

Intramolecular Oxidative Phenol Coupling and Hydrazone-Initiated C-H Bond Insertion in Stemodane Synthesis: A Reproduction of Work by Samir Chatterjee



Morris Olumba, Jeremy A. May*

Department of Chemistry, University of Houston
Collage of Natural Sciences and Mathematics

Abstract

The replication of the report entitled "Regio- and Stereo-controlled Total Synthesis of the Stemodane Nucleus; an Unusual Diterpene Skeleton, a suspect publication by Dr. Samir Chatterjee", has been initiated. The Goal of this project is to evaluate the reproducibility of the synthetic pathway reported to produce the stemodane diterpene structre in figure 1, proposed by Dr. Chatterjee in 1979.

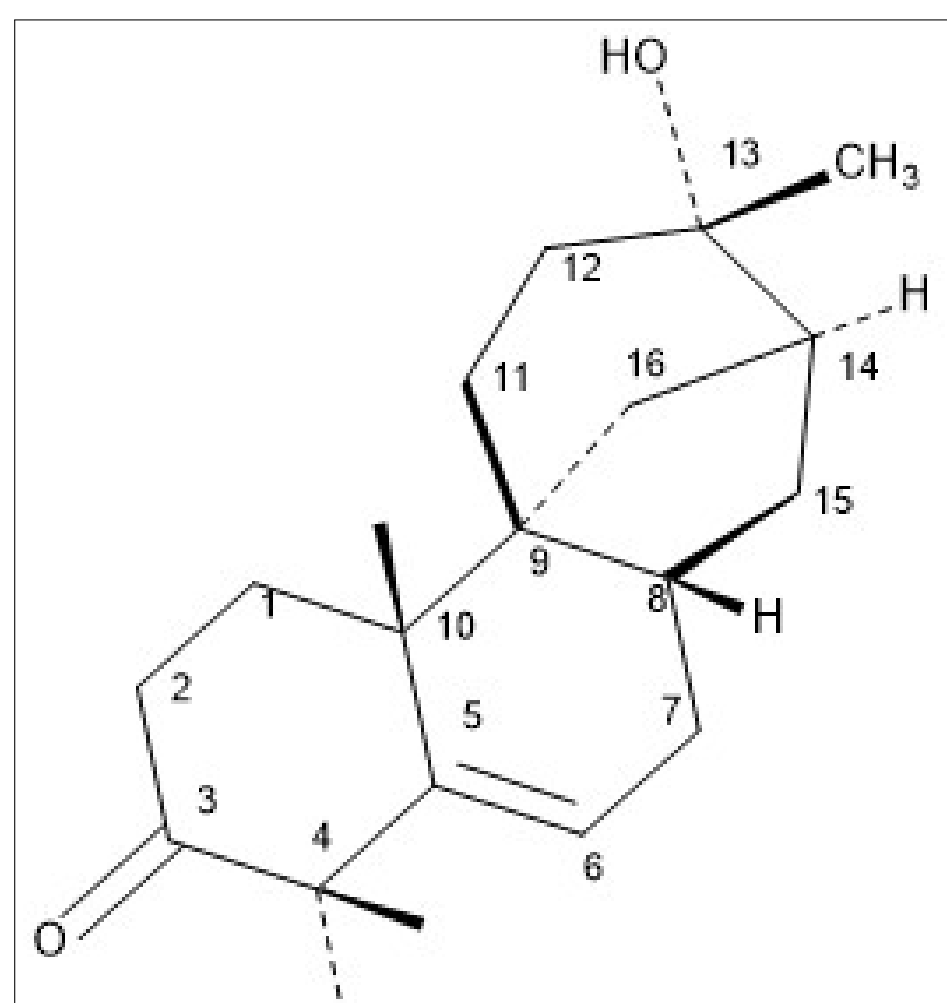


Figure 1: The desired Stemodane Nucleus [1].

In addition to other reports from this author having been refuted in published work[1][2], key elements of this stemodane report are believed to be inaccurate and improbable.

