,106,158 (1984)

2 $PdCl_2$(dppf) promotes the 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.The Pd-complex with the dppf ligand is also capable to promote the selective monoheteroarylation of several heteroarene di- or trihalides:A.Carpita,R.Rossi,C.A.Veracini,Tetrahedron,41,1919 (1985);A.Carpita,R.Rossi,Gazz.Chim.Ital.,115,575 (1985).

3 A.Carpita,R.Rossi, unpublished results.

4 All new compounds exhibited satisfactory spectral and physical properties.

5 B.V.Burger,M.le Roux,C.F.Garbers,H.S.C.Spies,R.G.Bigalke,K.G.R.Pachler,P.L.Wessels,V. Christ,K.H.Maurer,Z.Naturforsch. 31C,21 (1976)

6 For previous syntheses of (Z)-5-undecen-2-one see: K.Mori,T.Ara,M.Matsui,Agric.Biol.Chem. 41,2295 (1977);H.C.Brown,U.S.Racherle,D.Basavaniah,Synthesis,303 (1984).

7 Previously,we showed that when 1-alkynes are reacted with molar excesses of diastereoisomeric mixtures of 1-bromo-1-alkenes,under phase transfer conditions,in the presence catalytic amounts of $Pd(PPh_3)_4$ and CuI,internal conjugated (E)-enynes having ca.97% stereoisomeric purity are produced: R.Rossi,A.Carpita,P.Piccardi,in " Pesticide Chemistry, Human Welfare and the Environment ",J.Miyamoto ed.,Pergamon Press, pp 129-134 (1983).

8 The reaction of 1,2-dibromoalkanes with a suspension of 1.2 equiv of powdered KOH in vaseline oil at 90°C for 6 hr,in the presence of a catalytiv amount of Aliquat 336 (1 mole%) gives rise in ca.90% yield to mixtures constituted of equimolar amounts of 2-bromo-1-alkenes and 1-bromo-1-alkenes (Z/E ratio ca. 1) which are easily separable by fractional distillation using a Spaltrohr column.

9 GLC analyses were carried out using a Permaphase PEG capillary column (25m x 0.23 mm i.d.)

10 This compound was previously stereospecifically prepared by reacting (E)-β-methylthio-3,4-methylenedioxystyrene with a benzene solution of CH_3MgBr,in the presence of catalytic amounts of $NiCl_2(PPh_3)_2$: E.Wenkert,J.B.Fernandes,E.L.Michelotti,C.S.Swindell,Synthesis, 701 (1983).

11 J.S.Read,F.L.Warren Jr,P.H.Hewitt,Chem.Commun.,792 (1968).

12 H.T.Byron,R.Grigg,B.Kongkatip,A.R.Wade,J.Chem.Soc.Perkin Trans.I,1643 (1984).For these transformations these Authors used a 80:20 mixture of (E)- and (Z)-1,6-nonadiene.This diene was synthesized starting from ethyl nona-3,8-dienoate which was prepared by a Pd-catalyzed reaction of butadiene with CO and EtOH.This diene was then converted into threo- and erythro-3,4-dihydroxynon-8-ene which were cyclized by a Wacker-type catalyst. Careful purification of the cited diols was however necessary to eliminate the undesired stereoisomers deriving from the (Z)-diene.Our method allows to prepare (E)-1,6-nonadiene in a simpler way;moreover,owing to the high stereoisomeric purity of this diene,the purification of the derived diols is not necessary,or,however,is quite simple.

13 U.Kohnle,J.P.Vité,Naturwiss.,71,47 (1984).

14 R.M.Silverstein,R.G.Brownlee,T.E.Bellas,Science,159,889 (1968).

(Received in UK 24 March 1986)