Supplementary Information (SI) for ChemComm.

Supporting Information

Recent Transformations of Vinylidenecyclopropanes (VDCPs)

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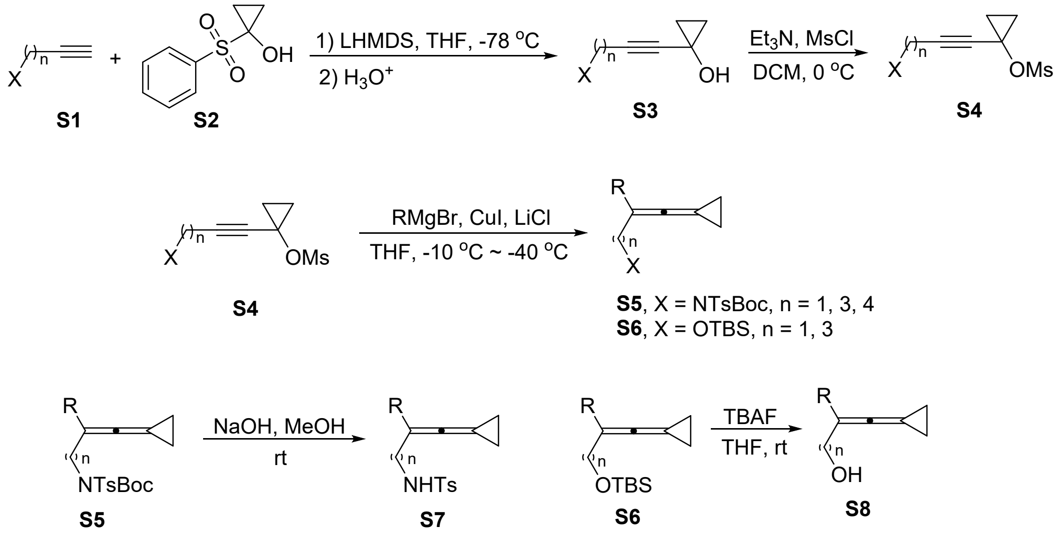
Preparation of the starting materials of vinylidenecyclopropanes (VDCPs)



Typical procedure:

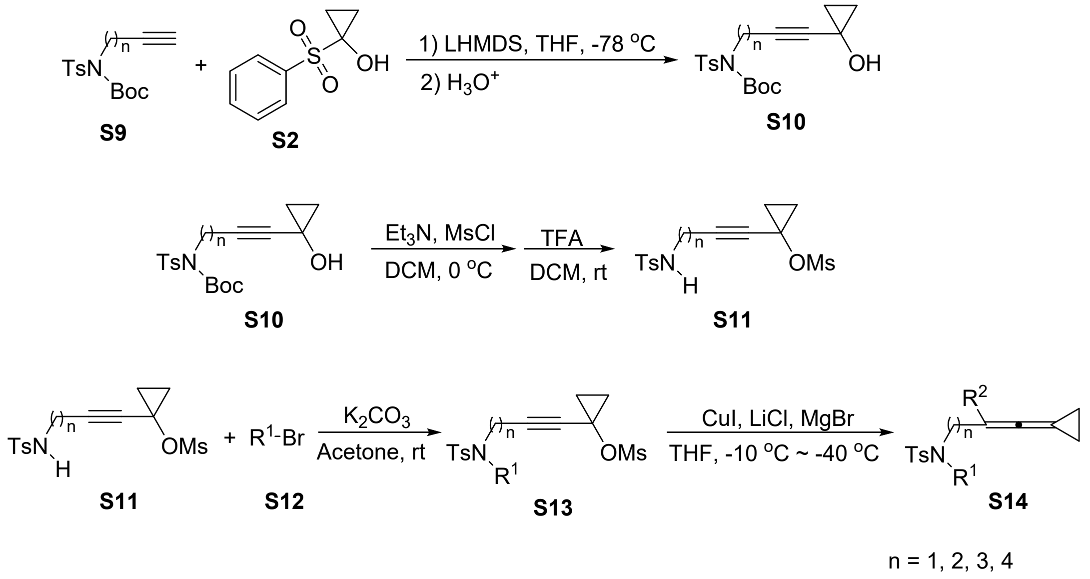
The procedure of preparing compounds **S5** and **S6** were slightly modified by the previous literature.[1] To the solution of compounds **S1** (20 mmol) in THF (30 mL) was added LMHDS (22 mmol, 1.0 M in THF) within 20 min at -78 °C under argon. The resulting solution was allowed to stir at -78 °C for 0.5 h before a solution of **S2** (10 mmol) in THF (10 mL) was added into the above mixture. Consequently, the reaction mixture was allowed to warm up to room temperature and was stirred for 8.0 h. Then, saturated NH_4Cl solution was added to quench the reaction. Extracted with ethyl ether, dried over anhydrous Na_2SO_4, filtered, the organic phase was purified by a flash column chromatography on silica gel to give the corresponding products **S3** (PE/EA: 4:1~2:1).

