Lewis acid-catalyzed formation of indene derivatives *via* tandem reactions of arylacetylenes with the cations generated from 2-silylmethyl cyclopropyl carbinols†

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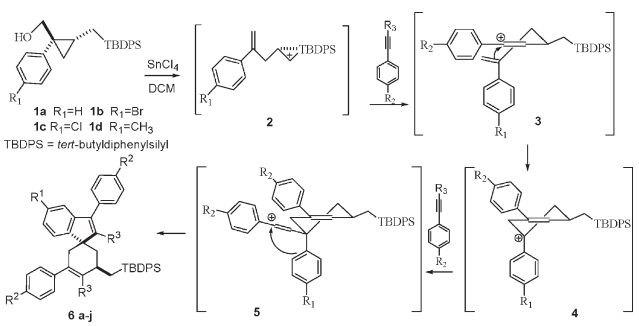
Vicinal silylmethyl-substituted cyclopropyl carbinols undergo tandem intermolecular cation–arylacetylene cyclization to generate indene derivatives.

Substituted indene derivatives are useful compounds that serve as building blocks for functional materials,[1a–d] pharmaceutical compounds, particularly oxytocin antagonists,[1e] antiproliferative agents,[1f] estrogen receptor modulators,[1g] and h5-HT6 serotonin receptor.[1h] Tandem reactions play a vital role in organic synthesis because they lead to the formation of two or more carbon–carbon bonds without adding additional reagents and catalysts.[2] The tandem intermolecular cation–olefin cyclization[3a] has advantages over intramolecular cation–olefin cyclization[3b–k] because one has choice to manipulate both the reactants. For some time, we have been involved in the synthesis of various carbocycles[4a,b] and heterocycles[4c–f] from cyclopropylmethylsilanes. Herein, we report a novel tandem intermolecular cation–arylacetylene cyclization for the synthesis of substituted indene derivatives[5] (**6a–j**) from vicinal silylmethyl-substituted cyclopropylcarbinols. The aryl groups, both in the cyclopropane substrate and the arylacetylene, were chosen so as to provide convenient handles for further manipulation.

The silicon-stabilized cation[6] **2**, generated from **1a** on treatment with $SnCl_4$, reacts with different aryl acetylenes.‡The subsequent intramolecular nucleophilic attack by the *in situ* formed olefin **3** on the aryl-stabilized vinyl cation results in another aryl-stabilized cation **4** (Scheme 1). The cation **4** reacts further with one more equivalent of the arylacetylene to generate yet another aryl-stabilized vinyl cation **5** that finally undergoes intramolecular Friedel–Crafts alkenylation to terminate the reaction.[7] The reaction generates four new carbon–carbon bonds, two new stereogenic centers, one being quaternary, and leads to the formation of two rings. The high stereoselectivity of the reaction is truly remarkable; the bulky silylmethyl group occupies an equatorial position in the six-membered transition state and the second molecule of arylacetylene enters exclusively from the equatorial site, as shown. Other substrates such as **1b**, **1c** and **1d** also reacted well with arylacetylenes (Table 1, entries 6–10).



Scheme 1 Working hypothesis for the tandem cation-arylacetylene cyclization.

The structural characterization of **6a** was achieved from spectral data, including COSY and NOE experiments.§ To demonstrate that one molecule of cyclopropylcarbinol had reacted with two molecules of the arylacetylene, **1a** was reacted with *p*-methylphenylacetylene. Two methyl signals were noted in ^{1}H and ^{13}C NMR spectra of the product **6b** (Table 1, entry 2). Further, a deuterium labelling experiment was carried out to ascertain that the olefinic ^{1}H signals at δ 6.19 and δ 5.57 in **6a** had indeed originated from the arylacetylene. Indeed, 1-deuterio-2-phenylacetylene reacted with **1a** to furnish the product **6c** in which the above ^{1}H signals were absent (entry 3).

The doubly activated 1-phenyl-2-trimethylsilylacetylene reacted to furnish the 1,2,4,5,6-pentasubstituted-1,3-cyclohexadiene **7a** as the sole product in 50% yield (Scheme 2).¶ The relative stereochemistry of the two C_{sp^3}-substituents was ascertained from X-ray structure analysis (Fig. 1).‖ A tentative mechanism for the formation of **7a** is depicted in Scheme 3. In *path a*, the H^+ generated from deprotonation after the first ring formation is captured by the electron-rich silylacetylene to generate a stable

Table 1 Reactions of **1** with different aryl acetylenes[a]

Entry	R^1	R^2	R^3	Product	Yield (%)
1	H	H	H	**6a**	65
2	H	CH_3	H	**6b**	55
3	H	H	D	**6c**	65
4	H	Cl	H	**6d**	55
5	H	Br	H	**6e**	50
6	Br	H	H	**6f**	65
7	Br	Br	H	**6g**	62
8	Cl	H	H	**6h**	57
9	Cl	Cl	H	**6i**	52
10	CH_3	H	H	**6j**	55

[a] All the reactions were carried out with 2 equiv. of $SnCl_4$ and 5 equiv. of arylacetylene in CH_2Cl_2 at $-50 \rightarrow 0$ °C for 3 h.

