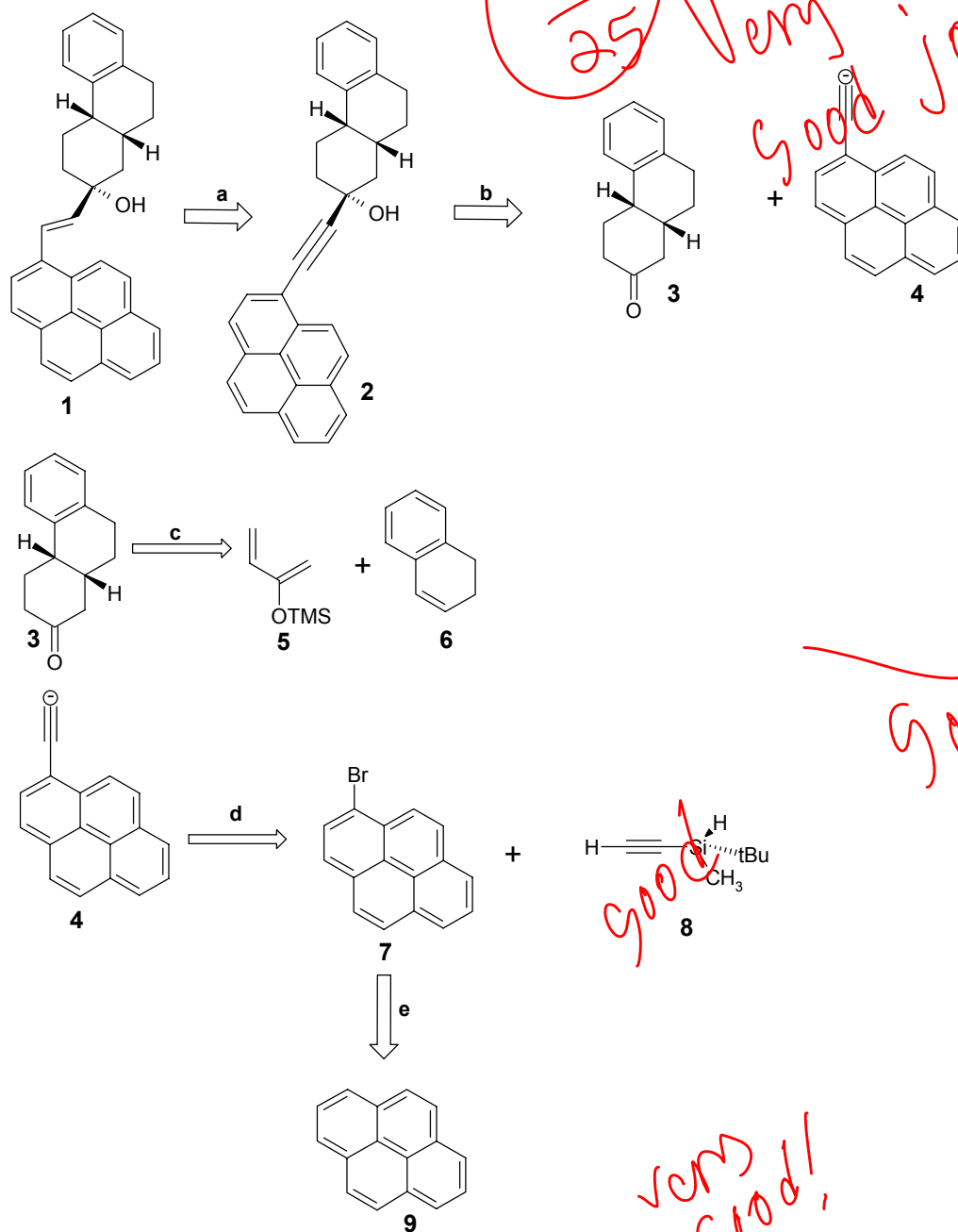


Assignment 1 CHE-535

Retrosynthetic route I



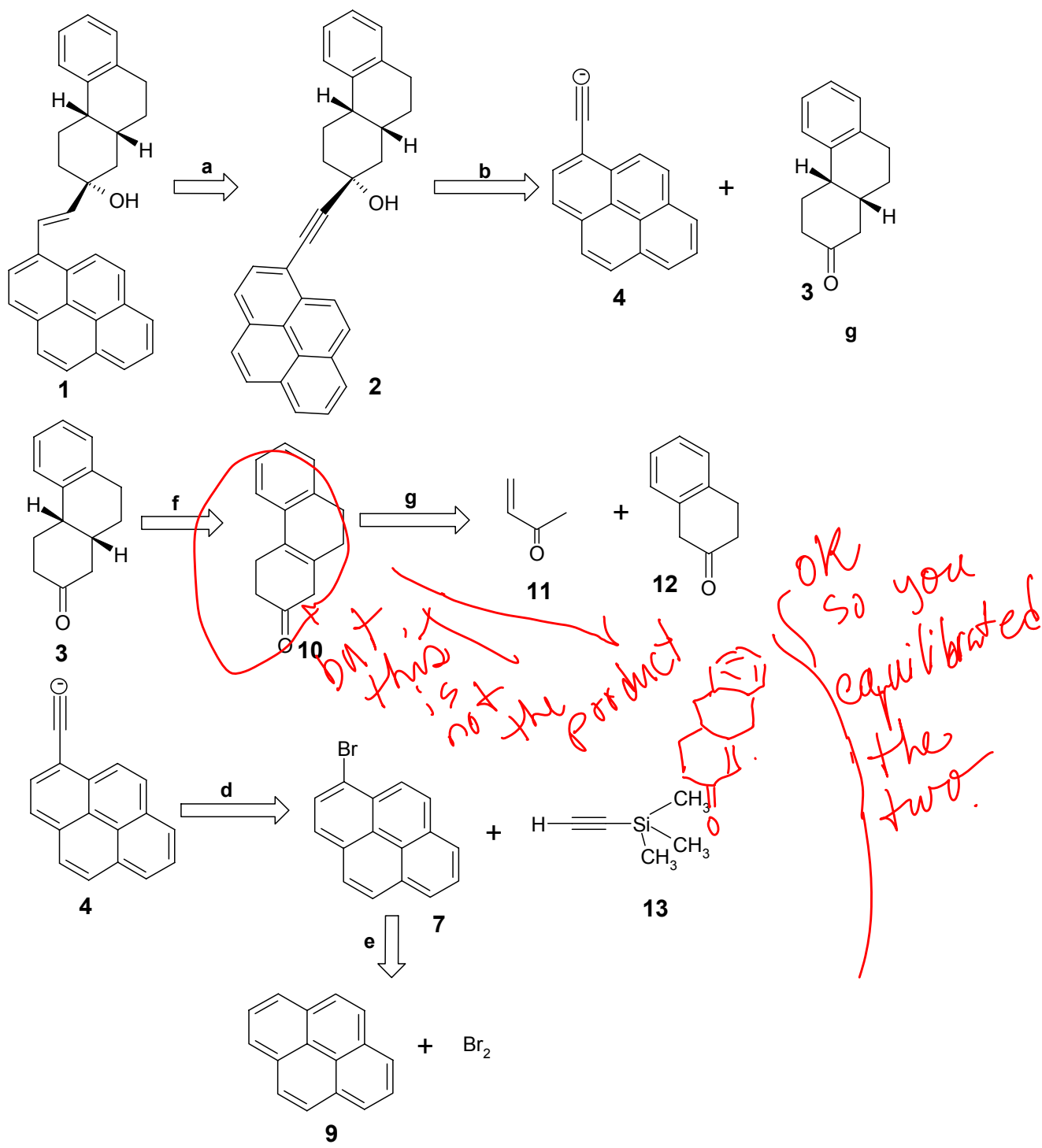
Scheme I. Retro synthetic route for the synthetic strategy of **1**.

This retrosynthetic analysis adopts a simple Diels-Alder reaction as a source of *syn* hydrogen stereochemistry for step **c**.¹ Bromopyrene (**7**) ~~could~~ ^{was} be easily prepared

stoichiometric bromination of pyrene in presence of carbon tetrachloride.² Sonogashira coupling was considered for the C-C bond formation between silyl acetylide (**8**) and bromopyrene.^{3,4} Taking advantage of facial preference, nucleophilic addition of acetylene-derived nucleophile (in conjunction with lithium treatment) and ketone, could lead to a good ~~enantio-selection~~ *diasterees* as reported previously.⁵ Finally, ~~enantioselective~~ (E-selective) reduction of alkyne to alkene could be achieved by treating the alkyne with triethoxy silane tetrabutylammonium fluoride (TBAF) and cuprous iodide as described previously.⁶

think about it

Retrosynthetic route II



Scheme II. Retro synthetic route for the synthetic strategy of **1**.

In this method, halogenation of pyrene was considered as described in the route I.

Sonogashira coupling of bromopyrene **9** with **13** could fulfill the requirement for step **d**.

