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Transition Metal-catalyzed Asymmetric Vinylcyclopropane-Cyclopentene Rearrangements. Asymmetric Synthesis of Cyclopentane Derivatives Using Chiral Sulfoxides as Chiral Sources

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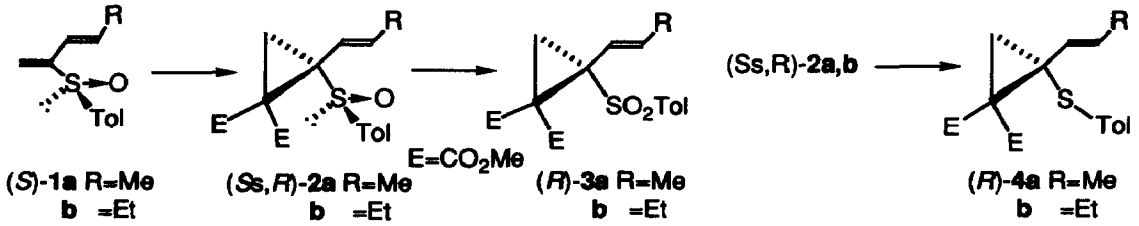
Abstract: Optically active α-olefinic cyclopropane derivatives, prepared by Michael addition of sodium bromomalonate to chiral vinylic sulfoxides followed by intramolecular asymmetric alkylation, led to facile transformation into chiral cyclopentane derivatives upon treatment with transition metals such as palladium, nickel, and platinum. The stereospecificity of the rearrangements was dependent on the catalysts and the reaction conditions employed. The palladium catalysts represented the highest stereospecificity.

A transition metal-mediated reaction has received much attention in recent years for the stereoselective new carbon-carbon bond formation . It facilitates in some cases the construction of complex organic structures which have been rather hard to access, with high stereoselectivity. We wish to communicate herein transition metal-catalyzed asymmetric rearrangements of chiral vinylcyclopropane systems into cyclopentene derivatives[1] by the use of the chirality of readily available optically active sulfoxides as the starting chiral sources. The thermal vinylcyclopropane-cyclopentene rearrangements require in general high reaction temperature,[2] whereas transition metals such as nickel,[3] palladium,[4] rhodium,[5] copper,[6] molybdenum,[7] chromium,[8] and iron[9] mediate the reactions to proceed under much milder reaction conditions. Therefore, the transition metal-catalyzed reactions seem more useful for the presentation of the high stereo- and enantioselectivity in organic synthesis.

Optically active cyclopropane compounds were prepared by Michael addition of dimethyl bromomalonate sodium enolate to vinyl sulfoxide derivatives bearing chiral sulfinyl groups as sole chiral sources, followed by intramolecular asymmetric alkylation.[10] Upon treatment with the sodium bromomalonate (in DME, at 0°C), chiral vinyl sulfoxides (*S*)-**1a,b** underwent Michael addition reactions followed by intramolecular asymmetric alkylations to obtain optically active cyclopropane derivatives (*Ss,R*)-**2a,b** in high optical yields (85%), which were isolated as diastereomerically pure forms by column chromatography on Silica gel . Michael addition of the sodium bromomalonate to (*S*)-2-*p*-toluenesulfinyl-1-penten-3-one followed by intramolecular alkylation gave dimethyl (*Ss,R*)-2-propionyl-2-*p*-toluenesulfinyl-1,1-cyclopropanedicarboxylate in a high optical yield (82%),



which was also isolated as a diastereomerically pure form by column chromatography on Silica gel. The $NaBH_4$ reduction of the ketone followed by dehydration of the resulting alcohol produced (*Ss,S*)-**2a**. It should be noted that the stereochemistry of the new chiral carbon center prepared asymmetrically from this (*S*)-α-propionylvinyl sulfoxide was opposite to that from (*S*)-**1a**.

