We have described a versatile protecting group (TBDMS) for $1,2\text{-}C_2B_{10}H_{12}$ that allows the efficient synthesis of monosubstituted and linked carboranes. The generality of the method coupled with the high yields obtained offers a valuable new tool for organic transformations on carborane cages. As shown previously, the silyl substituent on carborane cages provides unique reactivity, crystal growth and cage stability.[8] Work that extends to other areas of carborane chemistry is currently in progress.

Acknowledgment. We thank the National Institutes of Health for support of this research under Grant CA43904 and for an NIH MARC predoctoral fellowship (Grant GM11586) for F.A.G. We also thank the National Science Foundation for a postdoctoral fellowship (Grant NSF-CHE 90-01819) for S.E.J. We also thank Lai-Ling Ng and Carolyn Knobler for assistance.

Supplementary Material Available: Tables of bond distances and angles and positional and thermal parameters for **3**, details of the crystallographic data collection for **3**; experimental data on the preparation of **2–14**, and collection and reduction of X-ray data and solution and refinement of the structure of **3** (18 pages); table of observed and calculated structure factors for **3** (19 pages). Ordering information is given on any current masthead page.

---

(8) (a) Hosmane, N. S.; Maldar, N. N.; Potts, S. B.; Rankin, D. W.; Robertson, H. E. *Inorg. Chem.* **1986**, *25*, 1561. (b) Hosmane, N. S.; Islam, M. S.; Burns, E. G. *Inorg. Chem.* **1987**, *26*, 3237. (c) Hosmane, N. S.; Maguire, J. A. *Adv. Organomet. Chem.* **1990**, *30*, 99. (d) Hosmane N. S.; Barreto, R. D.; Tolle, M. A.; Alexander, J. J.; Quintana, W.; Siriwardare, U.; Shore, S. G.; Williams, R. E. *Inorg. Chem.* **1990**, *29*, 2698. (e) Siriwardare, U.; Zhang, H.; Hosmane, N. S. *J. Am. Chem. Soc.* **1990**, *112*, 9637.

Silicon-Promoted Nef Reaction by a γ-Effect

Jih Ru Hwu[*,†,‡] and Bryant A. Gilbert[†]

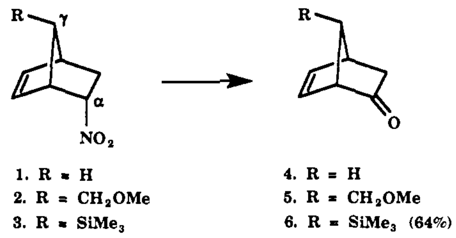
Department of Chemistry, The Johns Hopkins University
Baltimore, Maryland 21218
Department of Chemistry, National Tsing Hua University
Hsinchu, Taiwan 30043, Republic of China
Institute of Chemistry, Academia Sinica
Nankang, Taipei, Taiwan 11529, Republic of China

Received March 18, 1991

The γ-effect of silicon[1] results from the interaction between the back lobes of the Si–C_γ bond and the developing p orbital at the C_α position in a silicon-containing species. Studies on the solvolysis of γ-silyl-substituted compounds provide solid evidence to show the existence of the γ-effect.[2-8] Few examples, however, have demonstrated the use of this effect in synthesis.[9] We report herein the first systematic application of the silicon γ-effect to an organic reaction: a γ-trimethylsilyl group can assist nitro compounds to be converted to ketones under mild conditions.

Many methods have been developed for performance of the Nef reaction.[10] Nevertheless, some nitro compounds fail to be degraded to ketones under most conditions employed, such as the conversion of 5-nitrobicyclo[2.2.1]hept-2-enes **1** and **2** to the corresponding ketones **4** and **5**, respectively (Scheme I). The major products isolated are a cyclic hydroxamic ester and a lactone.[11-14] A compound possessing the skeleton of **1** would provide an ideal example to show the feasibility of the γ-silicon-promoted Nef reaction. Accordingly, we synthesized γ-trimethylsilyl nitro compound **3** by following Ranganathan's procedure.[15]