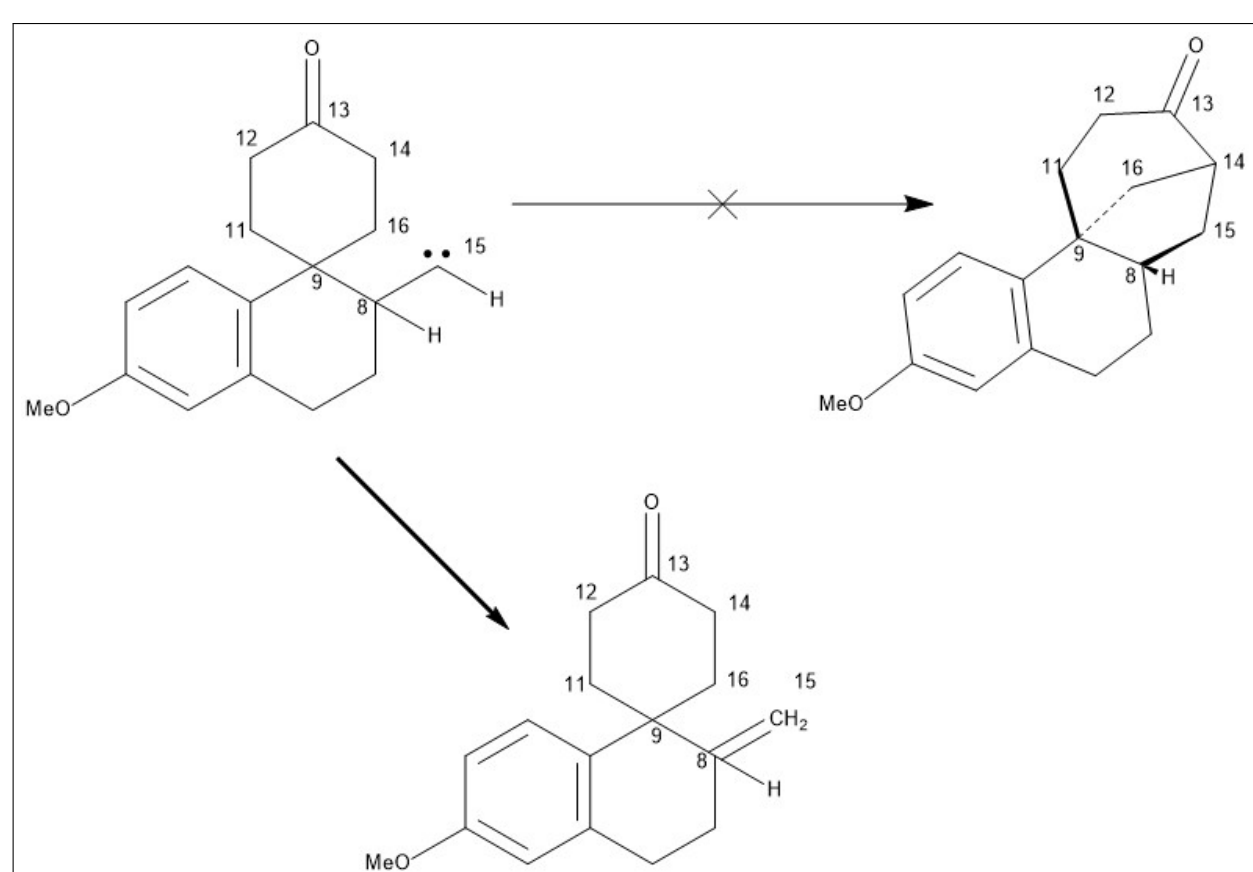


Figure 2: The suspect pathway [1].

Discussion

Based on the 3D renderings of the carbene intermediate, Figure 2, the geometric strain of this structure is evident. this suggests that C-15 to C-14 carbene bond formation is highly improbable.

