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SYNTHESIS OF STEREOISOMERICALLY PURE (E)-1,5-DIYN-3-ENES AND (E)-1-BROMO-3-YN-1-ENES BY DIASTEREOSELECTIVE PALLADIUM-CATALYZED CROSS-COUPLING REACTION OF 1-ALKYNYLZINC CHLORIDES WITH A STEREOISOMERIC MIXTURE OF 1,2-DIBROMOETHYLENE.

Adriano Carpita and Renzo Rossi

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

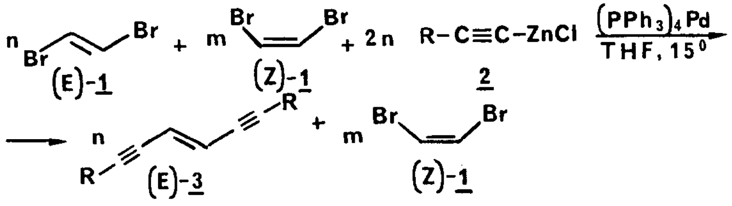
Summary : In the stereospecific palladium-catalyzed cross coupling reaction of 1-alkynylzinc chlorides,(E)-1,2-dibromoethylene reacts preferentially in the presence of (Z)-1,2-dibromoethylene.Products of di- or mono-substitution can be obtained according to the ratio of reagents.

During our studies on the development of new synthetic methods for preparing efficiently and in mild conditions stereodefined natural products,we have discovered and reported the first two examples of highly diastereoselective palladium-catalyzed reactions involving the use of diastereoisomeric mixture of 1-bromo-1-alkenes[1,2].The first example regarded the $(PPh_3)_4$Pd-CuI catalyzed reaction of diastereoisomeric mixtures of 1-bromo-1-alkenes with molarly deficient 1-alkynes,under phase-transfer conditions[1].This reaction gives rise in good yields to (E)-1,3-enynes having stereoisomeric purity higher than 97%.

The second example regards the reaction of diastereoisomeric mixtures of 1-bromo-1-alkenes with molarly deficient primary alkyl Grignard reagents,in the presence of catalytic amounts of dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium(II)[2].This reaction affords in satisfactory isolated yields (E)-alkenes having 95.5-99% stereoisomeric purity.

In continuation of these studies we now wish to report that a commercially available diastereoisomeric mixture of 1,2-dibromoethylene (1) can undergo a highly diastereoselective palladium-catalyzed mono- or di-alkynylation reaction.

Thus, when treated with 2n equiv. of an 1-alkynylzinc chloride (2) and 2 mole% of $(PPh_3)_4Pd$ in THF at room temperature for 16h, a diastereoisomeric mixture of 1 which contains n equiv. of (E)-1 affords in good isolated yields an (E)-1,5-diyn-3-ene (3) having stereoisomeric purity higher than 99.5%[3,4]. G.l.c. analysis of the crude reaction mixtures shows also the presence of unreacted (Z)-1, in addition to a small amount (2-4%) of the symmetrically disubstituted 1,3-diyne derived from the 1-alkyne used to prepare 2.



Interestingly, satisfactory stereoisomeric purities are also obtained using 2.8 n equiv. of 2. Some typical results are reported in Table 1[5].

TABLE 1

Diastereoselective coupling reaction between (E)/(Z)-1,2-dibromoethylene (1)[a] and 1-alkynylzinc chlorides (2): synthesis of (E)-1,5-diyn-3-enes (3).

Reagents			Product: (E)-3		
Compound 2		(E)-1/2 molar ratio	Compound 3	Stereoisomeric purity (%)	Isolated yield (%)[b]
2a	$R = n\text{-}C_4H_9$	2.8	3a	98.0	84
2a	$R = n\text{-}C_4H_9$	2.0	3a	>99.5	79
2b	$R = n\text{-}C_5H_{11}$	2.8	3b	94.0	98
2b	$R = n\text{-}C_5H_{11}$	2.0	3b	>99.5	77
2c	$R = SiMe_3$	2.8	3c	83.5	87
2c	$R = SiMe_3$	2.0	3c	>99.5	81
2d	$R = C_6H_5$	2.0	3d	>99.5	75

a) Commercially available 1,2-dibromoethylene containing 33% of (E)-stereoisomer was used.

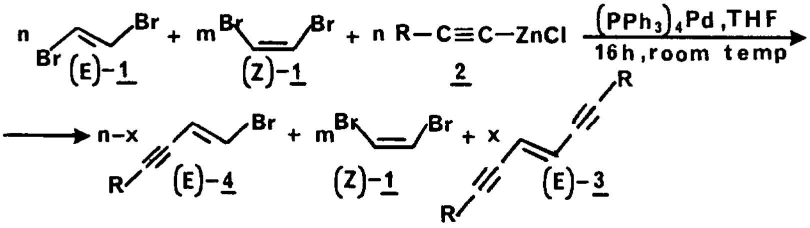
b) The reaction products were isolated by liquid chromatography on a silica gel column.