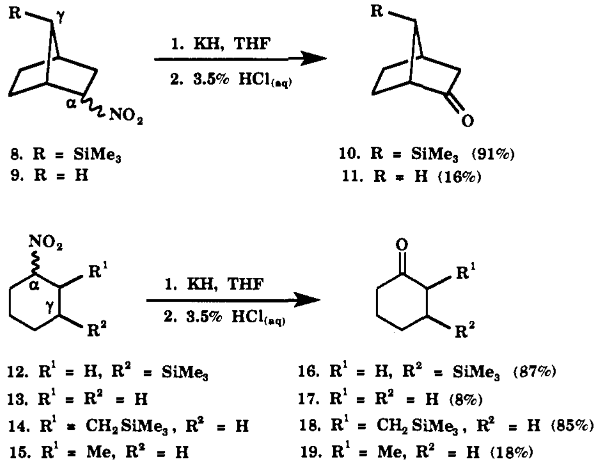
Scheme I



1. R = H
2. R = CH_2OMe
3. R = $SiMe_3$

4. R = H
5. R = CH_2OMe
6. R = $SiMe_3$ (64%)

Scheme II



8. R = $SiMe_3$
9. R = H

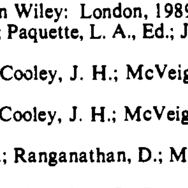
10. R = $SiMe_3$ (91%)
11. R = H (16%)

12. R^1 = H, R^2 = $SiMe_3$
13. R^1 = R^2 = H
14. R^1 = CH_2SiMe_3, R^2 = H
15. R^1 = Me, R^2 = H

16. R^1 = H, R^2 = $SiMe_3$ (87%)
17. R^1 = R^2 = H (8%)
18. R^1 = CH_2SiMe_3, R^2 = H (85%)
19. R^1 = Me, R^2 = H (18%)

We treated nitro compound **3** with 1.5 equiv of KH in THF at 0 °C–room temperature for 3 h and then with 3.5% aqueous HCl. After workup and purification, ketone **6** was obtained in 64% yield.

In comparison with failure of the Nef reaction for **1** and **2**, the successful conversion of **3** to **6** must be attributed to the Me_3Si group. We believe that the route from **3** to **6** involves the hydrated intermediate **7**,[16] in which the Me_3Si group is anti to the trihydroxyl moiety $HOCN(OH)_2$. Thus the silicon-promoted conversion must result from the γ-effect, not from the steric congestion caused by the Me_3Si group.



7

---

[*] Research fellow of the Alfred P. Sloan Foundation (1986–1990).

[†] The Johns Hopkins University.

[‡] Address correspondence to this author at National Tsing Hua University and Academia Sinica.

(1) For the pioneering work on the γ-effect, see: Sommer, L. H.; Dorfman, G. M.; Goldberg, G. M.; Whitmore, F. C. *J. Am. Chem. Soc.* **1946**, *68*, 488.

(2) Sommer, L. H.; van Strien, R. E.; Whitmore, F. C. *J. Am. Chem. Soc.* **1949**, *71*, 3056.

(3) Davis, D. D.; Black, R. H. *J. Organomet. Chem.* **1974**, *82*, C-30.

(4) Shiner, V. J., Jr.; Ensinger, M. W.; Kriz, G. S. *J. Am. Chem. Soc.* **1986**, *108*, 842.

(5) Shiner, V. J., Jr.; Ensinger, M. W.; Rutkowske, R. D. *J. Am. Chem. Soc.* **1987**, *109*, 804.

(6) Shiner, V. J., Jr.; Ensinger, M. W.; Huffman, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 7199.

(7) Kirmse, W.; Sollenbohmer, F. *J. Am. Chem. Soc.* **1989**, *111*, 4127.

(8) Grob, C. A.; Sawlewicz, P. *Tetrahedron Lett.* **1987**, *28*, 951.

(9) Davey, A. E.; Parsons, A. F.; Taylor, R. J. K. *J. Chem. Soc., Chem. Commun.* **1989**, 1853.

(10) For reviews on the Nef reaction, see: (a) Seebach, D.; Colvin, E. W.; Lehr, F.; Weller, T. *Chimia* **1979**, *33*, 1. (b) Nielsen, A. T. In *The Chemistry of Functional Groups: Nitrones, Nitronates and Nitroxides*; Patai, S., Rappoport, Z., Eds.; John Wiley: London, 1989; Chapter 1. (c) Pinnick, H. W. In *Organic Reactions*; Paquette, L. A., Ed.; John Wiley: New York, 1990; Vol. 38, Chapter 3.

(11) Noland, W. E.; Cooley, J. H.; McVeigh, P. A. *J. Am. Chem. Soc.* **1959**, *81*, 1209.

(12) Noland, W. E.; Cooley, J. H.; McVeigh, R. A. *J. Am. Chem. Soc.* **1957**, *79*, 2976.