Under argon atmosphere, compound **S3** (4.0 mmol) was dissolved in DCM (10.0 mL) at 0 °C, Et_3N (8.0 mmol) and MsCl (6.0 mmol) was added. After stirring for 1.0 h, the reaction was quenched with H_2O (10.0 mL), extracted with DCM (10 mL x 3), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (SiO_2) to give the corresponding product **S4** (PE/EA: 4:1).

Under argon atmosphere, CuI (2.2 mmol) and LiCl (2.2 mmol) in a three-necked bottle was dried upon heating. Then THF (10 mL) was added. at -10 °C, RMgBr (1.0 mol/L in THF, 2.0 mmol, 2.0 mL) was added to the reaction mixture. 10 minutes later, the flask was moved into a -40 °C bath and stirred for a while before a solution of **S4** (1.0 mmol) in THF (10 mL) was added dropwise into the above flask. After stirring at -40 °C for 8.0 h, the reaction was quenched with saturated NH_4Cl solution, extracted with EA (10 mL x 3), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (SiO_2) to give the corresponding product **S5** and **S6** (PE/EA: 10:1).

To the solution of **S5** (1.5 mmol) in MeOH (10 mL) was added NaOH (15 mmol). The resulting solution was stirred at room temperature for 8.0 h. The solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (SiO_2) to give the corresponding product **S7** (PE/EA: 4:1).

In a flame dried 20 mL vial, compound **S6** (2.0 mmol, 1.0 eq.) was combined with anhydrous THF (10 mL) under argon, and then TBAF (1.0 M solution in THF, 3.0 mL, 3.0 mmol, 1.5 eq.) was added all at once. The solution was left to stir at 0 ^{o}C for 1.0 h, and then was concentrated under reduced pressure and purified directly by a flash chromatography (SiO_2) to give product **S8** (PE/EA: 2:1).

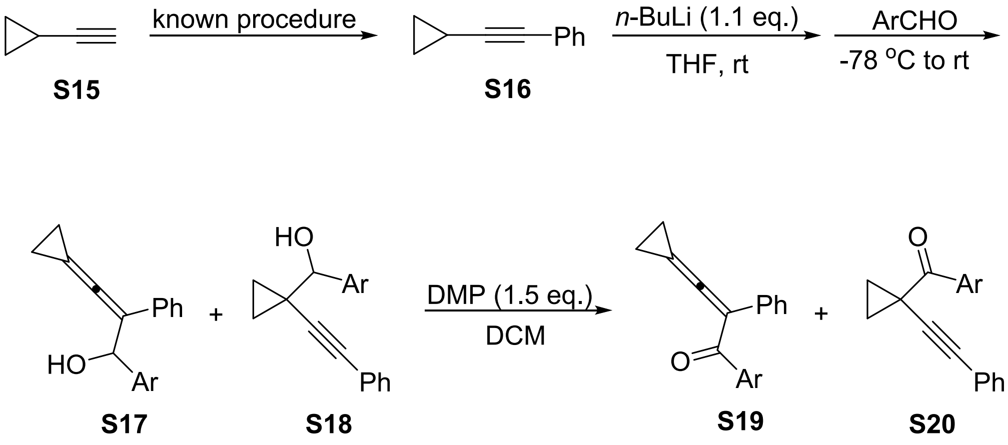


Typical procedure:

Compound **S10** was prepared in the same way as that of compound **S4**. Under argon atmosphere, compound **S10** (4.0 mmol) was dissolved in DCM (10.0 mL) at 0 °C, Et_3N (8.0 mmol) and MsCl (6.0 mmol) was added. After stirring for 1.0 h, the reaction was quenched with H_2O (10.0 mL), extracted with DCM (10 mL x 3), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was transferred into a 50 mL flask with 10 mL DCM. Then, trifluoroacetic acid (TFA, 40 mmol) was added dropwise. After stirring for 12 h, the reaction was quenched with saturated $NaCO_3$ solution, extracted with DCM (10 mL x 3), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (SiO_2) to give the corresponding product **S11** (PE/EA: 4:1~1:1).