As shown in Table 1, this new procedure allows to prepare in good yield stereoisomerically pure (E)-1,6-bis(trimethylsilyl)-hexa-1,5-diyn-3-ene (3c), a stable compound which can serve as a synthon for (E)-hexa-1,5-diyn-3-ene[6].

A preliminary investigation has been also carried out on the diastereoselective monoalkynylation reaction of (E)/(Z)-1 to point out the selectivity of this reaction. It has been found that the reaction of n equiv. of 2 (e.g. 2a or 2b) with (E)/(Z)-1 which contains n equiv. of (E)-1, under experimental conditions similar to those employed to prepare (E)-3, produces in modest yield the desired stereoisomerically pure (E)-1-bromo-3-yn-1-ene (4) (e.g. 4a or 4b) , together with a significant amount of the corresponding (E)-1,5-diyn-3-ene (3) (e.g. 3a or 3b) (Table 2). However, it has been also observed that treatment of trimethylsilylethynylzinc chloride (2c) with (E)/(Z)-1, under these experimental conditions, affords a reaction mixture in which the main product is the dialkynylated compound 3c.

TABLE 2

Diastereoselective synthesis of (E)-1-bromo-3-yn-1-enes (4)



Reagents	Products	
Compound 2	Compound (isolated yield) %	Stereoisomeric purity %
2a R = n-C_4H_9	4a (34)	>99.5
	3a (17)	>99.5
2b R = n-C_5H_{11}	4b (42)	>99.5
	3b (19)	>99.5
2c R = $SiMe_3$	4c (5)	n.d.
	3c (55)	> 99.5

No attempts have been so far carried out to improve the selectivity of these reactions by using molar excesses of (E)-1.

The results so far obtained suggest the following conclusions: i)the reactivity of (E)-1 toward 1-alkynylzinc chlorides, in the presence of a Pd(0) catalyst, is much higher than that of (Z)-1;ii)compounds 4 are more reactive than (Z)-1 and compound 4c is also more reactive than (E)-1.In our opinion the observed high diastereoselectivity could be explained taking into account that (E)-1 and (Z)-1 exhibit different reactivity toward $(PPh_3)_4Pd$. In other words,(E)-1 probably undergoes the oxidative addition more easily than (Z)-1.Efforts are being made to elucidate the real reasons for the observed high diastereselectivity and to delineate the full scope of these reactions and their synthetic potential. Particular care will be devoted to improve the selectivity of the monoalkynylation reactions. In fact,compounds 4 deriving from these reactions,although to our knowledge not yet described in the literature,are certainly valuable synthetic intermediates.The corresponding chloroderivatives^{8} may be used either to prepare conveniently stereodefined polyunsaturated natural products^{8b},or to obtain terminal and internal conjugated diynes^{8c}.

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REFERENCES AND NOTES

1) R.Rossi,A.Carpita,and P.Piccardi,in "Pesticide Chemistry,Human Welfare and the Environment" J.Miyamoto and P.C.Kearney Eds.,Pergamon Press,Vol 1,pp 129-134 (1983)

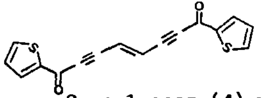
2) R.Rossi and A.Carpita,Tetrahedron Lett.,27,2529 (1986)

3) The stereochemistry of (E)-1,5-diyn-3-enes was established by IR analysis and confirmed by comparing them with stereoisomeric mixtures of (E)- and (Z)-3 prepared by treatment of (E)/(Z)-1 with molar excesses of 1-alkynylzinc chlorides (2).

4) The stereoisomeric purity of the reaction products was evaluated by GLC analysis on capillary columns (Permaphase Peg, OV 101).

5) All new compounds exhibited satisfactory spectral and physical properties.

6) Treatment of 3c with 2 equiv. of 2-chloroformylthiophen and 2 equiv.of $TiCl_4$ in CH_2Cl_2 at -78° for 7 h,followed by acidic hydrolysis afforded in 50% isolated yield the following diketone:



7) The stereochemistry of (E)-1-bromo-3-yn-1-enes (4) was established by IR and ^{1}HNMR analysis.These compounds exhibited characteristic IR bands at 2210,1680,and 920 cm^{-1}.Their ^{1}H NMR spectra showed olefinic coupling constants $J_{H,H}$(trans)≃14 Hz.Their stereoisomeric purity was evaluated by GLC.

8) For the preparation of (E)-1-choro-3-yn-1-enes see: a)V.Ratovelomana and G.Linstrumelle, Tetrahedron Lett.,22,315 (1981); b) V.Ratovelomana and G.Linstrumelle,Tetrahedron Lett., 25,6001 (1984); c) E.Negishi,N.Okukado,and F-T.Luo,J.Org.Chem.,49,2629 (1984)

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