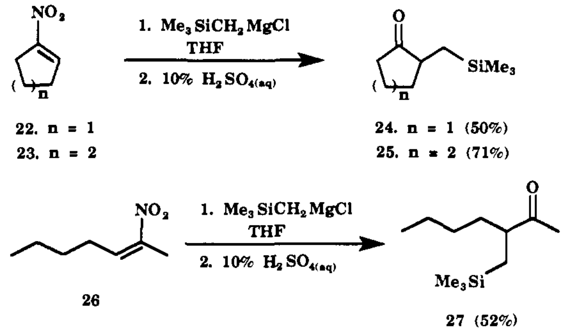
(13) Ranganathan, S.; Ranganathan, D.; Mehrotra, A. K. *J. Am. Chem. Soc.* **1974**, *96*, 5261.

(14) Wildman, W. C.; Saunders, D. R. *J. Org. Chem.* **1954**, *19*, 381.

(15) Ranganathan, D.; Rao, C. B.; Ranganathan, S.; Mehrotra, A. K.; Iyengar, R. *J. Org. Chem.* **1980**, *45*, 1185.

(16) Sun, S. F.; Folliard, J. T. *Tetrahedron* **1971**, *27*, 323.

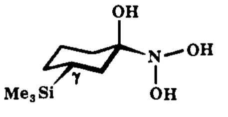
Scheme III



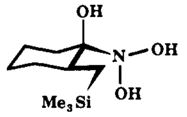
By the same procedure, we were able to convert the saturated silicon-containing nitro compound **8** to ketone **10** in excellent yield (91%, Scheme II). In contrast, the corresponding nitro compound **9**, without a γ-silyl group, gave ketone **11** in 16% yield under these mild conditions.

To prove the generality of the silicon-promoted Nef reaction, we reacted γ-silyl nitro compound **12** with KH and then with 3.5% aqueous HCl (Scheme II). The corresponding ketone **16** was obtained in 87% yield. Nonsilylated nitro compound **13**, however, gave ketone **17** in only 8% yield. Also, conversion of γ-silyl nitro compound **14** to ketone **18** (85% yield) was much more efficient than conversion of nonsilylated nitro compound **15** to ketone **19** (18% yield).

In the reaction **12** → **16**, the possible intermediate **20** can hold a "W" conformation for the Si–C–C–C–N backbone. The carbocation resulting from the C–N bond cleavage[16] in **20** can be stabilized by the γ-silicon. In the reaction **14** → **18**, however, the Si–C–C–C–N backbone in the intermediate may possess an "endo-Sickle" conformation[17] (see **21**) or have a "W" conformation through a ring flip. Shiner et al. reported that a γ-silyl substituent enhances the solvolytic reactivity of secondary alkyl sulfonate esters by a factors of 10–100;[4–6] the carbocation involved is stabilized by interaction with the back lobe of the Si–C bond in either a "W" or an "endo-Sickle" conformation.



20



21

To intensify the applicability of the silicon γ-effect to synthesis, we developed a "one-flask" method for the preparation of β-trimethylsilyl ketones from nitro olefins (Scheme III). We added 1-nitrocyclohexene (**23**) to a THF solution of Me_3SiCH_2MgCl (1.1 equiv) at −20 °C. After 30 min at 0 °C, the solution was acidified to pH 3.0 by addition of 10% aqueous H_2SO_4. The desired β-silyl ketone **25** was obtained in 71% yield. By the same procedure, we produced β-silyl ketone **24** in 50% yield from 1-nitrocyclopentene (**22**) and obtained β-silyl ketone **27** in 52% yield from 2-nitrohept-2-ene (**26**).

In conclusion, the γ-effect of silicon was found to facilitate the Nef reaction. The use of KH and aqueous HCl enabled conversion of nitro compounds with a γ-trimethylsilyl group to ketones much more efficiently than conversion of the corresponding nitro compounds without a silyl group. This unprecedented silicon-promoted Nef reaction was applied to a "one-flask" synthesis of β-silyl ketones from nitro olefins. β-Silyl ketones are valuable substrates for silicon-directed Norrish type I cleavage[18,19] and can be used in the development of silicon-containing photodegradable polymers.

Acknowledgment. For financial support, we thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Council of the Republic of China (NSC 80-0208-M007-85). B.A.G. thanks Dr. Henry Sonneborn III for a fellowship.

Supplementary Material Available: General experimental and preparation details and analysis (including ^1H NMR and IR) of **6**, **8**, **10–12**, **14**, **16–19**, **22**, and **24–27** (9 pages). Ordering information is given on any current masthead page.