Under palladium-mediated reaction conditions, chiral olefinic cyclopropyl sulfoxides (*Ss,R*)-**2a,b** thus obtained underwent asymmetric vinylcyclopropane-cyclopentene rearrangements to provide optically active cyclopentene derivatives. Treatment of (*Ss,R*)-**2a** with tetrakis(triphenylphosphine)palladium [$Pd(PPh_3)_4$] (0.15 equiv.) and triphenylphosphine (PPh_3) (0.66 equiv.) in acetonitrile (CH_3CN) (at 82°C) or dimethyl sulfoxide (DMSO) (at 80°C) gave (Ss,S)-**5a** in 50 or 45% yields with 89 or 68% stereospecificity, respectively. The nickel-catalyzed reactions of (*Ss,R*)-**2a** were carried out in the presence of bis(cyclooctadiene)nickel ($Ni(COD)_2$) and diphenylphosphinoethane (dppe) or diphenylphosphinobutane (dppb) in DMSO or CH_3CN at 80 or 82°C for 16 h to give (*Ss,S*)-**5a** in 50% (DMSO-dppe) and 38% (CH_3CN-dppe) yields with 24 and 14% stereospecificity, respectively. The platinum-catalyzed reactions of (*Ss,R*)-**2a** were undertaken in the presence of tetrakis(triphenylphosphine)platinum ($Pt(PPh_3)_4$)-dppb in DMSO at 80°C to give (*Ss,S*)-**5a** in a low yield with 31% stereospecificity. Upon treatment with $Pd(PPh_3)_4$ (0.15 equiv.)-PPh_3 (0.66 equiv.) in refluxing CH_3CN for 18 h, (*Ss,S*)-**2a** led to a facile conversion into (*Ss,R*)-**5a** with 89% stereospecificity in 50% yield. The palladium-catalyzed reactions of (*Ss,R*)-**2b**, prepared from (*S*)-**1b** in the similar way as described earlier, were carried out in CH_3CN at 82°C to give (*Ss,S*)-**5b** in 65% yield with 40% stereospecificity. The diastereomeric excess was calculated on the basis of the NMR spectral analysis. The results obtained under other reaction conditions are summarized in Table I.

The absolute configurations of the newly created carbons on the cyclopentene rings in **5a,b** were determined by chemical correlation to (*R*)-3-methyl- and ethylcyclohexanone (**7a,b**)[11] of known absolute configuration as follows. Oxidation of (*R*)-**7a,b** with selenium dioxide-hydrogen peroxide followed by esterification of (1*R*,2*R*)-**8a,b** gave (1*R*,2*R*)-**9a,b**.[12] α-Methoxycarbonylations of the esters (1*R*,2*R*)-**9a,b** with methyl

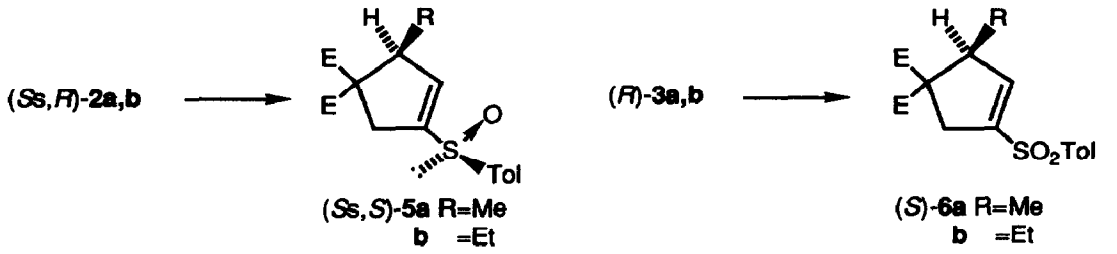


Table I. Transition Metal-Catalyzed Rearrangements of (*Ss*,*R*)-**2a,b**[a]

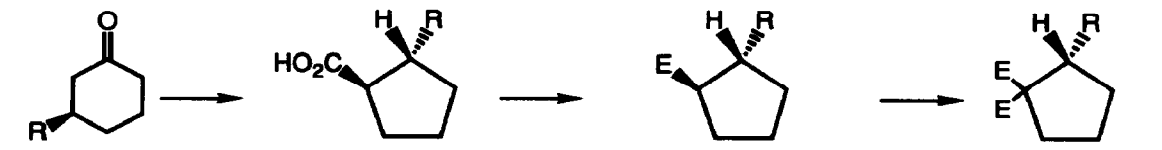
2	Catalysts	Solvent	Ligands	Reaction temp.(°C)	Reaction time(h)	Yield of **5a,b**(%)	Stereospecificity in **2a,b** —→**5a,b**[b]
2a	$Pd(PPh_3)_4$	CH_3CN	PPh_3	82	18	50	89
2a	$Pd(dba)_2$	CH_3CN	PPh_3	82	15	20	85
2a	$Pd(PPh_3)_4$	DMSO	PPh_3	80	18	45	68
2a	$Pd(PPh_3)_4$	THF	PPh_3	66	24	10	53
2a	$Pd(PPh_3)_4$	DME	PPh_3	82	24	18	51
2a	$Ni(COD)_2$	DMSO	dppe	80	16	50	24
2a	$Ni(COD)_2$	DMSO	dppb	80	16	22	26
2a	$Ni(COD)_2$	CH_3CN	dppe	82	16	38	14
2a	$Ni(COD)_2$	CH_3CN	dppb	82	16	18	18
2a	$Pt(PPh_3)_4$	DMSO	dppb	80	24	21	31
2a	$Pt(PPh_3)_4$	CH_3CN	dppb	82	24	11	9
2b	$Pd(PPh_3)_4$	CH_3CN	PPh_3	82	15	65	40
2b	$Pd(PPh_3)_4$	DMSO	PPh_3	80	15	23	29

a) The sulfinylcyclopropanes (*Ss*,*R*)-**2a,b** were treated with catalysts (0.15 equiv.)-ligands (0.66 equiv.).
b) The stereospecificity in the conversion of **2a,b** into **5a,b** was determind by d.e. of **5a,b** obtained.