Deprotection of silyl group followed by lithium treatment could generate a nucleophile

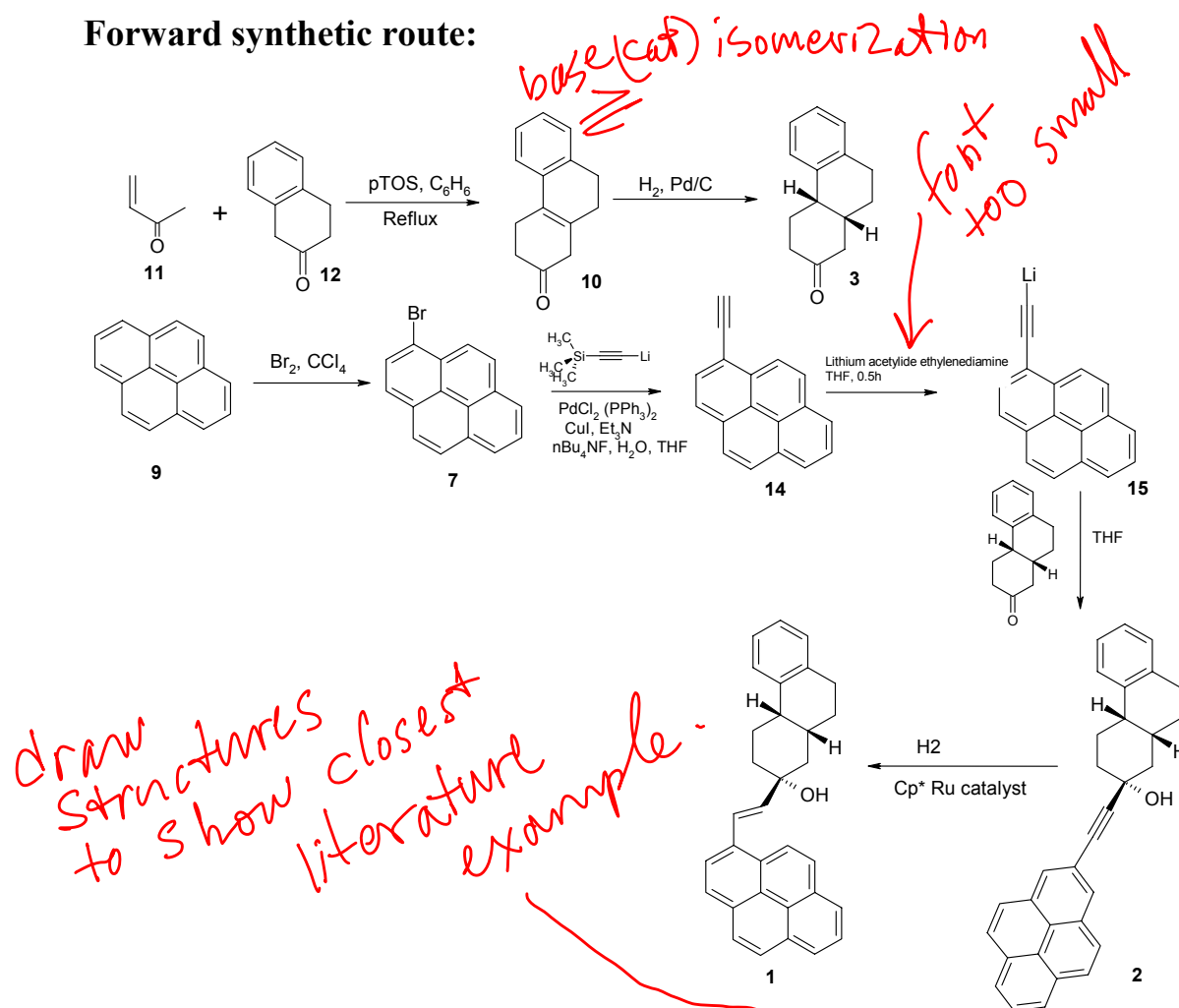
4.^{3,4} Robinson annulation-type reaction of tetralone with methyl vinyl ketone followed by

hydrogenation has already been reported for step **f** and **g**.⁸ Distereoselective addition of

nucleophile **4** to carbonyl carbon of **3** could result **2**.⁵ The final reduction could be carried

out as described in scheme **1**.^{6,7}

Forward synthetic route:



Scheme III. The synthetic scheme for the laboratory preparation of **1**.

Since, exact synthetic route for **3** has already been reported, it is pretty straight

forward to adopt second scheme for synthesis of **1**. For the Diels-Alder reaction (of

scheme II), it is necessary to optimize the condition. All references taken are cited in the above schemes.

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