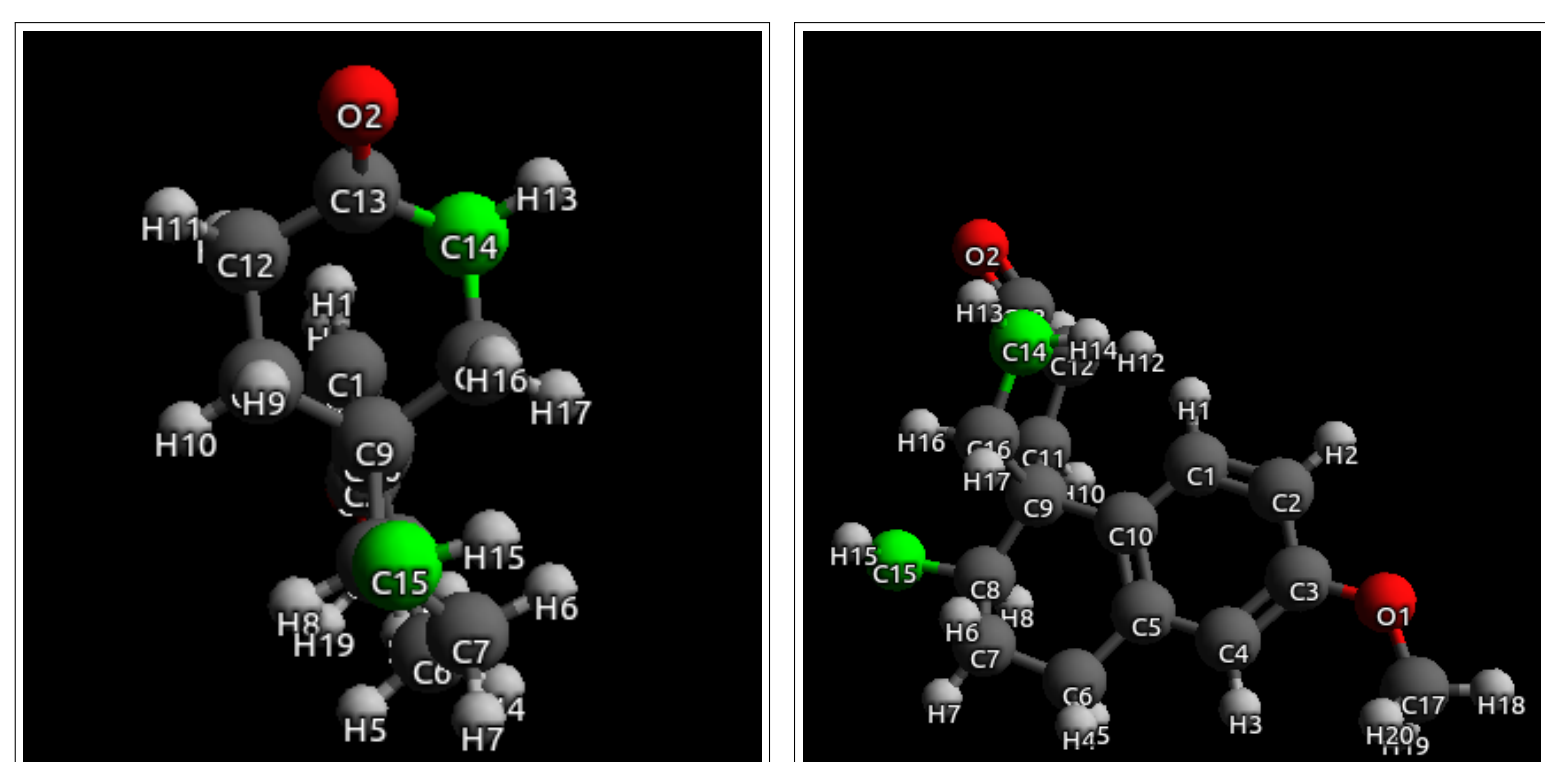


Figure 3: Left: The side view of the carbene intermediate
Right: The front view of the carbene intermediate.