To the solution of **S11** (1.5 mmol) and K_2CO_3 (1.8 mmol) in acetone (10 ml) was added **S12** (R^1-Br, 1.8 mmol). The resulting solution was allowed to stir at 70 °C for 8.0 h. Then, the reaction mixture was cooled to room temperature and the mixture was filtered through a celite. The filtrate was concentrated under reduced pressure and the residue was purified by a flash column chromatography (SiO_2) to give the corresponding product **S13** (PE/EA: 4:1~2:1).

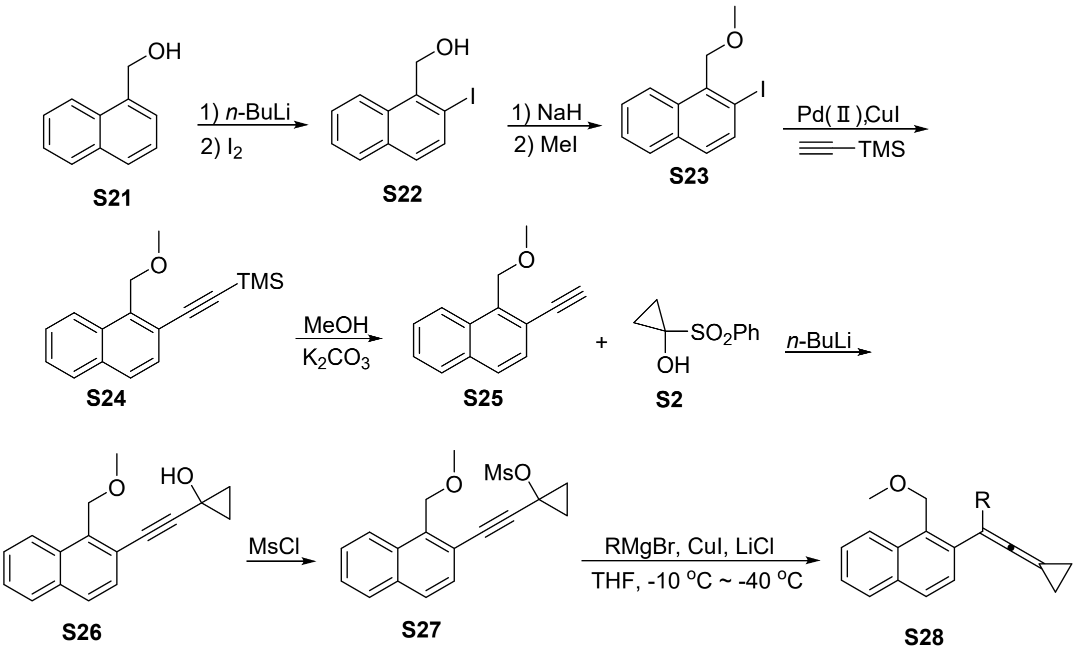
Under argon atmosphere, CuI (2.2 mmol) and LiCl (2.2 mmol) in a three-necked bottle was dried upon heating. Then THF (10 mL) was added. At -15 °C, R^2MgBr (1.0 M in THF, 2.0 mmol, 2.0 mL) was added to the reaction mixture. 10 minutes later, the flask was moved into a -40 °C bath and stirred for a while before a solution of **S13** (1.0 mmol) in THF (10 mL) was added dropwise into the above flask. After stirring at -40 ^{o}C for 8.0 h, the reaction was quenched with saturated NH_4Cl solution, extracted with EA (10 mL x 3), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (SiO_2) to give the corresponding product **S14** (PE/EA: 10:1).



Typical procedure:

The procedure of preparing compounds **S16** were slightly modified by the previous literature.[2,3,4] To the solution of compounds **S16** (9.8 mmol, 1.0 eq.) in anhydrous THF (20 ml) was added *n*-BuLi (4.3 mL, 2.5 **M** in hexane, 1.1 eq.) at room temperature; the resulting mixture was stirred for 1.0 h, and cooled to -78 °C. Then, ArCHO (9.8 mmol, 1.0 eq.) was added with a syringe to this mixture at -78 °C. After being stirred for 1.0 h, the mixture was allowed to warm up to room temperature, and the reaction was quenched with water, and the resulting mixture was extracted with ethyl acetate, dried over anhydrous MgSO$_4$, filtered, and evaporated. The residue was chromatographed through a silica gel column (petroleum ether/ethyl acetate 4:1 v/v) to afford the mixture of **S17** and **S18** (2:1) as yellow oil.

To a solution of the mixture of **S17** and **S18** (1.0 eq.) in 30 mL of DCM were added 1.5 equiv of DMP and after being stirred for 10 min, silica gel was added and the solvent was evaporated. The solid residue was purified by a column chromatography (petroleum ether/ethyl acetate 50:1 v/v) on a silica gel column to give the starting material **S19**.



