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TRANSFER OF ASYMMETRY BY THE PALLADIUM-CATALYZED ALKYLATION OF CHIRAL ALLYLIC SULFINATES[1)]

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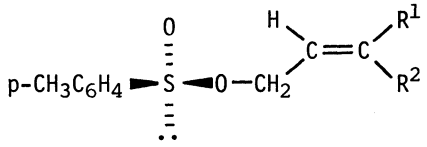
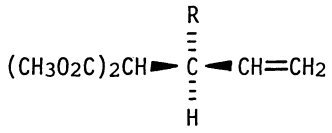
The palladium-catalyzed substitution of chiral allylic sulfinates was performed by the initial transformation of the sulfinates into allyl sulfones and the subsequent alkylation of the sulfones with retention of configuration. Reaction of trans- and cis-2-butenyl (S)-(-)-p-toluenesulfinate with the sodium salt of dimethyl malonate was undertaken in the presence of tetrakis(triphenylphosphine)palladium and triphenylphosphine to produce dimethyl (S)-(+)- and (R)-(-)-1-buten-3-ylmalonate, respectively, with the α-alkylated product, dimethyl 2-butenylmalonate.

In recent years much attention has been devoted by many investigators to the organic synthetic reactions catalyzed by organometallics, especially by palladium catalysts.[2)] Among them, the palladium-catalyzed allylic substitution is one of the most synthetically useful methods for the regio- and stereospecific carbon-carbon bond formation.[3)] Hitherto, allylic acetates,[4)] allylic lactonic carboxylates,[5)] and allylic epoxides[6)] have usually been used for the palladium-catalyzed allylic alkylation. We wish to communicate herein the stereospecific palladium-catalyzed alkylation of chiral allylic sulfinates involving chiral sulfur atoms as sole asymmetric sources.[7)]

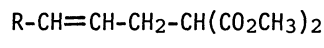
trans-2-Butenyl (S)-(-)-p-toluenesulfinate (1a) reacted with the sodium salt of dimethyl malonate in the presence of 0.15 equiv. of tetrakis(triphenylphosphine)palladium (2) and 0.66 equiv. of triphenylphosphine in refluxing tetrahydrofuran (THF) for 10 h to afford dimethyl (S)-(+)-1-buten-3-ylmalonate (3a) (83% stereospecificity) and dimethyl 2-butenylmalonate (4a) in 75% yield with a 1:1 ratio of 3a and 4a. In contrast, cis-2-butenyl (S)-(-)-p-toluenesulfinate (1b) reacted with the sodium salt of dimethyl malonate under the same condition to give

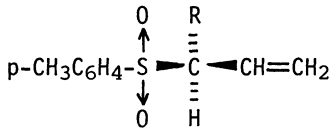


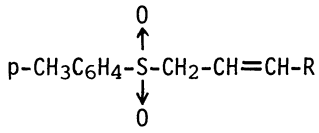
(S)-(-)-1a R^1=CH_3 , R^2=H
(S)-(-)-1b =H , =CH_3
(S)-(-)-1c =$(CH_2)_2CH_3$, =H
(S)-(-)-1d =H , =$(CH_2)_2CH_3$



(S)-(+)-3a R=CH_3
(S)-(+)-3b =$(CH_2)_2CH_3$







4a R=CH_3
4b =$(CH_2)_2CH_3$

(S)-(+)-5a R=CH_3
(S)-(+)-5b =$(CH_2)_2CH_3$

6a R=CH_3
6b =$(CH_2)_2CH_3$

(R)-(-)-3a (71% stereospecificity) and 4a in 65% yield with a 1:1 ratio of 3a and 4a. The reaction of (S)-(-)-1a with the sodium salt of dimethyl malonate was carried out without the palladium catalyst under the same condition employed above to recover the starting sulfinate completely. This means that the direct SN2 type substitution of the chiral allylic sulfinates with the sodium salt of dimethyl malonate could not occur under this condition and the presence of the palladium catalyst was required for the allylic alkylation of the sulfinates (1).

The palladium-catalyzed alkylation of trans-2-hexenyl (S)-(-)-p-toluenesulfinate (1c) under the same condition gave dimethyl (S)-(+)-1-hexen-3-ylmalonate (3b) (33% stereospecificity) and dimethyl 2-hexenylmalonate (4b) in 42% yield with a 2:3 ratio of 3b and 4b. cis-2-Hexenyl (S)-(-)-p-toluenesulfinate (1d) reacted with the sodium salt of dimethyl malonate in the same way to afford (R)-(-)-3b (21% stereospecificity) and 4b in 42% yield with a 2:3 ratio of 3b and 4b.

The absolute configurations of 3a and 3b were determined as (S)-(+)-3a and -3b by conversion of (+)-3a and -3b into (S)-(+)-3-methylvaleric acid[8] and (R)-(+)-3-ethylhexanoic acid[9] of known configuration, respectively, by hydrolysis of the esters (3a and 3b) followed by decarboxylation and the subsequent catalytic hydrogenation of the unsaturated acids.