Total Synthetic Pathway

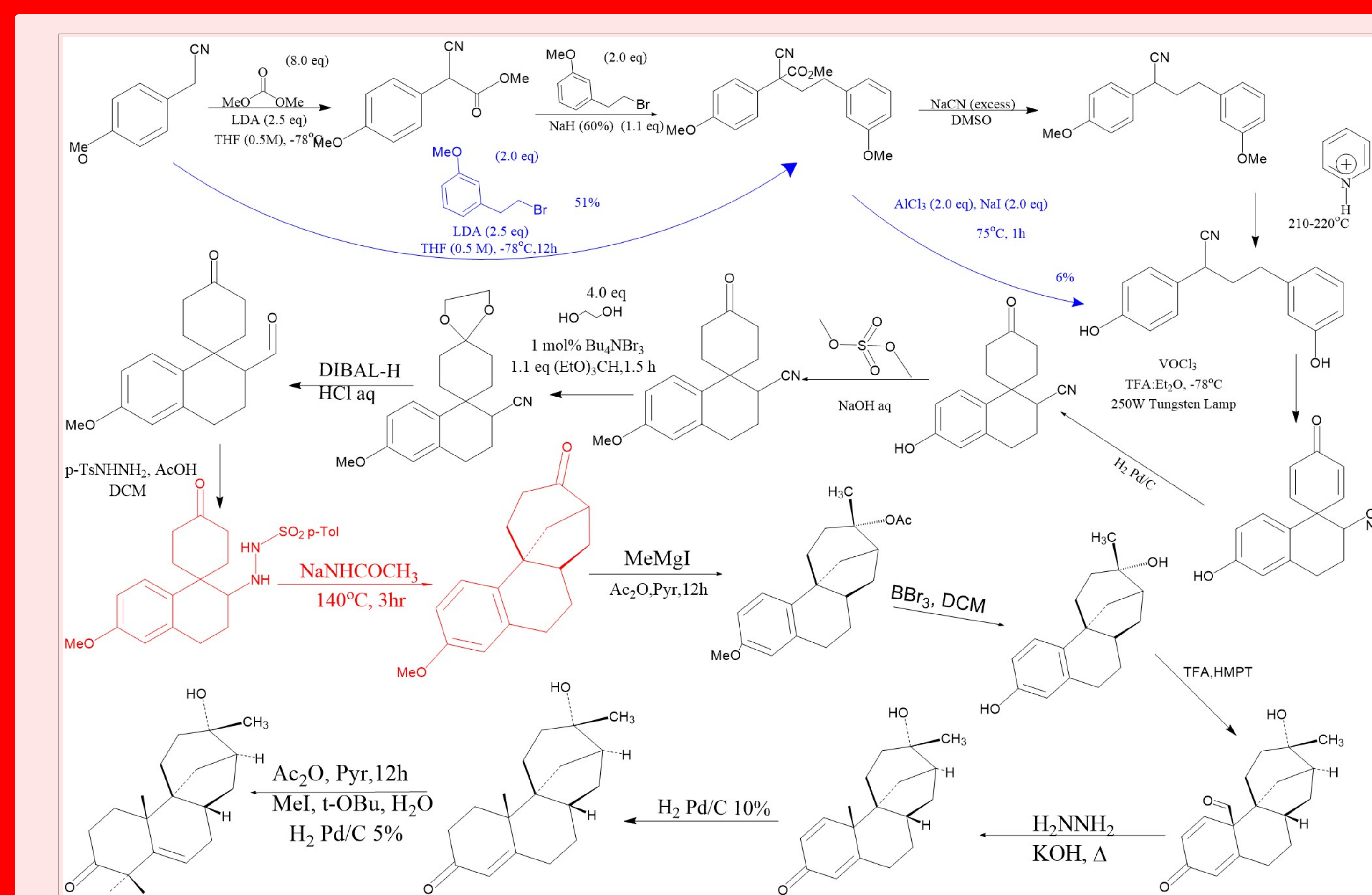


Figure 4: The total synthetic pathway detailed in [1].

Initial Reactions

*Initial Conditions(Black)

Reaction	Conditions	Results
26	KHMDS (2.0 eq) THF (75-80°C) 17h	-No desired product formation 21% Starting material recovered
27	LDA (1.5 eq) THF (75-80°C) 17h	-Starting material recovered
28	KHMDS (2.5 eq) THF (75-80°C) 17h	-Starting material recovered
52	Py-HCl (2.5 eq) (180°C) 3-8h	-Starting material recovered

Altered Reactions

*Altered Conditions (Blue)

Reaction	Conditions	Results
49	LDA (2.5 eq) THF (0.5M), (-78°C) 17h	56% Product yield, Product NMR confirmed
50	LDA (2.5 eq) THF (0.5M), (-78°C) 17h	44% Product yield, Product NMR confirmed
69	BBr ₃ (3.0 eq) DCM, (40°C) 12h	4% Product yield, Product IR confirmed
75	AlCl ₃ (2.0 eq),NaI (2.0 eq) (75°C) 1h	6% Product yield, Product IR confirmed

Figure 4 presents a mechanism in which the carbene intermediate at C-15 is stabilized by the electron inductive effects of the surrounding alkane carbons. However due to the highly reactive nature of carbenes leads to a hydride shift resulting in the formation of an olefin between C-8 and C-15; rather than proceeding with the theorized Hydrazone-initiated C-H insertion as the olefin reaction is significantly faster than the C-H insertion.

