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# ASYMMETRIC ENE REACTIONS OF CHIRAL ALLYLIC SULFONES VIA CHIRAL ALLYLIC SULFINATE-SULFONE REARRANGEMENTS

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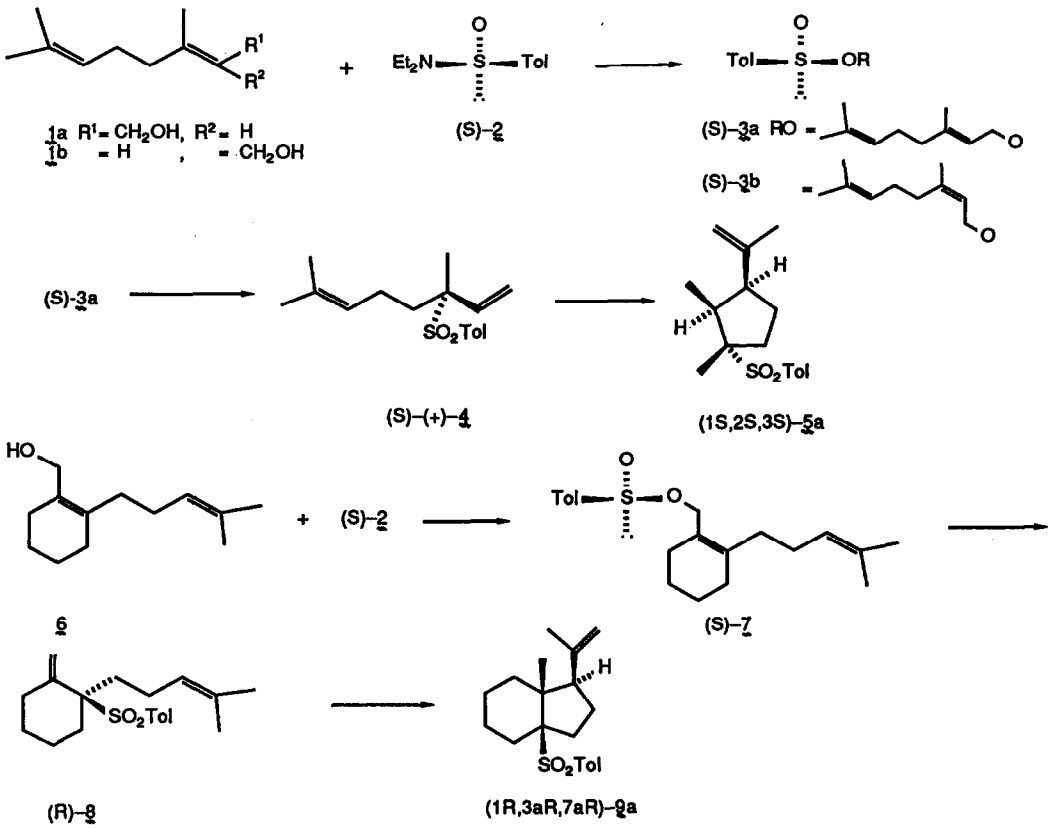
Abstract: Chirality of sulfur atoms in optically active allylic sulfinates was transfered to carbon centers via the allylic sulfinate-sulfone rearrangements and the subsequent ene reactions of the chiral allylic sulfones obtained provided chiral cyclic carbon compounds.

In recent years asymmetric synthesis with chiral organosulfur compounds has received much attention for the high enantioselectivity.[1] We have reported the successful results for transfer of asymmetry from sulfur to carbon atoms via chiral allylic sulfinate-sulfone rearrangements.[2] We have further continued investigation of the rearrangements for determination of the exact reaction mechanisms and explored a useful method in organic synthesis, utilizing chirality of allylic sulfones induced by chiral allylic sulfinates.