The stereospecificities of the alkylations of 1a,b and 1c,d were determined by the NMR analysis of 3a with a shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium [Eu(hfc)$_3$], and by comparison of the optical rotation of the acid derived from 3b, 3-ethylhexanoic acid, with that of the authentic acid.[9]

Table 1. The Palladium-catalyzed Alkylation of Chiral Allylic Sulfinates (S)-(-)-1a-d with the Sodium Salt of Dimethyl Malonate[a)]

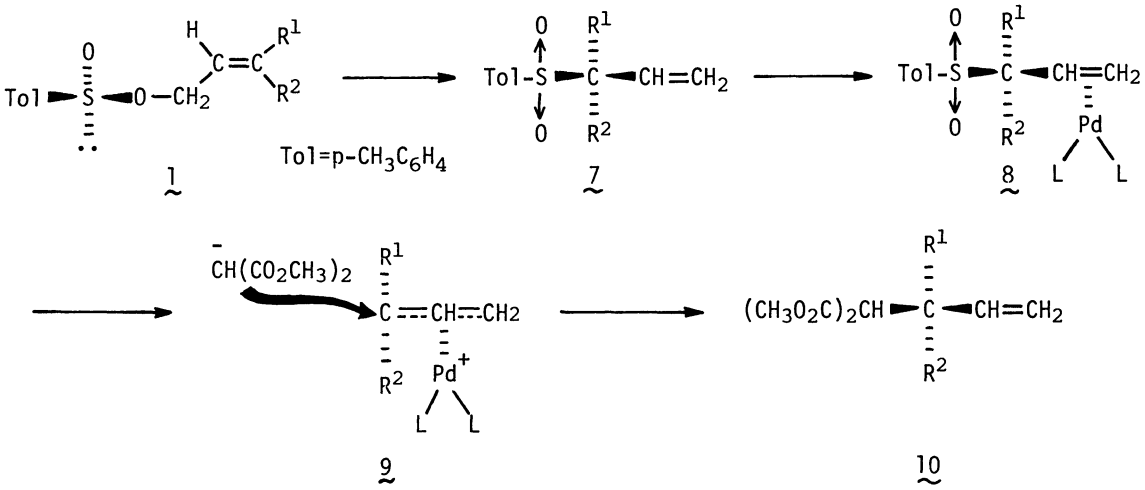
1a-d	1 e.e.(%)	Yield of 3 and 4 (%), (3 : 4)[b)]	Product 3 $[\alpha]_D$ (MeOH)	e.e.(%)	Stereospecificity in 1→3 (%)
1a	57.4	75 (1 : 1)	+7.1° (c 1.0)	45.4 [c)]	83
1b	56.8	65 (1 : 1)	-6.8° (c 0.7)	44.3 [c)]	78
1c	66.7	42 (2 : 3)	+4.3° (c 0.8)	21.8 [d)]	33
1d	58.7	42 (2 : 3)	-2.4° (c 0.9)	12.2 [d)]	21

a) Chiral allylic sulfinates (S)-1a-d reacted with the sodium salt of dimethyl malonate in refluxing THF for 10 h in the presence of 2 (0.15 equiv.) and triphenylphosphine (0.66 equiv.). b) Calculated by NMR analysis. c) Calculated by NMR analysis with a shift reagent [Eu(hfc)$_3$]. d) Determined by chemical correlation of (+)-3b to (R)-(+)-3-ethylhexanoic acid.

Detailed studies on these reactions revealed that the allylic sulfinates, (S)-1a,c and (S)-1b,d could smoothly be converted into the corresponding allyl sulfones, (S)-5a,b and (R)-5a,b, respectively, by the palladium-catalysis with 2.[10)] Therefore this palladium-catalyzed substitution of the allylic sulfinates would be accomplished by the initial transformation of the allylic sulfinates (1) into the allyl sulfones (5) and the subsequent alkylation of the allyl sulfones. Rather low degrees of stereospecificity in alkylation of 1c,d were explained by low stereospecificity of the palladium-catalyzed rearrangement of 1c,d to 1-hexen-3-yl p-tolyl sulfone (5b).[10)]

Recently we have reported a highly stereospecific transfer of chirality from chiral sulfur atoms to carbons by thermolysis of chiral allylic sulfinates.[11)] Thermolysis of (S)-(-)-1a,b and -1c,d in N,N-dimethylformamide provided (S)-(+)- and (R)-(-)-1-buten-3-yl p-tolyl sulfone (5a), and (S)-(+)- and (R)-(-)-5b, respectively, in good yields with exceedingly high stereospecificity. The stereospecific conversion of the carbon-sulfur bonds of the chiral allyl sulfones (5a,b) into the carbon-carbon bonds have been achieved by the palladium-catalyzed substitution reactions.[12)] Reaction of (S)-(+)-5a obtained above with the sodium salt of dimethyl malonate was carried out in the presence of 0.15 equiv. of 2 and 0.66 equiv. of triphenylphosphine by refluxing in THF for 10 h to produce (S)-(+)-3a (86% stereospecificity) and 4a in 72% yield with a 1:1 ratio of 3a and 4a. Analogously, the palladium-catalyzed substitution of (S)-(+)-5b with the sodium salt of dimethyl malonate produced (S)-(+)-3b (80% stereospecificity) and 4b in 40% yield with a 2:3 ratio of 3b and 4b.

On the basis of the stereochemical results obtained above, the mechanistic pathway for this palladium-catalyzed substitution of the chiral allylic sulfinates would be presented in the following way. The chiral allylic sulfinates 1 would



initially be transformed by the catalysis with 2 into 7,[10] which would be chelated with the palladium catalyst from the opposite side of the p-toluenesulfonyl group to form the intermediate 8. The dimethyl malonate carbanion would react to the ionic intermediate 9 from the opposite side of the coordinated palladium catalyst, producing 10. Therefore this allylic substitution of the chiral allyl sulfones was undertaken with retention of configuration.

References

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