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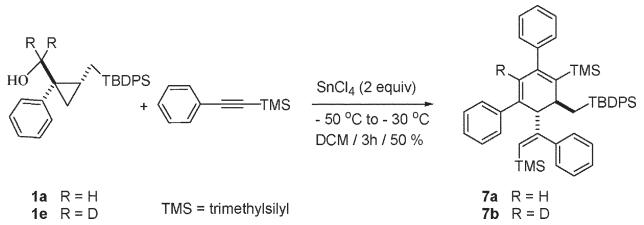
† Electronic supplementary information (ESI) available: Experimental details, spectroscopic and analytical details of all new compounds. See DOI: 10.1039/b700246g



Scheme 2 Reaction of **1a** and **1e** with 1-phenyl-2-trimethylsilylacetylene.

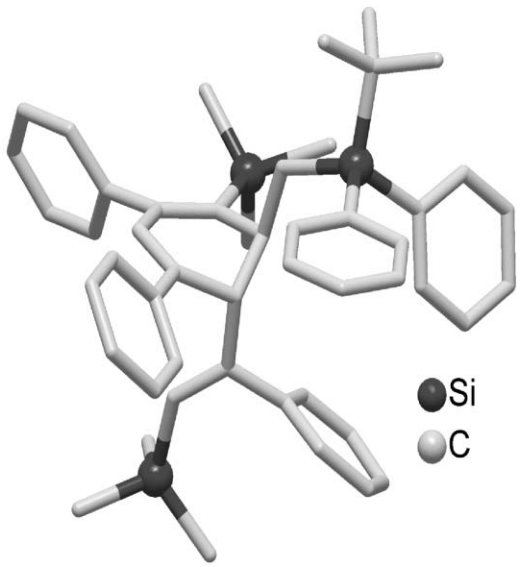
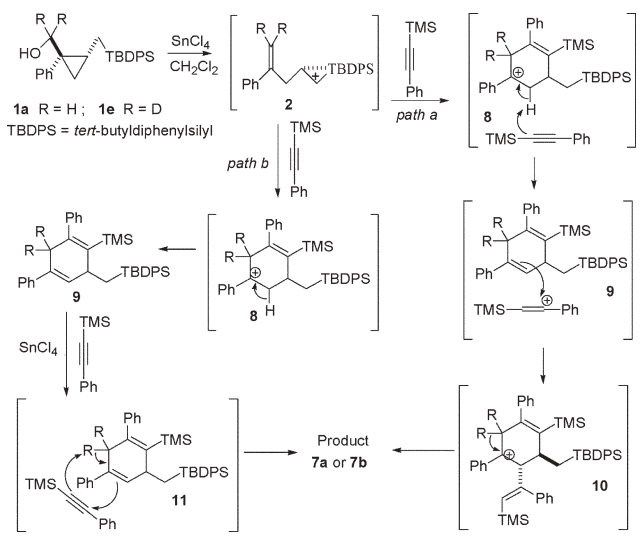
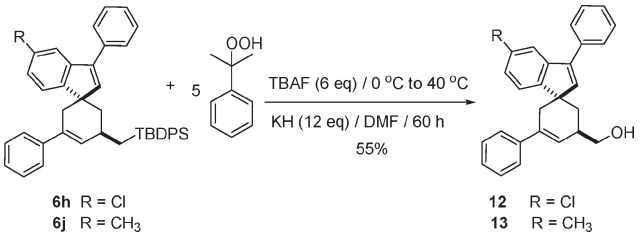


Fig. 1 X-Ray crystal structure of compound **7a**. Hydrogen atoms are omitted for clarity.

cation which reacts further with the styrene olefin to generate the observed product after yet another deprotonation. Alternatively, as shown in *path b*, the 1,4-cyclohexadiene formed above may undergo an ene reaction to generate the observed product. ^{1}H NMR of the product formed from **1e**, the –CD_2OH analogue of **1a**, showed absence of the vinylic hydrogen in the six-membered



Scheme 3 Tentative pathways for the formation of **7**.



Scheme 4 Oxidative cleavage of the C–$SiPh_2Bu^t$ bond into carbinol.

ring. However, it was present in the external vinylsilane motif. An ene mechanism will require migration of a deuterium atom from the ring position to the external vinylic position, as indicated in *path b*. The mechanism shown *via path a* is, therefore, more likely.