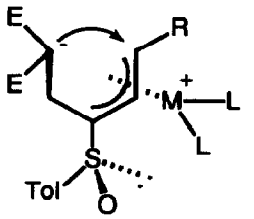
chloroformate (LDA,in THF, at -78°C) afforded (*R*)-(-)-**10a,b**. Reduction of the vinyl sulfoxides (*Ss*,*S*)-**5a,b** with Raney Ni gave (*S*)-(+)-**10a,b**. Thus, the absolute configurations of the newly created carbons on the cyclopentene rings prepared by the transition metal-catalyzed reactions of (*Ss*,*R*)-**2a,b** were determined as (S)-configuration.

The palladium-catalyzed reactions (Pd(PPh3)4-PPh3 in refluxing CH3CN for 18 and 15 h) of optically active *p*-toluensulfonylcyclopropane derivatives (*R*)-**3a,b** obtained by oxidation of the sulfoxides (*Ss*,*R*)-**2a,b** with *m*-CPBA afforded (*S*)-**6a,b** with the same stereospecificity (89 and 40%, respectively) as that of the sulfoxides (*Ss*,*R*)-**2a,b** (the compounds (*S*)-**6a,b** obtained by oxidation of (*Ss*,*S*)-**5a,b** with $NaIO_4$ showed the same optical rotation as that of (*S*)-**6a,b** derived from (*R*)-**3a,b**, starting both from the same cyclopropyl sulfoxides (*Ss*,*R*)-**2a,b**.). However, the palladium-catalyzed reactions of the sulfides (*R*)-**4a,b** obtained by reduction of the sulfoxides (*Ss*,*R*)-**2a,b** with titanium(III) chloride gave no rearrangement product, recovering the starting materials. This indicates that the new asymmetry on the cyclopentene rings would be created by the effect of the chirality on the cyclopropane rings in **2a,b**, not due to the chirality of the sulfinyl groups, during the rearrangements via palladium-coordinated transition states.

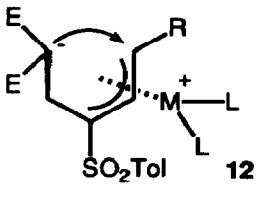
On the basis of the stereochemical results obtained above, the mechanistic pathway for this asymmetric rearrangement is presented as follows. A π-allylic transition metal complex **11** would be prepared with high stereospecificity by the coordination of the catalyst from the direction of the back side of the dissecting carbon-diethoxycarbonyl carbon bond of the cyclopropane ring in (*Ss*,*R*)-**2**. Nucleophilic substitution of the carbanion



(*R*)-**7a** R=Me b =Et (1*R*,2*R*)-**8a** R=Me b =Et (1*R*,2*R*)-**9a** R=Me b =Et (*R*)-(-)-**10a** R=Me b =E



11 R=Me
=Et



12 R=Me
=Et

in **11** would occur with rather high stereospecificity from the back side of the transition metal catalyst in the π-allyl transition metal complex intermediate to afford (*Ss*,*S*)-**5**. Similarly, the transition metal-catalyzed asymmetric rearrangement of the sulfonylcyclopropane derivative (*R*)-**3** would proceed through the transition metal-coordinated intermediate **12** from the back side of the transition metal catalyst, giving (S)-**6** with rather high stereospecificity. The stereospecificity of these rearrangements was dependent on the transition metal catalysts used, presumably due to the enantiomeric stability of the chiral π-allyl transition metal complexes under the reaction conditions employed.

Thus this transition metal-catalyzed rearrangement in the cyclopropane systems provides a facile entry to chiral cyclopentane derivatives under mild reaction conditions, starting from readily available chiral vinyl sulfoxide. Moreover, this method provides a great advantage for the preparation of both enantiomeric cyclopentane derivatives, on the use of palladium catalysts with rather high enantiomeric excess, by selecting the starting materials, chiral α-acylvinyl or α-olefinic vinyl sulfoxides. It should be also marked that the chirality on the cyclopropane rings affected the transition metal-catalyzed vinylcyclopropane-cyclopentene rearrangements with retention of configuration with rather high stereospecificity.

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