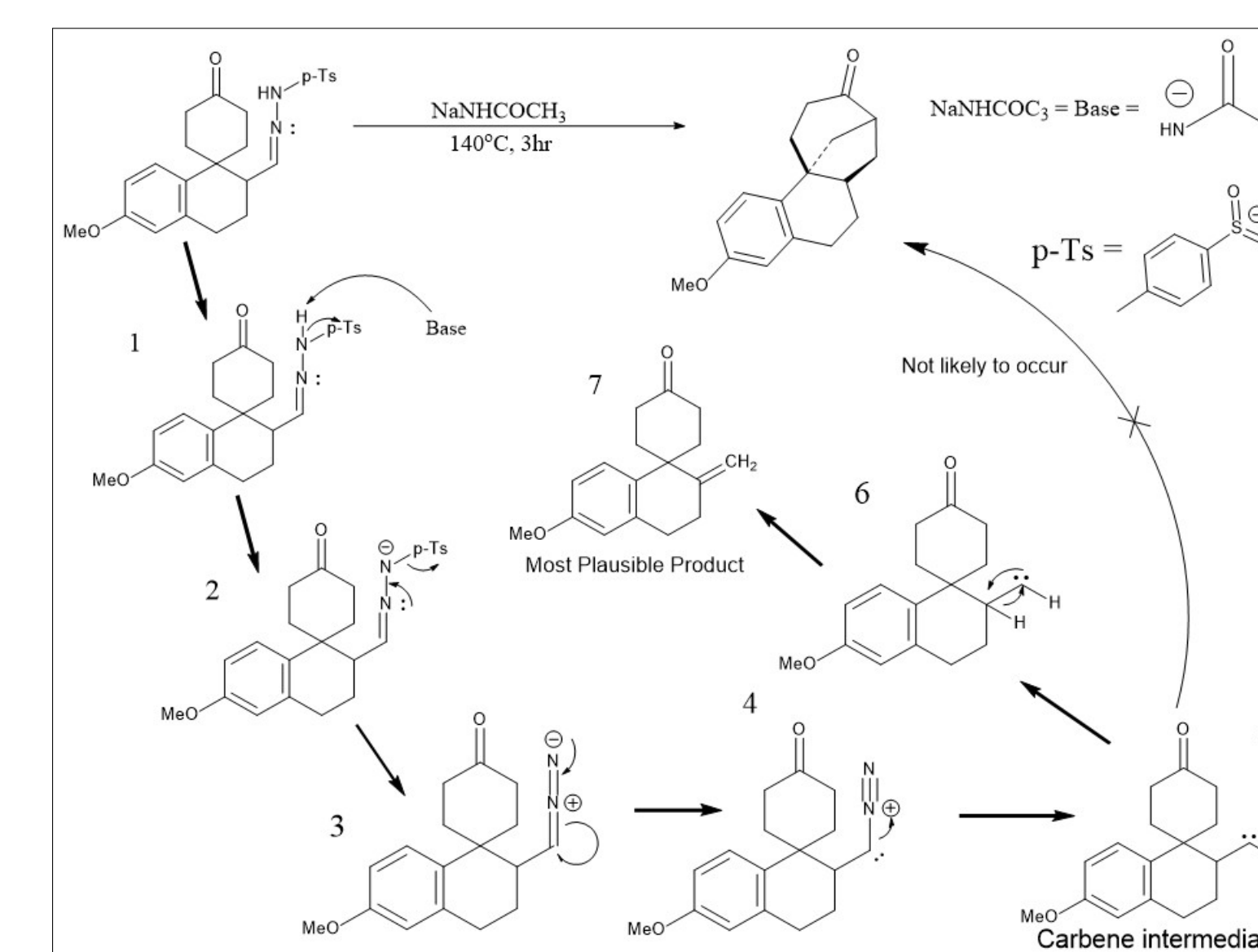


Figure 5: The mechanistic steps of the hydrazone initiated C-H insertion

References

- [1] Samir Chatterjee.
Regio- and stereo-controlled total synthesis of the stemodane nucleus; an unusual diterpene skeleton.
J. Chem. Soc., Chem. Commun., pages 622–623, 1979.
- [2] John Cornforth, W.
Comment on a paper by samir chatterjee.
Tetrahedron Lett., pages 709–710, 1980.
- [3] John Cornforth, W and Tony Pangelly.
Failure to verify a reported synthesis of the aconitine skeleton.
Tetrahedron Lett., pages 2213–2216, 1982.
- [4] Leo A. Paquette and Yeun-Kwei Han.
Total synthesis of (+,-)-isocomene, a naturally occurring triquinane.
Journal of the American Chemical Society, 103(7):1835–1838, 1981.
- [5] Douglas J. Raber, Patrick Gariano, Albert O. Brod, Anne Gariano, Wayne C. Guida, Anne R. Guida, and Mark D. Herbst.
Esterification of carboxylic acids with trialkyloxonium salts.
The Journal of Organic Chemistry, 44(7):1149–1154, 1979.

Acknowledgements

Dr. Jeremy A. May as well as the Graduate students within the May Group provided crucial support for this project. I am very grateful to them for their invaluable direction and mentorship; Additionally I am thankful to Dr. May for providing me with this research opportunity.