We wish to communicate herein stereochemical studies on asymmetric ene reactions[3] starting from chiral sulfinates by means of a new method of chiral allylic sulfinate-sulfone rearrangememts which we have explored previously.[2]

Reaction of geraniol (1a) with (S)-(+)-N,N-diethyl-p-toluenesulfinamide (2) was carried out in toluene at 0 °C for 4 h in the presence of boron trifluoride etherate (1.5 equiv.)[4] to give geranyl (S)-p-toluenesulfinate (3a) in 98% yield with 96% stereospecificity. Reaction of nerol (1b) with (S)-(+)-2 under the same conditions produced neryl (S)-p-toluenesulfinate (3b) in 87% yield with 91% stereospecificity. The absolute configuration of the sulfur atoms in 3a,b and the enantiomeric purity were determined by conversion of the products 3a,b into (R)-(+)-phenyl p-tolyl sulfoxide of known absolute configuration[5] by treatment of the sulfinates 3a,b obtained with phenylmagnesium bromide.[2c]

Thermolysis of (S)-3a or -3b in N,N-dimethylformamide (DMF) at 100 °C for 12 h gave (S)-(+)-4 or (R)-(-)-4 in 84 or 78% yield with 89 or 90% stereospecificity, respectively. Palladium-catalyzed reaction[2d] of (S)-3a or -3b was performed in tetrahydrofuran (THF) at 0 °C for 3 or 5 h in the presence of 0.15 equiv. of tetrakis(triphenylphosphine)palladium [$Pd(PPh_3)_4$] and 0.66 equiv. of triphenylphosphine ($PPh_3$) to afford (S)-(+)-4 or (R)-(-)-4 in 92 or 76% yield with 65 or 60% stereospecificity, respectively.




The absolute configuration of the produced allylic sulfone 4 was deduced on the basis of the mechanistic pathway for this thermolysis reported by us previously.[2c] The stereospecificity of the above reactions was calculated by NMR spectral analysis with a shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-d-camphorato]europium(III) [Eu(hfc)$_3$].

Ene reaction of (S)-(+)- or (R)-(-)-4 was smoothly achieved by treating with zinc(II) bromide in dichloromethane at room temperature for 15 h, or with diethylaluminum chloride in dichloromethane at -78 °C for 8 h to furnish (1S,2S,3S)- or (1R,2R,3R)-5a in 55 or 31% yield, respectively, without any loss of chirality. The structure of the product was determined by NMR spectral analysis. The stereochemistry was confirmed by observation of the Nuclear Overhauser effects between the methyl groups at $C_1$ and $C_2$ positions and the vinylic hydrogen of the isopropenyl group at $C_3$ in the NMR spectrum.

These transformations were applicable to cyclic systems. Sulfinylation of alcohol 6 was underwent, in the same way as described above, on treating 6 with (S)-(+)-2 in toluene at 0 °C for 6 h in the presence of boron trifluoride etherate (1.5 equiv.) to afford (S)-(-)-7 in 81% yield with 94% stereospecificity. The absolute configuration of the sulfur atom in the product 7 and stereospecificity of the reaction were determined by transformation of the sulfinate 7 obtained into (R)-(+)-phenyl p-tolyl sulfoxide, in the same way as described earlier. Thermolytic or palladium-

Table I. Thermal and Palladium-catalyzed Transformation of Chiral Allylic Sulfinates (S)-3a,b and (S)-7 into Allylic Sulfones 4 and 8

| Sulfinates (e.e. %) | Reaction conditions[a] Catalyst | Solvent | Reaction temp.(°C) | Reaction time(h) | Product | Yield (%) | e.e. (%) | Stereospecificity(%)[b] |
|---|---|---|---|---|---|---|---|---|
| (S)-3a(77.3) | - | DMF | 100 | 12 | (S)-4 | 84 | 68.6 | 89 |
| (S)-3a(77.3) | Pd | THF | 0 | 3 | (S)-4 | 92 | 49.5 | 65 |
| (S)-3b(74.0) | - | DMF | 100 | 12 | (R)-4 | 78 | 66.2 | 90 |
| (S)-3b(71.0) | Pd | THF | 0 | 5 | (R)-4 | 76 | 42.5 | 60 |
| (S)-7 (56.0) | - | DMF | 90 | 12 | (R)-8 | 63 | 33.0 | 59 |
| (S)-7 (48.0) | Pd | THF | 0 | 16 | (R)-8 | 71 | 18.0 | 38 |

a) The palladium-catalyzed reactions were carried out in the presence of $Pd(PPh_3)_4$ (0.16 equiv.) and $PPh_3$ (0.66 equiv.).

b) The enantiomeric excess (e.e.%) was determined by the NMR analysis with a shift reagent [$Eu(hfc)_3$].