---

(17) Nickon, A.; Werstiuk, N. H. *J. Am. Chem. Soc.* **1967**, *89*, 3914.

(18) Hwu, J. R.; Gilbert, B. A.; Lin, L. C.; Liaw, B. R. *J. Chem. Soc., Chem. Commun.* **1990**, 161.

(19) Tietze, L. F.; Wünsch, J. R. *Synthesis* **1990**, 985.

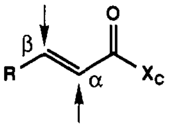
New Chiral Auxiliary for Asymmetric Thermal Reactions: High Regio- and β-Stereoselectivity in Asymmetric Radical Addition Reactions to Mixed Fumarimides

Jeffrey G. Stack, Dennis P. Curran,*[1] Julius Rebek, Jr.,*[2] and Pablo Ballester[2]

Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15260

Received April 16, 1991

Porter and Giese have recently reported the first examples of high α-stereoselection in the additions of achiral radicals to amide-substituted alkenes containing the 2,5-dimethylpyrrolidine auxiliary; however, there is no stereocontrol if the radicals attack the β-position (see eq 1).[3] Because ester- or amide-based chiral auxiliaries normally direct attack of nucleophilic radicals to the β-position, a more natural approach is to develop auxiliaries that control β-stereochemistry. We now report high regio- and β-stereoselection in the addition of achiral radicals to a mixed fumarimide substituted with a new chiral auxiliary derived from Kemp's triacid.[4]



α-attack, good stereocontrol with
X_C = *trans*-2,5-dimethylpyrrolidine (1)
β-attack, no stereocontrol

The chiral auxiliary used in this study is prepared from Kemp's triacid in six steps and 62% overall yield, as outlined in eq 2.[5] Imide formation is accomplished in 91% yield by heating Kemp's triacid and urea in triglyme at 200 °C. Treatment of the imide acid with $SOCl_2$ followed by 2-aminophenol gives the imide amide **2** in 92% yield. Two-step reduction of the imide with $NaBH_4$ and triethylsilane affords a lactam amide (84%), which upon heating with $SOCl_2$ affords the racemic auxiliary **3** in 89% yield. Resolution of the auxiliary is effected by acylation of the lactam with (−)-menthyl chloroformate, separation of the diastereomers by flash chromatography, and regeneration of the optically active auxiliaries with trifluoroacetic acid (40% and 36% yields). The absolute configuration of the enantiomers was determined by a single-crystal X-ray structure of one of the menthyl carbamate diastereomers.[6] Standard lactam acylation procedures gave poor yields (<40%) of the desired fumarimide substrate **4**, so we developed a high-yielding hybrid of existing lactam acylation technology. The key to the success of this procedure is the in situ

---

(1) Dreyfus Teacher-Scholar, 1986–1991. NIH Research Career Development Awardee, 1987–1992. ICI Pharmaceuticals Awardee, 1990.

(2) Current address: Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA 02139.

(3) (a) Porter, N. A.; Scott, D. M.; Rosenstein, I. J.; Giese, B.; Veit, A.; Zeitz, H. G. *J. Am. Chem. Soc.* **1991**, *113*, 1791–9. (b) Scott, D. M.; McPhail, A. T.; Porter, N. A. *Tetrahedron Lett.* **1990**, *31*, 1679–82. (c) Porter, N. A.; Scott, D. M.; Lacher, B.; Giese, B.; Zeitz, H. G.; Lindner, H. J. *J. Am. Chem. Soc.* **1989**, *111*, 8311–2. (d) Porter, N. A.; Lacher, B.; Chang, V. H.-T.; Magnin, D. R. *J. Am. Chem. Soc.* **1989**, *111*, 8309–10.

(4) (a) Kemp, D. S.; Petrakis, K. S. *J. Org. Chem.* **1981**, *46*, 5140–3. (b) Askew, B.; Ballester, P.; Buhr, C.; Jeong, K. S.; Parris, K.; Williams, K.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1989**, *111*, 1082–90. (c) Rebek, J., Jr.; Askew, B.; Killoran, M.; Nemeth, D.; Lin, F.-T. *J. Am. Chem. Soc.* **1987**, *109*, 2426–31.

(5) For preparation and applications of members of the first generation of this class of chiral auxiliaries, see: Curran, D. P.; Jeong, K.-S.; Heffner, T. A.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1989**, *111*, 9238–40.

(6) We thank Dr. Steven Gieb for solving this crystal structure. A full paper describing the preparation of the auxiliary and the structure assignments is being prepared.

0002-7863/91/1513-5918$02.50/0