It is important to oxidatively cleave the C–$SiPh_2Bu^t$ bond into alcohol to provide a convenient handle for further synthetic modifications. Our attempt at achieving this transformation by employing a literature protocol[8a] using $BF_3{\cdot}2HOAc$, CH_2Cl_2, 40 °C, 4 h followed by H_2O_2, KF, $NaHCO_3$, THF–MeOH, 25 °C, 24 h was unsuccessful as a complex mixture of products was obtained. We ascribe this failure to the acid-sensitive character of the styrene double bond. The desired transformation was achieved conveniently by the employment of a slightly modified version of a literature protocol[8b] that was originally used for the oxidative cleavage of a C–$SiPhMe_2$ bond (Scheme 4). Compounds **6h** and **6j** were transformed into the corresponding alcohols **12** and **13**, respectively, each in 55% yield (Scheme 4).

In summary, we have developed the synthesis of highly substituted indene derivatives *via* a highly diastereoselective tandem protocol that leads to the formation of four new carbon–carbon bonds, two new stereogenic centers and two rings, in all, in a single pot. It is significant to note that one of the two stereogenic centers is quaternary. The halogen derivatives are likely to serve as strategic substrates for organometal-promoted reactions such as Suzuki–Miyura[9] and Sonogashira[10] couplings for further elaborations leading to fine tuning of the photoluminescence behavior that are eminent of indenes.

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Notes and references

‡ General experimental procedure for the $SnCl_4$-induced reaction of 2-silylmethyl cyclopropyl carbinol **1** with arylacetylenes: A solution of cyclopropylcarbinol (0.5 mmol) and an arylacetylene (2.5 mmol) in CH_2Cl_2 (4 mL) was cooled to −50 °C in a round bottom flask and mixed with a solution of $SnCl_4$ (1.0 mmol, 1 mL of 1.0 M solution) in CH_2Cl_2 dropwise over 15 min using a motor-driven syringe. The reaction was allowed to warm gradually to 0 °C over 3 h when it was quenched with saturated aqueous $NaHCO_3$ and stirred vigorously for 10 min. The layers were separated and the aqueous solution was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic solution was washed with brine, dried, filtered, and concentrated. The crude material was purified by radial chromatography.

§ *Spectroscopic data* for **6a**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.50 (3H, m), 7.43–6.88 (17H, m), 6.83–6.81 (2H, m), 6.65–6.63 (2H, m), 6.19 (1H, s), 5.57 (1H, br s), 2.60–2.55 (1H, d, J = 17.4 Hz), 2.47–2.17 (1H, dt, J = 17.4, 3.1 Hz), 1.99–1.95 (1H, dd, J = 12.2, 4.4 Hz), 1.69 (1H, m), 1.50–1.47 (1H, t, J = 12.2 Hz), 1.27–1.22 (1H, dd, J = 14.9, 6.6 Hz), 1.17–1.12 (1H, dd, J = 14.9, 7.8 Hz), 0.93 (9H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5, 141.0, 140.3, 138.3, 136.1, 136.05, 134.8, 132.6, 131.6, 129.0, 128.96, 128.6, 128.1,

128.06, 127.7, 127.6, 127.5, 126.7, 126.5, 125.5, 124.7, 46.5, 44.0, 36.4, 29.6, 27.8, 18.2, 16.8. FTIR: ν_{max}/cm^{-1} 3054, 3026, 2929, 2856, 1598, 1493, 1427, 1266, 1105, 1028, 738, 700. Anal. Calc. for $C_{43}H_{42}Si$: C, 88.00; H, 7.21. Found: C, 88.20; H, 7.25%.

¶ Experimental procedure for the $SnCl_4$-induced tandem reaction of **1a** with 1-phenyl-2-trimethylsilylacetylene: A solution of cyclopropyl carbinol **1a** (0.5 mmol), 1-phenyl-2-trimethylsilylacetylene (2.5 mmol) in CH_2Cl_2 (8 mL) was cooled to −50 °C in a round bottom flask and mixed with a 1.0 M solution of $SnCl_4$ in CH_2Cl_2 (1 mL, 1.0 mmol) dropwise using a motor-driven syringe over 30 min. The reaction was allowed to warm gradually to *ca.* 30 °C and stirred for 3 h before quenching with saturated aqueous $NaHCO_3$ (10 mL) and further vigorous stirring for 10 min. The layers were separated and the aqueous solution was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude material was purified by chromatography.

‖ *Crystal data* for **7a**: $C_{49}H_{58}Si_3$, M = 731.22, monoclinic, space group $P2_1$, a = 10.3025(7), b = 17.9876(13), c = 23.1998(17) Å, β = 92.4830(10)°, V = 4295.3(5) Å^3, Z = 4, D_c = 1.131 Mg m^{-3}, μ = 0.142 mm^{-1}, $F(000)$ = 1576, crystal size = 0.20 × 0.18 × 0.14 mm, T =100(2) K, λ = 0.71073 Å, reflections collected = 28467, θ range for data collection: 2.09–28.35°, final R indices [$I > 2\sigma(I)$]: R_1 = 0.0691, wR_2 = 0.1455; R indices (all data): R_1 = 0.1048, wR_2 = 0.1612. The structure was refined on F^2 value using program SHELXL-97. CCDC 632633. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b700246g

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