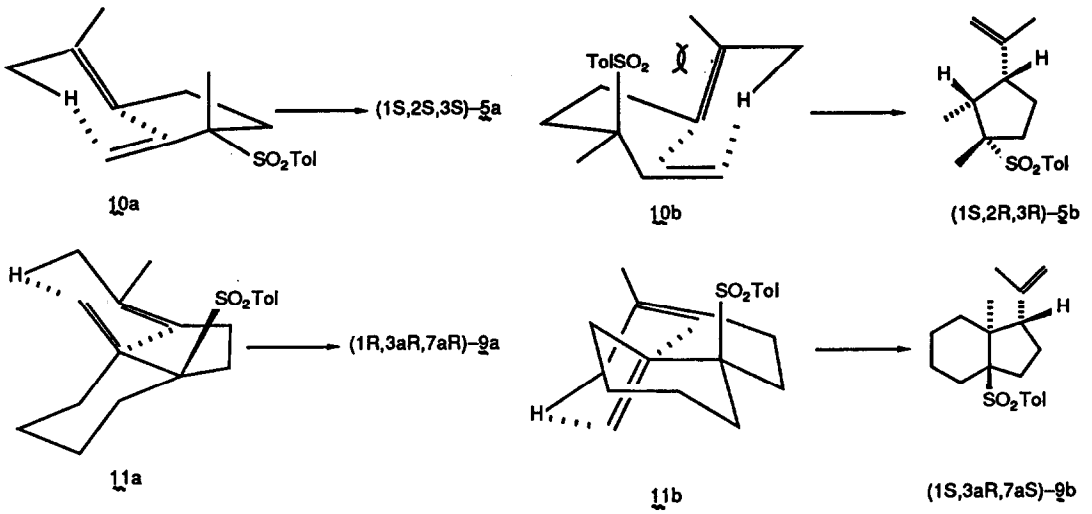
catalyzed reaction of (S)-7 was performed under the same conditions as mentioned above to provide (R)-(+)-8[2c] in 63 or 71% yield with 59 or 38 % stereospecificity,respectively. The lower stereospecificity in the palladium-catalyzed reaction was rationalized by the ionic reaction mechanism.[2b,6] Upon treatment with zinc(II) bromide (1.2 equiv.) in dichloromethane at room temperature for 16 h, (R)-8 underwent an intramolecular ene reaction without any racemization to afford (1R,3aR,7aR)-(+)-9a stereoselectively in 58% yield. The structure of the product was determined on the basis of NMR spectral analysis. The results of transformation of chiral allylic sulfinates to sulfones and the ene reactions of the chiral allylic sulfones are summarized in Table I and II.

The stereochemistry of the products obtained by the ene reactions was deduced on the basis of the mechanistic pathway as follows. Among two transition states 10a and 10b having cis five-six membered rings in the ene reaction of (S)-4,10a is more preferrable to 10b, because of steric interfer-

Table II. The Lewis acid-catalyzed Asymmetric Ene Reactions of Chiral Allylic Sulfones

| Sulfones | Reaction conditions[a] Lewis acid | Reaction temp.(°C) | Reaction time (h) | Product | Yield (%) |
|---|---|---|---|---|---|
| (S)-4 | $ZnBr_2$ | r.t. | 15 | 5a | 55 |
| (S)-4 | $Et_2AlCl$ | -78 | 8 | 5a | 31 |
| (R)-8 | $ZnBr_2$ | r.t. | 16 | 9a | 58 |
| (R)-8 | $Et_2AlCl$ | -78 | 8 | 9a | 21 |

a) The ene reactions of (S)-4 (51.8% e.e.) or (R)-8 (35.3% e.e.) were carried out in dichloromethane in the presence of $ZnBr_2$ (1.2 equiv.) or $Et_2AlCl$ (3.0 equiv.).




ence induced by the axial p-toluenesulfonyl group in 10b. Therefore, the ene reaction of (S)-4 provides (1S,2S,3S)-5a via the transition state 10a, and the reaction of (R)-4 produced the enantiomer, (1R,2R,3R)-5a. The stereochemistry of the product 9 could be rationalized with the same argument as described earlier. On the inspection of a Dreiding model of the ene reaction of (R)-8 having the cis six-membered ene reaction site, the transition state 11a, which has the cis-cis configuration to the five-membered ring, is more preferred to 11b (cis-trans configuration). Therefore the ene reaction of (R)-8 proceeds exclusively through 11a to furnish (1R,3aR,7aR)-9a.

Thus, chirality of the original asymmetric sulfur atoms in starting sulfinates was transfered to carbon centers in these procedures to lead in smooth formation of chiral cyclic carbon compounds.

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