Typical procedure:

To a flame dried, argon purged 250 mL round-bottom flask was added Et_2O (10 mL), then n-BuLi (45.8 mL, 110 mmol, 2.4 M in hexane) and TMEDA (16.5 mL, 110 mmol) was added at -78 °C. After stirring for 30 min, **S21** (7.9 g, 50 mmol) in 60 mL of Et_2O was added during 40 min via a syringe at room temperature. The resulting mixture was stirred for 4.0 h and I_2 (15.2 g, 60 mmol) in 60 mL of diethyl ether was added quickly at 0 °C. Quenched by saturated aqueous $Na_2S_2O_3$, extracted by Et_2O three-times (50 mL each), the combined the organic phase was dried over anhydrous $MgSO_4$. After filtration, the solution was concentrated under reduced pressure and the residue was purified by a silica gel flash column chromatography with petroleum ether-EtOAc as an eluent to give the corresponding products **S22**.

To a flame dried, argon purged round bottom flask was added **S22** (6.0 g, 21 mmol) dissolved in anhydrous THF (50 mL), and then NaH (1.0 g, 60 %, 25 mmol) was added in portions at 0 °C. After stirring for 1.0 h, MeI (1.56 mL, 25 mmol) was added slowly via a syringe. The reaction mixture was stirred at room temperature for 1.0 h. Quenched by water, extracted by Et_2O three-times (20 mL each), the combined the organic phase was dried over anhydrous $MgSO_4$. After filtration, the solution was concentrated under reduced pressure and the residue was purified by a silica gel flash column chromatography with petroleum ether-EtOAc as an eluent to give the corresponding products **S23**.

S23 (6.2 g, 21 mmol), $Pd(PPh_3)_2Cl_2$ (147 mg, 0.21 mmol) and CuI (65 mg, 0.35 mmol) were added to a flame dried, three-necked flask. Then $^{i}Pr_2NH$ (50 mL) was added to afford a yellow suspension.

Ethynyltrimethylsilane (3.3 mL, 23 mmol) was added dropwise via a syringe and the resulting mixture was stirred for another 30 min at room temperature. After filtration, the solution was concentrated under reduced pressure, which was directed used for the next reaction without further purification.

To a 250 mL round bottom flask was added **S24** in MeOH (50 mL), which was prepared by the previous step. Then K_2CO_3 (5.5 g, 40 mmol) was added and the resulting mixture was stirred for 2.0 h at room temperature. After filtration, the solution was concentrated under reduced pressure and the residue was purified by a silica gel flash column chromatography with petroleum ether-EtOAc as an eluent to give the corresponding products **S25**.

To a flame dried, argon purged three-necked flask (marked as flask 1) was added **S25** (3.4 g, 17 mmol) dissolved in THF (50 mL). To another flame dried, argon purged three-necked flask (marked as flask 2) was added **S2** (3.76 g, 19 mmol) dissolved in THF (50 mL). The two flasks were set in a dry ice-acetone bath and cooled down to -78 ^{o}C. When the temperature reached, *n*-BuLi (7.9 mL, 2.4 M in hexane) was added dropwise to each of the flasks via syringes at the same temperature. The reaction mixtures were stirred at that temperature for 2.0 h. Then, the resulting mixture in flask 1 was transferred to flask 2 and the reaction vessel was removed from the bath and naturally warmed to room temperature. The reaction mixture was stirred at room temperature for 4.0 h. After that, the reaction was quenched with water (20 mL) and the resulting dark mixture was extracted with ethyl acetate (45 mL) for three times. The organic phase was concentrated under reduced pressure and the residue was purified by a silica gel flash column chromatography with petroleum ether-EtOAc as an eluent to give the corresponding products **S26**.

The steps for the synthesis of compound **S27** from compound **S26** are the same as the steps for the synthesis of compound **S5** from compound **S3** as that above mentioned procedure.

2 References

1. (a) W. Yuan, X. Tang, Y. Wei and M. Shi, *Chem*. *Eur*. J., 2014, **20**, 3198-3204; (b) S. Yang, K.-H. Rui, X.-Y. Tang, Q. Xu and M. Shi, *J. Am*. *Chem*. *Soc*., 2017, **139**, 5957-5964.

2. H. Siebeneicher, S. Doye, *Eur*. *J. Org*. *Chem*., 2002, 1213.

3. C.-Y. Yang, M.-S. Lin, H.-H. Liao, R.-S. Liu, *Chem*. *Eur*. *J*., 2010, **16**, 2696.

4. S. Ye, Z.-X. Yu, *Org*. *Lett*., 2010, **12**, 804.